Effect of Substitution on Pyrimidine. The Crystal Structures of Pyrimidine and its 5-Methyl, 2-Chloro and 2-Amino Derivatives

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Substituent effects in pyrimidine have been studied by X-ray crystallographic methods. The crystal structures of the title compounds were derived from data collected at 107 K. Only high-order data ($\sin \theta/\lambda > 0.60$) were used for the determination of non-hydrogen parameters. The final R-values lie in the range $0.033 - 0.054$ and the e.s.d.'s in bond lengths are about 0.002 Å. In addition to the influence of substitution on bond angles, small but probably significant changes occur in the ring bonds adjacent to the substitution position. Chlorine substitution is found to shorten these bonds by 0.009(2) Å whereas introduction of methyl and amino groups causes lengthenings of 0.006(2) and 0.019(3) Å, respectively.

The electron density difference maps for the four compounds have been compared.

It is well known that substituents cause slight modifications in the geometry of aromatic rings.[1,2] Direct information on the changes occurring on substitution in benzene has been obtained by micro-wave spectroscopy in some cases.[1,3] X-Ray diffraction investigations have provided values for the angular distortions,[2,4] whereas the changes in bond lengths in general have not been established, mainly due to the large thermal vibrations of the atoms at room temperature. The aim of the present work was to provide such information by studying a series of related simple compounds at low temperature. In order to facilitate comparisons, the same experimental and computational procedures were applied to all compounds. Attempts were also made to observe changes in electron density directly. Pyrimidine was chosen as the aromatic compound because of its biological importance and our general interest in its structural chemistry.[5] Derivatives with substituents in the 2- and 5-positions were chosen in order to make use of the $2m$ symmetry of the ring.

In the following the compounds will be referred to as HP (pyrimidine), MeP (5-methylpyrimidine), ClP (2-chloropyrimidine) and AmP (2-aminopyrimidine).

The crystal structures of two of the compounds, HP and AmP, have been reported in the literature,[6,7] but the data were collected at room temperature and the structure of HP is not sufficiently accurate for the present purpose.

EXPERIMENTAL. STRUCTURE ANALYSIS

The compounds were supplied by Sigma Chemical Company and used without further purification. Suitable crystals of MeP and ClP were found in the samples, whereas crystals of AmP were obtained by recrystallization from alcohol, and of HP by slowly cooling the melt from 21 to 17 °C. The crystals were then rapidly transferred to the diffractometer at 107 K. They were all stable at this temperature.

Crystal data derived from diffractometer measurements are given in Table 1. About 15 reflections were used for the determination of the lattice constants.

The intensity measurements were carried out on a Syntex $P\bar{1}$ automatic diffractometer using monochromatic Mo$K\alpha$ radiation ($\lambda = 0.71069$ Å). The $\omega/2\theta$ scan mode with scan speed $1-6°$/min was employed. The temperature at the crystal site was 107 K. Crystal sizes are given in Table 1. No entirely satisfactory crystal could be found for HP. The one used yielded somewhat oblique peaks presumably due to slight splitting of the crystals. The MeP crystal is on the large side, but the influence of this on atomic positions is thought to be negligible.

The intensities of three standard reflections were measured for each 60th reflection. They

Table 1. Crystal data (107 K).

	HP	MeP	ClP	AmP
Formula	$C_4N_2H_4$	$C_5N_2H_6$	$C_4N_2H_3Cl$	$C_4N_3H_5$
Space group	$Pna2_1$	$P2_1/c$	Pbca	Pbca
a (Å)	11.555(8)	10.557(1)	11.518(2)	14.862(2)
b (Å)	9.461(5)	10.194(2)	7.083(1)	10.884(2)
c (Å)	3.693(2)	11.059(1)	23.548(4)	5.633(1)
β (°)	90	121.03(1)	90	90
V (Å³)	403.7	1019.9	1921.2	911.2
Z	4	8	16	8
D_x (g cm⁻³)	1.32	1.23	1.58	1.39
μ (MoKα) (mm⁻¹)	0.087	0.086	0.637	0.111
Melting point (°C)	21 – 22	28 – 30	65 – 66	127 – 128
Crystal size (10⁻² mm)	35 × 35 × 35	40 × 40 × 60	25 × 25 × 40	12 × 22 × 28

Table 2. Number of observed reflections and agreement indices. H.O. data are reflections with $\sin \theta/\lambda > 0.60$.

