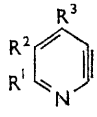
Polyhalogenoaromatic Compounds. Part VII.[1] Reaction of 4-Substituted Tetrachloropyridines with n-Butyl-lithium, the Generation of 2-Pyridynes, and their Trapping as Adducts with Furan[2]

By **J. D. Cook** and **B. J. Wakefield,*** Department of Chemistry and Applied Chemistry, University of Salford, Lancs., M5 4WT

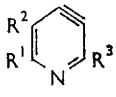
The reactions of n-butyl-lithium with 2,3,5,6-tetrachloro-4-dimethylamino-, tetrachloro-4-pyrrolidino-, and tetrachloro-4-piperidino-pyridine lead to the corresponding 2,5,6-trichloro-4-dialkylamino-3-pyridyl-lithiums. The same reaction with 2,3,5,6-tetrachloropyridine gives tetrachloro-4-pyridyl-lithium; reaction with tetrachloro-4-methylpyridine gives (tetrachloro-4-pyridyl)methyl-lithium; and reaction with 3-bromo-2-chloropyridine gives 2-chloro-3-pyridyl-lithium. In the presence of furan, the 2-chloro-3-pyridyl-lithium compounds gave the 5,8-dihydro-5,8-epoxyquinoline derivatives expected from the cycloaddition of the corresponding 2-pyridynes to furan. Some other derivatives of the 2-pyridynes, formed by cycloaddition or by addition of organolithium compounds, are described. The evidence for 2-pyridyne intermediates is discussed.

THE chemistry of ' hetarynes,' *i.e.* heterocyclic analogues of arynes, has attracted much interest.[3-5] Two types of pyridyne may be envisaged, conveniently designated 2-pyridynes (I) and 3-pyridynes (II). However, whereas 3-pyridyne (II) and its derivatives are evidently formed as intermediates in a number of reactions, and have been trapped by furan [6] and by aromatic hydrocarbons,[7] evidence for 2-pyridyne intermediates has



(I)

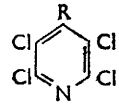
a; $R^1 = R^2 = R^3 = H$
b; $R^1 = R^2 = R^3 = Cl$
c; $R^1 = R^2 = Cl$, $R^3 = C_5H_{10}N$
d; $R^1 = R^2 = Cl$, $R^3 = C_4H_8N$
e; $R^1 = R^2 = Cl$, $R^3 = NMe_2$



(II)

a; $R^1 = R^2 = R^3 = H$
b; $R^1 = R^2 = R^3 = Cl$

proved extremely difficult to obtain. Evidence from *cine*-substitution reactions may be misleading,[3-5,8,9] and prior to the work described here the only clear evidence from trapping was the formation of quinoline in low yield in the reaction of 3-bromo-2-chloropyridine with lithium amalgam in the presence of furan.[10] Since our work was completed, it has been suggested [11] that products obtained by pyrolysis of quinolinic anhydride in the presence of thiophen are best rationalised in terms of 1,4- and 1,2-addition of 2-pyridyne to thiophen. There seems no obvious reason for the elusiveness of such intermediates; indeed, molecular orbital calculations have indicated that 2-pyridyne (Ia) should be stabilised by interaction on the lone pair on nitrogen with the partially occupied orbitals associated with the ring carbon atoms.[12]



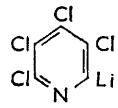
(III)

a; R = Li
b; R = $C_5H_{10}N$
c; R = C_4H_8N
d; R = NMe_2
e; R = H
f; R = Me
g; R = NO_2
h; R = OMe
i; R = OPh
j; R = CH_2Li
k; R = $CH_2{\cdot}CO_2H$
l; R = Et

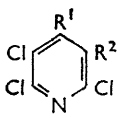
Our experiments on the reaction of n-butyl-lithium with pentachloropyridine [13] gave promise of a convenient route to both trichloro-2-pyridyne (Ib) and trichloro-3-pyridyne (IIb). However, while adducts of the 3-pyridyne (IIb) were indeed readily obtained from

