[CONTRIBUTION FROM THE CAMBRIDGE UNIVERSITY CHEMICAL LABORATORY]

CONDITIONS OF SALT FORMATION IN POLYAMINES AND KINDRED COMPOUNDS. SALT FORMATION IN THE TERTIARY 2-PYRIDYLAMINES, PHOSPHINES AND ARSINES

FREDERICK GEORGE MANN AND JAMES WATSON

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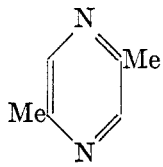
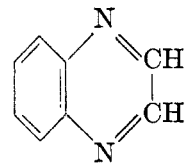
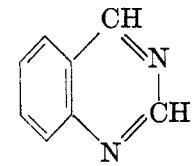
It is well recognized that if in an organic molecule there are two or more amine groups, which by virtue of their nature and bonding should possess the normal basic properties of such groups, their mutual proximity may prevent these groups showing simultaneously these basic properties; for example, they may not all form salts even with strong acids, nor, if they are tertiary amine groups, may they all form quaternary salts. This inhibition of complete quaternary salt formation also applies to molecules containing more than one tertiary phosphine or arsine group. As examples of this phenomenon, both pyrazine (I) and 2,5-dimethylpyrazine form only a monohydrochloride and monomethiodide (1), quinoxaline (II) behaves similarly (2), and quinazoline (III) even when heated with an excess of



I

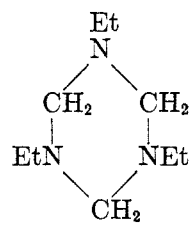


II

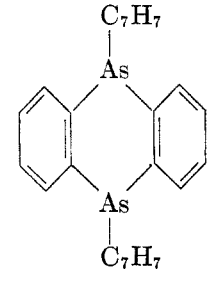


III

methyl iodide at 100° gives only a monomethiodide on the 3-nitrogen atom (3). Triethyltrimethylenetriamine (IV) forms only a monoethiodide (4). In the arsenic field, Chatt and Mann (5) have shown that each of the geometrically isomeric 5,10-di-*p*-tolyl-5,10-dihydroarsanthrenes (V) forms only a monomethiodide. Very many similar examples could be quoted.



IV



V

To explain this phenomenon, Mann *et al.* (5, 6) have pointed out, that when in such molecules the first nitrogen or arsenic atom forms a salt, the positive pole thus produced on the nitrogen or arsenic atom has a very strong inductive effect, particularly in quaternary salts (7, 8), and that this inductive effect towards the positive pole will tend to draw electrons away from a neighboring nitrogen or arsenic atom; this electronic drag from these latter atoms will reduce the activity

of the lone pair of electrons on these atoms, and their normal salt-forming properties may thus be reduced or even entirely suppressed. In suitable polyamines this deactivating effect on one nitrogen atom may be reinforced by salt formation on two or more neighboring amine groups.

If these theoretical considerations are correct, the deactivating influence caused by the inductive effect can operate only between two atoms which are in comparatively close proximity, if they are linked by a saturated chain; in such cases the effect *must* fall off rapidly as the distance between the two atoms is increased. Considerable support for the theory arises therefore from the work of Mann and Pope (9), who showed that tri-2-aminoethylamine, $N(CH_2CH_2NH_2)_3$, gave a tetrahydrochloride from cold concentrated hydrochloric acid, but that this salt on exposure to the air spontaneously lost one molecule of hydrochloric acid and gave the trihydrochloride (VI); on the other hand, tri-3-aminopropylamine gave an extremely stable tetrahydrochloride (VII).

$N(CH_2CH_2NH_2 \cdot HCl)_3$ VI

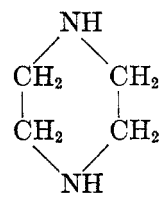
$HCl \cdot N(CH_2CH_2CH_2NH_2 \cdot HCl)_3$ VII

It is thus evident that in the trihydrochloride (VI), the combined influence of the positive poles on the three primary amine groups so weakens the reactivity of the tertiary nitrogen atom that it can show its normal basic properties only in the presence of strong acids; in the tetrahydrochloride (VII) however, this combined influence of the three primary amine salt groups is now too distant to affect appreciably the basic properties of the tertiary nitrogen atom, which therefore itself forms stable salts.

It is noteworthy that di-2-aminoethylamine and di-2-aminoethylmethylamine form the stable trihydrochlorides (VIII) and (IX) respectively (10).

$HCl \cdot HN(CH_2CH_2NH_2 \cdot HCl)_2$ VIII

$HCl \cdot MeN(CH_2CH_2NH_2 \cdot HCl)_2$ IX



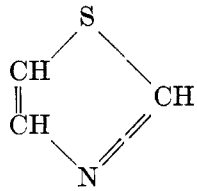
X

This is precisely what one would expect; if the combined effect of the three positive poles in the trihydrochloride (VI) is to weaken but not entirely suppress the activity of the "central" nitrogen atom in this compound, that of the two positive poles on the primary amine salt groups in VIII and IX will not seriously impair the basic properties of the remaining nitrogen atom in the presence of a strong acid. Other examples of this cumulative effect arise in our present work.

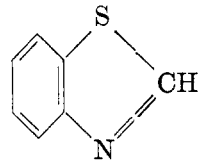
In contrast to the behavior of pyrazine (I), it should be noted that piperazine (X) gives a dihydrochloride (11), and N,N-dimethylpiperazine gives both

a dihydrochloride and a dimethiodide (12). It is clear therefore that when two nitrogen atoms are linked by a suitable conjugated chain as in the pyrazine (I), the electronic attraction exerted by the positive pole on one nitrogen (in the monohydrochloride) is readily transmitted by the mesomeric effect through this chain, and the second nitrogen atom is thus strongly affected. When, however, the chain is saturated, the electronic attraction is necessarily carried solely by the inductive effect and is (as would be expected) much weaker when transmitted an equivalent distance. Hence, in the piperazine molecules the second nitrogen atom is not detectably affected by the charge on the first nitrogen atom, and in the saturated aliphatic polyamine (VI) the cumulative effect of three positive poles is required to transmit effectively the deactivating influence over this distance.

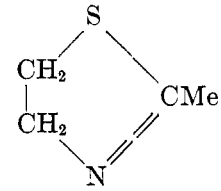
This deactivating effect by positive poles is not limited to compounds of the Group V B elements, although it appears most strongly in such compounds. It is known that thiazole (XI) and its 2-methyl and 2,4-dimethyl derivatives and also benzothiazole (XII) when heated with an excess of methyl iodide form only monomethiodides (13), the methyl iodide adding solely to the nitrogen. It might be objected that the sulfur atom in these compounds has however, much of the "semi-aromatic" inactivity of the sulfur atom in thiophene, and would therefore be unlikely to form a sulfonium salt. Nevertheless, the same condition of monomethiodide formation applies also to, for example, 2-methylthiazoline (XIII) and to 2-methyldihydro-1,3-thiazine (XIV) (14, 15, 18), to which the above objection cannot apply.



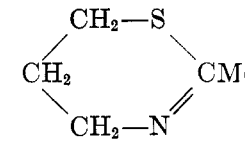
XI



XII

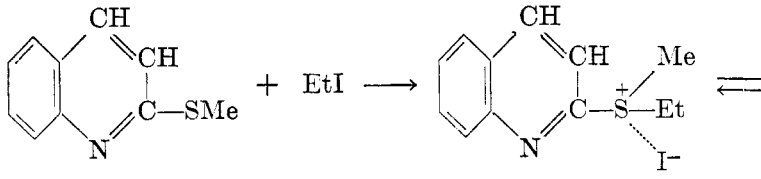


XIII

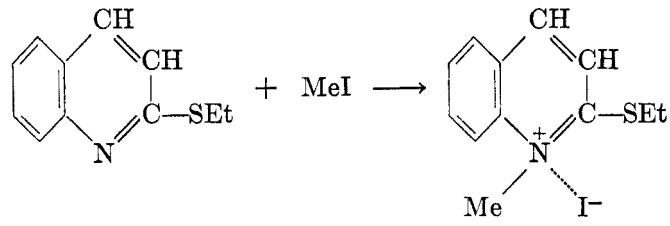


XIV

Valuable confirmation of our theoretical considerations also arises in the work of Beilenson and Hamer (16), who showed that 2-methylthioquinoline (XV), when heated with methyl iodide at 100° for 24 hours, formed only a monomethiodide, the position of the methyl group on the nitrogen atom being proved. When however, 2-methylthioquinoline (XV) was similarly treated with ethyl iodide, 2-ethylthioquinoline methiodide (XVIII) was formed.



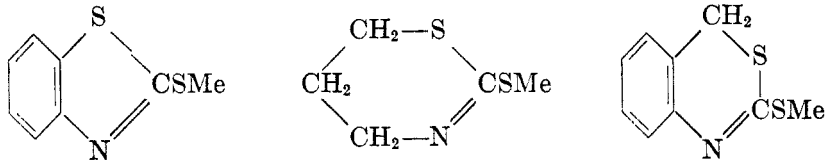
XV XVI



XVII XVIII

The only probable mechanism for this transformation is that the initial attack of the ethyl iodide is on to the aliphatic sulfur atom of the 2-methylthioquinoline (XV) to give the sulfonium salt (XVI). The latter then dissociates to give 2-ethylthioquinoline (XVII) and methyl iodide. It is almost certain that this dissociation is reversible (since such dissociation-equilibria are commonly encountered in the alkyl sulfonium halides), but the highly reactive methyl iodide thus liberated also combines with the nitrogen atom to give the quaternary ammonium salt (XVIII). The positive pole on this nitrogen (being more powerful than that on a sulfonium group) immediately deactivates the divalent sulfur atom in XVIII, and consequently the ultimate reaction is entirely in favor of this salt.

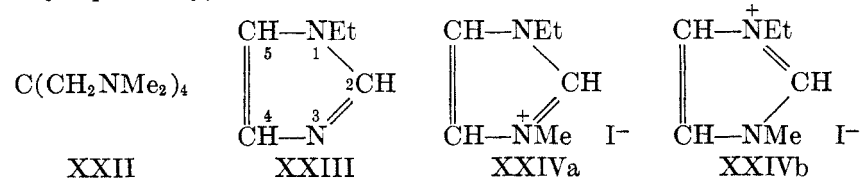
This is not an isolated example. It has been shown (17, 18) that 2-methylthiobenzothiazole (XIX), 2-methylthiodihydro-1,3-thiazine (XX) and 3-methylthio-2,4-benzothiazine (XXI), when heated with methyl iodide, give only quaternary monomethiodides, but with ethyl iodide again give the quaternary monomethiodide of the ethylthio derivatives.



XIX XX XXI

In all these four types of compound, therefore, initial attack by the alkyl halide must be on the aliphatic sulfur atom, and the instability of the sulfonium salt then allows attack at the nitrogen atom, with consequent inactivation of the sulfur.

The phenomenon of inductive deactivation which we have briefly outlined above is so widely spread and occurs in such a variety of compounds that other influences must often come into play. We do not suggest that our theory of inactivation by the inductive effect of neighboring groups represents the only effect which is present in such molecules: this effect may be blended with, or even entirely replaced by, other influences.

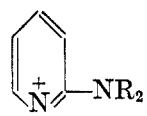


XXII XXIII XXIVa XXIVb

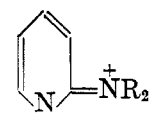
For example, it has been shown by Mann *et al.* (19, 6) that tetrakis-dimethylaminomethylmethane (XXII) forms a stable tetrahydrochloride, but when heated with an excess of methyl, ethyl, allyl, or benzyl iodide forms only a diquaternary salt; the dimethiodide when heated to its decomposition point will, however, give a small yield of the tetramethiodide, a reaction which is not shown by the other three diquaternary salts. The existence of the stable tetrahydrochloride shows clearly that in spite of the close proximity of the four tertiary nitrogen atoms, the cumulative effect of the positive poles is not sufficient to deactivate any one of these nitrogen atoms. Consequently one would not expect the inductive effect to prevent the formation of the tetramethiodide under normal conditions of quaternary salt formation. In this case, therefore, steric effects probably play a major part; protons can readily add on to the four amine groups in the tetramine (XXII), but the tetrahedral arrangement of these groups around the central carbon atom makes the ingress of methyl (or other alkyl) groups increasingly difficult for spatial reasons, and hence only the dimethiodide is normally formed. The violent conditions of thermal decomposition are required to force four methyl groups on to the tetramine, and even this method fails with larger alkyl groups. The use of Stuart models confirms this steric argument.