	HP	MeP	ClP	AmP
No. of refl.	1170	2904	3371	1195
No. of H.O.	761	1367	1852	581
R, all data	0.052	0.046	0.033	0.052
R, H.O. data	0.047	0.054	0.034	0.054
R_w, all data	0.053	0.052	0.034	0.046
R_w, H.O. data	0.042	0.040	0.034	0.049
S, all data	6.08	6.72	1.60	3.42
S, H.O. data	1.32	1.37	1.02	1.08

Table 3. Positional (× 10⁵ for non-hydrogens, × 10³ for hydrogens) and thermal (× 10⁴) parameters for pyrimidine. The anisotropic temperature factor is $\exp[-(B_{11}h^2 + ... + B_{23}kl)]$. Parameters for non-hydrogens are derived from data with $\sin \theta/\lambda > 0.6$, those for hydrogens from all data.

Atom	x	y	z	$B_{11}(B)$	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
N1	12643(10)	39921(9)	2901(0)	30(1)	34(1)	517(11)	− 2(1)	− 13(5)	− 27(5)
N3	1088(9)	19039(11)	1867(82)	27(1)	41(1)	523(10)	− 8(1)	2(4)	− 28(5)
C2	2859(10)	32784(12)	8149(66)	26(1)	40(1)	444(11)	7(1)	5(4)	− 31(5)
C4	10153(12)	11734(12)	− 10817(70)	33(1)	36(1)	508(11)	0(1)	− 27(5)	− 56(5)
C5	20796(11)	18063(13)	− 17116(69)	27(1)	49(1)	403(10)	13(1)	− 9(4)	− 52(5)
C6	21564(10)	32421(13)	− 9815(83)	25(1)	47(1)	491(11)	− 9(1)	2(4)	− 10(6)
H2	− 39(1)	386(2)	170(7)	2.3(4)					
H4	84(2)	21(2)	− 168(8)	3.2(4)					
H5	268(2)	126(2)	− 257(7)	3.1(5)					
H6	286(1)	379(2)	− 112(7)	2.7(4)					

did not vary significantly for any of the compounds during the data collection. Reflections with $I < 2.5\sigma(I)$ were considered unobserved and not included in the refinements. In Table 2 the numbers of observed reflections are given. Correction for extinction was not applied and only the chlorine derivative was corrected for absorption.[8] The transmission factors were $0.79 - 0.88$. The atomic form factors were those of Doyle and Turner,[9] except for hydrogen.[10]

The structures were solved by vector (ClP) or direct (MeP) methods. The hydrogen atoms were located by Fourier difference syntheses. The structures were refined by full-matrix least squares calculations. The weighting scheme was based on standard deviations from counter statistics and 2 % fluctuations in diffractometer stability. Anisotropic temperature factors were applied to the non-hydrogen atoms, isotropic ones to the hydrogen atoms. The final parameters for the non-hydrogen atoms were derived from refinements based on high-order reflections only ($\sin \theta/\lambda > 0.60$) in order to reduce errors

due to bonding and lone-pair electrons. The agreement indices are given in Table 2, the atomic parameters in Tables 3 − 6, and the corresponding bond lengths and angles in Table 7. Lists of observed and calculated structure factors may be obtained from the authors (S.F.)

Rigid-body thermal motion analyses were carried out.[17] The r.m.s. differences between the atomic vibration tensor components and those derived from the model are 0.0002 Å² for HP and 0.0005 − 0.0006 Å² for MeP, ClP and AmP. The corrected bond lengths are found in Tables 7 − 8. In Fig. 1 the differences in bonds and angles between the derivatives and pyrimidine are presented.

Residual electron density maps in the ring planes (Fig. 2) were calculated using the full data sets and a scale factor derived from a separate refinement on all reflections with fixed high-order parameters. The contributions from the hydrogens were not included in the calculated structure factors and the maps con-

Table 4. Parameters for 5-methylpyrimidine. Given as in Table 3.

