S 43. *The Synthesis of Thyroxine and Related Substances. Part II. The Preparation of Dinitrodiphenyl Ethers.*

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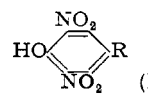
A new and facile synthesis of 2 : 6-dinitrodiphenyl ethers is described. Quaternary salts of the type (VI) are treated with phenols under a variety of conditions. Such quaternary compounds may also be prepared from the appropriate halogenodinitrobenzenes, derived from the corresponding phenol by reaction with phosphoryl chloride and a tertiary base, preferably diethylaniline. Similarly, certain other salts have been used satisfactorily in the diphenyl ether synthesis.

Although the synthesis of thyroxine described in the preceding paper was not wholly satisfactory, the new procedure for preparing 2 : 6-di-iododiphenyl ethers from the corresponding dinitro-derivatives, as there elaborated, suggested many new alternatives if the appropriate 2 : 6-dinitrodiphenyl ethers could be procured. The necessity for preparing the latter from halogeno-2 : 6-dinitrobenzenes rather than from the related phenols was also discussed. As phenols of the required orientation are more readily available than the corresponding halogeno-compounds, it was deemed necessary that such derivatives should be employed as starting materials for any simple thyroxine synthesis. To this end the replacement of the hydroxyl by halogen in a number of dinitrophenols, and also possible means of circumventing this operation, have been investigated.

As models for this study we chose the 3 : 5-dinitro-derivatives of *p*-hydroxybenzaldehyde (I; R = CHO), *p*-cresol (I; R = Me), and ethyl β-(*p*-hydroxyphenyl)propionate (I; R = $CH_2 \cdot CH_2 \cdot CO_2Et$). The first (I; R = CHO) was prepared by nitration of *p*-hydroxybenzaldehyde, a necessary modification of Hodgson and Beard's method (*J.*, 1927, 2375) being used whereby it could be isolated in 40% yield on crystallisation from aqueous acetic acid. Crystallisation of the crude product from carbon tetrachloride gave as the first crop the *picrate* of (I; R = CHO), which could be split into the two components by treatment with aqueous acetic acid.



(I.)

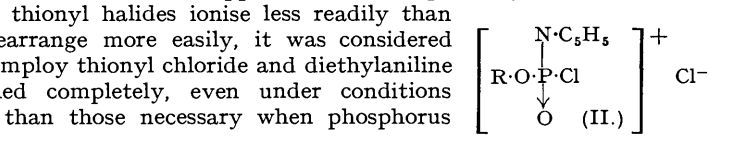
A thorough examination of the action of phosphorus pentachloride in various proportions on (I; R = CHO) and (I; R = $CH_2 \cdot CH_2 \cdot CO_2Et$) under a variety of conditions produced no tractable products, although in both instances hydrogen chloride was copiously evolved. Our attention was then drawn to a paper (Baddiley and Topham, *J.*, 1944, 678) on the use of phosphoryl chloride and diethylaniline for the conversion of 4-hydroxy- and 4 : 6-dihydroxy-pyrimidines into the corresponding chloro-compounds. As the hydroxyl groups in these compounds may be considered to be influenced in a similar manner to those *o*- or *p*- to nitro-groups in an aromatic ring, the analogy was tested by applying the method to the above dinitrophenols (I). The reaction with (I; R = CHO) proved extremely easy, being completed in five minutes at room temperature to give 4-*chloro*-3 : 5-*dinitrobenzaldehyde* in 90% yield. It has been claimed by Mittal (*J. Indian Chem. Soc.*, 1942, **19**, 408) that this compound arises by acid hydrolysis of the condensation product of *p*-nitrosodimethylaniline with 4-chloro-3 : 5-dinitrotoluene of obscure origin, but the m. p.s of his product (78°) and of its phenylhydrazone

(109°) do not agree with those of the materials prepared by our procedure, namely, 107° and 217°, respectively. The orientation of our product follows unambiguously from the method of preparation and from its oxidation to 4-chloro-3 : 5-dinitrobenzoic acid identical in all respects with an authentic specimen (Ullmann, *Annalen*, 1909, **366**, 92).

Phosphoryl chloride and diethylaniline were also applied successfully to (I; R = Me) to yield 4-chloro-3 : 5-dinitrotoluene and to (I; R = $CH_2 \cdot CH_2 \cdot CO_2Et$) to give *ethyl* β-(4-*chloro*-3 : 5-*dinitrophenyl*)*propionate*, though the reactions were less facile and required heat. Similar success attended the application of the method to picric acid, methyl 3 : 5-dinitro-4-hydroxybenzoate, 3 : 5-dinitro-4-hydroxyacetanilide, 3 : 5-dinitro-4-hydroxy-*tert.*-butylbenzene, and 2 : 4-dinitrophenol, but *p*-nitrophenol proved refractory.

Boyer, Spencer, and Wright (*Canadian J. Res.*, 1946, **24***B*, 200) used a similar method for the preparation of picryl chloride from the pyridine salt of picric acid by the action of carbonyl chloride or phosphoryl chloride. Although this method may prove useful when the pyridine salt is available, we have found that the yield falls if excess of pyridine is used. The superiority of diethylaniline over pyridine for the present purpose resides in the greater tendency shown by the latter for reaction with the products to give quaternary compounds whose formation and reactions are discussed in more detail later in this paper. Thus the yield (80%) of 4-chloro-3 : 5-dinitrobenzaldehyde when 1 equiv. of diethylaniline was employed remained steady at 86% for 1·2—4 equivs., whereas the yields obtained on using 1, 1·2, 2, and 4 equivs. of pyridine were 64, 77, 50, and 4% respectively. Similarly quinoline, and with less facility triethylamine, may be employed as the tertiary base, and the reaction can be effected, though in poorer yield, in solvents such as benzene or methyl cyanide. The use of phosphorus pentachloride instead of the oxychloride necessitates the use of solvents and gives very poor yields. Phosphoryl bromide proved less reactive towards (I; R = CHO) in the presence of diethylaniline and attacked the formyl group, under the more vigorous conditions required, to give 4-*bromo*-3 : 5-*dinitrobenzylidene dibromide*.

In view of the inability of phosphoryl chloride alone to effect the above conversions, the mechanism, proceeding *via* an intermediate (II), suggested by Kenyon *et al.* (*J.*, 1931, 382; see also Gerrard, *J.*, 1944, 85) for the reaction when applied to alcohols, probably holds true for the above examples. Hence, as thionyl halides ionise less readily than those of phosphorus, but rearrange more easily, it was considered significant that attempts to employ thionyl chloride and diethylaniline in the above reaction failed completely, even under conditions considerably more vigorous than those necessary when phosphorus oxychloride was used.