Yet another factor probably enters into the behavior of 1-ethyliminazole (XXIII), which when heated with an excess of methyl iodide gives only the 3-methiodide (XXIVa), the N-ethyl group refusing to unite with a second methyl iodide molecule (20). It will be seen however that the cation in XXIVa produced by the initial addition of methyl iodide is at once stabilized by resonance hybrid formation with the cation XXIVb; hence each nitrogen atom is partly tertiary and partly quaternary, and this effect again probably predominates over any inductive effect, which can of course exist only in the separate canonical forms.

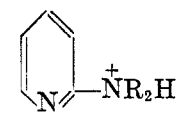
One further example of inactivation by a neighboring polar group may be cited, because it is closely connected to our present work. 2-Aminopyridine, 2-monoalkylaminopyridines, and 2-dialkylaminopyridines all act as monoacidic bases, forming for example monohydrochlorides and monopicrates (21). The position of proton attack in this salt formation is uncertain, but it is probably onto the pyridyl nitrogen, as the cation thus formed would be stabilized by resonance hybrid formation between XXVa and XXVb (R = H or alkyl), whereas the cation formed by proton attack at the side chain (XXVI) lacks this stabilizing factor.



XXVa



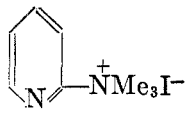
XXVb



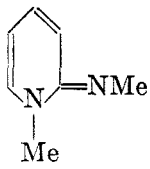
XXVI

Nevertheless, it is known that 2-dimethylaminopyridine reacts even with an excess of methyl iodide at 100° to give the compound XXVII (22), the attack at

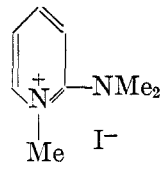
the side chain recalling the initial behavior of the methylthiol compounds cited above.



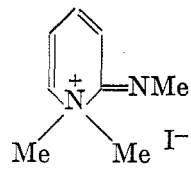
XXVII



XXVIII



XXIX



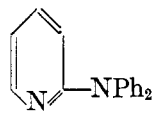
XXX

The constitution of XXVII is known, because cold methyl iodide reacts readily with 1-methyl-2-methylimino-1,2-dihydropyridine (XXVIII) to give a salt which with silver oxide or caustic alkali yields dimethylamine and N-methyl-2-pyridone. Hence this salt must be XXIX and not XXX, and since it is isomeric with the compound XXVII, the latter must have the structure stated. Here again the cation of the salt XXIX should be stabilized by resonance of precisely the same type as that given above between XXVa and XXVb. The fact that in spite of this stabilizing influence this compound is not formed by the action of methyl iodide on 2-dimethylaminopyridine must apparently be due to the tertiary nitrogen in the side chain of the latter compound having greater reactivity than the pyridyl nitrogen group; hence when stable quaternary salt formation occurs on the side chain, the pyridyl nitrogen atom immediately becomes inactivated. Consideration of structures XXVII and XXIX confirms the experimental fact that steric hindrance is not a controlling factor in the formation of either compound. In all these 2-aminopyridine derivatives, however, the deactivation of one amino group by a positive pole on the other group is particularly striking.

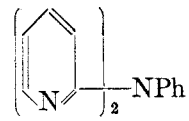
It will be clear that an inductive effect arising from a cause other than a full positively charged pole may also tend to produce the above deactivation. For example, phenyldiethylarsine, $C_6H_5As(C_2H_5)_2$, undergoes ready atmospheric oxidation to the arsine oxide, whereas phenyl-bis(2-cyanoethyl)arsine, $C_6H_5As(C_2H_4CN)_2$, when molten or in solution, is not perceptibly affected by exposure to air; nevertheless, the latter compound combines with methyl iodide on warming to give the methylarsonium iodide, $[C_6H_5(CH_3)As(C_2H_4CN)_2]I$. The positive inductive effect of the cyano groups has thus reduced but not suppressed the reactivity of the tertiary arsenic atom. A similar reduction in the activity of the tertiary arsenic atom occurs also in the amidine salts and the carboxylic acids derived from 2-cyanoethylarsines of the above type (40). As a further example, azobenzene can be readily oxidized to azoxybenzene, $C_6H_5\overset{\downarrow}{N}O{:}NC_6H_5$, but a similar oxidation of the second nitrogen cannot be accomplished, and compounds of the type $C_6H_5\overset{\downarrow}{N}O{:}\overset{\downarrow}{N}OC_6H_5$ are unknown, although there is apparently no steric obstruction to their formation, particularly in the *trans* form. There is little doubt, therefore, that in azoxybenzene the strong inductive effect from the first nitrogen atom to the contiguous oxygen atom completely inactivates the second nitrogen atom. The same factor may be responsible for the apparent

non-existence of disulfoxides of type R·SO·SO·R, the many compounds to which this structure had initially been allocated having been shown later to be sulfone-sulfides of type R·SO_2·SR (41).

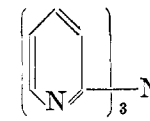
In the course of a chemotherapeutic investigation carried out in the second half of World War II, we had occasion to prepare the complete series of tertiary amines, phosphines, and arsines which systematically would arise from the step-by-step replacement of the phenyl groups in triphenyl-amine, -phosphine, and -arsine by 2-pyridyl groups. Thus, mono-2-pyridyldiphenylamine (XXXI), originally obtained by Tschitschibabin (21), was prepared by the interaction of 2-bromopyridine and diphenylamine in the presence of potassium carbonate and copper powder. Mono-2-pyridyldiphenyl-phosphine and -arsine were prepared by the action of magnesium-2-pyridyl bromide on diphenylmonochloro-phosphine and -arsine respectively. Di-2-pyridylmonophenylamine (XXXII) was prepared by the interaction of 2-bromopyridine and aniline [Wibaut and Tilman (23)], and the corresponding phosphine and arsine by the action of magnesium-2-pyridyl bromide on phenyldichloro-phosphine and -arsine in turn. Finally



XXXI



XXXII



XXXIII

tri-2-pyridylamine (XXXIII) was prepared by the interaction of 2-bromo-pyridine and 2-aminopyridine [Wibaut and La Bastide (24)], and tri-2-pyridyl-phosphine and -arsine by the action of an excess of the above Grignard reagent on phosphorus trichloride and arsenic trichloride respectively [Davies and Mann (25)].

Quite apart from chemotherapeutic properties, however, these nine compounds form a unique series for the comparative study of salt formation, for in each compound there is a theoretical possibility of quaternary salt formation on the "central atom" (*i.e.*, nitrogen, phosphorus, and arsenic), and of salt formation by the addition of acids or of alkyl halides on the pyridyl nitrogen atoms; moreover all these atoms are in sufficiently close proximity to permit considerable mutual influence. Although the wartime conditions of this work did not allow us to investigate these properties under the rigidly comparable conditions that we should have desired, we have been able to study this question in some detail. For this purpose, we have first added an ethanolic solution of the compound to a considerable excess of saturated ethanolic hydrogen chloride, and the hydrochloride of the compound which separated has then been confined in a vacuum over powdered sodium hydroxide. The composition of the hydrochloride thus obtained is shown in the third column of Table I. It must be emphasized that these values indicate the maximum number of molecules of hydrochloric acid that can be *stably* united to the compounds; in certain cases higher poly-hydrochlorides may possibly have been initially formed and then reverted to the lower and more stable salts during isolation and drying. Further evidence of salt

formation was obtained by similarly adding ethanolic solutions of each of the nine compounds in turn to a considerable excess of ethanolic picric acid (fourth column, Table I). The picrates thus obtained have been purified by recrystallization: since however it was possible that a poly-picrate which was stable in the presence of free picric acid might lose picric acid on recrystallization, the identity of the "crude" and the recrystallized picrate was always checked by analyses or mixed melting point determinations. The comparative reaction with these two acids is of value, because it may indicate the partial suppression of the basic properties of an amino group; such a group might remain sufficiently basic for combination with a strong acid such as hydrochloric acid, but insufficiently so for combination with the much weaker picric acid.

We have then investigated quaternary salt formation under four different conditions (cf. columns 5–8, Table I). Most of our compounds have been (a) refluxed with a benzene solution of methyl iodide, (b) refluxed with pure methyl iodide, (c) heated with methyl iodide in nitromethane solution at *ca.* 50°, (d) heated with methyl iodide in methanol at 100° in a sealed tube; in all these experiments a considerable excess of methyl iodide was of course employed. Theoretical considerations indicate that (a)–(d) provide increasingly favorable conditions for maximum quaternary salt formation, and our experience has confirmed this indication. Menschutkin (26) has shown that the rate of quaternary salt formation is increased in solvents of high dielectric constant. Benzene has the low constant of 2.3, whereas nitromethane has the high value of 38.2 (27), and is known to promote vigorously quaternary salt formation with methyl iodide (25). Methanol has also a high constant of 32.5 (27); moreover the use of a sealed tube in the experiments with methanolic methyl iodide enabled a comparatively high temperature to be employed without serious risk of dissociation of the quaternary salt.

In the case of the phosphine and arsine derivatives, further information regarding the position of the acid or alkyl residues could be obtained by first converting the tertiary phosphine or arsine group to the 4-covalent state. For this purpose, each of the tertiary phosphines was also converted to the corresponding phosphine sulfide, and the latter then subjected to the above treatment with acids and with methyl iodide. The mono-2-pyridyldiphenylarsine and the tri-2-pyridyl-phosphine and -arsine were also converted to the corresponding oxides, and the behavior of the latter towards picric acid then investigated.

The results for the nine original compounds and for the sulfide and oxide derivatives are collected in Table I; for convenient reference, the melting points of the parent compounds are collected in the second column.

The interpretation of the results incorporated in Table I rests on the following three well-established facts.

(i) The additive properties (as shown in salt formation) of trivalent Group V B elements in an organic molecule may be profoundly influenced by the near presence of a positive charge in the molecule. This point has already been discussed.

(ii) The nitrogen atom in the pyridine molecule tends to withdraw electrons

from the 2 and the 4 positions, and pyridine consequently bears a chemical resemblance to nitrobenzene [Bradley and Robinson (28)]. This inductive effect away from the 2 and the 4 positions in pyridine is supported by many chemical properties which are too familiar to require citation. It is also to be expected on theoretical grounds. Since nitrogen is more electronegative than

TABLE I

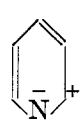
REACTIONS OF AMINES, PHOSPHINES, ARSINES, AND DERIVATIVES

Py = 2-Pyridyl Ph = Phenyl

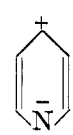
COMPOUND	M.P. °C	COMBINATION WITH ACIDS		COMBINATION WITH METHYL IODIDE			
				Moles Methyl iodide in			
		Moles HCl	Moles Picric Acid	(a) Boiling Benzene	(b) Boiling Methyl iodide	(c) Nitromethane at *ca.* 50°	(d) Methanol at 100°
$PyPh_2N$	105		1		1		1
$PyPh_2P$	85		1		1	1	1
$PyPh_2As$	62		1	1	2		
Py_2PhN	94		1		1	1 + 2	2
Py_2PhP	96	2	2		1	1	(d)
Py_2PhAs	88	2	2		2		2
Py_3N	130	2	1		1	1 + 2	2
Py_3P	115	3	2	1		1 + (e)	(d)
Py_3As	85	3	2	2	2	2	3
$PyPh_2PS$	119		0		0	1	1 + (g)
$PyPh_2AsO$			1				
Py_2PhPS	141	2	1	0	0	1	(d)
Py_3PS	161		1		1	1	(d) + (f)
Py_3PO	209		1				(d)
Py_3AsO			1				

(d) 2,2′-Dipyridyl dimethiodide.
(e) Di-2-pyridylmonomethylphosphine dimethiodide monohydrate.
(f) Mono-2-pyridyldimethylphosphine sulfide monomethiodide.
(g) Trimethylsulfonium iodide.

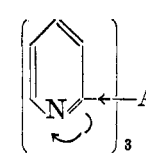
carbon, canonical forms of pyridine such as XXIVa and XXIVb will play a much more prominent part in the resonance hybrid than any analogous forms in the benzene hybrid [Pauling (29)].