[1] Part VI, J. I. Hollies, D. Price, and H. Suschitzky, preceding paper.
[2] Preliminary communications, J. D. Cook and B. J. Wakefield, *Chem. Comm.*, 1968, 297; The Chemical Society, Autumn Meeting, Keele, 1968, Abstract F8.
[3] T. Kauffmann, *Angew. Chem. Internat. Edn.*, 1965, **4**, 543.
[4] H. J. den Hertog and H. C. van der Plas, *Adv. Heterocyclic Chem.*, 1965, **4**, 121.
[5] R. W. Hoffmann, ' Dehydrobenzene and Cycloalkynes,' Academic Press, New York, 1967, ch. 6.
[6] T. Kauffmann and F.-P. Boettcher, *Chem. Ber.*, 1962, **95**, 949.
[7] (*a*) J. D. Cook and B. J. Wakefield, *Tetrahedron Letters*, 1967, 2535; (*b*) J. D. Cook, B. J. Wakefield, H. Heaney, and J. M. Jablonski, *J. Chem. Soc.* (*C*), 1968, 2727.
[8] M. G. Reinecke and H. W. Adickes, *J. Amer. Chem. Soc.*, 1968, **90**, 511.
[9] T. Kauffmann, R. Nürnberg, and K. Udluft, *Angew. Chem.*, 1968, **80**, 614.
[10] (*a*) R. J. Martens and H. J. den Hertog, *Tetrahedron Letters*, 1962, 643; (*b*) R. J. Martens and H. J. den Hertog, *Rec. Trav. chim.*, 1964, **83**, 621.
[11] E. K. Fields and S. Meyerson, in ' Organosulfur Chemistry,' ed. M. J. Janssen, Interscience, New York, 1967, p. 156.
[12] H. L. Jones and D. L. Beveridge, *Tetrahedron Letters*, 1964, 1577.
[13] (*a*) J. D. Cook, B. J. Wakefield, and C. J. Clayton, *Chem. Comm.*, 1967, 150; (*b*) J. D. Cook and B. J. Wakefield, *J. Organometallic Chem.*, 1968, **13**, 15.

tetrachloro-4-pyridyl-lithium (IIIa),[7] tetrachloro-2-pyridyl-lithium (IV) did not appear to eliminate lithium chloride to give the 2-pyridyne (Ib); only a small amount of an adduct of this pyridyne was obtained, as a mixture with other adducts. In this respect, our observations were consistent with an earlier suggestion [3,14] that 3-chloro-2-pyridyl-lithium would not readily lose lithium chloride. Zoltewicz and Smith have also shown that base-catalysed deuterium exchange at the 2-position of 3-chloropyridine is extremely slow, suggesting that formation of 3-chloro-2-pyridyl anion (V), a reasonable intermediate in the conversion of 3-chloro-2-pyridyl-lithium into 2-pyridyne, is an unfavourable process.[15] On the other hand, the formation of quinoline from the reaction of 3-bromo-2-chloropyridine with lithium amalgam in the presence of furan presumably involved the elimination of lithium chloride from 2-chloro-3-pyridyl-lithium.[10] Similarly, the mesitylene


(IV)


(V)


(VI)

a; R^1 = Cl, R^2 = Li
b; R^1 = $C_5H_{10}N$, R^2 = Li
c; R^1 = C_4H_8N, R^2 = Li
d; R^1 = NMe_2, R^2 = Li
e; R^1 = $C_5H_{10}N$, R^2 = H
f; R^1 = C_4H_8N, R^2 = H
g; R^1 = NMe_2; R^2 = H
h; R^1 = $C_5H_{10}N$, R^2 = CO_2H

adducts of trichloro-2-pyridyne (Ib) [7] could have been derived from the small proportion of tetrachloro-3-pyridyl-lithium (VIa) present in the mixture of tetrachloropyridyl-lithium compounds.

In view of these considerations, we examined 2-chloro-3-lithiopyridines as potential precursors for 2-pyridynes. In order to avoid the concomitant formation of 3-pyridynes, the presence of a 4-substituent was desirable. We therefore investigated the reactions of some 4-substituted 2,3,5,6-tetrachloropyridines (IIIb—i) with n-butyl-lithium. In the case of 4-dialkylamino-derivatives (IIIb—d) metal–halogen exchange occurred smoothly in diethyl ether at −70° to give solutions of 2,5,6-trichloro-4-dialkylamino-3-lithiopyridines (VIb—d). The identity of these lithium compounds was established by hydrolysis to 2,5,6-trichloro-4-dialkylaminopyridines (VIe—g), and in the case of the piperidino-compound by reaction with carbon dioxide to give 2,5,6-trichloro-4-piperidinopyridine-3-carboxylic acid (VIh). The position at which metallation had taken place was inferred from the ^{1}H n.m.r. spectra of the hydrolysis products. These showed, in addition to the signals due to the amino-substituents, singlets at τ 3·31 (VIe), 3·58 (VIf), and 3·32 (VIg); protons at the 2-position of a pyridine ring give signals below τ 2.[16]

Metallation in the 3-position is probably favoured by co-ordination of the n-butyl-lithium with the amino-substituent, although the contrast between this system and *N*-pentachlorophenylpiperidine, where no metallation adjacent to the piperidino-group is observed,[17] is difficult to account for.

