

Aryne Chemistry. Part XIII.¹ Polychloroaromatic Compounds. Part III.² The Generation and Reactions of Trichloropyridynes³†

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Trichloro-3-pyridyne was generated by the elimination of lithium chloride from tetrachloro-4-pyridyl-lithium, and trapped in the form of 1,4-adducts with benzene, *p*-xylene, *p*-di-isopropylbenzene, mesitylene, and 1,2,4,5-tetramethylbenzene. Polar and steric factors affecting the addition reactions are discussed. The action of furan on tetrachloro-4-pyridyl-lithium gave polychlorobipyridyls, but with 1,3-diphenylisobenzofuran, the expected adduct was obtained.

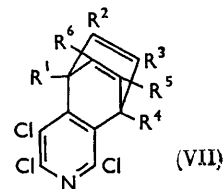
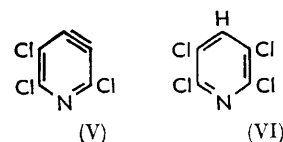
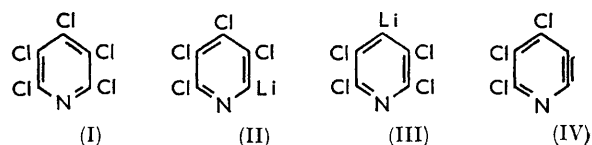
A mixture containing two isomeric adducts of trichloro-2-pyridyne was obtained when *n*-butyl-lithium and pentachloropyridine were heated in the presence of mesitylene.

Tetrafluorobenzene⁴ and tetrachlorobenzene^{1,5} have aroused considerable interest because of their exceptionally high reactivity towards aromatic hydrocarbons. These intermediates give 1,4-adducts even with monocyclic arenes, including benzene itself. The tetrahalogenobenzene intermediates are conveniently generated by thermal elimination of metal halide from the appropriate pentahalogenophenyl-lithium compound or pentahalogenophenylmagnesium bromide. Our discovery^{2,6} that solutions of tetrachloropyridyl-lithium compounds may be readily prepared by the reaction of *n*-butyl-lithium with pentachloropyridine suggested that trichloropyridynes could be generated from these lithium compounds, although a reported attempt to generate trifluoro-3-pyridyne from tetrafluoro-4-pyridylmagnesium bromide was unsuccessful.⁷

We have demonstrated^{2,6} that the reaction of *n*-butyl-lithium with pentachloropyridine (I) in a hydrocarbon solvent yields mainly tetrachloro-2-pyridyl-lithium (II), whereas in diethyl ether the main product is tetrachloro-4-pyridyl-lithium (III). Thus, in principle, both trichloro-2-pyridyne (IV) and trichloro-3-pyridyne (V) could be generated, by elimination of lithium chloride from the lithium compounds (II) and (III), respectively. In practice, the trichloro-3-pyridyne (V) could be readily generated and trapped, but our attempts to trap the trichloro-2-pyridyne (IV) have met with only limited success.

Tetrachloro-4-pyridyl-lithium eliminated lithium chloride only slowly at room temperature, and even after being heated in benzene for 30 min. gave largely 2,3,5,6-tetrachloropyridine (VI) on hydrolysis. However, when

heated for a long time in a series of aromatic hydrocarbon solvents, the compounds formed by 1,4-addition



- a; $R^1 = R^2 = R^3 = R^4 = R^5 = R^6 = H$
 b; $R^1 = R^3 = R^4 = R^6 = H, R^2 = R^5 = Me$
 c; $R^1 = R^3 = R^4 = R^6 = H, R^2 = R^5 = Pr^i$
 d; $R^1 = R^3 = R^5 = H, R^2 = R^4 = R^6 = Me$
 e; $R^1 = R^4 = H, R^2 = R^3 = R^5 = R^6 = Me$
 f; $R^1 = R^4 = Me, R^2 = R^3 = R^5 = R^6 = H$
 g; $R^1 = R^4 = Pr^i, R^2 = R^3 = R^5 = R^6 = H$
 h; $R^1 = R^2 = R^4 = R^6 = Me, R^3 = R^5 = H$
 i; $R^1 = R^3 = R^5 = Me, R^2 = R^4 = R^6 = H$

of the pyridyne (V) to the hydrocarbons were obtained. The structures of the adducts (VIIa—e) formed from benzene, *p*-xylene, *p*-di-isopropylbenzene, mesitylene,