XXXIVa



XXXIVb



XXXV

Consequently the 2-pyridyl radical will be more electronegative than the phenyl radical, and therefore the central nitrogen, phosphorus or arsenic atoms in, for example, the tri-2-pyridyl derivatives (XXXV, where A = N, P, or As) will be less reactive than those in the triphenyl analogs, because the inductive effect away from each central atom will place a greater restraint on its lone pair of electrons.

(iii) The third factor, originally suggested by Ingold (7, 30), is that the inductive effect is transmitted more readily through a nitrogen atom than through the larger phosphorus and arsenic atoms. The evidence for this statement can be briefly outlined. It is well known that the direct attachment of an atom bearing an integral positive charge to the benzene nucleus causes almost exclusively *meta*-substitution irrespective of the nature of the atom [Vorländer (31)]. If a CH_2 group is inserted between the atom and the benzene ring, the *meta*-substitution will still persist in the benzyl group, but will be less prominent because of the weaker inductive effect of the more distant positively charged atom. Ingold *et al.* (7, 8) have determined the amount of *meta*-nitration which phenyltrimethyl-ammonium, -phosphonium, -arsonium and -stibonium picrates

TABLE II

AMOUNT OF *meta*-NITRATION IN PHENYLTRIMETHYL- AND BENZYLTRIMETHYL-AMMONIUM, -PHOSPHONIUM, -ARSONIUM, AND -STIBONIUM PICRATES

	N	P	As	Sb
$PhMe_3$ derivative	100%	100%	98%	86%
$BzMe_3$ "	88	10	3.4	—

undergo, and also that shown by the corresponding benzyltrimethyl derivatives. Their results are summarized in Table II.

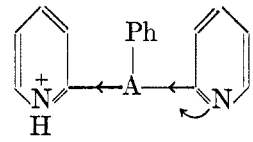
They suggest, in explanation of these results, that the charge on the above cations resides in the nucleus of the Group V B atom concerned, and that the influence of this charge will consequently be less the greater the number of outer electronic shells which this atom possesses. Hence the larger atoms could be regarded as exerting a damping action on the inductive effect initiated by the charge; therefore the amount of *meta*-substitution, dependent on this effect, falls steadily from nitrogen through to antimony.

Independent confirmation of this factor has been obtained by Davies and Lewis (32), who have studied the effect of a *para*-substituent X upon the rate of reaction of tertiary amines and phosphines, p-$XC_6H_4AR_2$ (A = N or P), with alkyl halides. Thus the introduction of a *para*-methyl group into the amine $C_6H_5NR_2$ increased its reactivity towards methyl iodide twice as much as that caused by the introduction of the same group into the corresponding phosphine $C_6H_5PR_2$; similarly the introduction of a *para*-chloro group into the above amine decreased its reactivity almost twice as much as that of the phosphine. Further, the introduction of *para*-substituents had less effect on the basic strengths of the above phosphines than on that of the amines (33). In all these examples it is

clear that the electronic influence of the *para*-substituent is being transmitted less readily through the phosphorus than through the nitrogen atom.

In interpreting the reactions summarized in Table I, the action of the acids on the parent compounds will be considered first, and then that of methyl iodide. From the above discussion it is clear that the "central" nitrogen, phosphorus, and arsenic atoms in the nine tertiary amines, phosphines, and arsines must be neutral, and that salt formation with acids therefore can occur only at the pyridyl nitrogen atoms. Each of the three mono-2-pyridyldiphenyl derivatives forms a monopicrate, clearly by salt formation at the 2-pyridyl nitrogen atom. The mono-2-pyridyldiphenylphosphine sulfide does not form a picrate, however. This is not unexpected, because the positive charge on the phosphorus atom (due to the polar P^+-S^- link) will tend to deactivate the basic nitrogen atom. It is noteworthy that Davies and Mann (25) found that neither phenyl-*p*-bromophenyl-2-pyridylphosphine sulfide nor phenyl-*p*-bromophenyl-*p*-dimethylaminophenylphosphine sulfide would form salts with acids, the same deactivating mechanism being present. In the case of the mono-2-pyridyldiphenylarsine oxide, $PyPh_2AsO$, a new factor enters, and the arsine oxides will be discussed later.

In the di-2-pyridylmonophenyl series, it is significant that whereas the phosphine and arsine exerted their normal basicity and formed dipicrates, the amine formed only a monopicrate. It is clear that directly one of the pyridyl groups forms a salt (XXXVI), the inductive effect initiated by this positive pole will



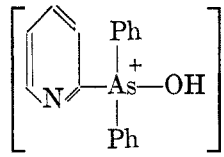
XXXVI

tend to deactivate the nitrogen atom of the second pyridyl group. When in the pyridylamine these two groups are separated only by the light central nitrogen atom (XXXVI, A = N), this inductive effect is not seriously impeded, and the nitrogen atom of the second pyridyl group is forced into inactivity. When, however, the two groups are separated by the larger phosphorus and arsenic atoms (XXXVI, A = P or As), the inductive effect is so damped that the nitrogen atom of the second pyridyl group remains sufficiently basic for salt formation, and dihydrochlorides and dipicrates result. In the di-2-pyridylmonophenylphosphine sulfide, the positive charge on the phosphorus atom will however strengthen the inductive effect away from the second pyridyl nitrogen atom, which now becomes partly inactivated, and consequently the sulfide molecule, although forming a rather unstable dihydrochloride, now forms only a monopicrate.

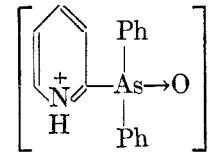
Precisely similar results are furnished by the tri-2-pyridyl compounds. In the presence of a strong acid such as hydrochloric acid, all three nitrogen atoms in the phosphine and arsine are sufficiently basic for salt formation, the central phosphorus and arsenic atoms again damping the inductive effect, but in the amine this effect is sufficiently strong to deactivate one of the pyridyl groups,

and only a dihydrochloride is formed. It is very interesting to note that this deactivating influence must be present in the phosphine and arsine also, although not sufficiently strongly to prevent trihydrochloride formation, because in these two compounds the third nitrogen atom cannot hold a molecule of the weaker picric acid, and the phosphine and arsine consequently form only dipicrates; in the pyridylamine the stronger inductive effect similarly deactivates a second pyridyl nitrogen atom towards picric acid (although not to the stronger hydrochloric acid), and this amine therefore forms only a monopicrate. The behavior of these three compounds with the two acids forms a striking confirmation of our theoretical suggestions. Again in the tri-2-pyridylphosphine sulfide, the basicity towards picric acid drops from two to one by the effect of the extra positive pole produced by combination with sulfur.

There is little doubt concerning the structure of the picrates given by the tertiary arsine oxides. It is well known that triarylarsines will not combine with picric acid, but that their oxides readily give crystalline picrates, and will combine even with such weak acids as *p*-toluenesulfonamide to give crystalline salts (34); these derivatives must therefore have the structure $[R_3AsOH]OC_6H_2(NO_2)_3$ and $[R_3AsOH]\cdot NHSO_2C_7H_7$ respectively (R = aryl group). It is therefore reasonably certain that the picrate formed by mono-2-pyridyldiphenylarsine oxide has the cation XXXVII. The possibility that the cation has the isomeric structure XXXVIII is discounted by the above argument and also by the following consideration.



XXXVII



XXXVIII

If the picrate had the cation XXXVIII, it would follow that the arsenic-oxygen link did not affect the pyridyl group, since the proton had united with the pyridyl nitrogen atom precisely as in the parent mono-2-pyridyldiphenylarsine itself. There should by analogy therefore be no difference between the behavior of tri-2-pyridylarsine and its oxide towards picric acid; yet the tertiary arsine unites with two molecules and the arsine oxide with only one molecule of picric acid. It follows that the cation of both arsine oxides is of type XXXVII, and that the positive charge on the arsenic atom is sufficiently strong to deactivate the pyridyl nitrogen atoms. A similar argument applies to the tri-2-pyridylphosphine oxide.

The interpretation of the results of quaternary salt formation with methyl iodide is clearly more complex, because an extra factor now enters, since theoretically the "central" nitrogen, phosphorus, or arsenic atom can also now unite with the methyl iodide. It is most convenient to discuss first the three amines, then the corresponding phosphines and arsines in turn.

It will be seen that mono-2-pyridyldiphenylamine combined with only one molecule of methyl iodide. Since the central nitrogen atom in this amine is less

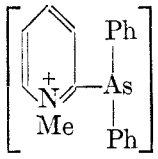
reactive than that in triphenylamine, and the latter does not combine with methyl iodide, it is certain that our monomethiodide has the quaternary group on the 2-pyridyl nitrogen atom. Furthermore, it is significant that di-2-pyridylmonophenylamine and tri-2-pyridylamine under like conditions behave precisely similarly with methyl iodide, and that a dimethiodide is the highest quaternary salt formed. It follows that one of the pyridyl nitrogen atoms in tri-2-pyridylamine must have been inactivated by the quaternary salt formation, and that the methyl iodide molecules have undoubtedly added on to the other two pyridyl nitrogen atoms; the positive pole on either of these atoms is insufficient to deactivate the other atom towards methyl iodide, but their combined effect does deactivate the third group. It is almost certain therefore that in the di-2-pyridylmonophenyl derivative, the methyl iodide units are also on the pyridyl nitrogen atoms. Incidentally, the behavior of both these tertiary amines towards methyl iodide illustrates vividly the increasing potency of the four sets of conditions (a)–(d) for methiodide formation that we have employed.

With regard to the three tertiary phosphines, it is highly significant that all three combined with only one molecule of methyl iodide. Now there is both qualitative and quantitative evidence [Davies and Lewis (32)] that under comparable conditions the rate of reaction of a tertiary phosphine with an alkyl iodide is greater than that of the corresponding arsine, which in turn is greater than that of the corresponding amine. Our results indicate strongly therefore that all our phosphines have combined with methyl iodide to give phosphonium salts, and the strong positive charge on the phosphonium atom has effectively deactivated all the pyridyl nitrogen atoms. The constitution of these methiodides is further confirmed by the following considerations. If the methyl iodide molecule, instead of combining with the phosphorus atom, had combined with the nitrogen atom of one of the pyridyl groups, the positive pole thus produced would have exerted a weaker deactivating effect on a neighboring pyridyl nitrogen atom than it would in the corresponding amine, because this effect would have to pass through the central phosphorus atom instead of the lighter nitrogen atom. Consequently our di- and tri-pyridylphosphines should have combined with more molecules of methyl iodide than the corresponding amines. Actually the reverse was the case: *e.g.*, di-2-pyridylmonophenylphosphine gave only a monomethiodide in nitromethane, whereas di-2-pyridylmonophenylamine gave both a mono- and a di-methiodide under these conditions. There is no doubt therefore that all our phosphine methiodides are quaternary phosphonium salts.

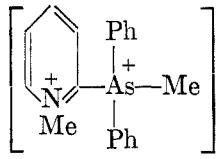
In the three tertiary phosphine sulfides, however, this phosphonium salt formation has been impossible; the positive charge on the phosphorus atom in the sulfides is however much weaker than that in the phosphonium salts, and the deactivating effect is therefore less intense; consequently in each of the sulfides one of the pyridyl nitrogen atoms has been able to combine with methyl iodide, although the conditions of combination were throughout more vigorous than those required for methyl iodide addition to the tertiary phosphines themselves.

Considering our tertiary arsines, it is noteworthy that mono-2-pyridyldiphenylarsine gave a monomethiodide with methyl iodide in benzene, but a di-

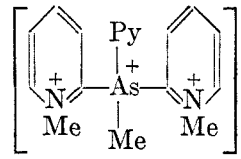
methiodide with methyl iodide alone. Now pyridine reacts much more vigorously with methyl iodide than triphenylarsine does, and it would be expected therefore that methyl iodide would attack the pyridyl nitrogen first, and then attack the tertiary arsenic atom only under more vigorous conditions. Consequently our monomethiodide should have the cation XXXIX and the dimethiodide the cation XL.



XXXIX



XL



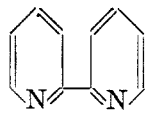
XLI

The suggestion that methyl iodide addition here occurs preferentially on the pyridyl nitrogen atoms receives strong support from the results obtained with the other arsines. It will be noticed that under the most vigorous conditions (methyl iodide in methanol at 100°), di-2-pyridylmonophenylarsine gave a dimethiodide and tri-2-pyridylarsine a trimethiodide. Now if the latter had been an arsonium salt, *i.e.* had it possessed the cation XLI, there is no reason why di-2-pyridylmonophenylarsine should not also have formed a similar trimethiodide. It follows that in both this dimethiodide and the trimethiodide, the addition of methyl iodide has occurred solely at the pyridyl nitrogen atoms, and that the tertiary arsenic atom has remained unchanged. This indicates that in the quaternary salts of the arsines a positive charge on at least two pyridyl nitrogen atoms is required to deactivate the arsenic atom under the conditions we have employed.