Atom	x	y	z	$B_{11}(B)$	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
Molecule A									
N1	60215(13)	27260(14)	60627(12)	52(1)	65(1)	52(1)	29(2)	40(1)	− 12(1)
N3	36844(15)	27576(17)	39217(13)	64(1)	83(1)	42(1)	5(2)	29(1)	7(2)
C2	50685(16)	23407(17)	47428(14)	69(1)	72(1)	50(1)	17(2)	52(2)	− 22(2)
C4	32081(14)	36303(17)	45026(15)	51(1)	68(1)	58(1)	24(2)	43(2)	43(2)
C5	40830(13)	40798(12)	58858(15)	59(1)	46(1)	64(1)	24(1)	76(2)	26(1)
C6	55103(13)	35919(13)	66159(12)	52(1)	52(1)	48(1)	11(1)	45(1)	− 5(1)
C7	35358(29)	50268(23)	65528(28)	127(2)	69(1)	132(2)	74(3)	190(4)	26(3)
H2	540(1)	169(1)	432(1)	3.3(3)					
H4	223(1)	392(1)	390(1)	2.8(2)					
H6	620(1)	389(1)	755(1)	2.6(2)					
H7	285(2)	557(2)	594(2)	7.4(5)					
H8	434(2)	554(2)	730(2)	7.2(5)					
H9	304(2)	457(2)	684(2)	6.5(5)					
Molecule B									
N1	23847(14)	655(14)	50704(11)	61(1)	54(1)	48(1)	31(1)	39(1)	13(1)
N3	2422(13)	1274(13)	27645(11)	57(1)	55(1)	47(1)	3(1)	34(1)	− 11(1)
C2	15531(14)	− 3488(12)	37379(13)	61(1)	47(1)	53(1)	18(1)	55(2)	− 1(1)
C4	− 2680(12)	11350(13)	31690(13)	47(1)	52(1)	52(1)	11(1)	37(1)	11(1)
C5	5010(13)	16685(11)	45175(12)	64(1)	37(1)	56(1)	12(1)	75(2)	9(1)
C6	18476(15)	10749(13)	54430(12)	67(1)	50(1)	43(1)	9(2)	46(1)	− 1(1)
C7	− 819(27)	28095(15)	49384(25)	135(2)	47(1)	116(2)	35(2)	188(4)	7(2)
H2	193(1)	− 106(1)	347(1)	2.4(3)					
H4	− 119(1)	148(1)	247(1)	3.0(3)					
H6	243(1)	140(1)	639(1)	3.1(2)					
H7	− 108(2)	269(2)	470(2)	5.8(4)					
H8	− 3(2)	362(2)	447(2)	4.6(3)					
H9	51(2)	295(2)	598(2)	5.6(4)					

Table 5. Parameters for 2-chloropyrimidine. Given as in Table 3.

Atom	x	y	z	$B_{11}(B)$	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
Molecule A									
Cl	16461(3)	16279(7)	12614(2)	26(0)	120(1)	7(0)	−4(1)	5(0)	6(0)
N1	21354(10)	25737(23)	2212(6)	22(1)	97(2)	6(0)	8(2)	−3(0)	2(1)
N3	37185(10)	17183(25)	8286(6)	19(1)	108(2)	6(0)	5(2)	−3(0)	1(1)
C2	26074(11)	20212(21)	7068(6)	19(1)	72(2)	6(0)	−0(2)	0(0)	0(1)
C4	44523(12)	20100(26)	3941(7)	20(1)	115(3)	7(0)	6(2)	−0(1)	−3(1)
C5	40803(13)	25883(28)	−1378(7)	25(1)	121(3)	7(0)	−0(2)	3(1)	2(1)
C6	28936(13)	28629(28)	−2037(7)	28(1)	109(3)	6(0)	11(2)	−2(1)	5(1)
H4	525(1)	179(2)	48(1)	1.9(3)					
H5	460(1)	279(2)	−43(1)	2.1(3)					
H6	258(1)	327(2)	−56(1)	2.2(3)					
Molecule B									
Cl	10378(3)	44719(6)	35641(2)	24(0)	97(1)	7(0)	8(1)	6(0)	−3(0)
N1	23756(10)	35099(22)	27229(5)	24(1)	92(2)	5(0)	−6(2)	−1(0)	−5(1)
N3	32838(11)	47690(19)	35555(6)	26(1)	87(2)	6(1)	2(2)	−3(1)	−6(1)
C2	23901(11)	42124(20)	32436(6)	20(1)	68(2)	6(0)	0(2)	1(0)	−0(1)
C4	43238(13)	45786(26)	33032(7)	23(1)	93(2)	7(0)	−7(2)	−6(1)	−3(1)
C5	44427(13)	38402(26)	27581(7)	23(1)	104(2)	7(0)	−5(2)	1(1)	1(1)
C6	34291(12)	33251(25)	24802(6)	26(1)	106(2)	5(0)	−3(2)	1(1)	−1(1)
H4	499(1)	499(2)	350(1)	2.7(4)					
H5	518(1)	375(2)	258(1)	2.6(3)					
H6	343(1)	281(2)	212(1)	1.4(3)					

Table 6. Parameters for 2-aminopyrimidine. Given as in Table 3.