† The referees have pointed out that it is conceivable, though unlikely, that the adducts described in the paper are derived from trichloro-2,3-pyridyne, rather than from trichloro-3,4-pyridyne. However, the fact that identical adducts are obtained in 8% yield (with *p*-di-isopropylbenzene) and 17% yield [with 1,2,4,5-tetra(—)methylbenzene] from tetrachloro-4-pyridylmagnesium chloride (contaminated with less than 1% of isomeric Grignard reagents²), proves that the structures assigned are correct.

¹ Part XII, H. Heaney and J. M. Jablonski, *J. Chem. Soc. (C)*, 1968, 1895.

² Part II, J. D. Cook and B. J. Wakefield, *J. Organometallic Chem.*, 1968, 13, 15.

³ Preliminary account, J. D. Cook and B. J. Wakefield, *Tetrahedron Letters*, 1967, 2535.

⁴ (a) J. P. N. Brewer and H. Heaney, *Tetrahedron Letters*, 1965, 4709; (b) D. D. Callander, P. L. Coe, and J. C. Tatlow, *Chem. Comm.*, 1966, 143; (c) J. P. N. Brewer, I. F. Eckhard, H. Heaney, and B. A. Marples, *J. Chem. Soc. (C)*, 1968, 664; (d) T. D. Petrova, T. I. Savchenko, and G. G. Yakobson, *Zhur. obshechi. Khim.*, 1967, 37, 1170; (e) I. N. Vorozhtsov, N. G. Ivanova, and V. A. Barkhash, *Izvest. Akad. Nauk, S.S.S.R., Ser. khim.*, 1967, 1514; (f) S. C. Cohen, D. E. Fenton, A. J. Tomlinson, and A. J. Massey, *J. Organometallic Chem.*, 1966, 6, 301; (g) J. L. W. Pohlmann and F. E. Brinckman, *Z. Naturforsch.*, 1965, 20b, 5.

⁵ H. Heaney and J. M. Jablonski, *Tetrahedron Letters*, 1966, 4529.

⁶ J. D. Cook, B. J. Wakefield, and C. J. Clayton, *Chem. Comm.*, 1967, 150.

⁷ R. D. Chambers, F. G. Drakesmith, J. Hutchinson, and W. K. R. Musgrave, *Tetrahedron Letters*, 1967, 1705.

and 1,2,4,5-tetramethylbenzene were established from their elemental analyses and ^1H n.m.r. spectra (see below and Table).

^1H N.m.r. spectra of adducts (VII) of trichloro-3-pyridyne (V) (CDCl_3 solution; 60 MHz)

	τ	Number of protons	Multiplicity	Assignment
(VIIa)	3.05	4	m	$\text{R}^2, \text{R}^3, \text{R}^5, \text{R}^6$
	4.61	2	m	R^1, R^4
(VIIb)	3.65	2	m	R^3, R^6
	5.15	2	m	R^1, R^4
	8.05	6	d	R^2, R^5 (Me)
(VIIC)	3.72	2	m	R^3, R^6
	5.01	2	m	R^1, R^4
	7.52	2	m	R^2, R^5 (Pr^i)
	8.96	12	d	R^2, R^5 (Pr^i)
(VIId)	3.97	2	qi *	R^3, R^6
	5.36	1	t	R^1
	7.87	3	s	R^4 (Me)
	8.03	6	d	R^2, R^5 (Me)
				(Me)
(VIIe)	5.34	1	s	R^1
	5.49	1	s	R^4
	8.19	12	s	$\text{R}^2, \text{R}^3, \text{R}^5, \text{R}^6$

* Quintet.

The spectrum of the benzene adduct was complex, and could not be completely analysed. However, the positions and intensities of the two multiplets were clearly consistent with the formulation of the adduct as 1,3,4-trichloro-5,8-dihydro-5,8-ethenoisquinoline (VIIa). The spectrum was further elucidated by a triple irradiation experiment, carried out at 100 MHz; irradiation at τ 3.04 and 3.13 caused the multiplet with centre at τ 4.61 to collapse to two singlets.

