

Polyhalogenoaromatic Compounds. Pa_{Coc}XXIII.¹ Synthesis and Reactions of Heptachloro-3-lithio-4,4'-bipyridyl²

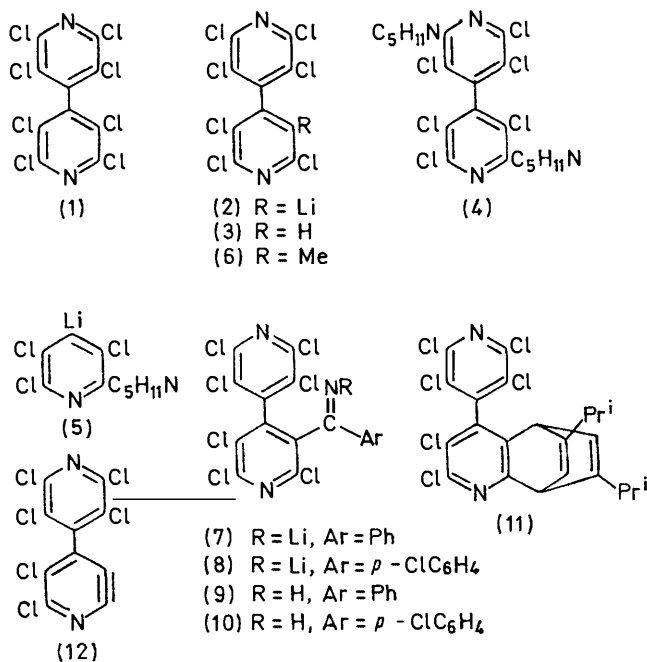
By J. D. Cook, N. J. Foulger, and B. J. Wakefield,* Department of Chemistry and Applied Chemistry, University of Salford, Salford M5 4WT

Metal-halogen exchange between *n*-butyl-lithium and octachloro-4,4'-bipyridyl gave heptachloro-3-lithio-4,4'-bipyridyl, whereas nucleophilic substitution of the bipyridyl by piperidine took place at the 2- and 2'-positions. The reactions of the 3-lithio-compound with water, dimethyl sulphate, and aromatic nitriles gave the expected products. On heating in the presence of *p*-di-isopropylbenzene the 3-lithio-compound gave an adduct of 5,6-dichloro-4-(tetrachloro-4-pyridyl)-2-pyridyne.

PREVIOUS studies have shown that many tetrachloro-4-pyridyl derivatives undergo metal-halogen exchange reactions with *n*-butyl-lithium (or *t*-butyl-lithium). With most substituents (dialkylamino,² alkoxy,³ aryl⁴), the exchange occurred exclusively at the 3-position. Only in the cases of the 4-thiolate⁵ and the 4-phenolate⁶ was any exchange at the 2-position observed. The behaviour of the tetrachloro-4-pyridyl derivatives was thus anomalous, since in a variety of other systems, exchange occurred at the position(s) most susceptible to nucleophilic substitution (see ref. 7 for discussion and references). In all the tetrachloro-4-pyridyl derivatives so far examined, the substituents are potentially capable of co-ordinating with the organolithium reagent, and thus diverting its attack into the 3-position. We have therefore examined a compound, *viz.* octachloro-4,4'-bipyridyl (1), where the 4-substituent (tetrachloro-4-pyridyl), although it possesses a π -system, is strongly electron-withdrawing, and unlikely to co-ordinate with the reagent.

The starting material (1) is obtainable by the reaction of tetrachloro-4-pyridyl-lithium with titanium tetrachloride⁶ and by vapour-phase chlorination of 4,4'-bipyridyl.⁸ On treatment with *n*-butyl-lithium in diethyl ether at -75° , followed by warming to room temperature, it gave heptachloro-3-lithio-4,4'-bipyridyl (2), whose identity was confirmed by hydrolysis to 3*H*-heptachloro-4,4'-bipyridyl (3). The location of the hydrogen atom was established by the n.m.r. spectrum [τ 2.9(s) (*cf.* ref. 9)]. Apparently co-ordination by the substituent does not determine the orientation of metal-halogen exchange in tetrachloro-4-pyridyl derivatives, and another explanation must be sought. In order to eliminate the possibility that the strongly electron-withdrawing tetrachloro-4-pyridyl group might promote nucleophilic substitution at the 3- rather than at the 2-positions, we examined the reaction of octachloro-4,4'-bipyridyl with piperidine. Under conditions similar to those used for the analogous reaction with

pentachloropyridine,¹⁰ the product was 2,2',3,3',5,5'-hexachloro-6,6'-dipiperidino-4,4'-bipyridyl (4), identical with the compound obtained from the reaction of



2,3,5-trichloro-4-lithio-6-piperidinopyridine⁷ (5) with titanium tetrachloride.