Atom	x	y	z	$B_{11}(B)$	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
N1	15248(13)	38644(16)	56057(33)	13(1)	21(1)	88(4)	−0(1)	13(3)	−8(3)
N2	7120(15)	36114(16)	90678(36)	18(1)	22(1)	102(5)	4(1)	19(3)	12(3)
N3	6627(13)	55240(15)	72735(33)	13(1)	19(1)	89(4)	2(1)	8(3)	−1(3)
C2	9788(15)	43562(16)	72791(35)	12(1)	19(1)	74(4)	−1(1)	2(3)	−4(3)
C4	9554(14)	62444(18)	55030(42)	15(1)	22(1)	108(4)	3(11)	−1(3)	4(4)
C5	15513(17)	58517(20)	37689(46)	17(1)	26(1)	102(5)	3(1)	13(3)	21(4)
C6	18052(16)	46244(19)	38895(38)	15(1)	27(1)	82(4)	1(1)	14(3)	2(4)
H1	102(1)	291(2)	931(3)	2.1(4)					
H3	35(1)	391(2)	18(4)	2.3(4)					
H4	73(1)	707(1)	551(3)	1.6(4)					
H5	177(1)	639(1)	252(3)	1.8(4)					
H6	222(1)	423(1)	272(3)	2.2(4)					

sequently exhibit high peaks due to these atoms. The maximum electron densities in the bond peaks are given in Table 9. Electron density sections perpendicular to the bonds through their mid-points were calculated for HP and AmP. All calculations were carried out on CYBER-74 using the programs of Ref. 11.

Table 7. Bond lengths (Å) and angles (°). Lower values are corrected for libration. When not given, the e.s.d.'s are 0.002 Å and 0.1° for bonds and angles involving non-hydrogens, and 0.01 − 0.03 Å and 1 − 2° for those involving hydrogens.[a]

	HP	MeP,mol.A	MeP,mol.B	ClP,mol.A	ClP,mol.B	AmP
N1 − C2	1.331	1.335	1.337	1.326	1.324	1.354
	1.335	1.342	1.343	1.329	1.327	1.356
C2 − N3	1.337	1.331	1.332	1.329	1.325	1.355
	1.340	1.338	1.338	1.332	1.328	1.357
N3 − C4	1.340	1.338	1.339	1.343	1.344	1.341(3)
	1.341	1.344	1.344	1.346	1.346	1.343
N1 − C6	1.337	1.336	1.338	1.344	1.348	1.339(3)
	1.338	1.342	1.343	1.347	1.350	1.341
C4 − C5	1.388	1.395	1.390	1.386	1.393	1.386(3)
	1.391	1.402	1.397	1.389	1.395	1.388
C5 − C6	1.388	1.384	1.391	1.390	1.387	1.390(3)
	1.391	1.391	1.398	1.392	1.390	1.392
C5 − C7		1.500	1.498			
		1.504	1.502			
C2 − Cl				1.735(1)	1.741(1)	
				1.738	1.743	
C2 − N2						1.353(3)
						1.355
C2 − H2	1.01	0.97	0.95			
C4 − H4	0.96	0.94	0.95	0.95	0.94	0.96
C5 − H5	0.92			0.91	0.95	0.97
C6 − H6	0.97	0.96	0.96	0.95	0.93	1.00
C7 − H7		0.89	0.95			
C7 − H8		0.98	0.99			
C7 − H9		0.95	1.00			
N2 − H1						0.91
N2 − H3						0.89
N1 − C2 − N3	126.8	126.5	126.5	129.0	129.5	125.2(2)
C2 − N3 − C4	116.3	115.9	116.0	114.6	114.7	116.0(2)
C3 − C4 − C5	121.9	123.0	123.0	122.7	122.2	123.4(2)
C4 − C5 − C6	116.6	115.3	115.4	116.5	116.8	115.8(2)
C5 − C6 − N1	122.5	123.1	122.8	122.3	122.2	123.0(2)
C6 − N1 − C2	115.9	116.1	116.1	114.9	114.7	116.4(2)
C4 − C5 − C7		123.1	122.5			
C6 − C5 − C7		121.6	122.1			
N1 − C2 − Cl				115.8	115.5	
N3 − C2 − Cl				115.2	115.1	
N1 − C2 − N2						117.2(2)
N3 − C2 − N2						117.5(2)
N1 − C2 − H2	115	118	116			
N3 − C2 − H2	118	116	117			
N3 − C4 − H4	114	115	116	115	117	116
C5 − C4 − H4	124	122	121	121	119	121
C4 − C5 − H5	119			121	121	123
C6 − C5 − H5	125			122	121	122
C5 − C6 − H6	125	121	120	120	122	123
N1 − C6 − H6	113	116	118	116	115	114

[a] The atoms of the methyl group are denoted C7, H7, H8 and H9, of the amino group N2, H1 and H3. The angles at C7 are 103 − 114°, at N2 118 − 121°.