The spectra of the *p*-xylene and *p*-di-isopropylbenzene adducts were consistent with their formulation as 1,3,4-trichloro-5,8-dihydro-6,9-dimethyl-5,8-ethenoisquinoline (VIIb) and 1,3,4-trichloro-5,8-dihydro-6,9-di-isopropyl-5,8-ethenoisquinoline (VIIC), respectively. The signals near τ 5.0 were clearly due to the bridgehead protons (R^1 and R^4), and there was no indication of the presence of any of the alternative isomers (VIIf or VIIg) with alkyl groups at the bridgeheads. These adducts of *p*-xylene and *p*-di-isopropylbenzene are potentially resolvable.

The duren adduct is similarly formulated as 1,3,4-trichloro-5,8-dihydro-6,7,9,10-tetramethyl-5,8-ethenoisquinoline (VIIe) rather than the isomer (VIIh), as no signals attributable to olefinic protons were observed. Two signals were observed for the bridgehead protons. We attribute the signal at τ 5.34 to R^1 and that at τ 5.49 to R^4 , on the grounds that the shielding effect of the chlorine atom at C-4 should be greater than that of the chlorine atom at C-1, because of the buttressing effect of the chlorine atom at C-3.

We had expected to obtain two isomeric mesitylene adducts, 1,3,4-trichloro-5,8-dihydro-6,8,10-trimethyl-5,8-ethenoisquinoline (VIId) and 1,3,4-trichloro-5,8-dihydro-5,7,9-trimethyl-5,8-ethenoisquinoline (VIIi). In fact, the product obtained gave no evidence of being a mixture (t.l.c. and g.l.c.) and the ^1H n.m.r. spectrum

showed only one signal for a bridgehead proton, whereas the spectrum of the duren adduct indicated that protons at R^1 and R^4 should have different chemical shifts. The position of the signal for the bridgehead proton (τ 5.36) was close to that for the proton at R^1 in the duren adduct (τ 5.34), and we therefore assign structure (VIId) to the mesitylene adduct. Further arguments in favour of this structure are advanced below.

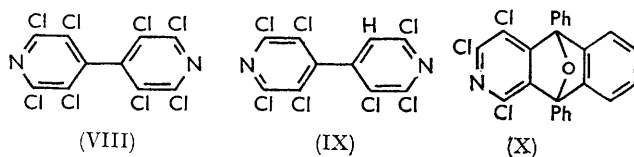
The efficiency of aromatic hydrocarbons in trapping polyhalogenobenzenes increases with the number of electron-releasing alkyl groups in the hydrocarbons,^{4c} and with the degree of electron withdrawal by the halogens in the arynes.⁸ Our results with trichloro-3-pyridyne agree with these observations. Thus, the yields of the adducts increased in the order: benzene < *p*-xylene < mesitylene < 1,2,4,5-tetramethylbenzene < *p*-di-isopropylbenzene, and an experiment in which the 4-lithio-compound (III) was heated in a mixture of equal volumes of the hydrocarbons showed that the ratio of the rates of the reactions with benzene and *p*-di-isopropylbenzene was *ca.* 1 : 23. The competition data for reactions of tetrachlorobenzene with benzene and *p*-di-isopropylbenzene were similar; when tetrachloroanthranilic acid was used as the arylene precursor the ratio was 1 : 19.5, and when pentachlorophenyl-lithium was used the ratio was 1 : 24.¹ Besides these polar factors, steric factors appear to be of considerable importance in these reactions. Thus, both the earlier studies^{4c} and those now reported indicate that where a choice is available, the hydrocarbon is attacked at an unsubstituted position in preference to an alkylated position. In this connection, the case of the mesitylene adduct of the 3-pyridyne (V) is particularly interesting. We have argued, above, that the n.m.r. evidence favours structure (VIId) rather than structure (VIIi) for the adduct. Steric factors also favour structure (VIId); the 4-position of the pyridyne is more hindered than the 3-position, because of the buttressing effect of the chlorine atom at the 6-position in the pyridine ring, and the mesitylene is attacked in the direction such that a carbon atom carrying a methyl group becomes attached to the less hindered 3-position.