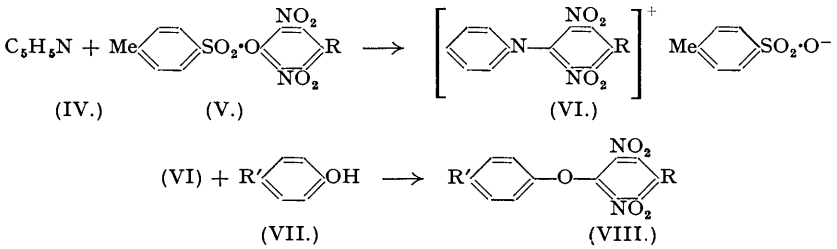
The Ullmann and Nadai procedure for the preparation of chlorodinitrobenzenes by treatment of the analogous dinitrophenols with toluene-*p*-sulphonyl chloride and diethylaniline appears to be satisfactory for a wide variety of examples (Ullmann *et al.*, *Ber.*, 1908, **41**, 1870; 1911, **44**, 3730; Sané and Joshi, *J.*, 1924, **125**, 2481; *J. Indian Chem. Soc.*, 1928, **5**, 299; Sen, *ibid.*, 1945, **22**, 183; 1946, **23**, 53), although a few exceptions are on record (Sané and Joshi, *J. Indian Chem. Soc.*, 1932, **9**, 59). That the reaction proceeds *via* a quaternary compound as represented in the following formulæ has been shown by Borsche and Feske (*Ber.*, 1927, **60**, 157), who prepared these intermediates, using diethylaniline and pyridine as tertiary bases.

$$R \cdot OH + (p)\text{-}C_6H_4Me \cdot SO_2Cl \longrightarrow RO \cdot SO_2 \cdot C_6H_4Me(p) \xrightarrow{C_5H_5N}$$
$$[R \cdot NC_5H_5]^+ [SO_3 \cdot C_6H_4Me(p)]^- \xrightarrow{HCl} RCl + C_5H_5N, HO_3S \cdot C_6H_4Me(p) \quad \text{(III.)}$$

Treatment of (I; R = CHO) with toluene-*p*-sulphonyl chloride and pyridine or diethylaniline under a variety of conditions failed to yield a chloro-compound or the toluene-*p*-sulphonyl ester, whereas application of similar methods to (I; R = Me) and (I; R = $CH_2 \cdot CH_2 \cdot CO_2Et$) yielded the esters but no halogen compounds. The latter ester (V; R = $CH_2 \cdot CH_2 \cdot CO_2Et$) could not be prepared in aqueous alkali, the *toluene*-p-*sulphonyl acid* (V; R = $CH_2 \cdot CH_2 \cdot CO_2H$) being obtained.

Although it was recognised that toluene-*p*-sulphonyl esters of simple phenols do not react with potassium iodide (Rodionov, *Bull. Soc. chim.*, 1926, **39**, 305; Tipson and Block, *J. Amer. Chem. Soc.*, 1944, **66**, 1880; Tipson *et al.*, *J. Org. Chem.*, 1947, **12**, 133), it was hoped that the nitro-groups in the above esters would facilitate their reaction with lithium chloride to yield chlorodinitro-derivatives, a procedure of value with the aliphatic toluenesulphonyl esters (Kenyon *et al.*, *J.*, 1929, 1700). No chloro-compounds resulted from a number of these experiments.

The properties of the pyridinium quaternary salts mentioned above suggested a new approach to the synthesis of diphenyl ethers. The formation of diphenylamines by reaction of the toluene-*p*-sulphonyl esters of dinitrophenols with aromatic amines proceeds with facility (Ullmann *et al.*, *loc. cit.*; Joshi and Sané, *J. Indian Chem. Soc.*, 1933, **10**, 459), and occasionally succeeds when the Ullmann and Nadai procedure (see above) for halogenating the dinitrophenols fails (Sané and Joshi, *ibid.*, 1932, **9**, 59). Reaction of 2 : 4-dinitrophenyl toluene-*p*-sulphonate with phenol in an aqueous solution of sodium hydroxide at 160°, with phenol and sodium acetate, or with sodium phenoxide and diethylaniline at 210°, yielded no diphenyl ether but only phenyl toluene-*p*-sulphonate by trans-esterification. However, Borsche and Feske's interpretation (III) (*loc. cit.*) of the Ullmann and Nadai reaction suggested that replacement of the mineral acid (HCl) by phenol might result in the formation of a diphenyl ether. This speculation was confirmed by a preliminary experiment in which the quaternary pyridinium salt of 2 : 4-dinitrophenyl toluene-*p*-sulphonate, prepared *in situ*, gave after treatment with phenol 2 : 4-dinitrodiphenyl ether in 83% yield, identical in all respects with the material prepared from 1-chloro-2 : 4-dinitrobenzene and phenol (Raiford and Colbert, *loc. cit.*). Extended investigation of this reaction has revealed it to be remarkably good in many respects and to possess a certain amount of flexibility and has made several diphenyl ethers available directly from dinitrophenols. The following formulæ indicate the general character of the reaction :



(IV.) (V.) (VI.)

(VII.) (VIII.)

Investigation of the reaction with (VII; R′ = OMe), employing (V; R = Me or R = CH_2·CH_2·CO_2Et) as the nitrophenol components and assessing the usefulness of the conditions by the yield of diphenyl ether (VIII; R′ = OMe, R = Me or CH_2·CH_2·CO_2Et) isolated, showed that pyridine was the most effective of several tertiary bases tested. 2 : 4 : 6-Collidine, dimethylaniline, and triethylamine also permitted isolation of diphenyl ethers in reasonable yields, though with them some p-*methoxyphenyl toluene*-p-*sulphonate* was obtained as a by-product in addition to the diphenyl ethers. Employing pyridine as the tertiary base it was possible to isolate the intermediate *pyridinium* quaternary compounds (VI; R = Me or CH_2·CH_2·CO_2Et) by treating the respective esters (V) for a short period (9—10 mins.) on the steam-bath with dry pyridine, though prolonged heating (1·5 hrs.) of (V; R = CH_2·CH_2·CO_2Et) with pyridine gave (V; R = CH_2·CH_2·CO_2H). In the original experiments (cf. Table, Expts. 1, 2, 4) excess (15 equivs.) of (VII; R = H or OMe) was employed as the solvent to yield the new *ethers* (VIII; R = Me, R′ = H or OMe). Reducing the amount of phenol (Expt. 3) resulted in a fall in yield. However, with pyridine as solvent (Expts. 5, 6, 8) excellent yields were obtained even when the quantity of (VII) employed was reduced to about 3 equivs. The facility of the reaction was indicated by the formation at room temperature of a diphenyl ether (Expt. 7) in 26% yield. The isolation of the quaternary salt (VI) is unnecessary,

Examples of the Preparation of 2 : 6-*Dinitrodiphenyl Ethers.*

Expt.	Source of 2 : 6-dinitrophenyl moiety.	R′ in (VII).	Solvent.	Temp.	Time, hrs.	Yield of (VIII), %.
1	(VI; R = Me)	H	15 Equivs. of (VII; R′ = H)	180°	3	86
2	,,	H	,,	120	3	69
3	,,	H	2 Equivs. of (VII; R′ = H)	180	3	50
4	,,	OMe	15 Equivs. of (VII; R′ = OMe)	170	3	27
5	,,	OMe	Pyridine	170	2	70
6	,,	OMe	,,	114	1	94
7	,,	OMe	,,	R.T.	18	26
8	,,	OH	,,	114	1	60
9	(V; R = CH_2·CH_2·CO_2Et)	OMe	,,	114	1	95
10	(I; R = Me)	H	15 Equivs. of (VII; R′ = H)	180	3	60
11	,,	OMe	Pyridine	114	1	95

as demonstrated by the preparation of the ether (VIII; R = CH_2·CH_2·CO_2Et, R′ = OMe) from the reaction (Expt. 9) of (V; R = CH_2·CH_2·CO_2Et) with (VII; R′ = OMe) in pyridine; sometimes the preparation of the toluene-*p*-sulphonyl ester (V) may be avoided, for excellent yields of the ethers (VIII; R = Me, R′ = H or OMe) resulted when (I; R = Me) was treated directly (Expts. 10, 11) with pyridine, toluene-*p*-sulphonyl chloride, and the phenol (VII; R′ = H or OMe), although undoubtedly the reaction still proceeded by the same mechanism.