With various 4-substituents other than dialkylamino-groups, reactions involving the substituent occurred in preference to metal–halogen exchange. The substituents tried were hydrogen (IIIe), methyl (IIIf), and nitro-(IIIg); with the 4-methoxy- (IIIh) or 4-phenoxy-compound (IIIi), the action of n-butyl-lithium leads to replacement of the 4-substituent by a butyl group.[18]* With 2,3,5,6-tetrachloropyridine (IIIe), as expected, metal–hydrogen exchange occurred, to give a solution of tetrachloro-4-pyridyl-lithium (IIIa). With 2,3,5,6-tetrachloro-4-methylpyridine (IIIf), the methyl group was metallated, to give a solution of (tetrachloro-4-pyridyl)-methyl-lithium (IIIj), characterised by reaction with carbon dioxide to give (tetrachloro-4-pyridyl)acetic acid (IIIk) and with dimethyl sulphate to give 2,3,5,6-tetrachloro-4-ethylpyridine (IIIl). The tetrachloro-compound (IIIf) behaved like 4-methylpyridine, and not like 2,3,5,6-tetrafluoro-4-methylpyridine, in which the methyl group is not metallated by n-butyl-lithium.[20] It has been reported [21] that *o*-bromonitrobenzenes undergo metal–halogen exchange with n-butyl-lithium at *ca.* −100°, but we were unable to obtain any recognisable products from the reaction of tetrachloro-4-nitropyridine (IIIg) with n-butyl-lithium.

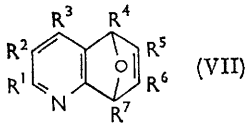
Besides the experiments described here, we are aware of a few others which might have led to precursors of 2-pyridynes. The reaction of tetrachloro-4-mercaptopyridine with n-butyl-lithium (2 mol.) followed by hydrolysis gave various products, including some 2,3,6-trichloro-4-mercaptopyridine,[22] and the reaction of n-butyl-lithium with 2,3,5,6-tetrachloro-4-trimethylsilylpyridine led to products which were probably derived from 5,6-dichloro-4-trimethylsilyl-2-pyridyne *via* 2,5,6-trichloro-4-trimethylsilyl-3-pyridyl-lithium [23] (see later).

The most promising approach to adducts of 2-pyridynes was thus that using 2,3,5,6-tetrachloro-4-dialkylaminopyridines (IIIb—d). Accordingly, the piperidino- (IIIb),

* Since our work was completed, it has been reported [19] that the reaction of 2,3-dibromo-4-ethoxypyridine with lithium amalgam leads to adducts of 4-ethoxy-2-pyridyne, presumably *via* 2-bromo-4-ethoxy-3-pyridyl-lithium.

[14] T. Kauffmann and F.-P. Boettcher, *Chem. Ber.*, 1962, **95**, 1528.
[15] J. A. Zoltewicz and C. L. Smith, *J. Amer. Chem. Soc.*, 1966, **88**, 4766.
[16] R. M. Silverstein and G. C. Bassler, ' Spectrometric Identification of Organic Compounds,' 2nd edn., Wiley, New York, 1967, p. 140.
[17] D. J. Berry, I. Collins, S. M. Roberts, H. Suschitzky, and B. J. Wakefield, *J. Chem. Soc.* (*C*), 1969, 1285.
[18] J. D. Cook and B. J. Wakefield, unpublished work; H. Heaney, personal communication.
[19] H. N. M. van der Lans and H. J. den Hertog, *Rec. Trav. chim.*, 1968, **87**, 549.
[20] R. D. Chambers, B. Iddon, W. K. R. Musgrave, and L. Chadwick, *Tetrahedron*, 1968, **24**, 877.
[21] G. Kobrich and P. Buck, *Angew. Chem.*, 1966, **78**, 1062.
[22] E. Ager and B. Iddon, personal communication.
[23] S. S. Dua and H. Gilman, *J. Organometallic Chem.*, 1968, **12**, 299.

pyrrolidino- (IIIc), and dimethylamino- (IIId) compounds were converted into the 3-lithio-derivatives (VIb—d) by n-butyl-lithium at −70°. Furan was added to the solutions, which were then allowed to warm to room temperature. In each case, the adduct (VIIa—c) of the 5,6-dichloro-4-dialkylamino-2-pyridyne (Ic—e) with



(VII)

a; $R^1 = R^2 = Cl$, $R^3 = C_5H_{10}N$, R^4—$R^7 = H$
b; $R^1 = R^2 = Cl$, $R^3 = C_4H_8N$, R^4—$R^7 = H$
c; $R^1 = R^2 = Cl$, $R^3 = NMe_2$, R^4—$R^7 = H$
d; R^1—$R^7 = H$

furan was obtained. The structures of these adducts were established by their elemental analyses and ^1H n.m.r. spectra (Table).

however its ^1H n.m.r. spectrum (Table) showed it to be 5,8-epoxy-5,8-dihydroquinoline (VIId). It was characterised in the form of its adduct (X) with 2,3-dimethylbuta-1,3-diene, which was solid, and more stable.