Attempts to trap the 3-pyridyne (V) with furan were unsuccessful (as was the reported attempt to trap trifluoro-3-pyridyne⁷). In this connection, whereas tetrachlorobenzene, generated from tetrachloroanthranilic acid, is trapped by furan, none of the adduct was obtained when furan was added to a solution of pentachlorophenyl-lithium and the mixture was heated.¹ Instead of the adduct, the main product obtained when a solution of the 4-lithio-compound (III) in furan was set aside at room temperature was a mixture of hepta- and octachlorobipyridyls, as indicated by mass spectroscopy, elemental analysis, and ^1H n.m.r. (singlet, τ 2.83, of very low intensity). No pure component of the mixture has been isolated, but the main constituent had the same gas chromatographic retention volume as octachloro-4,4'-bipyridyl (VIII) [prepared by reaction of 2,3,5,6-

⁸ R. Harrison and H. Heaney, *J. Chem. Soc. (C)*, 1968, 889.

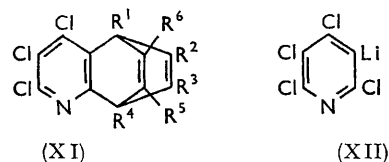
tetrachloropyridyl-lithium (III) with titanium tetrachloride⁹]. We suggest that the polychlorobipyridyls arise from nucleophilic attack by the 4-lithio-compound (III) either on unreacted pentachloropyridine [leading to the octachlorobipyridyls, such as (VIII)] or on another molecule of the lithium compound (leading, after hydrolysis, to heptachlorobipyridyls). An alternative route to heptachlorobipyridyls could involve addition of the 4-lithio-compound (III) to the 3-pyridyne (V), which would probably give the heptachlorobipyridyl (IX); some support is given to this possibility by the ¹H n.m.r. spectrum, which suggests that the proton is at the 3-position of a pyridine ring.

Although no furan adduct of the 3-pyridyne (V) could be isolated, we did obtain the expected adduct (X) with 1,3-diphenylisobenzofuran. The structure of the adduct (X) was confirmed by elemental analysis and ¹H n.m.r. spectroscopy.



Although tetrachloro-2-pyridyl-lithium (II) might reasonably be considered as a precursor for trichloro-2-pyridyne (IV), attempts to trap this aryne by heating the 2-lithio-compound in the presence of benzene, *p*-di-isopropylbenzene, durene, anthracene, *N*-methylpyrrole, and *N*-methylindole were unsuccessful; in the cases of the monocyclic hydrocarbons, small amounts of the adducts (VII) of the 3-pyridyne (V) were formed, presumably from the small proportion of the 4-lithio-compound (III) present in the solution.^{2,6} However, when the 2-lithio-compound (II) was heated in mesitylene, a mixture of products was obtained. The ¹H n.m.r. spectrum of the mixture indicated the presence of three adducts, which we believe to be 1,3,4-trichloro-5,8-dihydro-6,8,10-trimethyl-5,8-ethenoisoquinoline (VIId), 2,3,4-trichloro-5,8-dihydro-6,8,10-trimethyl-5,8-ethenoquinoline (XIa), and 2,3,4-trichloro-5,8-dihydro-5,7,9-trimethyl-5,8-ethenoquinoline (XIb). The spectrum of the mixture was in most respects similar to that given in the Table for (VIId). However, besides the triplet at τ 5.36, triplets were present at τ 5.23 and 5.57; we attribute these to the protons R¹ in adduct (XIa) and R⁴ in adduct (XIb), respectively. There is thus clear evidence for the trichloro-2-pyridyne intermediate (IV), although a pure adduct was not isolated. However, other investigations¹⁰ have suggested that 3-halogeno-2-lithiopyridines do not function as precursors for 2-pyridynes, and in view of the low yield of adduct, we suspect that the 2-pyridyne (IV) was formed not from the 2-lithio-compound (II), but from the small amount of the 3-lithio-compound (XII) also present in the solu-

tion^{2,6} (cf. ref. 11). The fate of the 2-lithio-compound (II) is not clear; it does not remain unchanged during the reactions, and it seems unlikely that it decomposes by way of the 2-pyridyne (IV), as 2-pyridynes, once formed do appear to form adducts as expected.¹¹ In an attempt to determine whether the 2-pyridyne was



a; R¹ = R³ = R⁵ = H, R² = R⁴ = R⁶ = Me
b; R¹ = R³ = R⁵ = Me, R² = R⁴ = R⁶ = H

formed at a low temperature, furan was added to a solution of the 2-lithio-compound (II) at -75° , but only polymeric materials (similar to those formed on the addition of diethyl ether²) were obtained. An intriguing possibility is that the chlorine atom at the 6-position is eliminated, to form 3,4,5-trichloro-2,6-dehydropyridine (cf. ref. 10a), but we have not yet succeeded in obtaining evidence for or against the presence of such an intermediate.