The above synthesis is therefore effectively an extension of the Borsche and Feske (*loc. cit.*) method of using hydrogen chloride to prepare chlorodinitrobenzenes; *i.e.*, the phenoxide ion apparently acts analogously to that of chlorine. As lithium chloride has been used (see above) to effect the exchange of a toluene-*p*-sulphonyloxy-group for halogen in certain instances, we attempted likewise to prepare 2 : 6-dinitrodiphenyl ethers by reaction of (V; R = Me) with lithium phenoxide and *p*-methoxyphenoxide. However, in both cases only trans-esterification occurred to give the toluene-*p*-sulphonyl esters of the two phenols. The lithium salts reacted normally with the quaternary compound (VI; R = Me) to produce the required diphenyl ethers.

Further investigation showed that the new reaction was not limited to the use of quaternary compounds prepared from toluene-*p*-sulphonyl esters of dinitrophenols, for those derived from benzenesulphonyl esters and 2 : 6-dinitrohalogenobenzenes were just as effective. Thus N-(2 : 6-*dinitro*-4-*methylphenyl*)*pyridinium bromide* * and N-(2 : 6-*dinitro*-4-2′-*carbethoxyethylphenyl*)-*pyridinium chloride*, on treatment with quinol monomethyl ether, gave the respective ethers (VIII; R = Me, R′ = OMe) and (VIII; R = CH_2·CH_2·CO_2Et; R′ = OMe) in excellent yields. Although the *ether* (VIII; R = CO_2Me, R′ = OMe) was prepared satisfactorily from methyl 4-chloro-3 : 5-dinitrobenzoate and (VII; R′ = OMe) in refluxing pyridine, similar treatment of 4-chloro-3 : 5-dinitrobenzaldehyde proved unsuccessful. The latter was shown to react with pyridine to produce an unstable quaternary compound, N-(2 : 6-*dinitro*-4-*formylphenyl*)-*pyridinium chloride*, which decomposed at 80°. Treatment of this quaternary compound in pyridine with (VII; R′ = OMe) at room temperature gave rise to the required *diphenyl ether* (VIII; R′ = OMe, R = CHO) in 70% yield. The same substance was prepared independently by the Ullmann reaction (*Ber.*, 1905, **38**, 2211) from 4-chloro-3 : 5-dinitrobenzaldehyde and the potassium salt of quinol monomethyl ether at 140°. The choice of the phenolic component is not restricted to phenol and quinol monomethyl ether, for *diphenyl ethers* (VIII; R = Me, R′ = CH_3, OH, NO_2, or CO_2Me) were also prepared by using *p*-cresol, quinol, *p*-nitrophenol, and methyl *p*-hydroxybenzoate.

Numerous solvents for the reaction were tested and it was found that in general only those with a dielectric constant of less than 15 at or about room temperature were suitable, *e.g.*, benzene, ethyl and amyl acetates, pyridine, diethylaniline, and phenol, whereas the reaction failed in solvents having constants substantially greater than this. Therefore it was deemed of interest to attempt the reactions in liquid sulphur dioxide and liquid ammonia, both solvents possessing suitable dielectric constants at their boiling points (13·7 and 14·9, respectively).

The reaction in liquid sulphur dioxide is somewhat erratic. The quaternary salt (VI; R = Me) gave, with quinol monomethyl ether, a 77% yield of (VIII; R = Me; R′ = OMe), whilst with phenol it gave only a 12% yield of the diphenyl ether (VIII; R = Me; R′ = H); (VI; R = CH_2·CH_2·CO_2Et) failed to react with quinol monomethyl ether at all under the conditions used, *viz.*, 3 hours at −10°. On the other hand, with liquid ammonia as the solvent excellent yields of diphenyl ethers were obtained in all the instances mentioned.

An explanation of this extreme facility of reaction in these solvents cannot reside alone in their dielectric constants, especially in view of the low temperatures involved. Both solvents are recognised to be capable of solvating carbonium ions, a property which might facilitate the preparation of the quaternary compounds (VI) from (V) and (IV). However, treatment of (V; R = Me) with pyridine in liquid ammonia did not give any quaternary salt, and in the absence of the tertiary base the ester was ammonolysed to give a mixture of the parent phenol (I; R = Me) and its ammonium salt. On the other hand in liquid sulphur dioxide quaternisation occurred to the extent of 17%.

The superiority of sulphur dioxide over ammonia in promoting the formation of quaternary salts from the toluenesulphonyl esters may be due to the fact that in the former solvent pyridine forms a salt-like complex (see Jander, Knöll, and Immig, *Z. anorg. Chem.*, 1937, **232**, 229). No quaternary formation occurred when pyridine sulphotrioxide was employed in liquid sulphur dioxide as the source of tertiary base. Attempts to obtain quaternary salts or diphenyl ethers using di-iodo- instead of dinitro-phenols failed, and hence it was not possible to extend the scope

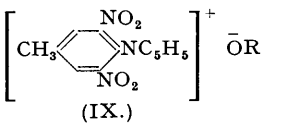
* In order to retain uniformity, this is not named as a 3 : 5-dinitro-*p*-tolyl derivative, and similarly for analogous compounds.—Ed.

of the reaction to include compounds such as *ethyl* 3 : 5-*di-iodo*-4-*toluene*-p-*sulphonyloxybenzoate*. However, although the latter was cleaved by dissolution in liquid sulphur dioxide in the presence of pyridine to yield *pyridinium toluene*-p-*sulphonate*, it was recovered unchanged when phenol was also present.

That this diphenyl ether synthesis does not depend only on the use of an *N*-arylpyridinium salt but also on the presence of two or more nitro-groups was indicated by the failure to prepare ethers from *N*-(*p*-methoxyphenyl)pyridinium chloride (Karrer, Schwarzenbach, and Utzinger, *Helv. Chim. Acta*, 1937, **20**, 72) or from the *N*-(*p*-nitrophenyl)pyridinium chloride or bromide ferric chloride complexes (König, *J. pr. Chem.*, 1904, **70**, 29, 31, 32). An attempt to obtain the free quaternary bromide from the ferric chloride complex by the usual procedure (Karrer *et al.*, *loc. cit.*) caused disruption of the molecule. Nor was it possible to prepare the pyridinium quaternary salt of the toluene-*p*-sulphonyl ester of *p*-nitrophenol by treatment with pyridine even under drastic conditions, or to effect the preparation of an ether by its formation *in situ*.

Diphenyl ethers containing nitro-groups, and more especially those with nitro-groups in both rings, are very susceptible to cleavage by nucleophilic reagents (Ungnade, *Chem. Reviews*, 1946, **38**, 405). Thus it has been shown (D.R.-P., 620,761) that pyridine cleaves 2 : 4 : 2′ : 4′-tetranitrodiphenyl ether to yield *N*-(2 : 4-dinitrophenyl)pyridinium 2 : 4-dinitrophenoxide. No example of such a cleavage of an asymmetrically substituted ether has been reported in the literature. However, this approach offered the possibility of preparing quaternary compounds of a type suitable for the purposes of the present investigation, and the subject has therefore now received some attention.