It will be seen therefore that our theory of deactivation by inductive effects initiated by neighboring positive poles both interprets and correlates the results summarized in Table I, which might otherwise seem largely disconnected in their apparent variety and differences.

One further point deserves mention, although strictly it lies beyond the scope of the above investigation. It will be noticed that certain tertiary phosphines and phosphine sulfides when exposed to the most vigorous methyl iodide attack underwent decomposition, with splitting off of the pyridyl groups. These decompositions usually gave a mixture of products which were difficult to separate; in no case do we claim to have isolated every component of the mixture, but the nature of the pure components that we have isolated leaves little doubt that the process consists essentially of a progressive replacement of 2-pyridyl groups by methyl groups. Thus both di-2-pyridylmonophenylphosphine and tri-2-pyridylphosphine under the most vigorous conditions of methyl iodide attack gave the dimethiodide of 2,2′-dipyridyl (XLII), but the latter phosphine also gave the dimethiodide of di-2-pyridylmonomethylphosphine (XLIII). When tri-2-pyridylphosphine sulfide was similarly treated, the process went one stage further, with the formation of the monomethiodide of mono-2-pyridyldimethylphosphine sulfide (XLIV) in addition to the dimethiodide of 2,2′-dipyridyl. It is clear

therefore that the 2-pyridyl groups must initially break off as free radicals, which then unite in pairs.



XLII $(C_5H_4N)_2CH_3P$ XLIII $(C_5H_4N)(CH_3)_2PS$ XLIV $(CH_3)_3SI$ XLV

The ultimate fate of the sulfides is strongly indicated by the fact that mono-2-pyridyldiphenylphosphine sulfide, similarly treated, gave trimethylsulfonium iodide (XLV). We have no evidence that phenyl groups are evicted in this way, and it is probable that the 2-pyridylphenylphosphines would ultimately give the corresponding phenylmethylphosphonium iodides, whilst tri-2-pyridylphosphine would give tetramethylphosphonium iodide, and that the phosphine sulfides behave similarly, with the sulfur atom splitting off as trimethylsulfonium iodide. No similar degradation of the corresponding amines and arsines with methyl iodide has been detected. It is noteworthy however that when tri-2-pyridylamine was treated with tin and hydrochloric acid in an attempt to prepare tri-2-piperidylamine, the only product isolated was di-2-pyridylamine, $(C_5H_4N)_2NH$, one of the pyridyl groups having thus been shed in this reaction also.

EXPERIMENTAL

2-Aminopyridine was prepared by the method of Tschitschibabin and Seide (21). 2-Bromopyridine, prepared by the method of Craig (37) in 85% yield, had b.p. 72–74°/10.5 mm., 79.5–82.5°/16 mm., and 90–92°/24 mm. Diphenylmonochlorophosphine was prepared by the action of diphenylmercury on phenyldichlorophosphine (38) and obtained as a colorless liquid, b.p. 193–194°/26 mm.

The letter (a), (b), (c), or (d) is given before each experiment with methyl iodide, in accordance with the conditions employed as cited in column 5, 6, 7, or 8 respectively in Table I.

Mono-2-pyridyldiphenylamine. A mixture of diphenylamine (16.9 g.), 2-bromopyridine (9.5 cc., 1 mole), anhydrous potassium carbonate (10 g.), copper bronze (0.25 g.), potassium iodide (*ca.* 0.2 g.), and amyl alcohol (5 cc.) was gently refluxed for 9 hours, and then steam-distilled to remove amyl alcohol and unchanged 2-bromopyridine. The cold residue was extracted with chloroform, and the chloroform layer then shaken thrice with dilute hydrochloric acid to extract the required amine, leaving unchanged diphenylamine in the chloroform. The united acid extracts were basified with sodium hydroxide, and the precipitated amine extracted with benzene. After drying, the benzene was distilled and the solid residue recrystallized from aqueous ethanol (charcoal). The amine had m.p. 105°; yield, 1.9 g. (7.7%). Tschitschibabin (21) gives m.p. 104°.

Monopicrate. A hot solution of the amine (0.3 g.) and picric acid (1.5 g., 5.3 moles) in ethanol (30 cc.) on cooling gave yellow crystals of the monopicrate, m.p. 174°, unchanged by recrystallization from ethanol.

Anal. Calc'd for $C_{17}H_{14}N_2 \cdot C_6H_3N_3O_7$: C, 58.1; H, 3.6.
Found: C, 58.4; H, 3.9.

Action of methyl iodide. (b). A solution of the amine (0.3 g.) in methyl iodide (5 cc., 66 moles) was refluxed for 4 hours, a yellow crystalline deposit separating very rapidly however. The excess of methyl iodide was evaporated, and the residue when recrystallized from ethanol gave the *monomethiodide*, m.p. 192°.

Anal. Calc'd $C_{18}H_{17}IN_2$: C, 55.7; H, 4.4.
Found: C, 56.2; H, 4.3.

(d) A solution of the amine (0.5 g.) in methanol (0.25 cc.) containing methyl iodide (0.4 cc., 3.2 moles) was heated in a sealed tube at 100° for 8 hours. The cold, clear, brown solution was poured into ether, and the precipitated crystals, when recrystallized from ethanol, had m.p. 192° alone and when mixed with the above monomethiodide.

Mono-2-pyridyldiphenylphosphine. The magnesium-2-pyridyl bromide required for this and for subsequent phosphine and arsine syntheses was prepared essentially by the method of Overhoff and Proost (39) as modified by Davies and Mann (25). One description in detail suffices for all. A round-bottomed flask of 1-liter capacity was fitted with a reflux water-condenser, stirrer, dropping-funnel, and an inlet-tube through which a current of nitrogen could be passed throughout the experiment; the necks of this condenser and dropping-funnel were closed with calcium chloride tubes. Magnesium turnings (15 g.) were placed in the flask, and a solution of ethyl bromide (1 cc., 0.02 mole) in ether (50 cc.) added. A crystal of iodine was also added to initiate the reaction. When the ether was boiling, the stirrer was started, and a solution of pure, dry 2-bromopyridine (28.8 cc., 0.49 mole) and ethyl bromide (10.5 cc., 0.23 mole) in ether (250 cc.) was run in at such a rate that gentle boiling continued. The addition required 75 minutes, and the formation of the Grignard reagent was then completed by refluxing the mixture for a further 2 hours. The mixture was then immersed in cold water (18–22°), and the stirring continued whilst a solution of diphenylmonochlorophosphine (43.2 g., 0.32 mole) in ether (275 cc.) was added over a period of 2 hours. The product was then refluxed for 2 hours, cooled in ice, and hydrolyzed by the cautious addition of a solution of ammonium chloride (140 g.) in cold water (275 cc.). The stirring and the passage of nitrogen were now stopped, the mixture filtered, and the ethereal layer separated, dried (sodium sulfate), and the solvent evaporated. The residue when fractionally distilled gave the fractions: (a) b.p. 37–114°/0.05 mm., (b) b.p. 132–155°/0.05 mm., (c) b.p. 160–180°/0.05 mm. Fraction (b) crystallized on scratching, and when recrystallized from aqueous methanol gave the pure mono-2-pyridyldiphenylphosphine, colorless crystals, m.p. 84–85°; yield 8.2 g. (16%). Fraction (c) was converted into the picrate described below, and the latter recrystallized: treatment with alkali gave a further crop of the phosphine, weighing 2.3 g. (4.4%), m.p. 85°. Fraction (a), which probably contained 2,2′-dipyridyl and other products, did not crystallize. It should be noted that in the first preparation fraction (b) refused to crystallize: the crude phosphine had to be converted to the picrate, purified as such, and then regenerated by the action of alkali (see corresponding arsine); this treatment gave the crystalline phosphine in 98% yield, and fraction (b) obtained in subsequent preparations then crystallized readily.

Anal. Calc'd for $C_{17}H_{14}NP$: C, 77.5; H, 5.3; N, 5.3
Found: C, 77.0; H, 5.5; N, 5.55.

Monopicrate. The addition of the phosphine (0.15 g.) to picric acid (0.4 g., 3 moles) each dissolved in ethanol, precipitated the phosphine monopicrate, m.p. 132–133.5°, increased to 137–138° by recrystallization from ethanol containing some acetone.

Anal. Calc'd for $C_{17}H_{14}NP \cdot C_6H_3N_3O_7$: C, 56.1; H, 3.5; N, 11.4.
Found: C, 55.5; H, 3.3; N, 11.5.

Action of methyl iodide. (b) A mixture of the phosphine (0.3 g.) and cold methyl iodide (5 cc., 70 moles) gave a clear solution, which however rapidly became cloudy and an oily layer collected on the surface. The mixture was refluxed for 30 minutes, during which the oil soon crystallized. The methyl iodide was then evaporated, and the residue purified by dissolving in ethanol, filtering, and adding much ether. The *monomethiodide* separated as colorless crystals, m.p. 141–142°.

Anal. Calc'd for $C_{18}H_{17}INP$: C, 53.5; H, 4.2.
Found: C, 52.55; H, 4.2.

This methiodide was converted in the usual way to the *monomethopicrate*, yellow crystals from ethanol, m.p. 98–99°.

Anal. Calc'd for $C_{24}H_{19}N_4O_7P$: C, 56.9; H, 3.9.
Found: C, 56.9; H, 4.0.

(c) A mixture of the phosphine (0.5 g.), nitromethane (3.5 cc.), and methyl iodide (2.0 cc., 17 moles) was heated at 47–50° for 48 hours. The solution remained clear on cooling, but the addition of ether precipitated a red oil, which crystallized on scratching. The crystals (0.7 g.), after purification as above, had m.p. 141–142°, unchanged by admixture, with the previous product.

(d) A mixture of the phosphine (0.5 g.), methanol (0.3 cc.), and methyl iodide (0.5 cc., 4.3 moles) was heated in a sealed tube at 100° for 8 hours. The cold product, consisting of a heavy red oil covered by a pale yellow liquid, would not crystallize. It was therefore extracted with cold ether, and the insoluble oil then dissolved in cold water: the aqueous solution, when treated with sodium picrate, precipitated the above monomethopicrate, m.p. 98–99° after crystallization from ethanol, unchanged by admixture with the above specimen.

Mono-2-pyridyldiphenylphosphine monosulfide. A solution of the phosphine (0.507 g.) and of sulfur (0.062 g., 1 atom) in benzene (10 cc.) was refluxed for 2 hours. The benzene was then evaporated and the residue, when recrystallized from ethanol, gave colorless crystals of the sulfide, m.p. 119°.

Anal. Calc'd for $C_{17}H_{14}NPS$: C, 69.1; H, 4.8.
Found: C, 69.1; H, 4.95.

This sulfide, which was only slightly soluble in cold ethanol, dissolved readily in saturated ethanolic hydrogen chloride, but the solution in the latter solvent when evaporated in a desiccator at room temperature gave a sticky, glassy residue which, when crystallized from ethanol, deposited the pure sulfide. It is probable, therefore, that the sulfide forms a hydrochloride in the acid solution, but the salt is too unstable for isolation.

A saturated ethanolic solution of the sulfide gave no precipitate when mixed with a similar solution of picric acid, whereas a saturated benzene solution of the acid merely dissolved the unchanged sulfide.

Action of methyl iodide. (b) A solution of the sulfide (0.15 g.) in methyl iodide (3 cc., 100 moles) was refluxed for 5 hours. Evaporation gave a residue of the unchanged sulfide, m.p. 118–119° after recrystallization from ethanol, unchanged by admixture with the original specimen.

(c) A solution of the sulfide (0.3 g.) in nitromethane (2.5 cc.) containing methyl iodide (1.5 cc., 24 moles) was maintained at 47–54° for 60 hours, and then cooled and poured into much ether. The solvent was then decanted from the sticky brown precipitate, which readily crystallized when rubbed with ethanol: recrystallization from ethanol then gave the *monomethiodide*, pale yellow crystals, m.p. 167.5–168.5° (effer.).

Anal. Calc'd for $C_{18}H_{17}INPS$: C, 49.4; H, 3.9.
Found: C, 48.9; H, 3.7.

