ON THE BIPYRIDYL FORMATION IN REACTIONS OF 2-CHLOROPYRIDINE DERIVATIVES WITH POTASSIUM AMIDE IN LIQUID AMMONIA*

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Dedicated to Dr Miroslav Protiva on the occasion of his 70th birthday.

In the reaction of 2,6-dichloropyridine and 2,6-dichloro-3-phenylpyridine with potassium amide in liquid ammonia at −70°C, formation of derivatives of 4,4′-bipyridyl and 3,4′-bipyridyl is observed. The 4,4′ coupling products are far in excess to the 3,4′ coupling products. When the reaction is carried out at −70°C in the presence of potassium permanganate, the corresponding 4-aminopyridines are the main products. 2-Chloro-6-phenoxypyridine is very unreactive with this aminating reagent at −70°C as well as −33°C, but in the presence of potassium permanganate at −33°C 4-amino-2-chloro-6-phenoxypyridine is formed in fair yield. The mechanisms of the formation of the bipyridyls and 4-aminopyridines are presented.

In several papers we described the reactivity of some (3-substituted) 2,6-di-X-pyridines (X = Cl, Br) towards potassium amide in liquid ammonia at −33°C. In some cases ring transformation took place leading to the formation of 4-amino-pyrimidine derivatives in modest yields[1−3]. This ring transformation has been proposed to be initiated by the addition of the amide ion at the C-(4) position of the pyridine ring, followed by ring opening, involving fission of the C(3)—C(4) bond, and a subsequent recyclisation to the pyrimidine system (ANRORC-mechanism).

In this paper we report on the reaction of 2,6-dihalogenopyridines when treated with potassium amide in liquid ammonia at −70°C, instead of −33°C.

RESULTS AND DISCUSSION

When a solution of 2,6-dichloropyridine (*I*) in 1,2-dimethoxyethane (DME) was added to potassium amide in liquid ammonia at −70°C a deep purple color arose,

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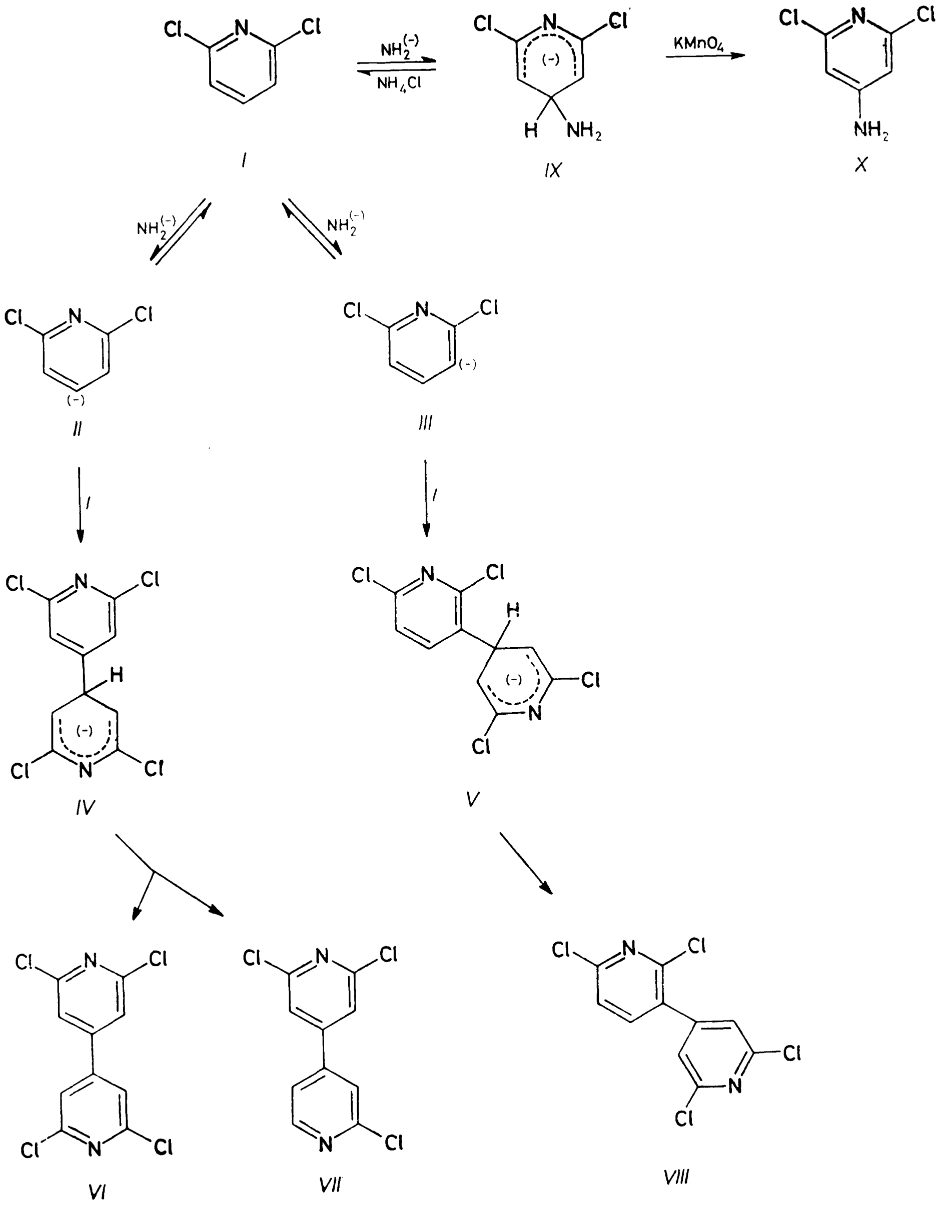
* For a previous paper in these series see ref.[3].

being in contrast to the dark brown color obtained when the reaction is carried out at −33°C. After quenching the reaction mixture at −70°C with ammonium chloride and work-up of the reaction mixture (see Experimental) we were able to isolate by



SCHEME 1

preparative TLC 2,2',6,6'-tetrachloro-4,4'-bipyridyl (*VI*), 2,2'6-trichloro-4,4'-bipyridyl (*VII*) and 2,2',6,6'-tetrachloro-3,4'-bipyridyl (*VIII*) in modest yields (see Scheme 1 and Table I). The 4,4' coupling products are far in excess to the 3,4' coupling products. Also some starting material could be recovered. 4-Amino-2-benzylpyrimidine, a possible product of a ring transformation reaction could not be detected in the reaction mixture.