In general, it was found unnecessary to isolate the intermediate diphenyl ethers, for, although the transient formation of these was demonstrated, the quaternary compounds were prepared directly from the halogenopolynitrobenzene and the polynitrophenol in hot pyridine. Thus treatment of 3 : 5-dinitro-4-hydroxytoluene (I; R = Me) with 1-chloro-2 : 4-dinitrobenzene in hot pyridine yielded N-(2 : 6-*dinitro*-4-*methylphenyl*)*pyridinium* 2 : 4-*dinitrophenoxide* [IX; R = 2 : 4-$(NO_2)_2C_6H_3$], which arose also by cleavage of 2 : 6 : 2′ : 4′-*tetranitro*-4-*methyldiphenyl ether* with pyridine. The structure of [IX; R = 2 : 4-$(NO_2)_2C_6H_3$] was established by the preparation from it of the *chloroplatinate*, identical with that obtained from (VI; R = Me). By the above method the *compound* [IX; R = 2 : 4 : 6-$(NO_2)_3C_6H_2$] was prepared and, as it failed to yield a chloroplatinate, it was identified by treatment with phenol to give (VIII; R = Me, R′ = H), which was also prepared from [IX; R = 2 : 4-$(NO_2)_2C_6H_3$]. The orientation of the two aryl moieties in the quaternary compounds prepared as above appeared to depend on the electron distributions in the initial reactants as determined by their respective substituents. Thus, in contrast to (I; R = Me) both 3 : 5-dinitro-4-hydroxybenzaldehyde and 4-chloro-3 : 5-dinitrobenzaldehyde when treated by the new procedure gave quaternary compounds [X; R = 2 : 4 : 6-$(NO_2)_3C_6H_2$ or 2 : 4-$(NO_2)_2C_6H_3$] in which the aldehyde moiety was present in the anion. The constitution of [X; R = 2 : 4-$(NO_2)_2C_6H_3$] was shown by the preparation of the known 2 : 4-dinitro-4′-methoxydiphenyl ether (Brewster and Choguill, *J. Amer. Chem. Soc.*, 1939, **61**, 2702) from [X; R = 2 : 4-$(NO_2)_2C_6H_3$] on treatment with quinol monomethyl ether and by the formation of a chloroplatinate (Vongerichten, *Ber.*, 1899, **32**, 2571) identical with that obtained from *N*-(2 : 4-dinitrophenyl)pyridinium chloride.



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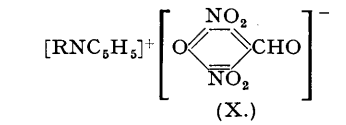

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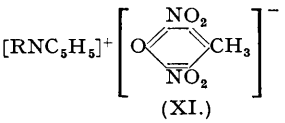

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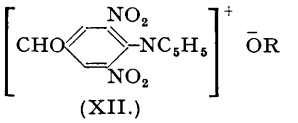

(XII.)

[R = 2 : 4-$(NO_2)_2C_6H_3$ or 2 : 4 : 6-$(NO_2)_3C_6H_2$.]

Compound [X; R = 2 : 4 : 6-$(NO_2)_3C_6H_2$] failed to form a chloroplatinate and was recovered unchanged after treatment with quinol monomethyl ether in pyridine. This structure was assigned to it after comparison with N-(2 : 6-*dinitro*-4-*formylphenyl*)*pyridinium* 2 : 4 : 6-*trinitrophenoxide* [XII; R = 2 : 4 : 6-$(NO_2)_3C_6H_2$], the melting point of which it depressed considerably. This compound, the other possible product of the cleavage of 2 : 6 : 2′ : 4′ : 6′-pentanitro-4-formyldiphenyl ether with pyridine, was prepared by treatment of *N*-(2 : 6-dinitro-4-formylphenyl)pyridinium chloride with picric acid in aqueous solution. It also failed to form

a chloroplatinate, but, unlike [X; R = 2 : 4 : 6-$(NO_2)_3C_6H_2$], it reacted with quinol monomethyl ether in pyridine, the product being the expected diphenyl ether (VIII; R = CHO, R′ = OMe). Reaction of *N*-picrylpyridinium chloride with (I; R = Me) yielded the quaternary salt [XI; R = 2 : 4 : 6-$(NO_2)_3C_6H_2$], in which the cation was characterised by conversion into a *chloroplatinate*, also prepared from the original chloride, and which was converted by treatment with phenol in hot pyridine into the *ether* (VIII; R = NO_2, R′ = H). On refluxing [XI; R = 2 : 4 : 6-$(NO_2)_3C_6H_2$] alone in pyridine there arose, presumably *via* the diphenyl ether, the quaternary compound [IX; R = 2 : 4 : 6-$(NO_2)_3C_6H_2$]. This again demonstrates the influence of the substituents on the final orientation of the quaternary compounds in hot pyridine.

The quaternary compounds with a polynitrophenoxide as anion are thus suitable for the preparation of diphenyl ethers by the new synthesis, but they are useful for the preparation of compounds of type (VIII) only where the relative electron distributions in the initial phenol and halogenobenzene are such that the nucleus of the former preferably enters the cation. However, they may prove of value where the more usual types of salts are unstable, for whereas [XII; R = 2 : 4 : 6-$(NO_2)_3C_6H_2$] is stable, the quaternary bromide corresponding to (VI; R = CHO) is heat labile and has to be used at room temperature.

Experimental.

3 : 5-*Dinitro*-4-*hydroxybenzaldehyde*.—3-Nitro-4-hydroxybenzaldehyde (80 g.) was added slowly to fuming nitric acid (230 ml.) at 5° with stirring. At the end of the addition the temperature was allowed to rise to 20° and remain there for 2 hours. The solution was poured on ice and the solid was filtered off, washed, dried, and crystallised from carbon tetrachloride, giving a small quantity of yellow plates (10 g.), m. p. 80°, which proved to be the *picrate* of 3 : 5-dinitro-4-hydroxybenzaldehyde (Found : C, 36·1; H, 1·5; N, 15·2. $C_{13}H_7O_{13}N_5$ requires C, 35·4; H, 1·6; N, 15·8%). The carbon tetrachloride mother-liquors were concentrated and the residue crystallised from acetic acid, giving the required 3 : 5-dinitro-4-hydroxybenzaldehyde (40 g.), m. p. 102° (lit., m. p. 102°).

Pyridine salt. Addition of a solution of the aldehyde in alcohol–ether to a similar solution of pyridine gave a precipitate of the pyridine *salt*, which separated as bright yellow needles from alcohol, m. p. 174° (Found : C, 49·3; H, 3·2; N, 13·3. $C_{12}H_9O_6N_3$ requires C, 49·5; H, 3·1; N, 14·4%).

4-*Chloro*-3 : 5-*dinitrobenzaldehyde*.—To a suspension of 3 : 5-dinitro-4-hydroxybenzaldehyde (4·25 g.) in phosphorus oxychloride (20 ml.), diethylaniline (4·3 ml.) was added at room temperature. After 5 minutes the mixture was poured on ice–water, and the solid was extracted with ether. The extract was washed with dilute sodium carbonate solution, filtered, and evaporated. The *aldehyde* crystallised from aqueous alcohol in the form of pale yellow needles (4 g.; 88%), m. p. 107° (Found : C, 36·8; H, 1·4; N, 12·2; Cl, 15·5. $C_7H_3O_5N_2Cl$ requires C, 36·5; H, 1·3; N, 12·1; Cl, 15·4%). The aldehyde was converted into the phenylhydrazone, m. p. 214°, in the usual manner, and into the *dinitrophenylhydrazone*, m. p. 270° after crystallisation from dioxan (Found : N, 20·3; Cl, 8·5. $C_{13}H_7O_8N_6Cl$ requires N, 20·5; Cl, 8·7%).

4-*Chloro*-3 : 5-*dinitrotoluene*.—3 : 5-Dinitro-*p*-cresol (0·8 g.) was heated on a steam bath for 1·5 hours with phosphorus oxychloride (6 ml.) and diethylaniline (10 ml.). The cooled mixture was poured on ice and the oil was extracted with ether. The extract was washed with dilute aqueous sodium carbonate solution, dried, filtered, and evaporated. The residue was crystallised from ethyl alcohol to give yellow needles (0·16 g.), m. p. 116° (lit., m. p. 114°).