(*d*) A mixture of the sulfide (0.35 g.), methanol (0.25 cc.), and methyl iodide (0.4 cc., 5.3 moles) was heated in a sealed tube at 100° for 7.5 hours. The cold product, which consisted of a deep red liquid containing some brown semi-solid material, was stirred with a small quantity of methanol, giving a solution containing some colorless crystals. The latter were filtered off, and the filtrate poured into much ether, whereby yellow crystals of the above monomethiodide were precipitated, m.p. 167.5–168.5° (effer.) (alone and mixed) after recrystallization from ethanol.

The colorless crystals were highly soluble in water, and were recrystallized from methanol; when heated in a capillary tube, the material dissociated and disappeared at

ca. 200°, depending on the rate of heating. The aqueous solution gave ionic iodine, and analysis showed that the compound was trimethylsulfonium iodide, although a low sulfur analysis was obtained.

Anal. Calc'd for C_3H_9IS: C, 17.6; H, 4.45; S, 15.7.
Found: C, 17.4; H, 4.7; S, 13.1.

It has previously been stated that when triphenylphosphine sulfide (35) and phenyl-*p*-bromophenyl-2-pyridylphosphine sulfide (25) are heated in a sealed tube with an excess of methyl iodide at 100°, tetramethylphosphonium iodide is formed, the latter having been identified by its properties and its iodine content. We have confirmed the iodine analysis quoted for these samples, but find that in spite of their excellent crystalline form they are actually impure samples of trimethylsulfonium iodide and hence have been incorrectly identified. To confirm this, we have heated triphenylphosphine sulfide (7.3 g.) with methyl iodide (15.5 cc., 10 moles) in a sealed tube at 100° for 4 hours. The crude product yielded unchanged triphenylphosphine sulfide, m.p. 159–160°, triphenylmethylphosphonium iodide, m.p. 166.5–167.5° (initially present largely as a polyiodide), and trimethylsulfonium iodide. The latter was recrystallized thrice from ethanol, and then dissociated at 201–203°, with preliminary softening.

Anal. Found: C, 17.3; H, 4.35.

Mono-2-pyridyldiphenylarsine. This was prepared precisely as the corresponding phosphine, the Grignard reagent being prepared from magnesium (5 g.), which was treated first with ethyl bromide (0.5 cc.) in ether (20 cc.) to initiate the reaction, and then with a mixture of 2-bromopyridine (9.6 cc., 0.49 mole) and ethyl bromide (3.5 cc., 0.23 mole) in ether (100 cc.). This reagent was treated with a solution of diphenylmonochloroarsine (11.5 g., 0.21 mole) in ether (100 cc.), then refluxed for 2 hours, and finally hydrolyzed at 0° by ammonium chloride (50 g.) dissolved in water (200 cc.). The crude product when distilled at 0.2 mm. pressure gave the fractions: (a) b.p. 94–160°; the first portion crystallized and was undoubtedly 2,2′-dipyridyl; (b) b.p. 160–192°, a liquid distillate; (c) b.p. 192–250°, a viscous syrup. Fraction (c) could not be induced to crystallize. It was therefore treated with an excess of ethanolic picric acid solution, which precipitated yellow crystals (3.7 g.) of the *monopicrate* of the arsine; this picrate, when recrystallized from ethanol containing a small amount of acetone, had m.p. 171.5–172.5°.

Anal. Calc'd for $C_{17}H_{14}AsN \cdot C_6H_3N_3O_7$: C, 51.5; H, 3.2.
Found: C, 52.0; H, 3.7.

This picrate was decomposed by shaking with a mixture of aqueous sodium hydroxide and ether until no solid remained; the ethereal solution was then separated, and repeatedly shaken with aqueous sodium hydroxide until colorless. It was then washed with water, dried (sodium sulfate), filtered, and evaporated. The residue, when recrystallized from aqueous ethanol (charcoal), gave colorless crystals of the arsine m.p. 62°.

Anal. Calc'd for $C_{17}H_{14}AsN$: N, 4.6. Found: N, 4.6.

In subsequent preparations, fraction (c) crystallized when seeded with the pure arsine. Solidification however was never complete, and purification was always effected through the picrate as before; evaporation of the ethereal solution gave the pure arsine without further crystallization. Yield of pure arsine, 9.4%.

Action of methyl iodide. (a) Methyl iodide (1.5 cc., 22 moles) was added to a solution of the arsine (0.34 g.) in benzene (10 cc.), and the mixture refluxed for 4 hours. The brown oil which separated did not crystallize on cooling. The solvent was therefore decanted, and the residual syrup stirred with ether; the latter was decanted and the residue stirred with a very small quantity of acetone. Yellow crystals of the *monomethiodide* remained, and were purified by precipitation from an ethanolic solution with ether; m.p. 160–162°.

Anal. Calc'd for $C_{18}H_{17}AsIN$: C, 48.1; H, 3.8.
Found: C, 47.85; H, 4.0.

The benzene which had been decanted was evaporated, and the residue readily crystallized; when purified by the above ethereal precipitation it furnished a second crop of the monomethiodide, m.p. 158–161° (alone and mixed) which was further identified as the monomethopicrate, m.p. 119°. It would appear therefore that this monomethiodide is the only product in this experiment.

(b) A solution of the arsine (0.5 g.) in methyl iodide (10 cc., 100 moles) was refluxed for 3.25 hours and then evaporated. The crystalline dark brown residue was too deliquescent for recrystallization. It was therefore mixed with an excess of sodium picrate, both in ethanolic solution: the yellow crystalline precipitate (m.p. 150.5–152°, increased to 152.5–153° by recrystallization from ethanol) was dried in a vacuum over phosphoric anhydride for several days and thus gave the *dimethopicrate monohydrate.*

Anal. Calc'd for $C_{31}H_{24}AsN_7O_{14}\cdot H_2O$: C, 45.8; H, 3.2; N, 12.1.
Found: C, 45.8; H, 2.5; N, 12.2.

Mono-2-pyridyldiphenylarsine dibromide and oxide. Bromine (0.075 cc., 1 mole) was added dropwise to a solution of the arsine (0.46 g.) in acetic acid (10 cc.) which was stirred meanwhile and cooled in water. The solution deposited colorless crystals of the arsine dibromide, which were washed with acetic acid and rapidly transferred to a vacuum desiccator. It was exceedingly deliquescent.

Anal. Calc'd for $C_{17}H_{14}As\,Br_2N$: Br, 34.2. Found: Br, 35.0.

The acetic acid mother liquor was poured into an excess of 30% aqueous sodium hydroxide and refluxed for 1 hour. The oil which had separated was extracted with chloroform, and the latter then washed with water, dried, and evaporated. The residual oil would not crystallize: it was therefore added to ethanolic picric acid solution. The yellow *arsine oxide monopicrate* thus obtained had m.p. 138–141.5°, increased to 144–145° by recrystallization from ethanol.

Anal. Calc'd for $C_{17}H_{14}AsNO\cdot C_6H_3N_3O_7$: C, 50.0; H, 3.1.
Found: C, 49.6; H, 3.4.

When hydrogen sulfide was passed through an ethanolic solution of the crystalline dibromide, a small amount of sulfur was deposited. The filtered solution was evaporated in a desiccator, but the residual oil did not crystallize. When treated with sodium carbonate solution, however, carbon dioxide was evolved, and the colorless solid arsine was deposited, m.p. 62° (alone and mixed) after crystallization from ethanol. The oil was therefore probably the hydrobromide of the arsine.

Di-2-pyridylmonophenylamine. This was prepared essentially by the method of Wibaut and Tilman (23). The crude product was recrystallized first from light petroleum (b.p. 60–80°) and then from aqueous ethanol; m.p. 94°, yield of pure material, 15%. Wibaut and Tilman give m.p. 93°.

Picrate. The amine (0.3 g.) was added to a hot solution of picric acid (1.5 g., 5.4 moles) in ethanol (30 cc.). On cooling, the monopicrate separated as yellow crystals, m.p. 149–150°, unchanged by recrystallization from ethanol: a mixture of the "crude" and the recrystallized picrate also had m.p. 149–150°.

Anal. Calc'd for $C_{16}H_{13}N_3\cdot C_6H_3N_3O_7$: C, 55.4; H, 3.4.
Found: C, 55.3; H, 3.6.

Action of methyl iodide. (b) The amine (0.3 g.) dissolved immediately in methyl iodide (5 cc., 66 moles) and a crystalline precipitate readily formed on warming; the mixture was however refluxed for 5 hours, and the methyl iodide then allowed to evaporate. The

residue, when twice recrystallized from ethanol, in which it was very soluble, gave the pure *monomethiodide*, which melted with effervescence over a range of 4–5° at *ca.* 193°, dependent on the rate of heating.

Anal. Calc'd for $C_{17}H_{16}IN_3$: C, 52.4; H, 4.15.
Found: C, 53.2; H, 3.95.

In view of the indefinite m.p., the iodide was added to aqueous sodium picrate solution, and the precipitated material when recrystallized from ethanol gave the yellow crystalline *monomethopicrate*, m.p. 131–132°.

Anal. Calc'd for $C_{23}H_{18}N_6O_7$: C, 56.3; H, 3.7.
Found: C, 56.1; H, 3.6.

(c) A solution of the amine (0.5 g.) in nitromethane (4 cc.) containing methyl iodide (2.5 cc., 20 moles) was maintained at 48–53° for 48 hours, although crystals separated after the first few hours. The cold mixture was filtered, and the crystals, which were only slightly soluble in hot pure ethanol, were recrystallized from aqueous ethanol. The crystalline *dimethiodide* thus obtained melted sharply at *ca.* 189° with vigorous effervescence, the m.p. depending on the rate of heating.

Anal. Calc'd for $C_{18}H_{19}I_2N_3$: C, 40.7; H, 3.6.
Found: C, 40.8; H, 3.8.

Addition of dry ether to the nitromethane mother liquor precipitated a crop of monomethiodide, which after crystallization from ethanol had m.p. 189–199° (effer.), and which gave the monomethopicrate, m.p. 131–132°, both alone and when mixed with the former specimen.

(d) A mixture of the amine (0.5 g.), methyl iodide (0.6 cc., 5 moles) and methanol (0.35 cc.) was heated in a sealed tube at 100° for 8 hours. The yellow crystalline product, when recrystallized from aqueous ethanol, gave the dimethiodide, m.p. 193° (effer.).

Anal. Found: C, 40.95; H, 3.7.

Di-2-pyridylmonophenylphosphine. This was prepared similarly to the diphenyl analog, a Grignard reagent prepared from magnesium (15 g.), ethyl bromide (11.5 cc., 0.25 mole), and 2-bromopyridine (28.8 cc., 0.49 mole) in ether (250 cc.) being treated with a solution of phenyldichlorophosphine (14 g., 0.13 mole) in ether (100 cc.). After the usual treatment and working-up, the residue from the evaporation of the solvent was distilled at 0.4 mm. pressure and gave the fractions: (i) b.p. 64–66°, a small quantity of a colorless liquid; (ii) b.p. 94–105°, which rapidly solidified and was undoubtedly 2,2′-dipyridyl; (iii) b.p. 160–196°, a pale yellow oil; (iv) b.p. 196–210°, a viscous red liquid which crystallized spontaneously. Fraction (iv) could be crystallized from methanol, ethanol, cyclohexane, or light petroleum (b.p. 60–80°); it was best crystallized from a mixture of ethanol and light petroleum (b.p. 40–60°) and afforded the pure phosphine, colorless crystals, m.p. 96°.

Anal. Calc'd for $C_{16}H_{13}N_2P$: C, 72.7; H, 5.0; N, 10.6.
Found: C, 72.3; H, 5.1; N, 11.1.

Dihydrochloride. An ethanolic solution of the phosphine (0.2 g.) was slowly added to a saturated ethanolic hydrogen chloride solution (30 cc.) with stirring and ice-cooling. No crystals separated, so the solution was evaporated in a vacuum desiccator over flaked sodium hydroxide. The pale yellow residual oil was finally obtained crystalline by repeated extractions with cold acetone, although the crystalline residue at this stage was extremely deliquescent. It was further purified by adding ether to its ethanol solution, whereby a sticky precipitate was formed which crystallized on scratching and was no longer deliquescent. These crystals of the dihydrochloride when heated in a capillary tube sintered at *ca.* 100° and melted at 185–187°; when the tube was plunged into a bath pre-

heated to 130°, the crystals melted with effervescence, resolidified and melted again at 185–187°.