Bipyridyl formation in reactions of halopyridines with strong base is not unprecedented. Reaction of 3-fluoropyridine with potassium amide in liquid ammonia leads to fluorinated bipyridyls; only to a limited extent nucleophilic substitution at position 3 took place[4].

The formation of *VI*, *VII* and *VIII* can be explained as follows: *I* is partly deprotonated at position 4 as well as at position 3 to give the anions *II* and *III*, respectively. Both σ-anions add to the neutral species *I*, yielding the anionic σ-adducts *IV* and *V*, respectively. Hydride removal from *IV* and *V* leads to products *VI* and *VIII* while *VII* is formed by an overall-chloride elimination. We observed that when the reaction mixture obtained at −70°C was treated with the oxidizing reagent potassium

TABLE I

Details on the preparative procedure

Substr.	mmol	ml DME	ml NH_3	eq. KNH_2	React. temp. °C	React. time min	mmol $KMnO_4$	Isolated compounds	Yield, %	
I	7·5	10	150	33	−70	15	—	*I*	25—30	
								VI	10—15	
								VII	7	
								VIII	10—13	
I	7·6	10	150	37	−70	15	25	*I*	6—10	*VII* and *VIII*
								VI	3—5	detected
								X	25—30	
XI	7·5	10	150	34	−70	15	—	*XI*	15—20	
								XVI	10—20	
								XVII	6	
								XVIII	10—15	
XI	7·5	10	150	35	−70	15	25	*XI*	3—10	*XVII* and *XVIII*
								XVI	15—20	detected
								XX	16—20	
XXI	5·1	8	50	27	−33	15	—	*XXI*	85	
XXI	5·1	8	50	27	−33	15	20	*XXIII*	60—70	
								XXIV	10	

TABLE II

Table of positional parameters and their estimated standard deviations for compound *XVII*. Starred atoms were refined isotropically. Anisotropically refined atoms are given in the form of the isotropic equivalent displacement parameter defined as:
$(4/3)^* [a^2 {}^* B(1, 1) + b^2 {}^* B(2, 2) + c^2 {}^* B(3, 3) + ab(\cos \gamma)^* B(1, 2) + ac(\cos \beta)^* B(1, 3) + bc(\cos \alpha)^* B(2, 3)]$

Atom	*x*	*y*	*z*	B(A2)
Cl1	0·81650(6)	0·05586(8)	0·70591(9)	4·03(2)
Cl2	1·61247(8)	0·61581(9)	0·8452(1)	5·36(2)
Cl3	1·20955(9)	0·6496(1)	1·0392(1)	6·05(2)
N4	1·4004(2)	0·6104(2)	0·9231(3)	3·69(6)
C5	1·4546(3)	0·5380(3)	0·8363(3)	3·20(7)
C6	1·3929(2)	0·4108(3)	0·7426(3)	2·76(6)
C7	1·2635(2)	0·3553(3)	0·7463(3)	2·72(6)
C8	1·2066(3)	0·4280(3)	0·8386(3)	3·39(7)
C9	1·2792(3)	0·5545(3)	0·9224(3)	3·76(8)
C10	1·4606(2)	0·3377(3)	0·6457(3)	2·85(7)
C11	1·5311(3)	0·2810(3)	0·6998(3)	3·91(8)
C12	1·5872(3)	0·2063(4)	0·6099(4)	4·96(9)
C13	1·5737(3)	0·1859(4)	0·4627(4)	5·2(1)
C14	1·5055(3)	0·2433(3)	0·4073(4)	4·65(9)
C15	1·4500(3)	0·3189(3)	0·4972(3)	3·46(7)
C16	1·1883(2)	0·2116(3)	0·6561(3)	2·71(6)
C17	1·2030(3)	0·1017(3)	0·7201(3)	3·20(7)
C18	1·1225(3)	0·0767(3)	0·8432(3)	3·27(7)
N19	1·0120(2)	0·0789(2)	0·8413(3)	3·27(6)
C20	0·9791(2)	0·1148(3)	0·7242(3)	2·98(7)
C21	1·0528(2)	0·1842(3)	0·6347(3)	2·77(6)
N22	1·1639(2)	0·0487(3)	0·9532(3)	4·49(7)
C23	1·0165(3)	0·2357(3)	0·5203(3)	3·16(7)
C24	0·9292(3)	0·2953(3)	0·5413(4)	4·43(8)
C25	0·8979(3)	0·3432(4)	0·4333(5)	6·0(1)
C26	0·9503(4)	0·3330(4)	0·3049(4)	6·4(1)
C27	1·0374(4)	0·2772(4)	0·2815(4)	5·5(1)
C28	1·0714(3)	0·2306(3)	0·3889(4)	4·03(8)
O29	0·4283(4)	0·0964(5)	0·9695(6)	8·6(2)
C30	0·4647(5)	0·0045(5)	0·9435(7)	10·0(2)
H8	1·125(2)	0·390(2)	0·842(2)	1·9(5)*
H11	1·537(2)	0·295(2)	0·801(3)	2·9(6)*
H12	1·631(3)	0·166(3)	0·650(3)	5·9(8)*
H13	1·613(3)	0·142(3)	0·399(3)	6·0(8)*
H14	1·499(3)	0·226(3)	0·303(3)	5·4(8)*
H15	1·402(2)	0·357(2)	0·457(3)	3·2(6)*
H16	1·217(2)	0·206(2)	0·569(2)	1·6(5)*