Heptachloro-3-lithio-4,4'-bipyridyl reacted with dimethyl sulphate to give the 3-methyl derivative (6). On treatment with benzonitrile and *p*-chlorobenzonitrile it gave the adducts, (7) and (8), respectively, which on hydrolysis gave the imines (9) and (10). Attempts to cause the adduct (7) to cyclise by nucleophilic attack at the 3'-position were unsuccessful, probably because the energy needed to force the pyridine rings into coplanarity is higher than that needed to reverse the addition of

¹ Part XXII, E. Ager, B. Iddon, and H. Suschitzky, *J.C.S. Perkin I*, 1972, 133.

² J. D. Cook and B. J. Wakefield, *J. Chem. Soc. (C)*, 1969, 1973.

³ R. A. Fernandez, H. Heaney, J. M. Jablonski, K. G. Mason, and T. J. Ward, *J. Chem. Soc. (C)*, 1969, 1908.

⁴ J. D. Cook and B. J. Wakefield, *J. Chem. Soc. (C)*, 1969, 2376.

⁵ E. Ager, B. Iddon, and H. Suschitzky, *J. Chem. Soc. (C)*, 1970, 193.

⁶ J. D. Cook, unpublished observations.

⁷ D. J. Berry, B. J. Wakefield, and J. D. Cook, *J. Chem. Soc. (C)*, 1971, 1227.

⁸ R. D. Bowden and M. B. Green, I.C.I. Ltd., Mond Division, personal communication.

⁹ J. D. Cook and B. J. Wakefield, *J. Organometallic Chem.*, 1968, 13, 15.

¹⁰ S. M. Roberts and H. Suschitzky, *J. Chem. Soc. (C)*, 1968, 1537.

benzotrile (*cf.* ref. 11). We were also unable to observe any addition of a second molar equivalent of benzotrile when an excess of this reactant was used.

When the 3-lithio-compound (2) was heated in the presence of *p*-di-isopropylbenzene, the adduct (11) of the 2-pyridyne (12) was obtained. Adducts of 2-pyridynes with furan and with *N*-methylpyrrole have been reported,^{2,3,12} but compound (12) is the first such adduct with an aromatic hydrocarbon to be isolated.* Its formation provides further evidence for 2-pyridynes as *echt*, rather than *ersatz*¹⁴ arynes.

EXPERIMENTAL

n-Butyl-lithium was used as a 2—3M-solution in hexane. All experiments involving organometallic reagents were carried out in anhydrous conditions under dry, oxygen-free nitrogen. Octachloro-4,4'-bipyridyl, prepared from tetrachloro-4-pyridyl-lithium⁶ or donated by Imperial Chemical Industries Ltd.,⁸ had m.p. 218—220° and showed no ¹H n.m.r. signal. ¹H N.m.r. spectra were recorded at 60 MHz with tetramethylsilane as internal reference. Calculated *m/e* values for molecular ions are based on ³⁵Cl.

Heptachloro-3-lithio-4,4'-bipyridyl (2).—To a stirred suspension of octachloro-4,4'-bipyridyl (1) (0.50 g) in diethyl ether (50 ml) at -75° was added a solution of *n*-butyl-lithium (1.3 mmol). The mixture was stirred at -75° during 30 min and at room temperature during 30 min.

Reactions of Heptachloro-3-lithio-4,4'-bipyridyl.—(a) *With water*. To a solution of the lithio-compound, prepared as just described, was added water (50 ml). Conventional work-up, followed by chromatography on silica (eluant 1 : 4 benzene-light petroleum) and recrystallisation from light petroleum gave 3H-heptachloro-4,4'-bipyridyl (3) (0.32 g, 70%), m.p. 171—172°, τ (CDCl₃) 2.9(s) (Found: C, 29.85; H, 0.45; N, 6.85%; *M*⁺, 394. C₁₀HCl₇N₂ requires C, 30.2; H, 0.25; N, 7.05%; *M*, 394).

(b) *With dimethyl sulphate*. To a solution of the lithio-compound [from octachloro-4,4'-bipyridyl (1.5 g)] at -75° was added dimethyl sulphate (5 ml). The solution was stirred during 30 min at -75° and 4 h at room temperature. Concentrated ammonia solution (50 ml) was added. Work-up as before gave 2,2',3,3',5,6,6'-tetrachloro-5'-methyl-4,4'-bipyridyl (6) (1.1 g, 77%), m.p. 224—225°, τ (CDCl₃) 7.85(s) (Found: C, 32.45; H, 0.85; N, 6.75%; *M*⁺, 408. C₁₁H₃Cl₄N₂ requires C, 32.1; H, 0.75; N, 6.8%; *M*, 408).