Table 8. Mean corrected values for ring bond lengths (Å) and angles (°). 2m symmetry assumed.

	HP el.diff.	HP	MeP	ClP	AmP Present work	AmP Ref. 7
Bond						
C2−N3	1.340(2)	1.338(2)	1.340(1)	1.329(1)	1.357(2)	1.358(2)
N3−C4	1.340(2)	1.340(2)	1.343(1)	1.347(1)	1.342(2)	1.339(2)
C4−C5	1.393(3)	1.391(2)	1.397(1)	1.391(1)	1.390(2)	1.384(2)
Angle						
N1−C2−N3	127.6(3)	126.8(1)	126.5(1)	129.2(1)	125.2(2)	125.1(1)
C2−N3−C4	115.5(2)	116.1(1)	116.0(1)	114.7(1)	116.2(2)	116.0(1)
N3−C4−C5	122.3	122.2(1)	123.0(1)	122.3(1)	123.2(2)	123.5(1)
C4−C5−C6	116.8	116.6(1)	115.4(1)	116.7(1)	115.8(2)	115.9(1)
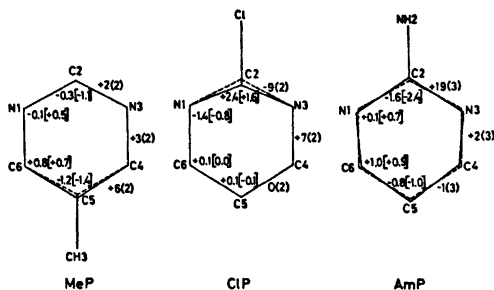
Fig. 1. Bond lengths (10⁻³ Å) and angles (°) minus those in pyrimidine. E.s.d.'s in bond lengths in parentheses. Those of the angles are 0.2°. Values in brackets are based on electron diffraction results on pyrimidine. The un-distorted pyrimidine ring is dotted.

Table 9. Maximum electron density (10^{-2} e $Å^{-3}$) in ring bonds. E.s.d.'s based on deviations from 2m symmetry in parentheses. Bracketed numbers are explained in text.

Bond	HP	MeP	ClP	AmP
C2−N3	37(3) [46]	44(5) [46]	32(4) [28]	38(8) [36]
N3−C4	25(1) [31]	31(2) [32]	26(4) [23]	49(9) [46]
C4−C5	30(3) [37]	53(2) [56]	40(3) [35]	41(3) [38]
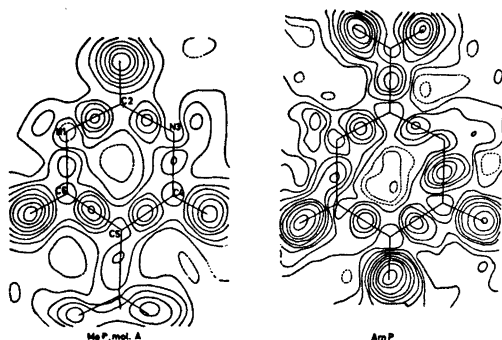
Fig. 2. Residual electron density in ring plane for MeP, mol. A and AmP, including that of the hydrogen atoms.

RESULTS AND DISCUSSION

The librational vibrations are considerable even at the low temperature. The corrections to the bond lengths lie in the range 0.002 − 0.007 Å; to the angles they are less than 0.1°. As the rigid body approximation would appear to be a reasonable one for this type of molecules, the discussion will be based on corrected values.

In MeP and ClP there are two molecules, A and B, in the asymmetric unit. The bond lengths and angles (Table 7) in A and B are equal within error in both compounds, the mean difference being 0.003 Å (1.5σ). The same holds when the two halves of each of the six molecules are compared, except for the C5−C bonds in molecule A of MeP, which differ by 0.011 Å. It appears justified to assume ring symmetry 2m

for all molecules and to use mean values when comparing them.

In Table 8 the results of a recent electron diffraction investigation of pyrimidine [12] (assuming equal C−N bonds) and those of the room temperature study of AmP are also included.[7] The agreement between the electron diffraction and present X-ray results for pyrimidine is satisfactory, although discrepancies of about 3σ occur for the ring angles at N and C2. Our results for AmP agree well with those of the room temperature study, especially when considering that different $\sin\theta/\lambda$-ranges are used. The librational corrections to the bond lengths in AmP are about 0.009 Å at room temperature and 0.002 Å in the present analysis.

