by Berggren (1971) has been called to our attention. This paper contains no essentially new conclusion relative to the Colville (1970) paper.

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The Crystal Structure of Clopidol (3,5-Dichloro-2,6-Dimethyl-4-Pyridinol)

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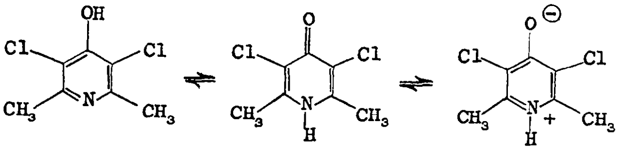
(*Received* 8 *May* 1972)

Clopidol (3,5-dichloro-2,6-dimethyl-4-pyridinol), $C_7H_7Cl_2NO$, is a commercially successful anticoccidial. The crystal and molecular structure of this heterocycle have been determined by single-crystal X-ray diffraction methods. Clopidol crystallizes (usually with twinning) in space group $P2_1/m$ with $a=6\cdot795\pm0\cdot009$, $b=6\cdot932\pm0\cdot013$, $c=8\cdot746\pm0\cdot015$ Å, $\beta=103\cdot56\pm0\cdot07°$, and $Z=2$. X-ray intensity data were gathered on a Picker automatic four-circle diffractometer (Mo $K\alpha$ radiation) using both the θ–2θ and ω scan techniques. The crystal structure was solved from the Patterson function and refined by full-matrix least-squares methods assuming anisotropic temperature factors for the nonhydrogen atoms. The final R values were $R_1=4\cdot4$ and $R_2=3\cdot5\%$ for the 421 reflections above background. The molecules are situated on the crystallographic mirror planes at $y=\frac{1}{4}$ and $\frac{3}{4}$, and form infinite hydrogen-bonded chains in the **a** direction. From the bond lengths and the location of the nonmethyl hydrogen atom, clopidol is shown to exist as the pyridone tautomer in the crystalline state.

3,5-Dichloro-2,6-dimethyl-4-pyridinol, or clopidol, is the active ingredient in a commercially sucessful anticoccidial* used to control coccidiosis in chickens. Since clopidol is in principle able to exist in forms (I)-(III) and because the nature of the hydrogen-bonding system in the crystalline state was not known, a three-dimensional X-ray diffraction study of its crystal structure was undertaken.



(I) (II) (III)

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Experimental

A. *Selection and characterization of crystal*

Crystals of clopidol form laths elongated along [010] and have prominently developed {100} faces (Table 1). The crystals are almost always twinned and exhibit apparent D_{2h} diffraction symmetry. The twin plane is (001); Fig. 1 illustrates the relative disposition of the reciprocal lattices of two individuals in the manner of Herbstein (1965). Overlap in twinned specimens occurs for $0kl$ and again for $5kl$ reflections; *e.g.* the $5k0$ reflection from one individual superimposes on the $5k3$ from another. The crystals are white and very fragile, and generally cleave parallel to the twin planes.

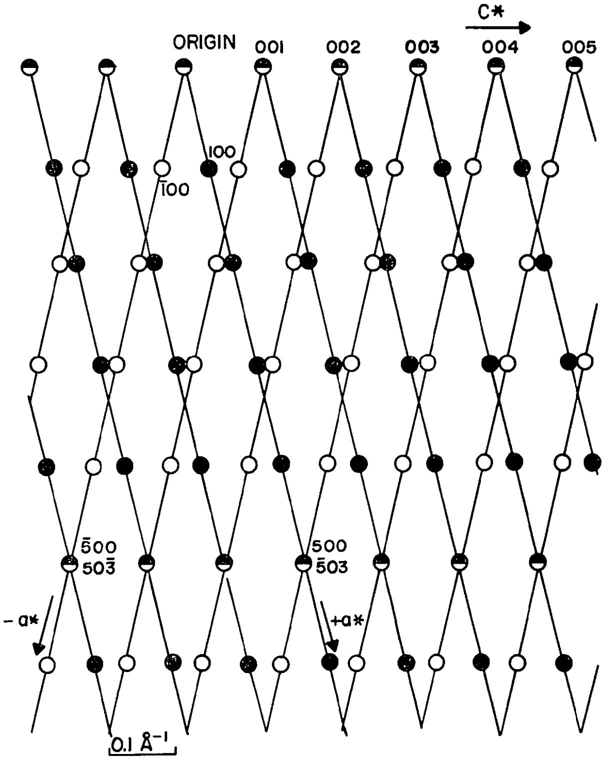

Fig. 1. Superimposed a^*c^* nets of two twinned individuals. Black circles belong to one individual, white circles to the other, and the split circles belong to both.