It has recently been pointed out [5] (*cf.* refs. 25 and 26) that the formation of adducts with furan may not provide conclusive evidence for aryne intermediates, as addition of furan may precede elimination of, *e.g.*, metal halide. We can also envisage a route from an *o*-halogenoaryl-lithium compound to an adduct, involving removal of the lithium and formation of a bond between the aromatic and furan rings before the halogen is displaced (*cf.* ref. 27). However, the simplest explanation of the results of our experiments, particularly in view of the mild conditions employed, is that 2-pyridynes were involved as intermediates, and that these intermediates, once generated, are normal in their behaviour

TABLE

^1H N.m.r. spectra of adducts of 2-pyridynes [a]

Chemical shift (τ) of signal for proton(s) at position indicated [b]

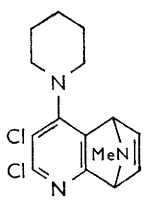
	R^1	R^2	R^3	R^4	R^5, R^6	R^7	R^8
(VIIa)			6·9(4), 8·3(6)	4·65(1)	2·95(2)	4·05(1)	
(VIIb)			6·42(4), 8·06(4)	4·58(1)	2·95(2)	3·88(1)	
(VIIc)			7·02(6)	4·53(1)	2·91(2)	3·89(1)	
(VIII) [c]			6·88(4), 8·32(6)	5·77(1)	3·20(2)	5·19(1)	7·82(3)
(VIId)	2·05(1) [d], 2·15(1) [d]	3·32(1) [e]	2·66(1) [d], 2·79(1) [d]	4·54(1)	3·00(2)	4·37(1)	

[a] 60 MHz. Solutions in carbon tetrachloride unless otherwise stated. [b] Number of protons in parentheses. All signals broadened singlets or unresolved multiplets unless otherwise stated. [c] Groups numbered as in (VII). R^8 = NMe. [d] dd. [e] m.

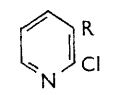
When 1-methylpyrrole was used in place of furan, 2,3,5,6-tetrachloro-4-piperidinopyridine (IIIb) gave 2,3-dichloro-5,8-methylimino-4-piperidino-5,8-dihydroquinoline (VIII), but attempts to prepare adducts of the 2-pyridynes with *p*-di-isopropylbenzene were unsuccessful. This last result was not unexpected, as the ready 1,4-addition of polyhalogenoarynes to monocyclic aromatic hydrocarbons is evidently associated with the presence of strongly electron-withdrawing groups in the aryne,[7b,24] particularly in the positions adjacent to the 'triple bond'; in our case the effect of the chlorine substituents and the pyridine ring nitrogen is opposed by that of the electron-releasing dialkylamino-group.

The fact that derivatives of 2-pyridyne were successfully generated, and behaved normally as dienophiles, encouraged us to attempt to trap 2-pyridyne itself. Accordingly, 3-bromo-2-chloropyridine (IXa) was treated with n-butyl-lithium in diethyl ether at −70°. Hydrolysis of the resulting solution gave a high yield of 2-chloropyridine (IXb), indicating that metal–halogen exchange had produced 2-chloro-3-lithiopyridine (IXc). When furan was added to the cold solution of this lithio-compound, and the solution was allowed to warm to room temperature, the principal product was an unstable oil, which could not be adequately purified;

towards trapping agents. It remains to be determined whether 2-pyridyne is, as predicted, more stable than benzyne or 3-pyridyne.

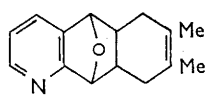


(VIII)

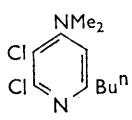


(IX)

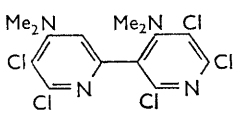
a; R = Br
b; R = H
c; R = Li



(X)



(XI)

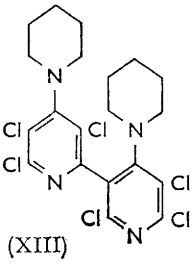


(XII)

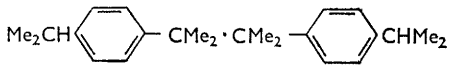
In the preparation of adducts of the 5,6-dichloro-4-dialkylamino-2-pyridynes (Ic—e), we observed small amounts of by-products. These were formed in larger amounts when n-butyl-lithium was added to the tetrachlorodialkylaminopyridines (IIIb—d) at room