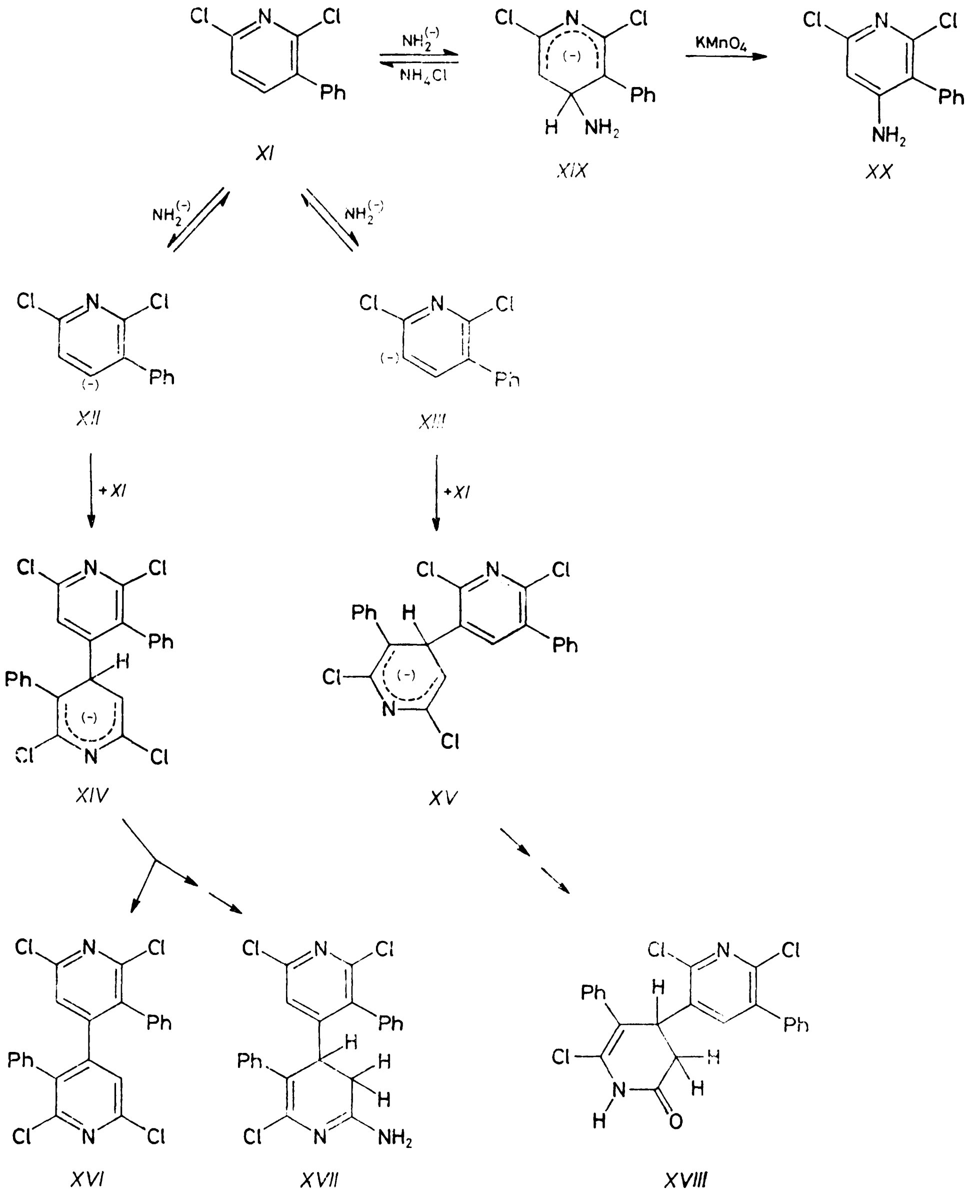
TABLE II
(Continued)

Atom	x	y	z	B(A2)
H17A	1·181(2)	0·025(3)	0·653(3)	3·6(6)*
H17B	1·287(2)	0·122(2)	0·746(3)	2·9(6)*
H22A	1·115(3)	0·022(3)	1·017(3)	5·0(8)*
H22B	1·234(3)	0·049(3)	0·944(3)	4·4(7)*
H24	0·898(2)	0·306(3)	0·629(3)	3·7(6)*
H25	0·837(3)	0·377(3)	0·448(4)	6·8(9)*
H26	0·924(3)	0·362(4)	0·239(4)	7(1)*
H27	1·068(3)	0·265(3)	0·193(4)	5·9(8)*
H28	1·127(2)	0·189(2)	0·367(3)	3·1(6)*

permanganate before quenching with ammonium chloride, 4-amino-2,6-dichloropyridine (*X*) was formed as main product; compound *VI* was only isolated in a small yield and the compounds *VII* and *VIII* could only be detected in trace amounts. All these results can be understood when we assume that in the liquid ammonia/potassium amide an equilibrium mixture of the anions *II* and *III* and adduct *IX* is present. At −70°C this adduct *IX* is too unreactive to react further and forms back the starting material *I*, when quenching the reaction mixture with ammonium chloride; only the anions *II* and *III* will react.

However, in the presence of potassium permanganate a fast oxidation of *IX* into *X* takes place and shifts the equilibrium of the anions *II* and *III* into *IX*. Oxidation of σ-NH_2 adducts with potassium permanganate is a well-known procedure to obtain amino products and this S_NH substitution reaction has been developed into a useful synthesis of amino heterocycles[5,6].