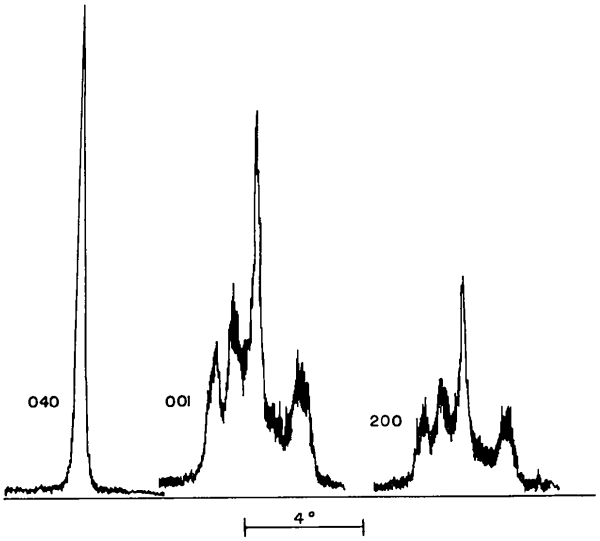

Fig. 2. ω-Scans of axial reflections of the clopidol crystal using a 4-circle diffractometer. The 040 reflection occurs at $\chi=90°$ and its width varies slightly as a function of $\varnothing$. The 001 and 200 reflections occur in the equatorial plane of the diffractometer ($\chi=0°$).

Table 1. *Crystal data*

Clopidol (2,6-dimethyl-3,5-dichloro-4-pyridinol)	
$C_7H_7Cl_2NO$	
M.W.	192·055
Space group	$P2_1/m$ (No. 11, C_{2h}^2)
a	6·795 (9) Å
b	6·932 (13)
c	8·746 (15)
β	103·56 (7)°
Z	2
D_{calc}	1·593 g.cm^{-3}
μ(Mo $K\alpha$)	4·09 cm^{-1}

To obtain crystals of a quality suitable for an X-ray structural study, we experimented with a variety of crystal growth techniques, including sublimation and controlled precipitation from a number of solvents. The most promising specimens were examined further by optical and then X-ray methods. While searching for a twinned crystal sufficiently well-formed for further work, we were fortunate enough to find a small untwinned crystal fragment in a batch of crystals grown from dimethylformamide. This specimen was 0·42 mm long (on **b**), 0·098 mm wide (on **a**) and varied in thickness between 0·033 and 0·072 mm from one end to the other. The diffraction profiles of its reflections indicated that this crystal possessed an irregular mosaic structure in the xz plane (see Fig. 2). However, since the mosaicity was not as severe as for most of the twinned specimens examined, we decided to use this crystal for intensity measurements.

The crystal was aligned on its b axis on a Weissenberg goniometer. Oscillation and Weissenberg photographs showed the reciprocal lattice symmetry to be C_{2h}. No systematic absences were observed on the $h0l$, $h1l$ or $h2l$ levels, but a careful scan of the $0k0$ row on a Picker four-circle diffractometer revealed the reflection conditions $0k0$, $k=2n$, indicating the space group to be $P2_1$ or $P2_1/m$. Lattice constants at 25°C were calculated by least-squares refinement of the setting angles of ten reflections on the diffractometer (Mo $K\bar{\alpha}$ radiation, $\lambda=0{\cdot}71069$ Å). The setting angles were taken to be the centers of the major peaks in the reflection scans (Fig. 2). Excellent precision was obtained in the least-squares analysis; the errors in Table 1 are the least-squares errors multiplied by an arbitrary factor of 10 to allow for possible systematic errors in these measurements. The presence of two molecules per unit cell may be accommodated either by general positions of space group $P2_1$ or by placing the molecules in the symmetry planes of space group $P2_1/m$.

B. Data collection and solution of structure

Intensity data were gathered on the diffractometer using Mo $K\bar{\alpha}$ radiation selected by the 002 reflection of a highly oriented graphite crystal monochromator. The take-off angle of the X-ray tube was 3°, and a counter aperture 6·0 × 6·0 mm square was positioned 30 cm from the crystal; 1·5 mm diameter incident- and exit-beam collimators restricted stray radiation. The reciprocal lattice was recorded out to the sphere limited by sin θ = 0·4063, containing a total of 679 unique reflections. About half of these were found to be absent using the statistical criteria described below. Attenuators were used to prevent count rates in excess of 12,000/sec. A test reflection $\bar{2}12$ was monitored after every 50 measurements and showed fairly good stability, with a maximum fluctuation of about 3% from the mean intensity. An error $\sigma(I)=[(0·02I)^2+N_o+k^2N_b]^{1/2}$ was assigned to the net intensity $I=N_o-kN_b$. Here N_o is the gross count, N_b is the background count, and k is the ratio of scan time to background time. The intensities were then corrected for Lorentz-polarization effects and for absorption (de Meulenaer & Tompa, 1965). Transmission coefficients ranged from 0·96 to 0·98.