EXPERIMENTAL

The ¹H n.m.r. spectra were recorded at 60 MHz., for solutions in deuteriochloroform, unless otherwise stated. Column chromatography was carried out with Kieselgel (0.05–0.02 mm.) and g.l.c. with 5% silicone SE301 on Celite at 290° .

Adducts of Trichloro-3-pyridyne (IV) with Aromatic Hydrocarbons.—(a) *With benzene.* A solution of *n*-butyllithium in hexane (2.7M; 10 ml.) was added to an ice-cold solution of pentachloropyridine (5.0 g.) in diethyl ether–benzene (1:4; 150 ml.). The solution was stirred for 15 min., while it attained room temperature. The ether was distilled off, and the remaining solution was heated under reflux for 4 hr. Water (50 ml.) was added with stirring, and the mixture was filtered and extracted with ether. The material from the ether extracts was dissolved in light petroleum (b.p. 40 – 60°) (some insoluble material was discarded), and chromatographed on silica. Light petroleum (b.p. 40 – 60°) eluted pentachloropyridine (0.35 g.), followed by a small amount of a mixture of 2,3,5,6-tetrachloropyridine and 2,3,4,6-tetrachloropyridine (identified by ¹H n.m.r.). Further elution with 4% ether–light petroleum (b.p. 40 – 60°) yielded a yellow viscous oil (0.28 g.). Repeated chromatographic purification, followed by vacuum sublimation, yielded 1,3,4-trichloro-5,8-dihydro-5,8-ethenoisoquinoline (0.25 g., 5%), m.p. 69 – 71° (Found: C, 51.1; H, 2.2; Cl, 40.9; N, 5.25. C₁₁H₆Cl₃N requires C, 51.1; H, 2.3; Cl, 41.2; N, 5.4%).

When the solution was heated under reflux for 30 min. instead of 4 hr., the main product isolated was 2,3,5,6-tetrachloropyridine, and none of the adduct was obtained.

(b) *With p-xylene.* The reaction was carried out essentially as described for the benzene adduct, and gave 1,3,4-trichloro-5,8-dihydro-6,9-dimethyl-5,8-ethenoisoquinoline as an oil (8%) (Found: C, 54.7; H, 3.9; Cl, 36.85; N, 5.2. C₁₃H₁₀Cl₃N requires C, 54.45; H, 3.5; Cl, 37.2; N, 4.9%).

⁹ J. D. Cook and B. J. Wakefield, unpublished work.

¹⁰ (a) T. Kauffmann, *Angew. Chem. Internat. Edn.*, 1965, **4**, 543; (b) H. J. den Hertog and H. C. van der Plas, *Adv. Heterocyclic Chem.*, 1965, **4**, 121.

¹¹ J. D. Cook and B. J. Wakefield, *Chem. Comm.*, 1968, 297.

(c) *With p-di-isopropylbenzene.* The reaction was carried out essentially as described for the benzene adduct, except that the solution of n-butyl-lithium was added at -75° . 1,3,4-Trichloro-5,8-dihydro-6,9-di-isopropyl-5,8-ethenoisoquinoline was recovered as an oil (2.02 g., 30.5%) which slowly solidified (m.p. $57-58^{\circ}$) (Found: C, 59.7; H, 5.3; Cl, 31.3; N, 4.0. $C_{17}H_{18}Cl_3N$ requires C, 59.6; H, 5.25; Cl, 31.0; N, 4.1%).