Ethyl β-(4-*Chloro*-3 : 5-*dinitrophenyl*)*propionate*.—The corresponding hydroxy-ester was prepared from β-(3 : 5-dinitro-4-hydroxyphenyl)propionic acid (Stohr, *Annalen*, 1884, **225**, 92) by an azeotropic method and was found to have m. p. 61° instead of the recorded m. p. of 72° (Stohr, *loc. cit.*); however, it had the correct analysis (Found : C, 46·7; H, 4·8; N, 10·2. Calc. for $C_{11}H_{12}O_7N_2$: C, 46·5; H, 4·2; N, 9·9%). Ethyl β-(3 : 5-dinitro-4-hydroxyphenyl)propionate (1·4 g.) in diethylaniline (5 ml.) was treated dropwise with phosphorus oxychloride (3 ml.) and heated on the steam-bath for one hour, during which the solution darkened considerably. After cooling, ethyl alcohol (20 ml.) was added and the reaction mixture was allowed to stand overnight to destroy excess of phosphorus oxychloride. The mixture was evaporated in a vacuum, the product extracted into benzene, and the benzene extract washed with dilute hydrochloric acid and water. After evaporation of the benzene, the residual *ester* was crystallised from alcohol, giving a feathery magma (0·9 g.; 60%), m. p. 52° (Found : C, 43·9; H, 3·6; N, 8·9; Cl, 11·3. $C_{11}H_{11}O_6N_2Cl$ requires C, 43·6; H, 3·7; N, 9·25; Cl, 11·7%).

1-*Chloro*-2 : 4-*dinitrobenzene*.—2 : 4-Dinitrophenol (1 g.), phosphorus oxychloride (5 ml.), and diethylaniline (1·2 ml.) were heated on the steam-bath for 20 minutes. The cooled solution was poured on ice, and the oil extracted into ether. The ether extract was washed with sodium carbonate solution and water, dried, and evaporated. The residue was sublimed in a vacuum (0·55 g., m. p. 50°) (lit., m. p. 51°).

4-*Bromo*-3 : 5-*dinitrobenzylidene Dibromide*.—3 : 5-Dinitro-4-hydroxybenzaldehyde (3 g.) was added to phosphorus oxybromide (10 g.) in xylene (10 ml.), and diethylaniline (3 ml.) was carefully added. The mixture was then heated on a steam-bath for 2 hours, diluted with chloroform (100 ml.), and cooled. Excess of phosphorus oxybromide was decomposed by shaking with water, and the chloroform layer was then washed with acid and alkali and evaporated. The *dibromide* crystallised from ethyl alcohol in yellow needles, m. p. 129° (40%) (Found : C, 20·1; H, 0·8; N, 6·45; Br, 56·5. $C_7H_3O_4N_2Br_3$ requires C, 20·1; H, 0·7; N, 6·7; Br, 57·3%).

Picryl Chloride.—Diethylaniline (*ca.* 1·8 ml.) was added dropwise to a solution of picric acid (1 g.) in phosphorus oxychloride (10 ml.) until the solution was brown. After being allowed to stand for 15 minutes, the mixture was poured into iced water, and the resultant pure picryl chloride filtered off, washed, and dried; m. p. and mixed m. p. 83° (1·05 g., 97%).

Methyl 4-*Chloro*-3 : 5-*dinitrobenzoate*.—Methyl 3 : 5-dinitro-4-hydroxybenzoate (1 g.) was treated with diethylaniline and phosphorus oxychloride exactly as above. Pale yellow lances of methyl 4-chloro-3 : 5-dinitrobenzoate were obtained; m. p. and mixed m. p. 102—103° (1·05 g., 98%).

4-*Chloro*-3 : 5-*dinitroacetanilide*.—A mixture of 3 : 5-dinitro-4-hydroxyacetanilide (3 g.), phosphorus oxychloride (10 ml.), and diethylaniline (6 ml.) was refluxed for 1 hour. Excess of phosphorus oxychloride was removed in a vacuum, and the residue triturated with dilute hydrochloric acid and extracted with ether. The extract was washed with sodium hydrogen carbonate solution, then water, and was dried and evaporated. The resultant 4-*chloro*-3 : 5-*dinitroacetanilide* recrystallised from a little ethanol as pale yellow lances, m. p. 232—234° (0·6 g., 19%) (Found : C, 37·5; H, 2·4; N, 16·1; Cl, 13·6. $C_8H_6O_5N_3Cl$ requires C, 37·0; H, 2·3; N, 16·2; Cl, 13·6%).

4-*Chloro*-3 : 5-*dinitro*-tert.-*butylbenzene*.—A mixture of 3 : 5-dinitro-4-hydroxy-*tert*.-butylbenzene (2 g.), phosphorus oxychloride (20 ml.), and diethylaniline (4 ml.) was refluxed for one hour. The cooled mixture was poured on ice, and the resultant solid recrystallised (charcoal) from 50% acetic acid solution as buff lances, m. p. 115° (1·2 g., 58%) (Found : N, 10·8; Cl, 13·7. $C_{10}H_{11}O_4N_2Cl$ requires N, 10·8; Cl, 13·7%).

2 : 4-*Dinitrodiphenyl Ether*.—2 : 4-Dinitrophenyl toluene-*p*-sulphonate (2·6 g.) (Ullmann and Nadai, *Ber*., 1908, **41**, 1872) was heated on a steam-bath for ½ hour with dry pyridine (10 ml.) to obtain the pyridinium quaternary salt. Excess of pyridine was then removed in a vacuum and the residue was heated with phenol (2·9 g.) to 210° for 6 hours. The cooled reaction mixture was dissolved in ether and washed with dilute sodium hydroxide solution. The residue obtained after evaporation of the dry ether solution was crystallised, giving the diphenyl ether, m. p. 70° (lit., m. p. 70°) (Found : N, 11·0. Calc. for $C_{12}H_8O_5N_2$: N, 10·8%).

Ethyl β-(3 : 5-*Dinitro*-4-*toluene*-p-*sulphonyloxyphenyl*)*propionate*.—Ethyl β-(3 : 5-dinitro-4-hydroxyphenyl)propionate (0·7 g.) in diethylaniline (2 ml.) was heated with toluene-*p*-sulphonyl chloride (0·6 g.) on the steam-bath for 4 hours. The cooled mixture was washed with dilute hydrochloric acid, and the residue triturated with ethyl alcohol and crystallised from aqueous acetic acid, yielding colourless prisms (0·7 g.; 63%), m. p. 103° (Found : C, 49·8; H, 3·9; N, 6·7; S, 7·2. $C_{18}H_{18}O_9N_2S$ requires C, 49·3; H, 4·1; N, 6·3; S, 7·3%).

The corresponding *acid* was obtained when the above *ester* (0·7 g.) was treated with toluene-*p*-sulphonyl chloride (0·6 g.) in 2N-sodium hydroxide (3 ml.) and water (20 ml.) containing enough acetone to achieve solution. At the end of one hour the solution was acidified and diluted with water; the insoluble precipitate was filtered off, and crystallised from aqueous ethyl alcohol or acetic acid in the form of glistening white plates (0·77 g.; 75%), m. p. 157° (Found : N, 6·6; S, 7·5. $C_{16}H_{14}O_9N_2S$ requires N, 6·8; S, 7·8%).

Ethyl β-(3 : 5-*Dinitro*-4-p-*methoxyphenoxyphenyl*)*propionate*.—The above toluenesulphonyl ester (0·22 g.) and quinol monomethyl ether (0·2 g.) were refluxed in pyridine for one hour. The warm reaction mixture was diluted with water and alcohol, and the crystals which deposited on cooling were filtered off and crystallised from ethyl alcohol, giving yellow needles of the *diphenyl ether* (0·19 g.; 95%), m. p. 104° (Found : C, 55·6; H, 4·9; N, 7·2. $C_{18}H_{18}O_8N_2$ requires C, 55·4; H, 4·6; N, 7·2%).