Three unique sets of intensity data were actually collected, two by the θ–2θ scan technique and the third by the ω-scan method. As we shall see, the ω-scan data were taken because of certain anomalies in the θ–2θ data to be discussed below. The first set, which we designate by the symbol $F(\theta_1)$, contained the hkl and $\bar{h}kl$ reflections. The $F(\theta_2)$ set contained the $hk\bar{l}$ and $\bar{h}k\bar{l}$ reflections. Both were collected at a scan speed of 0·5°/min over a 2θ scan angle of 2·6° + Δ, where Δ is the separation of the $K\alpha$ doublet. The set designated $F(\omega)$, containing the hkl and $\bar{h}kl$ reflections, was collected at a scan speed of 1°/min over an ω-scan angle of 5°. In all cases, background counts of 40 sec were taken at each end of the scan.

A rough crystal structure was obtained as follows from the $F(\theta_1)$ set of intensity data, while the remaining data were being gathered. A scale factor and overall temperature factor (B_o = 3·35 Å^2) were computed by Wilson's (1942) method and used to calculated a normal-sharpened Patterson function. Inspection of the map revealed that significant peaks occurred exclusively at $y=0$ and $y=\frac{1}{2}$, suggesting strongly that the space group was $P2_1/m$ with all non-hydrogen atoms located on the crystallographic mirrors. The crystal structure was readily deduced from an analysis of the Patterson peaks. Starting from a trial model a full-matrix least-squares refinement of atomic positions and temperature factors reduced $R_1\equiv\sum||F_o|-|F_c||/\sum|F_o|$ to 0·188 and $R_2\equiv\{\sum w[F_o-F_c]^2/\sum wF_o^2\}^{1/2}$ to 0·151 after 6 cycles. Distances, angles, and temperature factors all appeared quite reasonable for this stage of refinement.

However, inspection of the observed and calculated intensities revealed a fairly serious problem with the three $0k0$ reflections, for which the observed structure factors were too high by factors of 25 to 75%. (Recall that the calculated structure factors for $0k0$ are independent of the choice of atomic positions in space group $P2_1/m$ because the heavy atoms are constrained to the mirror planes.) A number of explanations for this phenomenon were considered, but it was eventually traced to the anisotropic nature of the mosaic structure of this crystal as discussed above. As Fig. 2 indicates, the distribution of intensity of the $0k0$ reflections along the ω axis is quite sharp. On the other hand for equatorial reflections, such as $h00$ and $00l$, the distribution is quite broad, of the order of 4°. With the exception of a few reflections (such as the $0k1$ row) near $\varphi=90°$ on the diffractometer, most general reflections had profiles similar to those found for equatorial reflections. Under our experimental conditions, the θ–2θ scan technique fails to count a certain fraction of this distribution; the situation is analogous to trying to measure a reflection with ω mis-set by up to 2°. The treatment of the data discussed below later indicated that the fraction of the distribution missed is apparently fairly constant over most of the data set, and that for most reflections no serious error is introduced by the θ–2θ technique. However, for the 'sharp' $0k0$ reflections, and to a lesser extent for $0kl$, the fraction missed is significantly smaller and these reflections appear relatively too intense with respect to the rest of the data set.

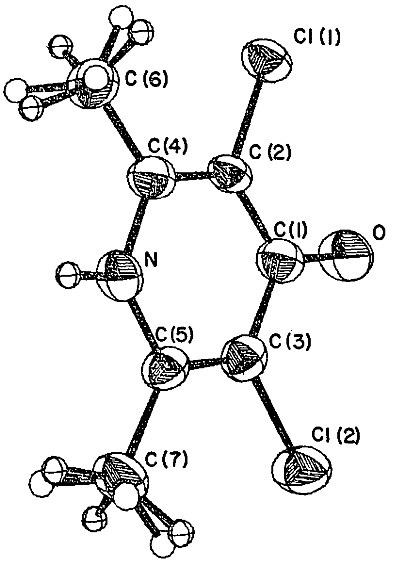

Fig. 3. The molecular structure of clopidol showing ellipsoids of thermal motion drawn at 50% probability. Both sets of hydrogen positions are shown for the disordered methyl groups, with hydrogens indicated by spheres of arbitrary radius.

To define the extent and nature of the problem, which was then not known, the decision was made to collect redundant data by the ω-scan method. Using this data much better agreement for the $0k0$ and $0k1$ reflections was obtained; accordingly the final observed structure factors for these two rows are based on $F(\omega)$

alone. For general reflections, however, the $F(\omega)$ data showed no better agreement with the model than the θ–2θ data. Indeed, our results showed that the average of any two of our data sets gave a significantly improved fit to the calculated F's than did any primary data set, and that merger of all three primary data sets gave the best agreement of all. The internal agreement of the primary data sets with each other, incidentally, was only about 15%. Much of the disagreement arises from counting statistics, so it is not really surprising that merging the data yielded a much improved fit to the calculated F's.