(d) *With mesitylene.* The reaction was carried out as described for the *p*-di-isopropylbenzene adduct, and gave 1,3,4-trichloro-5,8-dihydro-6,8,10-trimethyl-5,8-ethenoisoquinoline (0.67 g., 11%), m.p. $110-113^{\circ}$ [Found: C, 55.95; H, 4.3%; M^+ (mass spectrum), 299.002. $C_{14}H_{12}Cl_3N$ requires C, 55.95; H, 4.0%; M , 299.002].

(e) *With 1,2,4,5-tetramethylbenzene.* The reaction was carried out as described for the benzene adduct. After hydrolysis most of the durene was removed by steam distillation, and the remaining products were worked up as before, to yield 1,3,4-trichloro-5,8-dihydro-6,7,9,10-tetramethyl-5,8-ethenoisoquinoline (1.57 g., 25%), m.p. $101-102^{\circ}$ (Found: C, 57.0; H, 4.5. $C_{15}H_{14}Cl_3N$ requires C, 57.3; H, 4.45%).

Comparison of Reactivities of Benzene and p-Di-isopropylbenzene towards Trichloro-3-pyridyne.—To a solution of tetrachloro-4-pyridyl-lithium [from pentachloropyridine (3.0 g.)] in diethyl ether, was added a mixture of benzene (50 ml.) and *p*-di-isopropylbenzene (50 ml.). The ether was distilled off, and the remaining mixture was heated under reflux (b.p. ca. 85°) for 4 hr. The mixture of products was analysed by g.l.c., which showed peaks due to the benzene adduct (VIIa) and the *p*-di-isopropylbenzene adduct (VIIc) (1:22.8).

Action of Furan on Tetrachloro-4-pyridyl-lithium.—A solution of tetrachloro-4-pyridyl-lithium was prepared by the addition of n-butyl-lithium (10 ml. of 2.2M-solution in hexane) to pentachloropyridine (5.0 g.) in diethyl ether (100 ml.) at 0° . Furan (50 ml.) was added, and the solution was set aside at room temperature for 160 hr. Water (50 ml.) was added, and the products were isolated by ether extraction, etc. and chromatographed on silica. Light

petroleum (b.p. $40-60^{\circ}$) eluted a little pentachloropyridine, and 2% ether-light petroleum (b.p. $40-60^{\circ}$) then eluted a white crystalline solid mixture of heptachloro- and octachloro-bipyridyls (1.15 g.) (Found: C, 29.0; H, 0.5%; M^+ 394, 428. Calc. for $C_{10}Cl_8N_2$: C, 27.8%; M^+ 428. Calc. for $C_{10}HCl_7N_2$: C, 30.1; H, 0.25%; M^+ 394).

1,3,4-Trichloro-9,10-dihydro-9,10-diphenyl-9,10-epoxy-2-aza-anthracene (X).—1,3-Diphenylisobenzofuran (5.4 g.) was added to a solution of tetrachloro-4-pyridyl-lithium [from pentachloropyridine (5.0 g.)] in diethyl ether at 0° . The ether was distilled off, light petroleum (b.p. $80-100^{\circ}$) was added, and the mixture was then heated under reflux for 5 hr., cooled, washed with water, and dried ($MgSO_4$). The solvents were removed and the residue was chromatographed on alumina; elution with light petroleum (b.p. $60-80^{\circ}$) gave 1,3,4-trichloro-9,10-dihydro-9,10-diphenyl-9,10-epoxy-2-aza-anthracene (10%), m.p. 208° , τ 1.9–2.8 (complex multiplet) (Found: C, 66.7; H, 3.3; Cl, 23.8; N, 3.1. $C_{25}H_{14}Cl_3NO$ requires C, 66.6; H, 3.1; Cl, 23.6; N, 3.1%).

Adducts of Trichloro-2-pyridyne with Mesitylene.—A solution of n-butyl-lithium in hexane (2.7M; 10 ml.) was added to an ice-cold solution of pentachloropyridine (5.0 g.) in mesitylene (150 ml.), and the mixture was heated under reflux for 3 hr. The solvent was distilled off and the product was repeatedly chromatographed on silica to give a mixture of adducts (0.13 g.). Although t.l.c. and g.l.c. showed a partial resolution of the mixture of adducts, no separation was observed on column chromatography or preparative scale t.l.c. The 1H n.m.r. spectrum of the mixture is discussed above.

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