More or less the same observations were made with 2,6-dichloro-3-phenylpyridine (*XI*). When a solution of *XI* in 1,2-dimethoxyethane was reacted with a solution of potassium amide in liquid ammonia at −70°C for 15 min and the reaction mixture was worked-up the 4,4′-bipyridyls *XVI* and *XVII* were obtained together with the 3,4′-bipyridyl *XVIII* (Scheme 2). Their structures were assigned by IR, ^1H and ^{13}C NMR spectroscopy. Supporting evidence was obtained by crystal structure analysis of compound *XVII*. No evidence was found for the presence of a pyrimidine derivative. In the presence of potassium permanganate besides *XVI* 4-amino-2,6--dichloro-3-phenylpyridine (*XX*) was obtained in a modest yield. Also in these reactions we suppose the intermediacy of the σ-anions *XII* and *XIII* and the σ-adduct *XIX*. In the absence of potassium permanganate *XIX* does not react further and the σ-anions react into the bipyridyl σ-adducts *XIV* and *XV*. Via these σ-adducts the products *XVI*, *XVII* and *XVIII* are formed. It is assumed that pyridone *XVIII* is formed during work-up. During work-up σ-adduct *XIX* forms back the starting material *XI*.



SCHEME 2

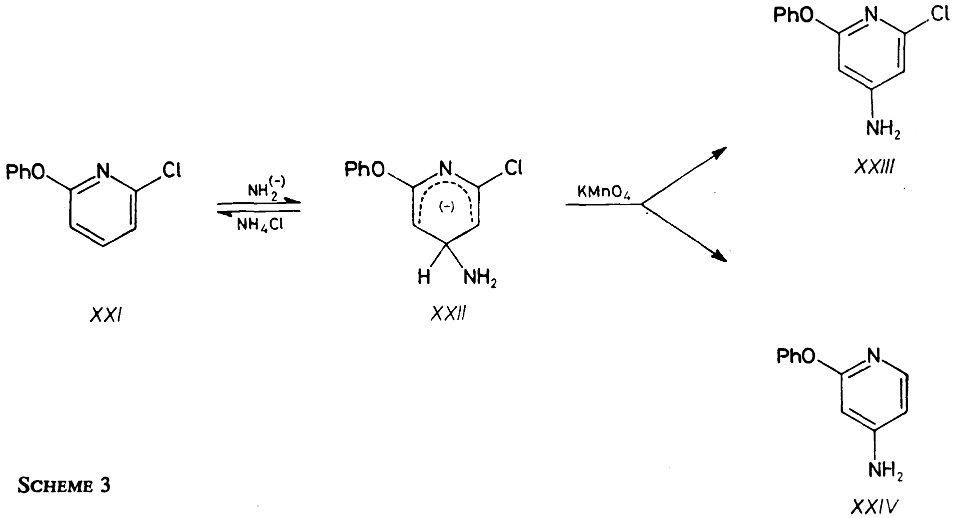
Extension of this study to the behaviour of 2-chloro-6-phenoxypyridine (*XXI*) in potassium amide/liquid ammonia showed that at −70°C as well as at −33°C *XXI* is completely unreactive (Scheme 3). However, when the reaction mixture obtained at −33°C was treated with potassium permanganate 4-amino-2-chloro-6-

TABLE III

Table of general displacement parameter expressions — *U*'s for compound *XVII*. The form of the anisotropic displacement parameter is: $\exp\,[2\,\mathrm{Pl}^2\{h^2a\,2\,\mathrm{U}(1,1) + k^2b\,2\,\mathrm{U}(2,2) + l^2c\,2\,\mathrm{U}(3,3) + 2hkab\,\mathrm{U}(1,2) + 2hlac\,\mathrm{U}(1,3) + 2klbc\,\mathrm{U}(2,3)\}]$, where *a*, *b* and *c* are reciprocal lattice constants

Atom	U(1, 1)	U(2, 2)	U(3, 3)	U(1, 2)	U(1, 3)	U(2, 3)
Cl1	0·0305(3)	0·0566(4)	0·0692(5)	0·0174(3)	0·0023(3)	0·0194(3)
Cl2	0·0498(4)	0·0634(5)	0·0743(5)	0·0038(4)	−0·0128(4)	0·0148(4)
Cl3	0·0828(5)	0·0820(5)	0·0625(6)	0·0497(3)	−0·0096(4)	−0·0222(4)
N4	0·054(1)	0·040(1)	0·041(1)	0·0160(9)	−0·012(1)	0·001(1)
C5	0·041(1)	0·039(1)	0·036(1)	0·009(1)	−0·007(1)	0·009(1)
C6	0·037(1)	0·036(1)	0·029(1)	0·010(1)	−0·004(1)	0·009(1)
C7	0·035(1)	0·035(1)	0·032(1)	0·012(1)	−0·004(1)	0·008(1)
C8	0·034(1)	0·047(1)	0·044(2)	0·015(1)	−0·004(1)	0·003(1)
C9	0·057(2)	0·051(1)	0·036(2)	0·026(1)	−0·008(1)	0·000(1)
C10	0·027(1)	0·038(1)	0·037(1)	0·005(1)	−0·001(1)	0·011(1)
C11	0·041(1)	0·062(2)	0·046(2)	0·020(1)	−0·003(1)	0·013(1)
C12	0·054(2)	0·076(2)	0·072(2)	0·038(1)	0·002(2)	0·019(2)
C13	0·058(2)	0·072(2)	0·067(2)	0·034(1)	0·018(2)	0·006(2)
C14	0·069(2)	0·063(2)	0·044(2)	0·027(1)	0·015(2)	0·012(2)
C15	0·047(1)	0·044(1)	0·041(2)	0·016(1)	0·002(1)	0·015(1)
C16	0·031(1)	0·035(1)	0·032(1)	0·0102(9)	0·001(1)	0·005(1)
C17	0·033(1)	0·034(1)	0·051(2)	0·011(1)	0·001(1)	0·007(1)
C18	0·037(1)	0·038(1)	0·047(2)	0·011(1)	−0·003(1)	0·012(1)
N19	0·035(1)	0·046(1)	0·044(1)	0·0160(8)	−0·001(1)	0·012(1)
C20	0·029(1)	0·036(1)	0·046(2)	0·0124(9)	−0·003(1)	0·005(1)
C21	0·033(1)	0·031(1)	0·038(1)	0·0103(9)	−0·004(1)	0·004(1)
N22	0·039(1)	0·078(1)	0·061(2)	0·021(1)	0·003(1)	0·032(1)
C23	0·037(1)	0·030(1)	0·046(2)	0·006(1)	−0·010(1)	0·008(1)
C24	0·048(2)	0·052(2)	0·071(2)	0·019(1)	−0·002(2)	0·019(1)
C25	0·059(2)	0·071(2)	0·111(3)	0·027(1)	−0·009(2)	0·041(2)
C26	0·084(2)	0·076(2)	0·091(2)	0·022(2)	−0·024(2)	0·043(2)
C27	0·095(2)	0·064(2)	0·049(2)	0·024(2)	−0·010(2)	0·019(1)
C28	0·056(2)	0·046(2)	0·050(2)	0·019(1)	−0·004(1)	0·009(1)
O29	0·074(2)	0·093(3)	0·162(4)	0·032(2)	−0·013(3)	0·032(3)
C30	0·120(3)	0·094(3)	0·166(5)	0·053(2)	−0·045(3)	−0·002(3)