With the accuracy problem of the F's near the b axis solved, and with the overall precision of the data set improved *via* merger,[*] the R values dropped to $R_1 = 0{\cdot}14$ and $R_2 = 0{\cdot}101$ after four more cycles of isotropic refinement. Upon introduction of anisotropic temperature factors for C, N, O and Cl atoms, R_1 and R_2 dropped to 0·060 and 0·063 respectively.

The location of the N hydrogen atom in an electron density difference map was straightforward, but chemically reasonable positions for all six methyl hydrogens could not be assigned unambiguously. However, the occurrence of significant electron density peaks at some of the expected hydrogen positions suggested that rotation about the $C–CH_3$ bonds might not be completely unrestricted. If we assume hydrogen atom positions consistent with the symmetry plane of the space group, each methyl group is permitted two conformations, one with the in-plane hydrogen toward the nitrogen end of the molecule, the other toward the oxygen end. Thus four possible ordered structures are allowed. In addition a disordered model can be postulated with both conformations given equal weight at each methyl group, and we may further consider the four combinations of an ordered structure on one methyl and a disordered structure on the other. R values were computed for all nine of these models (without refinement and assuming standard C–H bond lengths and tetrahedral bond angles at the methyl carbons). The calculations favored the completely disordered model (Fig. 3), which was then assumed throughout the final phase of refinement.

After three final cycles of least-squares refinement, convergence was obtained at $R_1 = 0{\cdot}044$ and $R_2 = 0{\cdot}033$ for the 421 reflections above background. In these calculations, the position and isotropic temperature factor of the N hydrogen atom had been permitted to vary, as had a common temperature factor for the 12 methyl hydrogen sites. In the final cycle no parameter shift exceeded $0{\cdot}05\sigma$. The final electron density difference map contained no peaks above 0·35 e.Å^{-3}.

Table 2 lists observed and calculated structure factors. Final atomic parameters and their standard deviations as calculated in the last cycle of least-squares refinement are given in Table 3. Intramolecular distances and angles with standard deviations obtained from the least-squares variance-covariance matrix are presented in Table 4. The amplitudes and directions of anisotropic thermal motion are illustrated in the form of thermal ellipsoids, drawn at 50% probability, in Fig. 3.

The atomic scattering factors for Cl, C, N, and O were taken from the *International Tables for X-ray Crystallography* (1962), as were the anomalous scattering factors used for the Cl atoms. The scattering factor for hydrogen is that given by Stewart, Davidson, and Simpson (1965). Fourier summations, least-squares refinements, and error analysis were based on adaptations of standard programs by Gvildys (1964, 1965, 1967) and illustrations were prepared using our own adaptation of the thermal ellipsoid plot program of Johnson (1965).

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[*] Weights were developed by the following scheme. The arithmetic mean (A) of the errors $\sigma(F)$ assigned to the three independent measurements was calculated. A parameter Δ was defined as the difference of $F(\omega)$ and $F(\theta)$, or 1, whichever was greater. The error $\sigma(F)$ was taken as the geometric mean of A and Δ. Term A brings in the effect of counting statistics, whereas the factor Δ serves to reduce somewhat the relative weight of reflections where the two kinds of experimental data were in poor agreement. Reflections for which $\sigma(F^2) \geq 0{\cdot}5F^2$ were taken as absent.

Table 2. *Observed and calculated structure factors in* $e \times 10$.