(c) *With benzotrile and p-chlorobenzotrile*. To a solution of the lithio-compound [from octachloro-4,4'-bipyridyl (3.0 g)] at -20° was added a solution of benzotrile (0.7 g) in diethyl ether (50 ml). The mixture was stirred at room temperature during 1 h, and water (50 ml) was added. Conventional work-up, followed by chromatography on silica (eluant chloroform) and recrystallisation

* When heated in the presence of mesitylene, a mixture of 2-, 3-, and 4-lithiotetrachloropyridine gives a mixture of products, one of which is probably an adduct of trichloro-2-pyridyne.¹³

¹¹ D. J. Berry and B. J. Wakefield, *J. Organometallic Chem.*, 1970, **23**, 1.

from benzene-light petroleum gave 3-benzimidoylheptachloro-4,4'-bipyridyl (9) (2.2 g, 62%), m.p. 182—184°, ν_{\max} 3280 (N-H str.) and 1620 (C=N str.) cm⁻¹, τ 0.0br (1H, NH) and 2.6br (5H, Ph) (Found: C, 41.1; H, 1.3; N, 8.6. C₁₇H₆Cl₇N₃ requires C, 40.8; H, 1.2; N, 8.4%).

A similar experiment with *p*-chlorobenzotrile gave the analogous *p*-chlorobenzimidoyl derivative (10) (56%), m.p. 194—196° (Found: C, 38.3; H, 1.2; N, 7.8. C₁₇H₅Cl₃N₃ requires C, 38.1; H, 0.9; N, 7.85%).

In attempts to obtain cyclised products or the addition of a second molar equivalent of benzotrile, solutions of the lithium imide were heated under reflux in diethyl ether, in tetrahydrofuran, and in dimethylformamide, and in the presence of an excess of benzotrile.

(d) *Decomposition in the presence of p-di-isopropylbenzene*. To a solution of the lithio-compound [from octachloro-4,4'-bipyridyl (1.2 g)] in diethyl ether (70 ml) was added *p*-di-isopropylbenzene (50 ml). Most of the ether was distilled off and the solution was heated under reflux for 4 h. Following hydrolysis with water and conventional work-up, chromatography on silica (eluant 1 : 4 benzene-light petroleum) gave 2,3-dichloro-5,8-dihydro-6,9-di-isopropyl-4-(2,3,5,6-tetrachloro-4-pyridyl)-5,8-ethenoquinoline (11) (0.31 g, 21%), as an oil, τ (CCl₄) 3.67 (2H, t), 5.25 (1H, dd), 6.08 (1H, dd), 7.56 (2H, m), and 9.00 (12H, m) (Found: C, 49.3; H, 3.3; N, 5.4%; *M*⁺, 520. C₂₂H₁₈Cl₂N₂ requires C, 50.5; H, 3.35; N, 5.35%; *M*⁺, 520).

2,2',3,3',5,5',6,6'-Hexachloro-6,6'-dipiperidino-4,4'-bipyridyl (4).—(a) Octachloro-4,4'-bipyridyl (7.5 g), piperidine (6.4 g), and dry benzene (200 ml) were heated under reflux during 5 h. Evaporation of the solvent and recrystallisation of the residue from ethanol gave the bipyridyl (4.5 g, 49%), m.p. 155—157° (Found: C, 45.5; H, 3.85; N, 10.55. C₂₀H₂₂Cl₆N₄ requires C, 45.4; H, 3.8; N, 10.6%).

(b) A solution of *n*-butyl-lithium (26 mmol) was added to a solution of 2,3,4,5-tetrachloro-6-piperidinopyridine (8.0 g) in diethyl ether (300 ml) at -70°. The solution was stirred at -70° during 15 min and at room temperature during 90 min, and then re-cooled to -70°. Titanium(IV) chloride (15 ml) was added, and the mixture was stirred at room temperature during 2 h and under reflux during 2.5 h. The crude product, obtained after hydrolysis with water and conventional work-up, was triturated with light petroleum. Chromatography of the solution on silica gave the bipyridyl (0.80 g), identical (*i.r.* spectrum; mixed m.p.) with the compound described in (a).

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¹² H. N. M. van der Lans and H. J. den Hertog, *Rec. Trav. chim.*, 1968, **87**, 549.

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¹⁴ M. G. Reinecke and H. W. Adickes, *J. Amer. Chem. Soc.* 1968, **90**, 511.