When the toluenesulphonyl ester (0·44 g.) was heated for 10 minutes in pyridine (2 ml.) and the cooled reaction mixture was diluted with ether, the quaternary salt, N-(2 : 6-*dinitro*-4-2′-*carbethoxyethylphenyl*)-*pyridinium toluene*-p-*sulphonate* was obtained. It crystallised from ethyl alcohol–ether in pale buff-coloured prisms (0·47 g.; 89%), m. p. 172° (Found : C, 53·8; H, 4·6; N, 7·95; S, 6·1. $C_{23}H_{23}O_9N_3S$ requires C, 53·4; H, 4·5; N, 8·1; S, 6·2%).

This quaternary salt (0·25 g.) and quinol monomethyl ether (0·2 g.) were dissolved in liquid ammonia (20 ml.), and the solution kept for 3 hours. After evaporation of the solvent, the residue crystallised from ethyl alcohol in the form of brown needles (0·18 g.; 97%), m. p. 102°, identical with the above diphenyl ether.

The corresponding quaternary pyridinium chloride also gave the diphenyl ether by treatment with liquid ammonia and quinol monomethyl ether in a similar fashion in 96% yield. The same diphenyl ether was formed when ethyl β-(3 : 5-dinitro-4-chlorophenyl)propionate was refluxed in pyridine for 1 hour with quinol monomethyl ether, the product being isolated in the usual manner.

p-*Methoxyphenyl Toluene*-p-*sulphonate*.—A solution of quinol monomethyl ether (1·2 g.) in aqueous sodium hydroxide (20 ml.; 0·5N) was treated on the steam-bath with toluene-*p*-sulphonyl chloride (1·9 g.). After 1 hour the cooled reaction mixture was extracted with ether, and the washed and dried extract concentrated to give the *ester*, which crystallised from light petroleum as long, colourless needles, m. p. 66—67° (Found : C, 60·9; H, 5·55; S, 11·4. $C_{14}H_{14}O_4S$ requires C, 60·5; H, 5·05; S, 11·5%).

2:6-*Dinitro*-4′-*methoxy*-4-*methyldiphenyl Ether* [3:5-*Dinitro*-4-(4′-*methoxyphenoxy*)*toluene*]*.—Treatment of the toluene-*p*-sulphonate of 3 : 5-dinitro-4-hydroxytoluene (1 g.) with dry pyridine (5 ml.) for 5 mins. on the steam-bath gave *N*-(2 : 6-dinitro-4-methylphenyl)pyridinium toluene-*p*-sulphonate as a crystalline product, which was filtered off after dilution of the reaction mixture with ether. It crystallised from ethyl alcohol (charcoal) as long, colourless needles (70% yield), m. p. 184° (Found : C, 52·9; H, 4·4. Calc. for $C_{19}H_{17}O_7N_3S$: C, 52·9; H, 4·0%) (cf. Borsche and Feske, *loc. cit*., reddish-yellow crystals, m. p. 179°).

This toluenesulphonate (1 g.) and quinol monomethyl ether (1 g.) were dissolved in pyridine (10 ml.), and the solution heated under reflux for one hour. The cooled mixture was poured into dilute sodium hydroxide solution, and the precipitated solid filtered off and crystallised from ethyl alcohol, forming yellow prisms, m. p. 142°, identical with the diphenyl ether previously prepared by a different method (see Part I).

The above quaternary salt (0·86 g.) was dissolved in liquid sulphur dioxide (20 ml.), quinol monomethyl ether (0·8 g.) was added, and the mixture left while solvent evaporated during about 3 hours, the flask being protected from air by a tube containing cotton-wool. The residue was extracted with

* Ethers are preferably named as such wherever possible. The alternative name, which has been omitted elsewhere, indicates the relation to other compounds described in the Experimental. Ed.

benzene, and the extract washed, dried, and evaporated. The residue recrystallised from ethyl alcohol to give the diphenyl ether as yellow prisms (0·47 g.; 77%), m. p. 142° not depressed on admixture with the above. The diphenyl ether was also obtained (82%, m. p. 142°) by the above method using liquid ammonia instead of liquid sulphur dioxide as solvent.

N-(2 : 6-*Dinitro*-4-*methylphenyl*)*pyridinium Bromide*.—The above quaternary toluene-*p*-sulphonate (2 g.) in liquid sulphur dioxide (15 ml.) was treated with bromine (0·2 ml.), whereupon a crystalline solid was deposited. Solvent was removed by warming, and the red crystalline residue was triturated with dry ether, yielding the perbromide as an orange powder (2·27 g.; 97%), m. p. 179°. This substance possessed all the characteristics of a perbromide and reacted with hot acetone, yielding bromoacetone and the quaternary *bromide*. The latter crystallised from dry methyl cyanide in colourless needles, m. p. 203° (Found : C, 41·0; H, 3·1; N, 11·7; Br, 23·4. $C_{12}H_{10}O_4N_3Br$ requires C, 42·4; H, 2·9; N, 12·3; Br, 23·5%).

The quaternary bromide (0·5 g.) in pyridine (5 ml.) was refluxed for one hour with quinol monomethyl ether (0·5 g.). After evaporation in a vacuum the residue was treated with dilute sodium hydroxide solution, and the diphenyl ether was filtered off and crystallised; m. p. and mixed m. p. 142°.

The corresponding quaternary *iodide* was obtained from the corresponding toluene-*p*-sulphonate (1·8 g.) in warm water (10 ml.) by treatment with an aqueous solution of sodium iodide (2·4 g. in 4 ml.). The deep orange platelets were recrystallised from water; m. p. 191° (decomp.) (Found : I, 32·4. $C_{12}H_{10}O_4N_3I$ requires I, 32·8%).

3 : 5-*Dinitro*-4-*benzenesulphonyloxytoluene* was prepared by treating 3 : 5-dinitro-*p*-cresol (5 g.) in water (10 ml.) containing sodium carbonate (0·5 g.) on a steam-bath with benzenesulphonyl chloride (1·3 ml.) while stirring. At the end of one hour the cooled reaction mixture was filtered, and the solid ester crystallised from glacial acetic acid as pale yellow plates (4·5 g.), m. p. 163° (Found : N, 8·4; S, 9·7. $C_{13}H_{10}O_7N_2S$ requires N, 8·3; S, 9·5%). The benzenesulphonyl ester was converted into the above diphenyl ether by treatment with pyridine and quinol monomethyl ether in the usual fashion.

2 : 6-*Dinitro*-4′-*hydroxy*-4-*methyldiphenyl Ether*.—*N*-(2 : 6-Dinitro-4-methylphenyl)pyridinium toluene-*p*-sulphonate (0·5 g.) was refluxed in pyridine for one hour with quinol (0·5 g.), and the cooled solution poured into water. The insoluble, rather gummy solid was crystallised from benzene–light petrol, giving yellow needles (0·2 g.; 60%), m. p. 166° (Found : C, 53·1; H, 3·6; N, 9·1. $C_{13}H_{10}O_6N_2$ requires C, 53·8; H, 3·45; N, 9·6%).

2 : 6-*Dinitro*-4-*methyldiphenyl Ether*.—3 : 5-Dinitro-*p*-cresol (5 g.), toluene-*p*-sulphonyl chloride (5 g.), and pyridine (20 ml.) were heated in an oil-bath to 110° for one hour. Phenol (20 g.) was added, and the mixture heated at 180—190° for 3 hours. The cooled melt was poured into dilute sodium hydroxide solution, and the precipitated solid was filtered off and crystallised from alcohol, forming yellow lances (yield 60%), m. p. 134° (Found : C, 57·0; H, 3·7; N, 10·4. $C_{13}H_{10}O_5N_2$ requires C, 56·9; H, 3·6; N, 10·2%).