K	L	FOBS	FCAL
•• H = 0 ••			
2	0	1297	1332
4	0	600	605
6	0	273	285
0	1	307	300
1	1	145	138
2	1	249	234
3	1	71	63
4	1	137	123
0	2	191	184
1	2	225	224
2	2	136	127
3	2	121	108
4	2	77	75
0	3	56	41
1	3	546	547
3	3	321	312
5	3	152	149
6	4	49	29
0	5	169	168
1	5	133	138
2	5	133	137
3	5	108	101
4	5	94	87
5	5	67	68
6	5	52	45
0	6	358	358
1	6	60	49
2	6	304	306
4	6	201	204
6	6	115	115
0	7	235	244
2	7	210	216
3	7	38	25
4	7	154	153
1	8	62	50
1	9	97	94
•• H = 1 ••			
0	0	450	458
1	0	191	189
2	0	366	355
3	0	170	160
4	0	235	205
5	0	83	82
6	0	136	116
7	0	48	33
-0	-1	193	195
0	1	31	29
1	1	230	241
-1	-1	101	110
-2	-1	155	140
3	1	195	188
-3	-1	48	42
-4	-1	82	67
5	1	114	98
6	1	41	37
7	1	62	41
-0	-2	251	253
0	2	151	149
1	2	73	63
-1	-2	93	90
-2	-2	237	238
2	2	119	119
3	2	48	59
-3	-2	36	28
-4	-2	161	154
4	2	79	74
-0	-3	330	330
0	3	368	367
1	3	79	72
-2	-3	280	273
2	3	312	309
-4	-3	166	157
4	3	192	199
-6	-3	84	72
6	3	94	95
-0	-4	149	148
0	4	198	202
1	4	188	184
-1	-4	69	64
-2	-4	130	130
2	4	172	174
3	4	116	109
-4	-4	88	94
4	4	110	110
-6	-4	66	63
6	4	53	55
-7	-4	51	25
-0	-5	76	77
0	5	69	60
-1	-5	265	263
-2	-5	64	57
2	5	63	57
-3	-5	199	199
4	5	48	43
-5	-5	120	119
-0	-6	94	93
0	6	132	136
1	6	146	152
-1	-6	169	166
-2	-6	87	84
2	6	121	123
3	6	118	115
-3	-6	123	120
-4	-6	84	69
4	6	88	90
5	6	65	66
-5	-6	70	64
-6	-6	65	52
-0	-7	187	192
1	7	102	104
-2	-7	169	170
2	7	40	24
3	7	86	79
-4	-7	110	116
-0	-8	113	112
0	8	53	63
1	8	68	67
-1	-8	79	82
-2	-8	87	97
2	8	55	53
3	8	63	51
-3	-8	64	65
-4	-8	69	62
-0	-9	67	69
0	9	111	112
2	9	87	99
•• H = 2 ••			
0	0	360	362
1	0	161	167
2	0	251	254
3	0	105	106
4	0	127	110
5	0	71	72
-0	-1	250	249
0	1	475	477
1	1	281	286
-1	-1	315	332
-2	-1	181	188
2	1	330	344
3	1	172	168
-3	-1	187	187
-4	-1	107	103
4	1	176	178
5	1	92	78
-5	-1	102	97
6	1	94	90
7	1	48	31
-7	-1	68	48
-0	-2	279	276
0	2	192	191
1	2	131	126
-1	-2	453	452
-2	-2	214	215
2	2	151	149
3	2	85	83
-3	-2	256	257
-4	-2	122	116
4	2	98	91
5	2	57	56
-5	-2	137	131
-6	-2	64	54
-7	-2	61	62
0	3	312	309
1	3	321	315
-1	-3	222	243
2	3	248	247
3	3	207	207
-3	-3	128	122
-4	-3	57	50
4	3	159	156
5	3	110	107
-5	-3	57	50
6	3	89	92
-0	-4	437	431
0	4	152	154
1	4	148	150
-1	-4	297	288
-2	-4	347	340
2	4	120	123
3	4	97	103
-3	-4	199	196
-4	-4	208	203
4	4	75	69
5	4	67	59
-5	-4	110	114
-6	-4	108	112
-0	-5	161	165
-1	-5	169	169
-2	-5	127	131
-3	-5	133	127
-4	-5	77	78
-5	-5	82	76
0	6	140	132
1	6	158	149
2	6	112	113
3	6	114	116
4	6	65	72
5	6	74	76
-0	-7	100	99
0	7	56	64
1	7	69	70
-1	-7	166	166
-2	-7	84	86
2	7	61	56
3	7	54	48
-3	-7	124	127
4	7	58	40
-5	-7	84	78
-0	-8	91	91
-1	-8	102	102
-2	-8	78	81
2	8	52	40
-3	-8	69	79
-4	-8	66	58
-0	-9	45	28