[24] R. Harrison and H. Heaney, *J. Chem. Soc.* (*C*), 1968, 889.
[25] K. Rasheed, *Tetrahedron*, 1966, **22**, 2957.
[26] M. D. Rausch, T. R. Criswell, and A. K. Ignatowicz, *J. Organometallic Chem.*, 1968, **13**, 419.
[27] H. Gilman and R. D. Gorsich, *J. Amer. Chem. Soc.*, 1957, **79**, 2625.

temperature, or if solutions of the trichlorolithio-compounds (VIb—d) were warmed in the absence of furan. The compounds derived from 2,3,5,6-tetrachloro-4-dimethylaminopyridine (VId) were shown to be 2-butyl-5,6-dichloro-4-dimethylaminopyridine (XI) and 2′,5,5′,6,6′-pentachloro-4,4′-bisdimethylamino-2,3′-bipyridyl (XII); their structures were deduced from their elemental analyses, mass spectra, and ^{1}H n.m.r. spectra. They evidently arise from addition of organolithium compounds to the 2-pyridyne (Ie), n-butyllithium leading to (XI), and 2,5,6-trichloro-4-dimethylamino-3-pyridyl-lithium leading to (XII). The aromatic ^{1}H n.m.r. signals in these compounds [τ 3·85 (XI) and 2·91 (XII)] indicate the presence of protons in the 3-position, and thus that the addition has occurred in the direction shown. This might be simply explained in terms of attack by the carbanion at the comparatively electron-deficient C-2, although considerations applying to attack on a pyridine do not necessarily apply to a pyridyne (*cf.* ref. 4, p. 133 and ref. 3, p. 556). In view of our results, it seems likely that a compound obtained by Dua and Gilman [23] from the reaction of n-butyllithium with 2,3,5,6-tetrachloro-4-trimethylsilylpyridine is 2-butyl-5,6-dichloro-4-trimethylsilylpyridine. A product obtained in low yield from the attempted preparation of the adduct of the piperidinopyridyne (Ic) with *p*-di-isopropylbenzene proved to be a hexachlorodipiperidinopyridine, as indicated by elemental analysis, ^{1}H n.m.r., and mass spectroscopy. The orientation of the substituents in this product is uncertain, but nucleophilic substitution of 2,3,5,6-tetrachloro-4-piperidinopyridine (IIIb) by 2,5,6-trichloro-4-piperidino-3-



(XIII)



(XIV)

pyridyl-lithium (VIb) might be expected to give 2′,3,5,5′,6,6′-hexachloro-4,4′-dipiperidino-2,3′-bipyridyl (XIII). Another by-product from this reaction was 1,2-bis-(*p*-isopropylphenyl)-1,1,2,2-tetramethylethane (XIV), presumably formed by some reaction involving hydrogen abstraction from the solvent. Its structure was apparent from its ^{1}H n.m.r. spectrum: τ 2·83 (m, 8H, aromatic), 7·13 (heptet, 2H, Me_2CH), 8·51 (s, 12H, Me), and 8·79 (d, 12H, Me_2CH), but it was unstable, and in a moist atmosphere was converted into *p*-isopropylphenol.

EXPERIMENTAL

Mass spectra were obtained with an A.E.I. MS 12 instrument, and ^{1}H n.m.r. spectra with a Varian A 60 instrument, with tetramethylsilane as internal standard. n-Butyl-lithium was used in the form of a commercially available solution in hexane (Pfizer).

4-Substituted Tetrachloropyridines.— (*a*) 2,3,5,6-Tetrachloro-4-piperidinopyridine and 2,3,5,6-tetrachloro-4-pyrrolidinopyridine were prepared as described by Roberts and Suschitzky.[28]

(*b*) 2,3,5,6-*Tetrachloro-4-dimethylaminopyridine*. To a mixture [28b] of 2,3,5,6-tetrachloro-4-methylaminopyridine and 2,3,4,5-tetrachloro-6-methylaminopyridine (4·0 g.) in diethyl ether (200 ml.) at −75° was added n-butyl-lithium solution (8·15 ml.). The mixture was stirred at −75° for 45 min., allowed to warm to room temperature during 1 hr., stirred for 30 min., and cooled to −75°. Dimethyl sulphate (2·05 g.) was added, and the solution was stirred at −75° for 10 min. and at room temperature for 5 hr. Following hydrolysis and work-up, the product was subjected to chromatography on silica, to yield the 4-dimethylamino-compound (1·3 g.), m.p. 90—92° (lit.,[28b] 92°), the 2-dimethylamino-compound (1·05 g.), and starting material (1·1 g.).