Anal. Calc'd for $C_{16}H_{13}N_2P \cdot 2HCl$: Cl, 21.05. Found: Cl, 21.5.

Dipicrate dihydrate. Prepared in the usual way from warm solution, the crude dipicrate dihydrate separated initially as yellow crystals, m.p. 128–130°, increased to 130–131° by one recrystallization from ethanol.

Anal. Calc'd for $C_{16}H_{13}N_2P \cdot 2C_6H_3N_3O_7 \cdot 2H_2O$: C, 44.3; H, 3.05.
Found: C, 44.1; H, 2.8.

Action of methyl iodide. (b) When the phosphine (0.3 g.) was added to methyl iodide (5 cc., 70 moles), the clear solution initially obtained soon became turbid, and a brown oil floated on the surface. The mixture was refluxed for 1 hour, and the methyl iodide then evaporated. The crystalline residue was dissolved in ethanol, and the latter then treated with much ether; the precipitated oil when scratched solidified to very deliquescent crystals. When these were dissolved in acetone, however, and ether again added, colorless non-deliquescent crystals of m.p. 133–134° were deposited. These were further purified by solution in ethanolic acetone and reprecipitation with ether. The pure *monomethiodide* was thus obtained, colorless crystals, m.p. 134–135°.

Anal. Calc'd for $C_{17}H_{16}IN_2P$: C, 50.2; H, 4.0.
Found: C, 50.35; H, 4.3.

(c) A solution of the phosphine (0.5 g.) in nitromethane (4.5 cc.) containing methyl iodide (2.5 cc., 21 moles) was kept at 48–52° for 8 hours. The product furnished only the above monomethiodide, m.p. 133–134°, alone and mixed.

(d) A clear yellow solution of the phosphine (0.5 g.) in methanol (0.5 cc.) containing methyl iodide (0.7 cc., 5.9 moles) was heated in a sealed tube at 100° for 9 hours. The cold solid red product was thoroughly mixed with methanol, and the yellow crystals which remained were then recrystallized from aqueous ethanol. They then had m.p. 247° (dec.) and when treated with aqueous sodium picrate gave a methopicrate, which after recrystallization from ethanolic acetone had m.p. 162–163°, unchanged by admixture with an authentic specimen of 2,2′-dipyridyl dimethopicrate.

Di-2-pyridylmonophenylphosphine sulfide. This was prepared by the union of the phosphine (0.694 g.) and sulfur (0.084 g., 1 atom) in boiling benzene, and when recrystallized from ethanol gave colorless crystals, m.p. 141°.

Anal. Calc'd for $C_{16}H_{13}N_2PS$: C, 64.8; H, 4.4.
Found: C, 64.5; H, 4.2.

Dihydrochloride. A solution of the sulfide (0.3 g.) in warm ethanol (5 cc.) was added to a cold saturated ethanolic solution of hydrogen chloride (35 cc.). The clear solution when partly evaporated in a vacuum desiccator deposited white crystals of the dihydrochloride, m.p. 165–171° (effer.).

Anal. Calc'd for $C_{16}H_{13}N_2PS \cdot 2HCl$: C, 52.0; H, 4.1; N, 7.6.
Found: C, 51.9; H, 4.0; N, 7.6.

Subsequent analysis indicated that this dihydrochloride, on prolonged confinement over sodium hydroxide in a vacuum desiccator, underwent slow dissociation to the monohydrochloride.

Monopicrate. When a solution of the sulfide (0.15 g.) and of picric acid (0.6 g., 5 moles) in ethanol (10 cc.) was allowed to cool, hard yellow crystals of the monopicrate, m.p. 141.5–142.5°, separated. Recrystallization from ethanol left the m.p. unaffected, and a mixed m.p. determination showed that no change had occurred.

Anal. Calc'd for $C_{16}H_{13}N_2PS \cdot C_6H_3N_3O_7$: C, 50.25; H, 3.1.
Found: C, 50.55; H, 3.6.

Action of methyl iodide. (a) A solution of the sulfide (0.2 g.) in benzene (5 cc.) containing methyl iodide (1 cc., 24 moles) was gently refluxed for 4 hours, during which a red coloration developed. The solvent was evaporated, and the residue, when recrystallized from aqueous ethanol, gave the unchanged sulfide, m.p. 139–140°, alone and mixed.

(b) A mixture of the sulfide (0.2 g.) and methyl iodide (4 cc., 95 moles) was refluxed for 3 hours. The clear hot solution was evaporated, but the residue on recrystallization furnished only the unchanged sulfide, m.p. 140–141°, alone and mixed.

(c) A solution of the sulfide (0.3 g.) in nitromethane (2.5 cc.) and methyl iodide (1.5 cc., 24 moles) was maintained at 49–54° for 50 hours. The clear brown solution was cooled and treated with ether; the precipitated brown gum could not be obtained crystalline, and was therefore converted to the methopicrate. Accordingly, the gum was extracted with boiling water, and the filtered chilled extract added to an excess of aqueous sodium picrate solution. The crude precipitated *monomethopicrate monohydrate* had m.p. 189–196°, and when recrystallized from ethanolic acetone had m.p. 200–202° (dec.) with sintering at 190°.

Anal. Calc'd for $C_{23}H_{18}N_6O_7PS \cdot H_2O$: C, 49.5; H, 3.6.
Found: C, 49.7; H, 3.7.

(d) A mixture of the sulfide (0.2 g.), methanol (0.2 cc.), and methyl iodide (0.3 cc., 7 moles) was heated in a sealed tube at 100° for 9 hours. The yellow crystalline product, when washed with methanol and recrystallized from aqueous ethanol, gave 2,2′-dipyridyl dimethiodide, melting with decomposition above 244°.

Anal. Calc'd for $C_{12}H_{14}I_2N_2$: I, 57.7. Found: I, 57.7.

This specimen was converted into the dimethopicrate, which after recrystallization from ethanolic acetone, had m.p. 161–162°, unchanged by admixture with an authentic sample.

Di-2-pyridylmonophenylarsine. To a Grignard reagent prepared from magnesium (15 g.) precisely as in the preparation of the phosphine analog, a solution of phenyldichloroarsine (17.5 g., 0.13 mole) in ether (100 cc.) was added over a period of 1.5 hours. After the usual refluxing and subsequent working up, the residue on distillation gave the fractions: (i) b.p. 80–196°/0.1 mm.; (ii) 196–230°/0.2 mm. The latter crystallized spontaneously; it was freely soluble in ether, benzene, methanol, and ethanol, but when recrystallized first from petroleum (b.p. 80–100°) and then aqueous ethanol (charcoal) gave the arsine in colorless crystals, m.p. 88°; 2.45 g., 10%.

Anal. Calc'd for $C_{16}H_{13}AsN_2$: C, 62.3; H, 4.25.
Found: C, 62.1; H, 4.4.

Dihydrochloride. The arsine (0.3 g.) dissolved readily in an ice-cold saturated ethanolic hydrogen chloride solution. The latter was evaporated in a desiccator, and the brown syrupy residue readily crystallized when stirred with ether. The crystals when dissolved in ethanol and reprecipitated with acetone, and finally dried in a vacuum over sodium hydroxide, gave the arsine dihydrochloride, colorless crystals, m.p 146–147°.

Anal. Calc'd for $C_{16}H_{13}AsN_2 \cdot 2HCl$: Cl, 18.6. Found: Cl, 18.4.

Dipicrate. A solution of the arsine (0.2 g.) and picric acid (1 g., 7 moles) in hot ethanol (20 cc.) when allowed to cool deposited a yellow oil which on scratching readily crystallized. These crystals of the dipicrate on being heated melted between 50° and 55°, appeared to resolidify, and then remelted at 136–142°; when recrystallized from ethanol containing a small quantity of acetone, they melted sharply at 142–143° without previous change; analysis indicated that their composition was unchanged.

Anal. Calc'd for $C_{16}H_{13}AsN_2 \cdot 2C_6H_3N_3O_7$: C, 43.85; H, 2.5; N, 14.6.
Found (before recrystallization): C, 43.6; H, 3.1.
(after recrystallization): C, 43.0; H, 2.5; N, 14.35.

Action of methyl iodide. (b) A solution of the arsine (0.3 g.) in methyl iodide (5 cc., 80 moles) was refluxed for 4 hours; during this period an oil which initially separated ultimately crystallized. The excess of methyl iodide was evaporated, and the residue, after two recrystallizations from ethanol containing *ca.* 3% of water, gave the *dimethiodide* as bright yellow crystals, m.p. 193–195° (dec.).

Anal. Calc'd for $C_{18}H_{19}AsI_2N_2$: C, 36.5; H, 3.2.
Found: C, 36.9; H, 3.6.

This dimethiodide was converted in the usual way into the *dimethopicrate*, yellow crystals from ethanol containing a small quantity of acetone; m.p. 190–191° (dec., with preliminary softening).

Anal. Calc'd for $C_{30}H_{23}AsN_8O_{14}$: C, 45.3; H, 2.9.
Found: C, 45.2; H, 3.1.

(d) A mixture of the arsine (0.3 g.), methanol (0.3 cc.), and methyl iodide (0.4 cc., 6.5 moles) was heated at 100° for 7 hours in a sealed tube. The dark red oily residue readily solidified, and when recrystallized as above furnished the dimethiodide, m.p. 192–195° (dec.).

Anal. Found: C, 36.3; H, 3.0.

Tri-2-pyridylamine. This was prepared essentially by the method of Wibaut and La Bastide (24); the amine after recrystallization from water had m.p. 130°. Wibaut and La Bastide give m.p. 130°.

Dihydrochloride. A solution of the amine (0.5 g.) in ethanol (5 cc.) was added to a cold saturated ethanolic hydrogen chloride solution (50 cc.). The highly deliquescent white crystalline precipitate of the dihydrochloride was filtered off and rapidly transferred to a vacuum desiccator containing sodium hydroxide.

Anal. Calc'd for $C_{15}H_{12}N_4 \cdot 2HCl$: N, 17.4; Cl, 22.1.
Found: N, 17.55; Cl, 22.5.

Monopicrate. A solution of the amine (0.3 g.) and picric acid (2.5 g., 9 moles) in hot ethanol (50 cc.) on cooling deposited yellow crystals of the monopicrate, m.p. 147–148°, which after recrystallization from ethanol had m.p. 147.5–148.5°; a mixture of the two samples had m.p. 147–148°.

Anal. Calc'd for $C_{15}H_{12}N_4 \cdot C_6H_3N_3O_7$: C, 52.8; H, 3.1.
Found: C, 52.5; H, 3.2.

Wibaut and La Bastide (24) prepared this compound, m.p. 150–151°.

Action of methyl iodide. (b) When a solution of the amine (0.4 g.) in methyl iodide (5 cc., 50 moles) was boiled under reflux, yellow crystals rapidly separated. After 4 hours' refluxing, the crystalline product was collected, recrystallized from ethanol, and then treated in aqueous solution with sodium picrate. The yellow crystalline *monomethopicrate* was thus obtained, m.p. 130–131° after recrystallization from ethanol; its m.p. was unchanged by admixture with the sample described below.

(c) A solution of the amine (1 g.) in nitromethane (10 cc.) containing methyl iodide (5 cc., 20 moles) was heated at 50–53° for 48 hours, yellow crystals separating meanwhile. After cooling, the crystals (0.8 g.) were filtered off, and when recrystallized from methanol gave the yellow *dimethiodide*, m.p. 202° (effer., with some sintering at 193°); the m.p. is affected by the rate of heating.

Anal. Calc'd for $C_{17}H_{18}I_2N_4$: C, 38.3; H, 3.4.
Found: C, 37.9; H, 3.5.

The addition of ether to the nitromethane-methyl iodide filtrate gave a pale yellow precipitate of the monomethiodide, which (unlike the dimethiodide) was freely soluble in hot ethanol, from which it was recrystallized, m.p. 198.5° (effer., with softening at 190°).

Anal. Calc'd for $C_{16}H_{15}IN_4$: C, 49.2; H, 3.9.
Found: C, 49.55; H, 3.9.

Wibaut and La Bastide (24) prepared only this monomethiodide, m.p. 204–206°.

This monomethiodide was converted to the *monomethopicrate*, yellow crystals from ethanol, in which it was readily soluble: m.p. 130.5–131°.

Anal. Calc'd for $C_{22}H_{17}N_7O_7$: N, 20.0. Found: N, 19.8.