-phenoxypyridine (*XXIII*) could be isolated in a yield of 60–70%, besides a small yield of 4-amino-2-phenoxypyridine (*XXIV*).



SCHEME 3

X-*Ray Structure Determination of* XVII

The crystal structure of *XVII* was determined by X-ray diffraction. Crystal data: $C_{22}H_{16}N_3Cl_3$; triclinic, space group *P1*; a = 11·738(1) Å, b = 10·859(1) Å, c =

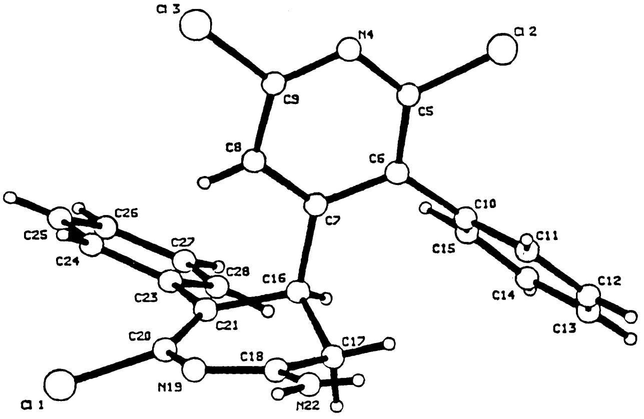


FIG. 1

The perspective view of the molecule *XVII* with atom numbering. Atom numbering; atoms O29 and C30 are part of the disordered solvent molecule

$= 9{\cdot}561(2)$ Å, $\alpha = 103{\cdot}27(2)°$, $\beta = 87{\cdot}60(1)°$, $\gamma = 112{\cdot}76(1)°$; $V = 1\,092{\cdot}3(6)$ Å^3; $Z = 2$; $\varrho_c = 1{\cdot}303$ g cm^{-3}; $\mu = 4{\cdot}31$ cm^{-1}.

Reflections were measured in the $\omega/2\vartheta$ scan mode, using graphite monochromated Mo K_α radiation, on a Philips PW 1100 diffractometer. The structure was solved by direct methods and refined with full-matrix least-squares methods. A total of 2 330 reflections with $F_\sigma^2 > 3\sigma(F_\sigma^2)$ were used in the refinement. The number of parameters refined was 338 [scale factor, extinction parameter, positional parameters of all atoms and thermal parameters (isotropic for H-atoms, anisotropic for others)]. The final R-factors were $R = 4{\cdot}0\%$, $R_w = 4{\cdot}1\%$. All calculations were done with SDP (ref.[7]). During the refinement two atoms were found near a symmetry center. The peaks were interpreted as disordered solvent ethanol molecules and included in the refinements. Figure 1 presents the perspective view of the molecule.

TABLE IV

Table of bond distances for compound *XVII*. Numbers in parentheses are estimated standard deviations in the least significant digits

Atom 1	Atom 2	Distance, Å	Atom 1	Atom 2	Distance, Å
Cl1	C20	1·765(3)	C16	H16	0·88(2)
Cl2	C5	1·710(3)	C17	C18	1·485(4)
Cl3	C9	1·741(4)	C17	H17A	0·89(2)
N4	C5	1·326(4)	C17	H17B	0·95(3)
N4	C9	1·312(4)	C18	N19	1·307(4)
C5	C6	1·396(3)	C18	N22	1·318(5)
C6	C7	1·403(4)	N19	C20	1·382(4)
C6	C10	1·486(4)	C20	C21	1·333(4)
C7	C8	1·373(4)	C21	C23	1·481(5)
C7	C16	1·529(3)	N22	H22A	0·84(4)
C8	C9	1·379(3)	N22	H22B	0·83(3)
C8	H8	0·89(2)	C23	C24	1·395(5)
C10	C11	1·381(5)	C23	C28	1·387(4)
C10	C15	1·392(4)	C24	C25	1·378(6)
C11	C12	1·370(6)	C24	H24	0·90(3)
C11	H11	0·95(3)	C25	C26	1·351(6)
C12	C13	1·380(5)	C25	H25	0·92(4)
C12	H12	0·93(4)	C26	C27	1·364(7)
C13	C14	1·371(6)	C26	H26	0·89(4)
C13	H13	0·91(4)	C27	C28	1·380(6)
C14	C15	1·371(6)	C27	H27	0·91(3)
C14	H14	0·98(3)	C28	H28	0·93(4)
C15	H15	0·95(3)	O29	C30	1·203(8)
C16	C17	1·527(5)	C30	C30′	1·432(6)
C16	C21	1·515(5)			