(*c*) 2,3,5,6-Tetrachloropyridine was prepared by hydrolysis of tetrachloro-4-pyridylmagnesium chloride.[13b]

(*d*) 2,3,5,6-*Tetrachloro-4-methylpyridine*. To a solution of tetrachloro-4-pyridyl-lithium [from pentachloropyridine (5·0 g.) [13b]] at −75° was rapidly added dimethyl sulphate (25 ml.). The solution was stirred for 10 min. at −75°. Following hydrolysis with conc. ammonium hydroxide, the product was isolated and purified by chromatography on alumina to yield 2,3,5,6-*tetrachloro-4-methylpyridine* (2·97 g., 64%), m.p. 82—83°, unchanged on recrystallisation from aqueous ethanol; τ 7·40 (s) (Found: C, 31·2; H, 1·4; N, 6·2. $C_6H_3Cl_4N$ requires C, 31·2; H, 1·3; N, 6·2%).

(*e*) Tetrachloro-4-nitropyridine was prepared by oxidising the 4-nitroso-compound with peroxytrifluoroacetic acid.[28c]

Reactions of 4-Substituted Tetrachloropyridines with n-Butyl-lithium.—(a) *General procedure*. To the pyridine derivative (1·0 g.) in diethyl ether (100 ml.) at −75° was added with stirring n-butyl-lithium (1·1 equiv.), and the solution was stirred at −75° for 10 min. before being treated as described in the following.

(b) *With tetrachloro-4-piperidinopyridine*. The solution, prepared as in (a), was stirred and allowed to warm to room temperature during 1 hr., hydrolysed with water (50 ml.), and worked up by conventional methods to yield 2,3,5-*trichloro-4-piperidinopyridine* (57%), m.p. 37—38°, τ 3·31 (1H, s), 6·32br (4H, s), and 8·32br (6H, s) (Found: C, 45·2; H, 4·1. $C_{10}H_{11}Cl_3N_2$ requires C, 45·65; H, 4·1%).

When carbon dioxide was passed into the solution, prepared as described in (a), as it warmed to room temperature and then for a further 2½ hr., and the solution was hydrolysed, and worked up *via* extraction with alkali, followed by reprecipitation with acid, the product was 2,5,6-*trichloro-4-piperidinopyridine-3-carboxylic acid* (31%), decomp. *ca.* 200°. The compound was further purified by repeated dissolution in aqueous potassium hydrogen carbonate, followed by reprecipitation with acid [Found: C, 43·0; H, 3·8%; *M* (mass spectrum), 308. $C_{11}H_{11}Cl_3N_2O_2$ requires C, 42·6; H, 3·6%; *M*, 308].

(c) *With tetrachloro-4-pyrrolidinopyridine*. The solution, prepared as in (a), was hydrolysed as in (b), to give 2,3,6-*trichloro-4-pyrrolidinopyridine* (39%), m.p. 118—119°, τ 3·58 (1H, s), 6·40 (4H, m), and 8·00 (4H, m) (Found: C, 43·4; H, 3·7. $C_9H_9Cl_3N_2$ requires C, 42·9; H, 3·6%).

(d) *With tetrachloro-4-dimethylaminopyridine*. The re-

[28] (*a*) S. M. Roberts and H. Suschitzky, *Chem. Comm.*, 1967, 893; (*b*) S. M. Roberts and H. Suschitzky, *J. Chem. Soc.* (*C*), 1968, 1537; (*c*) S. M. Roberts and H. Suschitzky, *ibid.*, p. 2844.

action and hydrolysis were carried out as in (c), to yield 2,3,6-*trichloro*-4-*dimethylaminopyridine* (45%), m.p. 107—108°, τ 3·32 (1H, s) and 7·00 (6H, s) [Found: C, 37·6; H, 3·3%; *M* (mass spec.) 223. $C_7H_7Cl_3N_2$ requires C, 37·25; H, 3·1%; *M* 223] and 2′,5,5′,6,6′-*pentachloro*-4,4′-*bisdimethylamino*-2,3′-*bipyridyl* (5·7%), m.p. 118—120°, τ 2·91 (1H, s), 7·32 (6H, s), and 7·40 (6H, s) (Found: C, 40·3; H, 3·25. $C_{14}H_{13}Cl_5N_4$ requires C,40·6; H, 3·1%).

When the n-butyl-lithium was added to the solution at room temperature, the main product (59%) was 2-*butyl*-5,6-*dichloro*-4-*dimethylaminopyridine*, m.p. 48—50°, τ 3·85 (1H, s), 6·95 (6H, s), 8·5 (2H, m), 8·7 (4H, m), and 9·02 (3H, t) [Found: C, 51·2; H, 6·1; N, 11·05%; *M* (mass spec.) 246. $C_{11}H_{16}Cl_2N_2$ requires C, 53·4; H, 6·45; N, 11·3%; *M* 246].