•• H = 3 ••			
1	0	142	141
3	0	115	109
5	0	65	74
-0	-1	148	149
0	1	217	214
1	1	186	185
-1	-1	309	306
-2	-1	137	141
2	1	175	183
3	1	122	126
-3	-1	198	197
-4	-1	107	106
4	1	105	114
5	1	65	62
-5	-1	111	102
-7	-1	58	47
-0	-2	225	221
0	2	127	125
1	2	103	102
-1	-2	173	180
-2	-2	174	182
2	2	87	95
3	2	94	92
-3	-2	112	124
-4	-2	100	101
-5	-2	70	70
-1	-3	79	78
-2	-3	63	39
-3	-3	52	53
6	3	40	18
-0	-4	169	167
0	4	131	135
1	4	165	169
-1	-4	186	181
-2	-4	131	136
2	4	116	116
3	4	127	128
-3	-4	141	149
-4	-4	73	81
4	4	77	71
5	4	73	73
-5	-4	91	99
-0	-5	134	135
0	5	57	59
1	5	101	101
-1	-5	140	140
-2	-5	111	110
2	5	71	58
3	5	68	69
-3	-5	94	93
-4	-5	67	74
5	5	37	36
-0	-6	105	108
-2	-6	93	95
2	6	52	48
-0	-7	182	193
0	7	102	93
1	7	110	103
-1	-7	96	100
-2	-7	158	163
2	7	98	79
3	7	82	81
-3	-7	78	79
-4	-7	116	115
-5	-7	59	52
-0	-8	71	67
-2	-8	52	54
-1	-9	86	80
-3	-9	63	60
•• H = 4 ••			
1	0	203	203
3	0	139	147
5	0	86	88
-0	-1	170	169
0	1	97	96
1	1	143	140
-1	-1	100	106
-2	-1	144	141
2	1	69	75
3	1	100	99
-3	-1	57	75
-4	-1	96	91
-5	-1	45	41
-0	-2	155	156
0	2	251	248
1	2	219	216
-1	-2	122	114
-2	-2	131	132
2	2	212	216
3	2	157	162
-3	-2	78	64
-4	-2	87	88
4	2	154	151
5	2	92	97
6	2	82	90
-0	-3	224	221
0	3	82	87
-2	-3	169	182
2	3	80	78
-3	-3	45	18
-4	-3	104	113
-0	-4	253	252
0	4	131	133
-1	-4	163	159
-2	-4	217	217
2	4	106	114
-3	-4	125	126
-4	-4	151	149
4	4	76	72
-5	-4	72	81
-6	-4	90	86
-0	-5	105	99
0	5	101	96
-2	-5	98	97
2	5	88	83
-4	-5	70	65
4	5	55	52
-6	-5	48	61
-1	-6	176	178
-3	-6	122	131
-5	-6	54	76
-0	-7	107	112
0	7	48	36
1	7	107	111
-2	-7	100	102
-4	-7	80	75
-0	-9	151	155
-2	-9	133	137
•• H = 5 ••			
1	0	91	94
2	0	69	61
3	0	73	72
1	1	93	98
-1	-1	189	188
2	1	54	46
3	1	72	64
-3	-1	134	134
-5	-1	73	73
0	2	290	297
1	2	110	101
2	2	253	259
3	2	81	82
4	2	167	177
5	2	69	55
-0	-3	95	86
1	3	61	69
-1	-3	99	93
-2	-3	73	76
3	3	61	58
-3	-3	70	72
-5	-3	55	46
-0	-4	304	301
0	4	51	33
-2	-4	261	261
-4	-4	176	176
-0	-5	194	199
1	5	112	117
-1	-5	171	176
-2	-5	180	177
-3	-5	128	129
-4	-5	126	127
-5	-5	87	72
-0	-6	65	65
-2	-6	78	73
-4	-6	55	48
-1	-7	89	86
-3	-7	53	65
-1	-8	94	90
•• H = 6 ••			
0	0	116	107
2	0	67	70
3	0	50	32
4	0	75	67
-0	-1	141	147
0	1	50	52
-1	-1	50	54
-2	-1	119	127
-3	-1	37	37
-4	-1	85	86
-0	-2	160	166
1	2	74	65
-1	-2	49	37
-2	-2	144	148
-4	-2	108	108
-0	-3	52	49
0	3	53	36
1	3	107	105
-1	-3	75	103
3	3	74	82
-3	-3	70	64
-2	-4	62	59
-0	-5	77	72
-2	-5	58	62
-3	-5	40	41
-0	-6	104	95
-1	-6	74	65
-2	-6	74	66
-3	-6	51	54
-2	-7	53	40
•• H = 7 ••			
0	0	63	60
1	0	71	59
1	1	105	96
-0	-2	171	178
0	2	54	46
-1	-2	64	51
-2	-2	154	157
-0	-3	57	48
-3	-3	49	41
-0	-5	81	74
-1	-5	129	127
-2	-5	67	63