TABLE V

Table of bond angles for compound *XVII*. Numbers in parentheses are estimated standard deviations in the least significant digits

Atom 1	Atom 2	Atom 3	Angle, °	Atom 1	Atom 2	Atom 3	Angle, °
C5	N4	C9	116·4(2)	C21	C16	H16	105(2)
C12	C5	N4	113·8(2)	C16	C17	C18	110·9(3)
C12	C5	C6	121·1(2)	C16	C17	H17A	108(2)
N4	C5	C6	125·1(3)	C16	C17	H17B	113(2)
C5	C6	C7	116·2(3)	C18	C17	H17A	109(2)
C5	C6	C10	121·8(2)	C18	C17	H17B	112(2)
C7	C6	C10	122·1(3)	H17A	C17	H17B	104(2)
C6	C7	C8	119·1(2)	C17	C18	N19	121·0(4)
C6	C7	C16	120·0(3)	C17	C18	N22	118·4(3)
C8	C7	C16	120·7(2)	N19	C18	N22	120·6(3)
C7	C8	C9	118·4(3)	C18	N19	C20	116·3(2)
C7	C8	H8	118(1)	C11	C20	N19	109·6(2)
C9	C8	H8	124(1)	C11	C20	C21	122·1(3)
C13	C9	N4	115·8(2)	N19	C20	C21	128·3(3)
C13	C9	C8	119·5(2)	C16	C21	C20	114·5(3)
N4	C9	C8	124·7(4)	C16	C21	C23	118·1(2)
C6	C10	C11	121·1(3)	C20	C21	C23	127·4(3)
C6	C10	C15	120·8(4)	C18	N22	H22A	119(2)
C11	C10	C15	118·1(3)	C18	N22	H22B	113(2)
C10	C11	C12	121·1(3)	H22A	N22	H22B	127(3)
C10	C11	H11	116(2)	C21	C23	C24	121·8(3)
C12	C11	H11	123(2)	C21	C23	C28	121·1(3)
C11	C12	C13	120·2(4)	C24	C23	C28	117·1(3)
C11	C12	H12	119(2)	C23	C24	C25	120·5(3)
C13	C12	H12	121(2)	C23	C24	H24	118(2)
C12	C13	C14	119·4(4)	C25	C24	H24	122(2)
C12	C13	H13	124(2)	C24	C25	C26	120·9(4)
C14	C13	H13	117(3)	C24	C25	H25	118(2)
C13	C14	C15	120·4(3)	C26	C25	H25	121(2)
C13	C14	H14	116(2)	C25	C26	C27	120·2(4)
C15	C14	H14	123(2)	C25	C26	H26	117(3)
C10	C15	C14	120·8(3)	C27	C26	H26	123(3)
C10	C15	H15	120(2)	C26	C27	C28	119·8(4)
C14	C15	H15	119(2)	C26	C27	H27	119(3)
C7	C16	C17	111·0(2)	C28	C27	H27	121(3)
C7	C16	C21	113·3(3)	C23	C28	C27	121·4(4)
C7	C16	H16	107(1)	C23	C28	H28	121(2)
C17	C16	C21	110·7(2)	C27	C28	H28	117(2)
C17	C16	H16	109(2)	O29	C30	C30′	116·6(5)

EXPERIMENTAL

Melting points are uncorrected. The ^{1}H NMR spectra were recorded on a Varian XL-100-15 spectrometer or on a Varian EM 390 spectrometer. ^{13}C NMR spectra were recorded on a Varian XL-100-15 spectrometer operating at 25·2 MHz, equipped with a Varian Fourier transform unit [the spectral width was 5 000 Hz (1·25 Hz/point)], and on a Bruker CXP-300 spectrometer operating at 75·460 MHz [SW 15 000 Hz (1·85 Hz/point)]. The IR spectra were recorded on a Hitachi EPI-G3 or on a Perkin–Elmer 237. Mass spectra were recorded on an AEI MS 902 instrument.

Amination Procedure

The procedure applied has been described previously$^{1-3}$. The reactions at −70°C have been carried out in an acetone–carbondioxide bath. The mol. ratio potassium amide/potassium permanganate/substrate was 4·3 : 3·3 : 1. The permanganate was grinded and added at once after the appropriate time.

Preparation of Starting Materials

2,6-Dichloropyridine (*I*) was obtained from Aldrich Corp. and 2,6-dichloro-3-phenylpyridine (*XI*) was prepared according to a procedure described in the literature[3,8].

2-Chloro-6-phenoxypyridine (*XXI*)

Nine Carius tubes, each of them containing a solution of sodium hydroxide (2·4 g, 60 mmol) in water (10 ml), phenol (6·0 g, 62·5 mmol) and 2,6-dichloropyridine (1·48 g, 10 mmol) were shaken during 24 h at 140°C. The combined reaction mixtures were then strongly basified and extracted with chloroform. After drying the chloroform layer and removing the solvent, a solid (17·1 g) was obtained which was recrystallized twice from petroleum ether (60—80°C). Yield of *XXI* 11·10 g (60%), m.p. 87—88°C. ^{1}H NMR (300 MHz, deuteriochloroform, δ) 7·61 dd, (1 H, H-4, $J = 7·9$); 7·40, 7·24, 7·16 (5 H, H-Ph); 7·03 d, (1 H, H-3, $J = 7·7$); 6·74 d, (1 H, H-5, $J = 8·4$). MS: $m/e = 205$ (Cl = 35). For $C_{11}H_8ClNO$ (205·6) calculated: 64·24% C, 3·92 H%; found: 64·21% C, 3·94% H.