Planarity of molecules. All molecules are essentially planar, the largest deviation of a ring atom from the least squares plane through the ring atoms being 0.003 Å (HP), 0.013 Å (MeP, mol. A), 0.008 Å (MeP, mol. B), 0.003 Å (ClP, mol. A), 0.004 Å (ClP, mol. B), and 0.022 Å (AmP). The atom furthest away from the plane is in all cases C2 and/or C5. All the six rings deviate from strict planarity in essentially the same manner, being slightly boat-shaped, with C2 and C5 at the "bows". This has been observed earlier in a number of other pyrimidine derivatives.[13]

The methyl carbon atoms in MeP are at distances of 0.049 and 0.023 Å from the ring planes in molecules A and B, respectively. The methyl groups are ordered, but differently oriented in the two cases. In molecule A the smallest torsion angle C6−C5−C7−H is 26.3°, in molecule B it is −10.8°.

Also in ClP and AmP the extra-ring atom nearly lies in the ring plane, the deviations being 0.017 Å (ClP, mol. A), 0.005 Å (ClP, mol. B) and 0.059 Å (AmP). The angle between the planes of the ring and the amino group is 17.9°. The amino hydrogens lie on the same side of the ring plane at distances 0.29 and 0.07 Å, respectively.

The effects of substitution. Three different types of substituents are present in the compounds studied, the chlorine atom being σ-electron-attracting, the methyl group σ-electron-releasing, and the amino group a π-electron donor. In the first two cases mainly inductive effects operate, whereas the amino group has a strong conjugative effect. As for the aromatic

system it may be expected that different aromatics, *e.g.* benzene and pyrimidine, should respond geometrically in essentially the same manner to substitution, although there may be differences in detail. It should also be borne in mind that the 2-position in pyrimidine differs markedly from the 5-position.

Inspection of Table 8 and Fig. 1 shows that the geometry of the pyrimidine ring is significantly influenced by all three types of substituents. As expected, the main effect is on the adjacent ring bonds and the angle between them. Variations caused by differences in crystal environment are believed to be negligible except for AmP.

Methyl substitution in the 5-position is found to increase the length of the C5−C bonds by 0.006 Å, which is probably significant. However, it cannot be excluded that the effect is due to some systematic error. The angle between the bonds decreases by 1.2° and the *ortho* angle becomes larger by 0.8°. The other bonds and angles are insignificantly influenced. The main geometric effect of methyl substitution is thus to move the C5 carbon atom outwards along the C2···C5 line. The distance C2···C5 is 2.666 Å in HP, 2.681 Å in MeP.

No changes in bond lengths appear to have been observed on methylation of benzene, but the angular deformations have been reported to be −1.9(1), 1.0(1), 0.3(1) and −0.7(1)° for *ipso*, *ortho*, *meta*, and *para* angles, respectively.[4] These values differ from those found in the present work, but it should be noted that a comparison based on the electron diffraction results for pyrimidine gives considerably better correspondence (Fig. 1).

The main effect of *chlorine substitution* in the 2-position is a movement of C2 towards the ring centre along the C2···C5 line (by 0.023 Å). The C2−N bonds are shortened by 0.009 Å, and the N−C2−N angle increases by 2.4°. The ring angles at N are correspondingly adjusted. A lengthening of the next bond, N3−C4, also appears to occur, presumably related to the shortening of C2−N3. The *meta* and *para* angles are hardly influenced, whereas all the angles have been reported to be significantly distorted on chlorine substitution in benzene, the deformations being 1.0(1), −1.1(1), 0.7(1) and −0.4(1)°, respectively, for the four angles.[4] These values were derived from X-ray data on

substituted benzenes. No changes in bond lengths were assumed to occur.

In a micro-wave analysis of chlorobenzene [14] the angular deformations were found to be small, about 0.2°, and no shortening of the ring bonds at the substitution position was observed. For fluorobenzene,[15] however, the changes in bond lengths and angles are similar to those found for ClP in the present work.

The changes occurring on substitution may be rationalized as hybridization effects.[2,15] When electrons are withdrawn from the ring by an electronegative substituent like chlorine, the *p*-character of the orbitals directed towards neighbouring ring atoms decreases. This causes a shortening of the bonds and an opening of the angle between them. Electron-releasing substituents, *e.g.* methyl groups, have the opposite effect, as is observed.