Results and discussion

The crystal structure shows that clopidol takes the oxo or pyridone form in the crystalline state. While this result is consistent with a widely held view (Katritzky & Lagowski, 1963) that α- and γ-hydroxypyridines exist predominantly as pyridones, we note that Boer & Turley (1972) have recently shown that tetrachloro-4-hydroxypyridine (TCHP) exists as the hydroxy or pyridinol tautomer in the solid. (β-Hydroxypyridines are of course expected to exist as pyridinols; a recent structure determination of the internally hydrogen-bonded dimer 2,2′-bis-(6-methyl-3-pyridinol) by Vogt & Wirth (1971) exemplifies this type of structure).

The structural arguments for the oxo form appear to be quite conclusive. The most important piece of evidence is the location of the hydrogen atom 0·81 ± 0·06 Å from the nitrogen. (The apparent N–H bond distance, in addition to being subject to a fairly large random error, is undoubtedly systematically shortened from the true internuclear separation [probably 1·00 Å or more (Sutton, 1965)] due to the bias of electron density from the hydrogen nucleus toward the N–H bond region and to the effects of vibrational motion. This hydrogen atom is clearly part of an N–H· · ·O hydrogen bond of length 2·755 Å. The N–H· · ·O angle of 167° is normal and supports the assignment of the hydrogen position. Chatar Singh (1965) has proposed an indirect test for the presence of an extra-annular hydrogen attached to nitrogen by noting that the internal bond angle at nitrogen atoms with an extra-annular hydrogen is significantly greater (and more than 120°) than at nitrogen atoms without an attachment (where the angle is generally less than 120°). The bond angle at nitrogen in clopidol is 123·0°, a value similar ($3{\cdot}5\sigma$) to the angle of 125·1° in α-pyridone (Penfold, 1953), where the hydrogen atom is also clearly associated with the nitrogen. In TCHP (Fig. 4) which has the pyridinol structure, and in pyridine (Bak, Hansen-Nygaard & Rastrup-Andersen, 1958) the respective bond angles are 116·6 and 116·8°.

The carbon-oxygen bond length would also be expected to be sensitive to the position of the hydrogen. The bond length in clopidol (1·253 Å) is within 3σ of

Table 3. *Final clopidol structure parameters*

Anisotropic temperature factors are in the form $\exp\left[-(h^2\beta_{11}+k^2\beta_{22}+l^2\beta_{33}+2hk\beta_{12}+2kl\beta_{23}+2hl\beta_{13})\right]$. The y coordinate of all atoms is 0·25. $\beta_{12}=\beta_{23}=0$.

	x	z	$10^4\times\beta_{11}$	$10^4\times\beta_{22}$	$10^4\times\beta_{33}$	$10^4\times\beta_{13}$
Cl(1)	0·5918 (3)	0·2629 (2)	226 (6)	202 (6)	103 (3)	76 (3)
Cl(2)	0·7553 (3)	0·8990 (2)	175 (6)	355 (8)	97 (3)	17 (3)
O	0·8499 (7)	0·5857 (5)	131 (14)	353 (21)	139 (9)	46 (9)
N	0·2502 (8)	0·5710 (6)	105 (14)	230 (20)	115 (10)	45 (11)
C(1)	0·6638 (11)	0·5792 (8)	206 (21)	158 (22)	102 (10)	44 (12)
C(2)	0·5113 (9)	0·4368 (7)	158 (19)	158 (23)	72 (10)	50 (12)
C(3)	0·5822 (10)	0·7178 (7)	166 (19)	152 (23)	96 (11)	16 (12)
C(4)	0·3109 (10)	0·4314 (8)	177 (20)	178 (23)	83 (11)	34 (11)
C(5)	0·3817 (10)	0·7126 (7)	138 (19)	191 (23)	77 (10)	4 (11)
C(6)	0·1450 (9)	0·2849 (8)	137 (19)	298 (29)	113 (12)	24 (13)
C(7)	0·2919 (10)	0·8525 (7)	152 (19)	309 (29)	106 (11)	58 (12)
H(N)	0·129 (10)	0·559 (8)		B(isotropic) = 5·1 Å^2		

Table 4. *Bond distances and angles for clopidol*

Standard errors as calculated from the least-squares variance-covariance matrix are given in parentheses. Asterisks indicate distances to molecule related by the **a** translation.

Distances (Å)

C(1)–C(2)	1·421 (9)	C(2)–Cl(1)	1·733 (6)
C(1)–C(3)	1·446 (9)	C(3)–Cl(2)	1·738 (7)
C(2)–C(4)	1·351 (8)	C(4)–C(6)	1·495 (9)
C(3)–C(5)	1·352 (8)	C(5)–C(7)	1·490 (8)
C(4)–N	1·370 (8)	N–H(N)	0·81 (6)
C(5)–N	1·353 (8)	H(N)· · ·O*	1·96 (6)
C(1)–O	1·253 (7)	N–H(N)· · ·O*	2·755 (7)