(e) *With* 2,3,5,6-*tetrachloropyridine*. Reaction and hydrolysis as described in (a) and (b) gave starting material (76%).

(f) *With* 2,3,5,6-*tetrachloro*-4-*methylpyridine*. Reaction and hydrolysis as described in (a) and (b) gave starting material (66%).

When a solution, prepared as described in (a), was allowed to warm to room temperature, re-cooled to −70°, and treated with dimethyl sulphate (1 mol.), the product after hydrolysis as in (b) and purification by sublimation was 2,3,5,6-tetrachloro-4-ethylpyridine (47%), m.p. 47—49° (lit.,[23] 74—75°), τ 6·94 (2H, q) and 8·76 (3H, t) (Found: C, 34·45; H, 2·4; N, 5·6. Calc. for $C_7H_5Cl_4N$: C, 34·3; H, 2·1; N, 5·7%).

A solution, prepared as described in (a), was allowed to warm to room temperature, then re-cooled to −70°, and a stream of dry carbon dioxide was passed in as the solution warmed to room temperature and for a further 2½ hr. Water (50 ml.) and 2N-sodium hydroxide (50 ml.) were added, with stirring. Acidification of the aqueous layer, followed by extraction with ether, and purification by dissolution in sodium hydrogen carbonate solution followed by re-precipitation with acid, gave 2,3,5,6-tetrachloro-4-pyridylacetic acid (73%), m.p. 182·5—183° (from light petroleum–benzene) (lit.,[29] 178—180°), τ −0·14 (1H, s) and 5·82 (2H, s) (Found: C, 30·55; H, 0·9; N, 5·4. Calc. for $C_7H_3Cl_4NO_2$: C, 30·55; H, 1·1; N, 5·1%).

Adducts of 5,6-*Dichloro*-4-*dialkylamino*-2-*pyridynes*.—(a) *With furan*. Solutions of 2,5,6-trichloro-4-dialkylamino-3-pyridyl-lithium compounds were prepared as already described above in diethyl ether at −70°. Equal volumes of furan were added at −70°, and the solutions were allowed to warm to room temperature, heated under reflux for 6 hr., and hydrolysed with water. The products were recovered by conventional procedures, and separated by chromatography on silica; light petroleum (b.p. 40—60°) eluted starting materials, 1 : 1 chloroform–light petroleum eluted the trichlorodialkylamino-compounds, and chloroform eluted the adducts. By this procedure, tetrachloro-4-piperidinopyridine gave a trace of the trichloro-compound and 2,3-*dichloro*-5,8-*epoxy*-4-*piperidino*-5,8-*dihydroquinoline* (50%), m.p. 117—118° (Found: C, 56·7; H, 4·6; Cl, 23·8; N, 9·3. $C_{14}H_{14}Cl_2N_2O$ requires C, 56·6; H, 4·7; C., 23·9; N, 9·4%).

Similarly, tetrachloro-4-pyrrolidinopyridine gave the trichloro-compound (17%) and 2,3-*dichloro*-5,8-*epoxy*-4-*pyrrolidino*-5,8-*dihydroquinoline* (22%), m.p. 138—139° (Found: C, 54·7; H, 4·5. $C_{13}H_{12}Cl_2N_2O$ requires C, 55·1; H, 4·2%).

Tetrachloro-4-dimethylaminopyridine gave traces of the trichloro-compound and bipyridyls, and 2,3-*dichloro*-4-*dimethylamino*-5,8-*epoxy*-5,8-*dihydroquinoline* (43%), m.p. 104—106° (Found: C, 51·45; H, 3·5; Cl, 27·8; N, 10·8. $C_{11}H_{10}Cl_2N_2O$ requires C, 51·3; H, 3·9; Cl, 27·6; N, 10·9%).

(b) *With* N-*methylpyrrole*. Procedure (a), with *N*-methylpyrrole in place of furan, converted tetrahydro-4-piperidinopyridine into the trichloro-compound (42%) and 2,3-*dichloro*-5,8-*methylimino*-4-*piperidino*-5,8-*dihydroquinoline* (18%), m.p. 114—115° (Found: C, 57·85; H, 5·6; N, 13·1. $C_{15}H_{15}Cl_2N_3$ requires C, 58·1; H, 5·5; N, 13·55%).