(d) A mixture of the amine (1 g.), methanol (0.7 cc.) and methyl iodide (1.2 cc., 5 moles) was heated in a sealed tube at 100° for 8 hours. The hard yellow crystals of the dimethiodide were washed with methanol and dried; m.p. 196° (dec.). They were recrystallized from methanol before analysis.

Anal. Calc'd for $C_{17}H_{18}I_2N_4$: N, 10.5; I, 47.7.
Found: N, 10.5; I, 48.3.

The dimethiodide was converted to the *dimethopicrate*, which was only slightly soluble in hot methanol, ethanol, or acetone but was freely soluble in hot water. After recrystallization from aqueous ethanol it was obtained as yellow crystals of the dihydrate, which melted slowly with effervescence over a range of 149–162°.

Anal. Calc'd for $C_{29}H_{22}N_{10}O_{14}\cdot 2H_2O$: C, 45.2; H, 3.4.
Found: C, 45.1; H, 3.9.

Tri-2-pyridylphosphine. This phosphine was prepared by the method of Davies and Mann (25); m.p. 115°. Davies and Mann give m.p. 113–114°.

Trihydrochloride. When a solution of the phosphine (0.4 g.) in hydrochloric acid (5 cc.) was added to an ice-cold saturated ethanolic hydrogen chloride solution, no solid material separated. The solution was therefore confined over solid sodium hydroxide in an atmospheric desiccator for 3–4 days, when colorless crystals of the trihydrochloride separated. These, drained and dried over sodium hydroxide, had m.p. 207.5–209.5° with slight preliminary softening.

Anal. Calc'd for $C_{15}H_{12}N_3P\cdot 3HCl$: Cl, 28.4. Found: Cl, 27.9.

Dipicrate. When a solution of the phosphine (0.25 g.) in ethanol (5 cc.) was added to one of picric acid (2 g., 10 moles) also in ethanol (40 cc.), yellow crystals of the dipicrate (0.66 g.) rapidly separated; m.p. 141–142°, increased to 142–143° by recrystallization from ethanol.

Anal. Calc'd for $C_{15}H_{12}N_3P\cdot 2C_6H_3N_3O_7$: C, 44.8; H, 2.5; N, 17.4.
Found (before recrystallization): C, 45.0; H, 2.6; N, 17.5.
(after recrystallization): C, 44.4; H, 2.8; N, 17.5.

Action of methyl iodide. (c) A solution of the phosphine (0.4 g.) in nitromethane (5 cc.) containing methyl iodide (3 cc., 32 moles) was maintained at 50–55° for 48 hours. The cold product was then mixed with ether, which precipitated a red oil. The ether was decanted off, and the red oil extracted with a small quantity of cold ethanol, which dissolved the greater part of the oil but left some crystalline material undissolved. The crystals were filtered off, and the ethanolic filtrate again treated with ether. The oil which was now precipitated could not be obtained crystalline; it was therefore dissolved in water and treated with aqueous sodium picrate. Yellow crystals of the *monomethopicrate monohydrate* were thus obtained, m.p. 157–158° after recrystallization from ethanol, unchanged by admixture with the preparation described below.

Anal. Calc'd for $C_{22}H_{17}N_6O_7P \cdot H_2O$: C, 50.2; H, 3.6.
Found: C, 49.9, 50.3; H, 3.6, 3.5.

The above crystalline material was dissolved in the minimum of cold ethanol, filtered and reprecipitated by the addition of ether. The colorless crystals, m.p. 190°, were soluble in water, in which they furnished ionic iodine; analysis indicated they were *di-2-pyridyl-monomethylphosphine dimethiodide monohydrate.*

Anal. Calc'd for $C_{13}H_{17}I_2N_2P \cdot H_2O$: C, 30.95; H, 3.8.
Found: C, 30.6; H, 4.0.

(d) A mixture of the phosphine (0.8 g.), methanol (0.5 cc.), and methyl iodide (0.8 cc., 4.3 moles) was heated in a sealed tube at 100° for 7.5 hours. The cold product formed a mass of yellow needles, which were washed with methanol, and thrice recrystallized from this solvent. Pale yellow crystals of 2,2'-dipyridyl dimethiodide, m.p. 239–242° (dec.), were thus obtained.

Anal. Calc'd for $C_{12}H_{14}I_2N_2$: C, 32.7; H, 3.2; N, 6.35; I, 57.7.
Found: C, 32.9; H, 3.1; N, 5.95; I, 57.9.

It is noteworthy that during the first two recrystallizations from methanol, the hot solution was deep red but became yellow on cooling, but during the third recrystallization the solution was yellow throughout.

To confirm the identity of this dimethiodide, a portion was converted to the dimethopicrate, which after recrystallization from acetone had m.p. 160.5–162°, unchanged by admixture with an authentic sample.

Tri-2-pyridylphosphine sulfide. This compound readily crystallized when a solution of the phosphine (0.85 g.) and sulfur (0.1 g., 1 atom) in benzene (20 cc.) was refluxed for 2 hours and allowed to cool. Recrystallization from ethanol gave colorless crystals, m.p. 161°.

Anal. Calc'd for $C_{15}H_{12}N_3PS$: C, 60.6; H, 4.1; N, 14.1.
Found: C, 61.2; H, 4.4; N, 14.0.

Monopicrate. A solution of the sulfide (0.3 g.) and picric acid (2 g., 8 moles) in hot ethanol (40 cc.) on cooling deposited yellow needles of the monopicrate, m.p. 156–158°, increased to 158–159° by recrystallization from ethanol, and not affected by admixture with the original sample.

Anal. Calc'd for $C_{15}H_{12}N_3PS \cdot C_6H_3N_3O_7$: C, 47.9; H, 2.9; S, 6.1.
Found: C, 48.1; H, 2.7; S, 6.3.

Action of methyl iodide. (b) A solution of the sulfide (0.35 g.) in methyl iodide (20 cc., 275 moles) was refluxed for 7 hours. A brown syrup separated, and later changed to yellow crystals. The cold solvent was decanted, and the crystals dissolved in ethanol; addition of ether precipitated the yellow crystalline *monomethiodide*, m.p. 156–157° (dec.).

Anal. Calc'd for $C_{16}H_{15}IN_3PS$: N, 9.6; I, 28.9.
Found: N, 9.4; I, 28.2.

An aqueous solution of this monomethiodide when treated with sodium picrate gave the *monomethopicrate*, yellow crystals from ethanol, m.p. 208–211° (effer.), unchanged by admixture with the sample described below.

(c) A solution of the sulfide (0.4 g.) in nitromethane (5 cc.) containing methyl iodide (3 cc., 36 moles) was maintained at 50° for 48 hours. The cold solution was poured into much ether, which precipitated a viscous brown gum; the ether was decanted, and the gum extracted with cold ethanol. After filtration of the extract, the gum was reprecipitated by the addition of ether. Since however the gum could not be induced to crystallize, it was dissolved in water and treated with sodium picrate. The monomethopicrate was precipitated, yellow crystals from ethanol, m.p. 209–211°. (dec.)

Anal. Calc'd for $C_{22}H_{17}N_6O_7PS$: C, 48.9; H, 3.2.
Found: C, 48.6; H, 3.3.

(d) A mixture of the sulfide (0.5 g.), methanol (0.3 cc.) and methyl iodide (0.5 cc., 4.8 moles) was heated in a sealed tube at 100° for 7 hours. The yellow crystalline product was washed with cold methanol, and twice recrystallized from methanol containing a small proportion of water. The product, which was sulfur-free, decomposed *ca.* 219–222°; when however its aqueous solution was treated with sodium picrate it gave 2,2′-dipyridyl dimethopicrate, m.p. 157–159° after solution in acetone and reprecipitation with ether. The m.p. was unchanged by admixture with an authentic sample.

The united aqueous methanol mother-liquors slowly deposited yellow crystals; these, recrystallized from aqueous methanol, gave pure 2,2′-dipyridyl dimethiodide, m.p. 244–246° (dec.).

Anal. Calc'd for $C_{12}H_{14}I_2N_2$: I, 57.7. Found: I, 58.0.

The united mother liquors were evaporated, but the residual red oil could not be crystallized. Its cold aqueous solution was therefore treated with aqueous sodium picrate; this gave an immediate yellow precipitate (A), and after filtration the solution slowly deposited more yellow crystals (B).

The compound (A) after recrystallization from methanol had m.p. 209–210° (dec.) unaffected by further recrystallization, but depressed to 186–193° (dec.) by admixture with the sulfide monomethopicrate. Its identity remains uncertain.

Anal. Found: C, 38.0; H, 2.5; N, 17.3.

The crystals (B) were recrystallized first from methanol and then from ethanol, the m.p. 145–147° being then unaffected. Analysis indicated that they were *mono-2-pyridyldimethylphosphine sulfide monomethopicrate.*

Anal. Calc'd for $C_{14}H_{15}N_4O_7PS$: C, 40.6; H, 3.65; N, 13.5.
Found: C, 40.8; H, 3.2; N, 13.9.

Tri-2-pyridylphosphine oxide. Aqueous hydrogen peroxide (20 cc., "20 vols") was added to a solution of the phosphine (0.9 g.) in acetone (8 cc.), the mixture becoming slightly warm and cloudy. After 5 days the solvent was removed in a vacuum. The colorless residual crystals of the oxide were recrystallized from ethanol, m.p. 209°.

Anal. Calc'd for $C_{15}H_{12}N_3OP$: C, 64.1; H, 4.3; N, 14.9.
Found: C, 64.4; H, 4.4; N, 15.15.

Action of methyl iodide. A mixture of the oxide (0.44 g.), methanol (0.3 cc.), and methyl iodide (0.5 cc., 5 moles) was heated in a sealed tube at 100° for 7 hours. The cold yellow crystalline product, when recrystallized from methanol, gave 2,2′-dipyridyl dimethiodide, m.p. 243–245° (dec.).

Anal. Found: I, 57.7.

For further identification, this compound was converted to the dimethopicrate, yellow crystals from acetone, m.p. 160.5–162°, unchanged by admixture with an authentic sample.

Action of Chloramine-T on tri-2-pyridylphosphine. (A) When solutions of the phosphine (1 g.) and of Chloramine-T (1.01 g., 1 mole), each in hot aqueous ethanol (10 cc.) were mixed, sodium chloride was at once precipitated. The mixture was refluxed for 1.5 hours, filtered, cooled, and taken to dryness in a desiccator. The oily residue, which crystallized on scratching, was dissolved in boiling water (20 cc.), and the solution on cooling deposited colorless crystals of *p*-toluenesulfonamide, m.p. 135°, alone and mixed.

The aqueous filtrate was divided into two portions. One portion when treated with aqueous sodium picrate gave yellow crystals of the *phosphine oxide monopicrate,* m.p. 144–148° after recrystallization from water.

Anal. Calc'd for $C_{15}H_{12}N_3OP \cdot C_6H_3N_3O_7$: C, 49.4; H, 2.9; N, 16.5.
Found: C, 49.7; H, 3.1; N, 16.9.

The second portion was evaporated, and the solid residue first extracted with boiling ether to remove *p*-toluenesulfonamide, and then recrystallized in turn from diethyl carbonate and from ethanol. Colorless crystals of the phosphine oxide were thus obtained, m.p. 207–209°, alone and mixed.

It is reasonably certain therefore that the original oily residue which crystallized was the hydroxyphosphine-*p*-toluenesulfonamide, $[(C_5H_4N)_3POH]NHSO_2C_7H_7$.

(B) When the condensation was repeated using anhydrous Chloramine-T in absolute ethanol, the crystalline residue when recrystallized from ethanol gave colorless crystals of *tri-2-pyridylphosphine-p-toluenesulfonylimine*, $(C_5H_4N)_3P \rightarrow NSO_2C_7H_7$, m.p. 177°.

Anal. Calc'd for $C_{22}H_{19}N_4O_2PS$: C, 60.9; H, 4.6; N, 12.9.
Found: C, 60.8; H, 4.4; N, 12.9.

Tri-2-pyridylarsine. This arsine, m.p. 85–85.5°, was prepared by the method of Davies and Mann (25), who give m.p. 85°.

Trihydrochloride. This salt was prepared precisely as that of the corresponding phosphine. Consistent m.p's. could only be obtained by preheating the immersion bath to within *ca.*10° of the m.p. and then raising the temperature at a fixed rate (2° per minute). M.p. 145.5–146.5° (dec.). When a solution of this salt in conc'd aqueous hydrochloric acid was poured into an excess of ethanolic hydrogen chloride, the white crystals of the salt were reprecipitated, m.p. 152° (dec.).