By *amino substitution* more complex changes take place than in the two cases described above. There is strong conjugation between the amino group and the ring, as evidenced by the short C2−N2 bond of 1.355 Å. On substitution the bond order of the extra-ring bond from C2 increases, causing a decrease in the C2−N ring bond order and a lengthening of this bonds (by 0.019 Å). The angle N−C2−N decreases correspondingly. This is compensated mainly by a change in the *meta* angle, whereas in methyl and chlorine substitution the *ortho* angle is adjusted. Furthermore, also the *para* angle

is significantly changed, as has been found also for amino benzenes.[16] Relative to pyrimidine the C2···C5 distance increases by 0.033 Å and N1···N3 by 0.021 Å, whereas C4···C6 becomes shorter by 0.008 Å.

In AmP and other aminopyrimidines the ring nitrogen atoms are engaged in hydrogen bond formation. This may cause small changes in ring geometry superimposed on the deformations due to amino substitution.

Electron density. Residual electron density maps in the ring plane were calculated for all six molecules. Two examples are given in Fig. 2. The maps exhibit the expected features: (1) Peaks of 0.6−1.0 e$Å^{-3}$ due to hydrogen atoms, (2) bonding electron densities in the ring bonds of 0.2−0.6 e $Å^{-3}$ and (3) peaks of 0.2−0.3 e $Å^{-3}$ at about 0.6 Å from the ring nitrogen atoms, corresponding to the lone-pair electrons. In Table 9 mean values for the peak heights of the ring bonds are given. The peak in the C2−NH$_2$ bond of AmP is 0.5 e $Å^{-3}$, in C5−CH$_3$ of MeP 0.2 e $Å^{-3}$ (in both molecules) and in the C−Cl bond of ClP less than 0.1 e $Å^{-3}$. The peak density values do not appear to be on quite the same scale for the different compounds, as the (mean) peak height of the hydrogen atoms vary, being 0.65, 0.71, 0.86 and 0.81 e $Å^{-3}$ for HP, MeP, ClP and AmP, respectively. When the maps are scaled so as to give equal (mean) hydrogen peak heights, the values in brackets in Table 9 are obtained. However, there are in
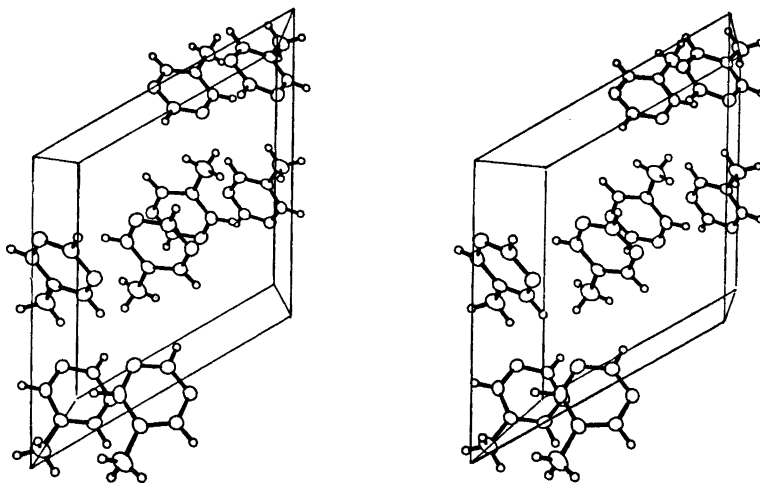

Fig. 3. The crystal structure of MeP viewed in the *b* direction. The *c* axis vertical.
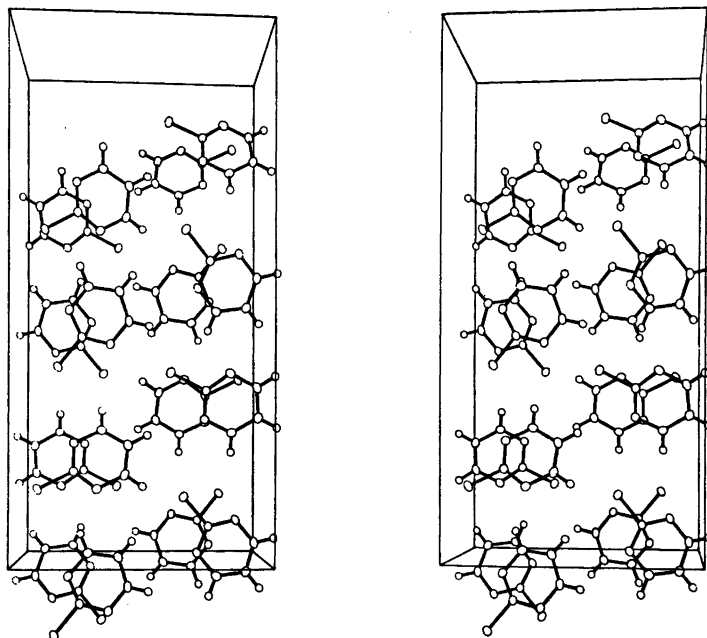
Fig. 4. The crystal structure of ClP viewed along *b*. The *a* axis horizontal.