Reaction of n-Butyl-lithium with Tetrachloro-4-*piperidinopyridine in* p-*Di-isopropylbenzene*.—To a solution of 2,5,6-trichloro-4-piperidino-3-pyridyl-lithium, from tetrachloro-4-piperidinopyridine (3·2 g.), in diethyl ether (100 ml.) was added *p*-di-isopropylbenzene (100 ml.). Most of the ether was distilled off, and the residue was heated under reflux at 160° for 5 hr. Following hydrolysis with water (50 ml.), the mixture of products was isolated by conventional means, and separated into its components by chromatography on silica. Light petroleum (b.p. 60—80°) eluted tri- and tetra-chloropiperidinopyridines and *p*-di-isopropylbenzene, and benzene–light petroleum (1 : 4) eluted 2′,3,5,5′,6,6′-*hexachloro*-4,4′-*dipiperidino*-2,3′-*bipyridyl* (0·16 g., 2·9%), m.p. 152—153°, τ 7·07 (8H, m) and 8·61 (12H, m) [Found: C, 45·1; H, 4·0%; *M* (mass spectrum), 525. $C_{20}H_{20}Cl_6N_4$ requires C, 45·4; H, 3·8%; *M*, 525]. The recovered *p*-di-isopropylbenzene was chromatographed on silica; light petroleum eluted *p*-di-isopropylbenzene, and chloroform eluted an oil (4·2 g.) formulated as 1,2-bis-(*p*-isopropylphenyl)-1,1,2,2-tetramethylethane. Attempts to purify this compound were unsuccessful; after it had been exposed to the atmosphere for some days, sublimation gave *p*-isopropylphenol, m.p. 60·5—61° (lit.,[30] 61°), τ (CCl_4) 3·19 (4H, m), 4·16 (1H, s, removed on addition of D_2O), 7·19 (1H, heptet), and 8·82 (6H, d).

3-*Bromo*-2-*chloropyridine*.—To 3-amino-2-chloropyridine (1·00 g.) in 45% hydrobromic acid (20 ml.) at −15° was added sodium nitrite (0·7 g.) in water (2 ml.), the temperature being kept below −10°. A solution of cuprous bromide (1·0 g.) in 45% hydrobromic acid (10 ml.) was added slowly, the temperature being maintained at −20 to −10°. The solution was made alkaline with 4N-sodium hydroxide, and the product was obtained *via* ether extraction and purified by chromatography, to give 3-bromo-2-chloropyridine (1·46 g., 97%), m.p. 54° (lit.,[31] m.p. 55·5—56·5°).

Reactions of 2-*Chloro*-3-*pyridyl-lithium*.—(a) *Hydrolysis*. n-Butyl-lithium solution (2·5 ml.) was added to 3-bromo-2-chloropyridine (1·0 g.) in diethyl ether (120 ml.) at −75°. The solution was stirred at −75° for 2 hr., water (50 ml.) was added, and the product (0·35 g., 52%) was isolated from the ether layer and shown to be identical (i.r., ^1H n.m.r., and g.l.c.) with an authentic specimen of 2-chloropyridine.

(b) *Generations of* 2-*pyridyne*. To a solution of 2-chloro-3-pyridyl-lithium [prepared as in (a), from 3-bromo-2-chloropyridine (1·50 g.)] in diethyl ether (100 ml.) at −75° was added furan (20 ml.). The mixture was stirred at −75° for 30 min. and at room temperature for 3 hr. Water (50 ml.) was added, and the product was isolated, and

[29] A. Roedig and K. Grohe *Chem Ber.*, 1965, **98**, 923.

[30] 'Handbook of Chemistry and Physics,' Chemical Rubber Publishing Co.

[31] H. J. den Hertog and N. A. I. M. Boelrijk, *Rec. Trav. chim.*, 1951, **70**, 578.

purified by chromatography on silica (chloroform eluant) to give 5,8-epoxy-5,8-dihydroquinoline (0·36 g., 31%), as an oil, which rapidly darkened and gradually became viscous.

The adduct (0·7 g.), prepared as already described, was dissolved in xylene (10 ml.), and 2,3-dimethylbuta-1,3-diene (5 ml.) was added, together with a trace of hydroquinone. The mixture was heated under reflux for 16 hr., and the solvents were removed *in vacuo*. Chromatography of the residue on silica (chloroform eluant), followed by vacuum sublimation, gave 1-*aza*-9,10-*epoxy*-6,7-*dimethyl*-5,8,8a,9,10,10a-*hexahydroanthracene* (0·66 g., 60%), m.p. 103—104°, as pale yellow crystals, which slowly darkened; τ ($CDCl_3$) 1·77 (1H, dd, H-2), 2·54 (1H, dd, H-4), 3·02 (1H, q, H-3), 4·99 (1H, s, H-9), 5·01 (1H, s, H-10), 7·85 (6H, m, H-5, -8, -8a, and -10a), and 8·30 (6H, s, Me) [Found: *M* (mass spectrum), 227·1311. $C_{15}H_{17}NO$ requires *M*, 227·1310].

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