Anal. Calc'd for $C_{15}H_{12}AsN_3 \cdot 3HCl$: Cl, 25.4; N, 10.0.
Found: Cl, 25.3; N, 10.0.

Dipicrate. Prepared similarly to that of the corresponding phosphine; yellow crystals, m.p. 152–153° (dec.), unchanged by recrystallization from ethanol; mixed m.p. of products before and after recrystallization, unchanged.

Anal. Calc'd for $C_{15}H_{12}AsN_3 \cdot 2C_6H_3N_3O_7$: C, 42.2; H, 2.35; N, 16.4.
Found: C, 42.4; H, 2.35; N, 16.7.

Action of methyl iodide. (a) A solution of the arsine (0.6 g.) in benzene (15 cc.) containing methyl iodide (2.2 cc., 18 moles) was refluxed for 4.5 hours. The cold solvent was decanted from the crystalline deposit, which when twice recrystallized from much ethanol (*ca.* 300 cc.) gave yellow crystals of the *dimethiodide monohydrate*. The m.p. depended on the rate of heating, owing to preliminary decomposition; values of 186° and 194° were recorded.

Anal. Calc'd for $C_{17}H_{18}AsI_2N_3 \cdot H_2O$: C, 33.4; H, 3.3.
Found: C, 33.7; H, 3.3.

When heated for 6 hours at 120°/15 mm., this compound gave the anhydrous *dimethiodide*, m.p. 213–215° (dec.).

Anal. Calc'd for $C_{17}H_{18}AsI_2N_3$: N, 7.1; I, 42.8.
Found: N, 7.1; I, 43.4.

(b) A solution of the arsine (0.3 g.) in methyl iodide (5 cc., 83 moles) was refluxed for 4 hours; the brown oil which rapidly separated crystallized during the heating. The methyl iodide was evaporated, and the residue when recrystallized from aqueous ethanol gave the above dimethiodide monohydrate, m.p. 183–193° (dec.).

Anal. Found: C, 32.6; H, 3.7.

A portion was converted to the *dimethopicrate*, yellow crystals from water, m.p. 180–182° (dec.).

Anal. Calc'd for $C_{29}H_{22}AsN_9O_{14}$: C, 43.8; H, 2.8.
Found: C, 44.3; H, 2.9.

(c) A solution of the arsine (0.5 g.) in nitromethane (5 cc.) containing methyl iodide (3 cc., 30 moles) was heated at 47–53° for 48 hours. The yellow crystals which separated were recrystallized from aqueous ethanol and furnished the above dimethiodide monohydrate, m.p. 188–197° (dec.).

Anal. Found: C, 33.1; H, 3.2.

(d) A mixture of the arsine (0.6 g.) and methyl iodide (2.5 cc., 21 moles) was heated in a sealed tube at 100° for 8 hours. The cold methyl iodide was decanted from a residual brown glass, which when twice recrystallized from aqueous ethanol, furnished the *trimethiodide*, m.p. 201.5–204.5° (dec.).

Anal. Calc'd for $C_{18}H_{21}AsI_4N_2$: C, 29.4; H, 2.9; N, 5.7; I, 51.8.
Found: C, 30.0; H, 3.3; N, 5.7; I, 51.1.

Action of Chloramine-T on tri-2-pyridylarsine. Solutions of the arsine (0.7 g.) and the hydrated Chloramine-T (0.8 g.), each in hot ethanol (15 cc.) were mixed, and refluxed for 1 hour. Precipitated sodium chloride was filtered off, and the filtrate evaporated. The semi-solid residue solidified immediately it was stirred with cold water. The colorless crystals proved to be *p*-toluenesulfonamide, m.p. 136–137°. The aqueous extract contained the arsine oxide, for treatment with aqueous picric acid precipitated large yellow needles of the *arsine oxide monopicrate*, m.p. 144–147° with preliminary softening.

Anal. Calc'd for $C_{15}H_{12}AsN_3O\cdot,C_6H_3N_4O_7$. C, 45.5; H, 2.7; N, 15.2.
Found: C, 45.4; H, 2.9; N, 15.3.

2,2'-Dipyridyl dimethiodide and dimethopicrate. Authentic samples of these compounds were required for direct comparison with the products arising in our work. The dimethiodide was made by the method of Blau (36), a mixture of 2,2'-dipyridyl (0.5 g.), methanol (0.25 cc.), and methyl iodide (0.5 cc., 2.5 moles) being heated in a sealed tube at 100° for 2 hours. The cold product formed yellow crystals, which when recrystallized from aqueous methanol had m.p. 237° (dec.). No m.p. is given by Blau (36).

When hot aqueous solutions of the dimethiodide and of an excess of sodium picrate were mixed and allowed to cool, an orange oil separated and ultimately solidified. Recrystallization from acetone gave the pure dimethopicrate, yellow crystals, m.p. 161.5–163°.

Anal. Calc'd for $C_{24}H_{18}N_8O_{14}$: C, 44.85; H, 2.8.
Found: C, 45.1; H, 2.9.

Attempted reduction of tri-2-pyridylamine. A mixture of the amine, (1 g.) granulated tin (10 g.), and concentrated hydrochloric acid (10 cc.) was warmed until vigorous effervescence occurred, and then more hydrochloric acid (40 cc.) added in small quantities at intervals over a period of 3 hours to maintain the reaction. The mixture was then refluxed for 1 hour, and much of the free acid finally removed by evaporation on a water-bath. The cold, almost solid product was treated with an excess of 30% aqueous sodium hydroxide and thrice extracted with benzene. The solvent was evaporated from the united dried benzene extracts, and the residue, when recrystallized from water, gave di-2-pyridylamine, m.p. 94–95°, unchanged by admixture with an authentic sample. Wibaut and La Bastide (24) give m.p. 95.5–96°.

Anal. Calc'd for $C_{10}H_9N_3$: C, 70.2; H, 5.25; N, 24.6.
Found: C, 70.4; H, 5.1; N, 25.1.

2-Methyldihydro-1,3-thiazine methiodide. This compound has hitherto been obtained only as an unanalyzed oil (18). When the thiazine (XIV) (1.1 g.) was dissolved in methyl iodide (4.1 g., 3 moles) in a closed flask, solid material began to separate within a few minutes. The mixture was set aside overnight, and then refluxed for 1 hour. The excess of methyl iodide was evaporated, and the residue when washed with ether gave the yellow

semi-solid deliquescent methiodide (2.2 g., 82%). The latter when twice recrystallized from ethanol gave pale yellow crystals, which after drying over phosphoric anhydride in a vacuum had m.p. 154–156° in a sealed tube.

Anal. Calc'd for $C_6H_{12}INS$: I, 49.4. Found: I, 49.9.

SUMMARY

1. Theoretical considerations are put forward to explain the fact that in many polyamines, not all the amino groups can exert simultaneously their normal reactivity towards acids, and—in the case of tertiary amines—towards alkyl halides. It is suggested that the positive pole created by the initial salt formation exerts a strong electronic attraction, and this attraction, relayed by the inductive or mesomeric effect, may virtually immobilize the lone pair of electrons on a neighboring nitrogen atom and so deactivate this atom. In certain cases, the cumulative effect of more than one positively charged atom may be required to exert this deactivating effect on a particular atom, depending on the nature of the molecule concerned. The same effect is observed in the reactivity of tertiary polyphosphines and arsines towards alkyl halides.

2. The theory is applied successfully to explain the reactivity towards acids and alkyl halides of mono-2-pyridyldiphenyl-amine, -phosphine, and -arsine, di-2-pyridylmonophenyl-amine, -phosphine, and -arsine, tri-2-pyridyl-amine, -phosphine, and -arsine and of certain of their derivatives.

CAMBRIDGE, ENGLAND

REFERENCES

(1) STOEHR, *J. prakt. Chem.*, [2], **47**, 455, 462 (1893); [2] **49**, 402 (1894); [2], **51**, 456, 462 (1895).
(2) HINSBERG, *Ann.*, **237**, 335 (1887); **292**, 245 (1896).
(3) GABRIEL & COLMAN, *Ber.*, **37**, 3651 (1904).
(4) GRAYMORE *et al.*, *J. Chem. Soc.*, 1311 (1938); 1787 (1939).
(5) CHATT & MANN, *J. Chem. Soc.*, 1184 (1940).
(6) GIBSON & MANN. *J. Chem. Soc.*, 175 (1942).
(7) INGOLD, INGOLD & SHAW, *J. Chem. Soc.*, 814 (1927).
(8) INGOLD, SHAW & WILSON, *J. Chem. Soc.*, 1280 (1928).
(9) MANN & POPE, *Proc. Roy. Soc. London*, A, **109**, 444 (1925): *J. Chem. Soc.*, 482, 489 (1926).
(10) MANN, *J. Chem. Soc.*, 461 (1934).
(11) SIEBER, *Ber.*, **23**, 326 (1890); MAJERT & SCHMIDT, *Ber.*, **23**, 3720 (1890).
(12) LADENBURG, *Ber.*, **24**, 2401 (1891); KNORR, *Ber.*, **37**, 3515 (1904).
(13) HANTZSCH, *Ann.*, **250**, 271 (1889); POPP, *Ann.*, **250**, 277 (1899); HOFMANN, *Ber.*, **13**, 16 (1880).
(14) BROOKER, *J. Am. Chem. Soc.*, **58**, 664 (1936).
(15) PINKUS, *Ber.*, **26**, 1077 (1893).
(16) BEILENSON & HAMER, *J. Chem. Soc.*, 143 (1939).
(17) SEXTON, *J. Chem. Soc.*, 470 (1939).
(18) HAMER & RATHBONE, *J. Chem. Soc.*, 243 (1943); BEILENSON, HAMER & RATHBONE, *J. Chem. Soc.*, 222 (1945).
(19) LITHERLAND & MANN, *J. Chem. Soc.*, 1588 (1938).
(20) WALLACH & SCHULZE, *Ber.*, **14**, 423 (1881); PINNER & SCHWARZ, *Ber.*, **35**, 2447 (1902).
(21) TSCHITSCHIBABIN *et al.*, *J. Russ. Phys.-Chem. Soc.*, **46**, 1231 (1914); **50**, 501, 521 (1920); MAGIDSON & MENSHIKOV, *Ber.*, **59**, 1209 (1926).
(22) TSCHITSCHIBABIN & KONOVALOVA, *Ber.*, **59**, 2055 (1926).

(23) WIBAUT & TILMAN, *Rec. trav. chim.*, **52,** 987 (1933).
(24) WIBAUT & LA BASTIDE, *Rec. trav. chim.*, **52,** 493 (1933).
(25) DAVIES & MANN, *J. Chem. Soc.*, 279 (1944).
(26) MENSCHUTKIN, *Z. physik. Chem.*, **6,** 41 (1890): *cf.* HAWKINS, *J. Chem. Soc.*, **121,** 1175 (1922); PICKLES & HINSHELWOOD, *J. Chem. Soc.*, 1356 (1936).
(27) WALDEN, *Z. physik. Chem.*, **54,** 131 (1906).
(28) BRADLEY & ROBINSON, *J. Chem. Soc.*, 1254 (1932).
(29) PAULING, "The Nature of the Chemical Bond", **1945,** p. 75.
(30) INGOLD, *Annual Reports Chem. Soc. Lond.*, **23,** 129 (1926).
(31) VORLÄNDER, *Ber.*, **52,** 263 (1919).
(32) DAVIES & LEWIS, *J. Chem. Soc.*, 1599 (1934).
(33) DAVIES & ADDIS, *J. Chem. Soc.*, 1622 (1937).
(34) MANN, *J. Chem. Soc.*, 958 (1932).
(35) LYON & MANN, *J. Chem. Soc.*, 667 (footnote) (1942).
(36) BLAU, *Monatsh.*, **10,** 382 (1889).
(37) CRAIG, *J. Am. Chem. Soc.*, **56,** 231 (1934).
(38) MICHAELIS, *Ber.*, **10,** 627 (1877).
(39) OVERHOFF & PROOST, *Rec. trav. chim.*, **57,** 179 (1938).
(40) COOKSON & MANN, *J. Chem. Soc.*, 618 (1947).
(41) SMILES *et al.*, *J. Chem. Soc.*, **125,** 176 (1924); **127,** 224 1821 (1925).