Identification of Isolated Product from Reaction of *I* with Potassium Amide/Liquid Ammonia

Analysis of the reaction mixture by TLC (silicagel/petroleum ether (60—80°C)–ethyl acetate, 4 : 1) gave *VI* (R_F 0·69), *I* (R_F 0·63), *VIII* (R_F 0·53) and *VII* (R_F 0·44). They were isolated by preparative TLC.

2,2',6,6'-*Tetrachloro*-4,4'-*bipyridyl* (VI): m.p. 260—261°C (ethanol–ethyl acetate). ^{1}H NMR (hexadeuterioacetone, δ) 7·98 s, H-3,5,3',5'). MS: accurate mass (−4 Cl); calculated for $C_{10}H_4N_2$ 152·0374; found 152·0378. For $C_{10}H_4Cl_4N_2$ (293·9) calculated: 40·85% C, 1·37% H; found: 41·15% C, 0·96% H.

2,2',6-*Trichloro*-4,4'-*bipyridyl* (VII): m.p. 180·5—181·5°C (ethanol). ^{1}H NMR (hexadeuteriodimethylsulfoxide, δ) 8·58 d, (1 H, H-6', $J = 5·1$); 8·13 s, (3 H, H-3,5,3'); 7·95 d, (1 H, H-5', $J = 5·1$; $J_{3',5'} = 1·5$). MS: accurate mass (−3 Cl); calculated for $C_{10}H_5N_2$ 153·04527; found 153·04531. For $C_{10}H_5Cl_3N_2$ (259·5) calculated: 46·28% C, 1·94% H; found: 46·30% C, 2·03% H.

2,2',6,6'-*Tetrachloro*-4,3'-*bipyridyl* (VIII): m.p. 154·0—155·0°C (ethanol). ^{1}H NMR (hexadeuterioacetone, δ) 8·05 d, (1 H, H-4', $J = 7·8$); 7·67 s, (2 H, H-3, 5); 7·65 d, (1 H, H-5', $J = 7·8$). MS: accurate mass (−4 Cl); calculated for $C_{10}H_4N_2$ 152·0374; found: 152·0374. For $C_{10}H_4Cl_4$.$.N_4$ (321·9) calculated: 40·85% C, 1·37% H; found: 41·14% C, 1·67% H.

Reaction of *I* with potassium Amide/Liquid Ammonia, Followed by Treatment with Potassium Permanganate

Analysis of the reaction mixture by TLC (silicagel/petroleum ether (60—80°C)–ethyl acetate 4 : 1) gave *I* (R_F 0·65), *X* (R_F 0·18) and traces of *VI*, *VII* and *VIII*. They were isolated by preparative TLC and identified with authentic samples.

4-*Amino*-2,6-*dichloropyridine* (X): m.p. 175—176°C. Mixed m.p. with an authentic sample[9] is 175—176°C. IR (KBr): 3 460, 3 300 (NH_2). ^1H NMR (hexadeuterioacetone, δ) 6·62 s, (H-3, 5); 6·10 br, (NH_2). For $C_5H_4Cl_2N_2$ (163·0) calculated: 36·38% C, 2·47% H; found: 37·06% C, 2·37% H.

Reaction of *XI* with Potassium Amide/Liquid Ammonia

Analysis of the reaction mixture by TLC (silicagel/petroleum ether (60—80°C)–ethyl acetate 17 : 3) gave *XI* (R_F 0·52), *XVI* (R_F 0·45), *XVIII* (R_F 0·10) and *XVII* (R_F 0·0). They were isolated by preparative TLC.

2,2′,6,6′-*tetrachloro*-3,3′-*diphenyl*-4,4′-*bipyridyl* (XVI): m.p. 155—156°C (ethanol). ^1H NMR (deuteriochloroform, δ) 7·40—7·17 m, (6 H, H_m - Ph + H_p - Ph); 7·12 s, (2 H, H-5 + H-5′); ~6·97—6·67 br s (4 H, H_o-Ph). ^1H NMR (deuteriochloroform, −40°C, δ) ~6·98—6·78 (m, 2 H, H_o-Ph); ~6·63—6·45 m, (2 H, H_o-Ph). ^{13}C NMR (deuteriochloroform, δ) 150·8 (C-2/C-4 + C-2′/C-4′); 149·3 (C-6 + C-6′); 148·5 (C-2/C-4 + C-2′/C-4′); 133·8 (C-3 + C-3′); 133·2 (C_1-Ph + C_1-Ph′); 130·1—128·8—128·3 ($C_{o\ m\ p}$-Ph); 124·0 (C-5 + C-5′, J = 172). MS: accurate mass (−4 ^{35}Cl); calculated for $C_{22}H_{12}N_2$ 304·1000; found 304·1013. For $C_{22}H_{12}Cl_4N_2$ (446·2) calculated: 59·22% C, 2·71% H; found: 59·00% C, 2·85% H.

6′-*Amino*-2,2′,6-*trichloro*-3,3′-*diphenyl*-4′,5′-*dihydro*-4,4′-*bipyridyl* (XVII) m.p. 215—216°C (ethanol). IR (chloroform): 3 500, 3 400 (NH_2). ^1H NMR (deuteriochloroform, δ) 7·43—7·03 m, (11 H, H-5 + H-Ph); 6·75—6·55 br s, (2 H, NH_2); 3·80 dd, (1 H, H-4′, J = 2·4; J = 9·0); 2·68 dd, (1 H, H-5′, J = 9·0; J = 16·1); 2·20 dd (1 H, H-5′, J = 2·4; J = 16·1). ^{13}C NMR (deuteriochloroform, δ) 158·3 (C-4); 154·6 (C-6′); 150·3, 150·1 (C-2 + C-6); 138·6, 137·6 (C-5 + C-5′); 134·8, 134·3 (C_1-Ph + C_1-Ph′); 129·1, 129·0, 128·8, 128·7, 128·1, 127·3 ($C_{o,m,p}$-Ph + $C_{o,m,p}$-Ph′); 121·7 (C-5, J = 170); 114·3 (C-2′); 39·7 (C-4′, J = 138); 32·8 (C-5′, J = 131). MS: accurate mass; calculated for $C_{22}H_{16}N_3Cl_3$ (Cl = 35) 427·0395; found 427·0410. For $C_{22}H_{16}Cl_3N_3$ (427·0) calculated: 61·62% C, 3·76% H; found: 61·43% C, 3·64% H.