N-(2 : 6-Dinitro-4-methylphenyl)pyridinium toluene-*p*-sulphonate (0·43 g.) was treated with phenol (0·4 g.) in liquid ammonia (25 ml.). After evaporation of the solvent the product was worked up by the usual procedure; m. p. and mixed m. p. 134° (0·21 g.; 78%).

2 : 6-*Dinitro*-4 : 4′-*dimethyldiphenyl Ether*.—The foregoing toluene-*p*-sulphonate (2·5 g.) was refluxed for 30 minutes in pyridine with *p*-cresol (2 g.). The cooled solution was poured into dilute sodium hydroxide solution, and the precipitated *ether* filtered off and crystallised from alcohol, giving yellow prisms (1·3 g.; 78%), m. p. 106—107° (Found : C, 58·3; H, 4·4; N, 9·9. $C_{14}H_{12}O_5N_2$ requires C, 58·3; H, 4·2; N, 9·7%).

2 : 6 : 4′-*Trinitro*-4-*methyldiphenyl Ether*.—This was prepared exactly as above from the quaternary salt and *p*-nitrophenol. The *product* crystallised from benzene–light petrol as cream-coloured prisms (1·1 g.; 60%), m. p. 172° (Found : N, 13·3. $C_{13}H_9O_7N_3$ requires N, 13·2%).

Methyl 3′ : 5′-*Dinitro*-4-(4′-*methylphenoxy*)*benzoate*.—*N*-(2 : 6-Dinitro-4-methylphenyl)pyridinium toluene-*p*-sulphonate (2 g.), methyl *p*-hydroxybenzoate (2 g.), and pyridine (10 ml.) were heated under reflux for 30 minutes, and the product worked up as usual. The *ester* crystallised from alcohol as bright yellow needles (1·2 g.; 78%), m. p. 137° (Found : C, 54·7; H, 3·9; N, 8·6. $C_{15}H_{12}O_7N_2$ requires C, 54·3; H, 3·6; N, 8·5%).

Methyl 3 : 5-*Dinitro*-4-(4′-*methoxyphenoxy*)*benzoate*.—Methyl 4-chloro-3 : 5-dinitrobenzoate (1 g.) was added to pyridine, in which it dissolved giving a deep red solution from which the quaternary salt separated. Quinol monomethyl ether (1 g.) was added, and the mixture heated under reflux for 30 minutes. The cooled solution was poured into dilute alkali and the precipitated solid crystallised from alcohol as bright yellow needles (0·4 g.), m. p. 129°, identical with the substance prepared (Part I) by a different method.

3 : 5-*Dinitro*-4-(4′-*methoxyphenoxy*)*benzaldehyde*.—4-Chloro-3 : 5-dinitrobenzaldehyde (6·9 g.), quinol monomethyl ether (3·72 g.), potassium hydroxide (1·68 g.), and water (24 ml.) were heated to 140° in an oil-bath for 2 hours. After cooling, the mixture was extracted with chloroform, the extract evaporated, and the residue crystallised from aqueous acetic acid, forming bright yellow needles (6·8 g.; 70%), m. p. 109° (Found : C, 53·3; H, 2·9; N, 8·6. $C_{14}H_{10}O_7N_2$ requires C, 52·8; H, 3·2; N, 8·8%).

4-Chloro-3 : 5-dinitrobenzaldehyde (1·15 g.) was dissolved in dry benzene (15 ml.) and pure anhydrous pyridine (0·5 ml.) was added dropwise to the solution with shaking. The precipitated N-(2 : 6-*dinitro*-4-*formylphenyl*)*pyridinium chloride* was filtered off at the end of one hour (1·3 g.; 80%); m. p. 80° (decomp.) (Found : N, 12·9. $C_{12}H_8O_5N_3Cl,H_2O$ requires N, 12·8%). The buff-coloured *chloroplatinate* had m. p. 256° (Found : N, 8·8; Pt, 20·1. $C_{26}H_{16}O_{10}N_6Cl_6Pt$ requires N, 8·8; Pt, 20·4%).

The diphenyl ether was prepared from 3 : 5-dinitro-4-chlorobenzaldehyde (0·58 g.) and quinol monomethyl ether (0·92 g.) in anhydrous pyridine by shaking for 26 hours at room temperature. The solution was diluted with chloroform and washed with acid and water. The dried chloroform solution was evaporated in a vacuum, the residue dissolved in ethyl alcohol, and the solution treated with an acid solution of 2 : 4-dinitrophenylhydrazine. The yellow *dinitrophenylhydrazone* which separated was filtered off, washed, and dried (0·88 g.; 70%), m. p. 249—250° (Found : N, 16·6. $C_{20}H_{14}O_{10}N_6$ requires N, 16·8%). The m. p. was not depressed on admixture with the derivative of an authentic specimen of the diphenyl ether.

Methyl 3:5-*Di-iodo*-4-*toluene*-p-*sulphonyloxybenzoate*.—Methyl 3:5-di-iodo-4-hydroxybenzoate (4·04 g.) in pyridine (14 ml.) was treated portionwise with toluene-*p*-sulphonyl chloride (2·2 g.) at 0° with stirring. After 2 hours, the mixture was diluted with water, and the insoluble product crystallised from ethyl acetate, yielding colourless triclinic prisms, m. p. 160° (Found: S, 5·4; I, 44·8. $C_{15}H_{12}O_5I_2S$ requires S, 5·7; I, 45·6%).

Solution of the above *sulphonic* ester (0·56 g.) in liquid sulphur dioxide in the presence of dry pyridine (0·08 ml.) gave after 4 hours *pyridinium toluene*-p-*sulphonate* (0·18 g.). This was isolated by evaporation of the solvent and extraction of the residue with water. The deliquescent salt crystallised from methyl cyanide–ether as thin transparent plates, m. p. 115—116·5° not depressed by the specimen prepared from pyridine and toluene-*p*-sulphonic acid (Found: C, 57·2; H, 5·7; N, 5·1. $C_{12}H_{13}O_3NS$ requires C, 57·3; H, 5·2; N, 5·6%).

2 : 6 ; 2′ : 4′-*Tetranitro*-4-*methyldiphenyl Ether*.—1-Chloro-2 : 4-dinitrobenzene (4 g.) and 3 : 5-dinitro-*p*-cresol (3·96 g.) were dissolved in nitrobenzene (20 ml.) and powdered potassium hydroxide (1·12 g.) and copper-bronze (0·15 g.) were added. The solvent was distilled off slowly while more was added to maintain the volume for a period of 1½ hours. The nitrobenzene was then steam-distilled, and the non-volatile product was extracted from the cooled aqueous residue with chloroform. The dried extract was evaporated, and the residue distilled in a high vacuum as a yellow oil (2·8 g.; 38%), b. p. 40—60°/10^{-4} mm. (Found: N, 14·9. $C_{13}H_8O_9N_4$ requires N, 15·3%).

The above *tetranitro*-compound (2·5 g.) was heated under reflux with pyridine (10 ml.) for 2 hours. Half of the pyridine was evaporated off in a vacuum, and the remainder on cooling deposited crystals, which were filtered off, washed with chloroform, and recrystallised from water or methyl cyanide, forming red prisms (1·6 g.; 52%), m. p. 229° (Found: C, 49·2; H, 3·0; N, 15·75. $C_{18}H_{13}O_9N_5$ requires C, 48·8; H, 3·0; N, 15·8%). This N-(2 : 6-*dinitro*-4-*methylphenyl*)*pyridinium* 2 : 4-*dinitrophenoxide* gave a buff-coloured *chloroplatinate*, m. p. 239°, identical with that prepared from the toluene-*p*-sulphonate (p. S 196) (Found: C, 31·0; H, 2·1; N, 9·0; Pt, 20·8. $C_{24}H_{20}O_8N_6Cl_6Pt$ requires C, 31·05; H, 2·2; N, 9·05; Pt, 21·0%).