some cases (AmP) large differences (up to 0.18 e Å⁻³) between densities in bonds assumed to be 2*m*-related, and only the main changes may possibly be significant when comparing the ring densities in different compounds. In MeP the main change relative to HP is an increase in the bond density of C5 − C, which may be related to the electron donating properties of the methyl group. In ClP electron withdrawal from the ring is possibly indicated by the reduction in the density of the C2 − N bonds. In AmP the electron density in the "middle" bond N3 − C4 is possibly increased, and the density in C2 − HN₂ is also high.

The electron density sections perpendicular to the ring bonds are, in general, elliptic with the longest axis approximately perpendicular to the plane of the molecule. Variations in the π-character of the ring bonds might possibly be observed in such sections, but no meaningful conclusions could be drawn on the basis of the present data, which probably are not sufficiently accurate for the study of such details. For the same reason no attempt was made to derive the electron density populations of the ring atoms.

Molecular packing. The arrangement of the molecules in the crystals of MeP is shown in Fig. 3, of ClP in Fig. 4. For HP and AmP the general crystal structures have been reported earlier.[6,7]

The building units in HP, MeP and ClP are stacks of parallel, or nearly parallel, molecules which overlap but little. The stacks run in the *c* direction in HP, in the *b* direction in ClP, and along the *ab* diagonals in MeP. In HP the molecules in a stack are related by translation, in MeP by centres of symmetry, and in ClP by glide planes. The stacks in MeP contain both A and B molecules, whereas those in ClP consist of either A or B molecules. Furthermore, molecules A and B are equally oriented in MeP, but not in ClP.

In all three compounds the shortest inter-stack contacts are between hydrogen atoms and the nitrogen atoms in neighbouring molecules. These H···N contacts, in which all the aromatic hydrogen atoms are involved, lie in the range 2.54 − 2.73 Å. In ClP there are in addition several H···Cl contacts (2.91 − 3.15 Å).

In crystals of AmP the building units con-

sist of centrosymmetrically related hydrogen-bonded pairs of molecules, which are linked to adjacent pairs by hydrogen bonds.[7] The lengths of the two types of hydrogen bonds are 3.047(2) and 3.074(3) Å, respectively.

REFERENCES

1. Bak, B., Christensen, D., Dixon, W. B., Hansen-Nygaard, L. and Rastrup-Andresen, J. *J. Chem. Phys. 37* (1962) 2027.
2. Domenicano, A., Vaciago, A. and Coulson, C. A. *Acta Crystallogr. B 31* (1975) 221.
3. Larsen, N. W. *J. Mol. Struct. 51* (1979) 175.
4. Norrestam, R. and Schepper, L. *Acta Chem. Scand. A 32* (1978) 889.
5. Furberg, S. and Aas, J. B. *Acta Chem. Scand. A 29* (1975) 713.
6. Wheatley, P. J. *Acta Crystallogr. 13* (1960) 80.
7. Scheinbeim, J. and Schempp, E. *Acta Crystallogr. B 32* (1976) 607.
8. Busing, W. R. and Levy, H. A. *Acta Crystallogr. 10* (1957) 180.
9. Doyle, P. A. and Turner, P. S. *Acta Crystallogr. A 24* (1968) 390.
10. Stewart, R. F., Davidson, E. R. and Simpson, W. T. *J. Chem. Phys. 42* (1965) 3175.
11. Groth, P. *Acta Chem. Scand. 27* (1973) 1837.
12. Fernholt, L. and Rømming, C. *Acta Chem. Scand. A 32* (1978) 271.
13. Furberg, S. and Solbakk, J. *Acta Chem. Scand. 24* (1970) 3230.
14. Michel, F., Very, H., Nösberger, P. and Roussy, G. *J. Mol. Struct. 30* (1976) 409.
15. Nygaard, L., Bojesen, I., Pedersen, T. and Rastrup-Andersen, J. *J. Mol. Struct. 2* (1968) 209.
16. Domenicano, A. and Vaciago, A. *Third European Cryst. Meeting*, Zürich 1976, p. 274.
17. Shomaker, V. and Trueblood, K. N. *Acta Crystallogr. B 24* (1968) 63.