2,2′,6-*Trichloro*-N′,4′,5′,6′-*tetrahydro*-6′-*oxo*-3,3′-*diphenyl*-3,4′-*bipyridyl* (XVIII): m.p. 200 to 201°C (ether, −30°C, dried in vacuo at 100°C). IR (chloroform) 3 490 (NH), 1 695 (C=O). ^1H NMR (deuteriochloroform, δ) 8·30 br s, (1 H, NH); 7·57 s, (1 H, H-4); 7·50—7·15 m, (10 H, H-Ph + H-Ph′); 4·50 dd, (1 H, H-4′, J = 3·6; J = 7·2); 3·14 dd, (H-5′, J = 7·2; J = = 16·8); 2·89 dd, (H-5′, J = 3·6; J = 16·8). ^{13}C NMR (deuteriochloroform, δ) 167·8 (C-6′); 147·8, 147·4 (C-2 + C-6); 140·1 (C-4, J = 162); 136·6, 135·9 (C-5, C_1-Ph, C_1-Ph′); 132·7 (C-3); 129·2, 128·9, 128·8, 128·6, 128·4, 128·1 ($C_{o\ m\ p}$-Ph + $C_{o\ m\ p}$-Ph′); 124·3 (C-3′); 114·2 (C-2′); 40·2 (C-4′, J = 135); 36·6 (C-5′, J = 127). MS: accurate mass (−3 Cl); calculated 328·1184; found 323·1178. For $C_{22}H_{15}Cl_3N_2O$ (429·7) calculated: 61·49% C, 3·52% H; found: 61·81% C, 3·67% H.

Reaction of *XI* with Potassium Amide/Liquid Ammonia, Followed by Treatment with Potassium Permanganate

Analysis of the reaction mixture by TLC (silicagel/petroleum ether 60—80°C–ethyl acetate 4 : 1) gave *XI* (R_F 0·58), *XVI* (R_F 0·48) and *XX* (R_F 0·24). They were isolated by preparative TLC.

4-*Amino-2,6-dichloro-3-phenylpyridine* (XX): m.p. 147—148°C (heptane). IR (KBr): 3 460, 3 380 (NH_2). ^1H NMR (deuteriochloroform, δ) 7·53—7·17 m, (5 H, H-Ph); 6·60 s, (1 H, H-5); 4·32 br s, (2 H, NH_2). ^{13}C NMR (deuteriochloroform, δ) 154·5 (C-4); 149·4, 149·0 (C-2, C-6); 132·9 (C_1-Ph); 129·8, 129·4, 128·8 ($C_{o,m,p}$-Ph); 119·9 (C-3); 107·7 (C-5). MS: accurate mass; calculated for $C_{11}H_8Cl_2N_2$ 238·0064 (Cl = 35); found 238·0061. For $C_{11}H_8Cl_2N_2$ (238·0) calculated: 55·25% C, 3·37% H; found: 55·11% C, 3·36% H.

Reaction of *XXI* with Potassium Amide/Liquid Ammonia, Followed by Treatment with Potassium Permanganate

Analysis of the reaction mixture by TLC (silicagel/chloroform-methanol 39 : 1) gave *XXIII* (R_F 0·59), *XXI* (R_F 0·94) and *XXIV* (R_F 0·23). They were isolated by preparative TLC.

4-*Amino-2-chloro-6-phenoxypyridine* (XXIII): m.p. 92·0—92·5°C (hexane–chloroform). IR (chloroform): 3 500, 3 400 (NH_2). ^1H NMR (deuteriochloroform, δ) 7·42—7·03 m, (5 H, H-Ph); 6·28 s, (1 H, H-3, $J_{3,5}$ = 1·6); 5·83 s, (1 H, H-5, $J_{3,5}$ = 1·6); 4·33 br s, (2 H, NH_2). ^{13}C NMR (deuteriochloroform, δ) 164·1 (C-6); 157·5 (C_1-Ph); 154·0 (C-4); 149·6 (C-2); 129·6, 124·6, 120·8 ($C_{m,p,o}$-Ph); 104·8 (C-5); 93·4 (C-3). MS: accurate mass; calculated for $C_{11}H_9ClN_2O$ (Cl = 35) 220·0404; found 220·0407. For $C_{11}H_9ClN_2O$ (220·0) calculated: 59·87% C, 4·11% H; found: 59·74% C, 4·03% H.

4-*Amino-2-phenoxypyridine* (XXIV) (*ref.*[2]). IR (*chlorforom*): 3 510, 3 410 (NH_2). ^1H NMR (deuteriochloroform, δ) 7·85 d, (1 H, H-2, $J_{2,3}$ = 5·7); 7·50—7·03 m, (5 H, H-Ph); 6·27 d, (1 H, H-3, $J_{2,3}$ = 5·7, $J_{3,5}$ = 1·8); 6·02 s, (H-5, $J_{3,5}$ = 1·8); 4·17 br s, (2 H, NH_2). MS: accurate mass; calculated for $C_{11}H_{10}N_2O$ 186·0793; found 186·0787.

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