The same compound was obtained when 2 : 4-dinitrochlorobenzene (2·03 g.) and 2 : 6-dinitro-*p*-cresol (1·98 g.) were boiled in anhydrous pyridine (5 ml.) for 2 hours. The cooled mixture was diluted with chloroform and the deposited solid collected and crystallised from methyl cyanide.

The above quaternary salt (1·1 g.) and quinol monomethyl ether (0·93 g.) were heated in pyridine (5 ml.) for 1½ hrs. The product after dilution with water was extracted into chloroform and the extract was washed successively with acid, alkali, and water. The residue after removal of chloroform from the dry extract crystallised from alcohol as yellow prisms (0·39 g.; 58%), m. p. 142—143°, not depressed by an authentic specimen of 2 : 6-dinitro-4′-methoxy-4-methyldiphenyl ether.

2 : 6-Dinitro-4-methyldiphenyl ether, m. p. and mixed m. p. 134°, was prepared in exactly the same way, phenol being used instead of quinol monomethyl ether.

N-(2 : 6-*Dinitro*-4-*methylphenyl*)*pyridinium Picrate*.—Picryl chloride (2·48 g.) and 3 : 5-dinitro-*p*-cresol (1·98 g.) were boiled with pyridine (5 ml.) for 2 hours. The cooled solution deposited a dark oil, from which the pyridine was decanted, and the oil was dissolved in hot water (30 ml.). The hot solution, after being decolorised with charcoal, was filtered through a thin pad of Kieselguhr and on cooling deposited red crystals (1·0 g.; 20%), m. p. 151°. The *picrate* recrystallised from alcohol–acetone as yellow needles, m. p. 156—158° (Found: C, 44·1; H, 2·5; N, 17·7. $C_{18}H_{12}O_{11}N_6$ requires C, 44·3; H, 2·5; N, 17·2%). This salt on treatment with phenol and pyridine in the usual manner gave 2 : 6-dinitro-4-methyldiphenyl ether in 33% yield; m. p. 134°.

N-(2 : 4-*Dinitrophenyl*)*pyridinium* 2 : 6-*Dinitro*-4-*formylphenoxide*.—3 : 5-Dinitro-4-hydroxybenzaldehyde (2·12 g.) was heated for 2 hours in pyridine (7 ml.) with 2 : 4-dinitrochlorobenzene (2·03 g.). The cooled solution deposited the quaternary *salt*, which was filtered off, washed with chloroform, and crystallised from water or ethanol–acetone, forming clusters of yellow needles (3·7 g.; 81%), m. p. 169—170° (Found: C, 46·7; H, 2·6; N, 15·3. $C_{18}H_{11}O_{10}N_5$ requires C, 47·3; H, 2·4; N, 15·3%). An identical quaternary compound arose on similar treatment of 4-chloro-3 : 5-dinitrobenzaldehyde and 2 : 4-dinitrophenol.

The quaternary salt, when dissolved in aqueous alcohol and treated with chloroplatinic acid, gave 2 : 4-dinitrophenylpyridinium chloroplatinate, m. p. 210° (Found: N, 9·4; Pt, 21·7. Calc. for $C_{22}H_{16}O_8N_6Cl_6Pt$: N, 9·3; Pt, 21·7%) (lit., m. p. 210°).

2 : 4-*Dinitro*-4-*methoxydiphenyl Ether*.—This was obtained when the above quaternary salt (0·92 g.) and quinol monomethyl ether (0·74 g.) were refluxed with pyridine (5 ml.) for 2 hours. The reaction mixture was diluted with chloroform and washed successively with acid, alkali, and water. The residue from the chloroform extract was crystallised from ethyl alcohol (0·31 g.; 58%); m. p. 110°, identical with an authentic specimen (lit., m. p. 110°).

Picrylpyridinium 2 : 6-*Dinitro*-4-*formylphenoxide*.—Picryl chloride (2·48 g.) and 3 : 5-dinitro-4-hydroxybenzaldehyde (2·12 g.) were boiled in pyridine for 2 hours. The product was worked up by dilution with chloroform in the usual fashion and crystallised from ethyl acetate and acetone as yellow prisms (2·92 g.; 58%), m. p. 167°, which sublimed at 100°/10^{-4} mm. (Found: N, 16·4. $C_{18}H_{10}O_{12}N_6$ requires N, 16·7%). The quaternary *compound* arose also on treatment of picric acid and 4-chloro-3 : 5-dinitrobenzaldehyde in a similar manner.

N-(2 : 6-*Dinitro*-4-*formylphenyl*)*pyridinium* 2 : 4 : 6-*Trinitrophenoxide*.—The corresponding quaternary chloride (0·81 g.) was dissolved in hot water (15 ml.) and a hot aqueous solution of picric acid (0·57 g.) was added; the precipitated *compound* (0·86 g.) was filtered off and crystallised from acetone–ethyl acetate; m. p. 167—168° (Found: N, 16·9. $C_{18}H_{10}O_{12}N_6$ requires N, 16·7%). An identical product was obtained on refluxing picrylpyridinium 2 : 6-dinitro-4-formylphenoxide for 1·5 hours in pyridine.

This quaternary salt was converted into 3 : 5-dinitro-4-(4′-methoxyphenoxy)benzaldehyde by treatment with quinol monomethyl ether in pyridine in the usual fashion. The aldehyde was isolated as the 2 : 4-dinitrophenylhydrazone in 78% yield; m. p. 248°.

2 : 4 : 6-*Trinitrodiphenyl Ether*.—Picrylpyridinium chloride was prepared by treating a solution of picryl chloride (12·4 g.) in anhydrous benzene (75 ml.) with pyridine (5 ml.), added dropwise. The

quaternary chloride (15·4 g.; 95%) was filtered off; m. p. 116—117°. This compound gave a *chloroplatinate* in the usual manner; m. p. 249—251° (Found : N, 11·0; Pt, 19·2. $C_{22}H_{14}O_{12}N_8Cl_6Pt$ requires N, 11·3; Pt, 19·7%).

The above quaternary chloride (4·1 g.) in hot water (50 ml.) on treatment with a solution of 3 : 5-dinitro-*p*-cresol (1·5 g.) in hot water (20 ml.) gave the quaternary salt *picrylpyridinium* 2 : 6-*dinitro*-4-*methylphenoxide* on cooling. The crude solid (2·25 g.; 37%) crystallised from acetone–light petrol as yellow needles, m. p. 219°, which could be sublimed at 180°/10^{-5} mm. (Found : N, 17·2. $C_{18}H_{12}O_{11}N_6$ requires N, 17·2%). On treatment with chloroplatinic acid the quaternary salt yielded picrylpyridinium chloroplatinate, m. p. and mixed m. p. 249—251°.

The above quaternary salt (0·98 g.) and phenol (0·56 g.) in boiling pyridine (5 ml.) gave 2 : 4 : 6-trinitrodiphenyl ether which was isolated in the usual fashion (0·35 g.; 57%), m. p. 151—152°, and found to be identical with that described by Willgerodt (*Ber.*, 1879, **12**, 1278).

When the quaternary compound was refluxed for 1·5 hrs. in absolute pyridine there was obtained *N*-(2 : 6-dinitro-4-methylphenyl)pyridinium picrate in 70% yield; m. p. and mixed m. p. 161°.

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