(*b*) Angles

C(4)–N—–C(5)	123·0 (6)	C(2)–C(1)–C(3)	113·0 (6)
C(4)–N—–H(N)	114 (5)	C(2)–C(1)–O	124·1 (6)
C(5)–N—–H(N)	123 (5)	C(3)–C(1)–O	122·9 (6)
C(1)–C(2)–C(4)	123·5 (6)	C(1)–C(3)–C(5)	123·5 (6)
C(1)–C(2)–Cl(1)	117·0 (5)	C(1)–C(3)–Cl(2)	117·0 (5)
C(4)–C(2)–Cl(1)	119·5 (5)	C(5)–C(3)–Cl(2)	119·5 (5)
C(2)–C(4)–N	118·6 (6)	C(3)–C(5)–N	118·3 (6)
C(2)–C(4)–C(6)	125·5 (6)	C(3)–C(5)–C(7)	125·1 (6)
N–C(4)–C(6)	115·8 (6)	N—–C(5)–C(7)	117·6 (6)
N–H(N)· · ·O*	167 (7)	H(N)· · ·O*–C(1)*	171 (2)
C(1)–O· · ·N*	174·7 (9)		

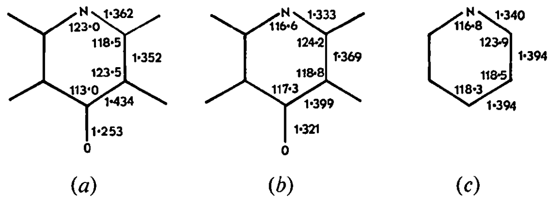

Fig. 4. A comparison of bond distances and angles in (*a*) clopidol, (*b*) tetrachloro-4-hydroxypyridine (Boer & Turley, 1972) and (*c*) pyridine (Bak, Hansen-Nygaard & Rastrup-Andersen, 1958). The values are averaged to C_{2v} symmetry.

that in α-pyridone (1·236 Å) and relatively close to the accepted value of 1·215 Å for aldehydes and ketones (Sutton, 1965). Values for pyridinol tautomers are considerably larger, [TCHP, 1·321 Å and 2,2′-bis-(6-methyl-3-pyridinol), 1·347 Å] and, within experimental error, overlap the range of values found for phenol derivatives [pentachlorophenol (Sakurai, 1962), 1·329 Å; catechol (Brown, 1966), 1·364–1·380 Å; resorcinol (Bacon & Curry, 1956), 1·34–1·36 Å; phloroglucinol (Maartmann-Moe, 1965), 1·37–1·38 Å].

Bond distances on the ring show strong evidence for a contribution from the localized canonical form (II) when compared to the corresponding values in TCHP and pyridine (Fig. 4). Thus, the bond lengths between the α- and β-carbons [C(2)–C(4), 1·351 ± 0·008 Å and C(3)–C(5), 1·352 ± 0·008 Å] are not a great deal longer than the accepted value for a carbon–carbon double bond, 1·335 Å (Sutton, 1965). Similarly, the bonds between β- and γ-carbons [C(1)–C(2), 1·421 ± 0·009 Å and C(1)–C(3), 1·446 ± 0·009 Å] approach the expected range (1·465–1·49 Å) for single bonds between sp^2 hybridized carbons (Sutton, 1965). The carbon–nitrogen bonds, 1·353 ± 0·008 and 1·370 ± 0·008 Å, are also significantly longer than the corresponding bonds in TCHP and pyridine. The facts remain, however, that neither the C(8)–O nor C(α)–C(β) bonds can be classified as pure double bonds, nor can the N–C(α) or C(β)–C(γ) bonds be called pure single bonds, and we must conclude that aromatic forms such as (III) make an important contribution to the valence structure of clopidol.

The crystal structure (Figs. 5 and 6) is based upon linear chains of clopidol molecules aligned head-to-tail and related by the cell translation in the **a** direction. In this arrangement, the hydrogen bonds are nearly, but not quite, collinear with the carbon–oxygen bonds, as evinced by the C–O···N(H) angle of 174·7°. Within a given layer, say at $y=\frac{1}{4}$, there are an infinite number of parallel chains proceeding in the same direction and related by the translation along **c**. In adjacent layers, however, the chains proceed in opposite directions. This structure is probably a consequence of the large dipole moment of the clopidol molecule: γ-pyridinol has a moment of 6·0 Debye (Albert & Phillips, 1956) and clopidol is probably even more polar since the electronegative chlorine substituents occur in the negatively polarized half of the molecule. The head-to-tail arrangement is of course a favorable way of aligning dipoles in a chain, and the close approach of opposed dipoles generated by the centers of symmetry directly above and below each molecule (at $\frac{1}{2},\frac{1}{2},\frac{1}{2}$ and $\frac{1}{2},0,\frac{1}{2}$) lends further stability to the structure.

The linear chain structure, as found in clopidol, may well be a relatively rare feature. In both TCHP and α-pyridone infinite *helical* chains occur based on C–O···N angles of 135·5 and 136° respectively. In all three of these systems, the lengths of the hydrogen bonds are very similar (clopidol, 2·755 Å; TCHP, 2·740 Å; α-pyridone, 2·77 Å).

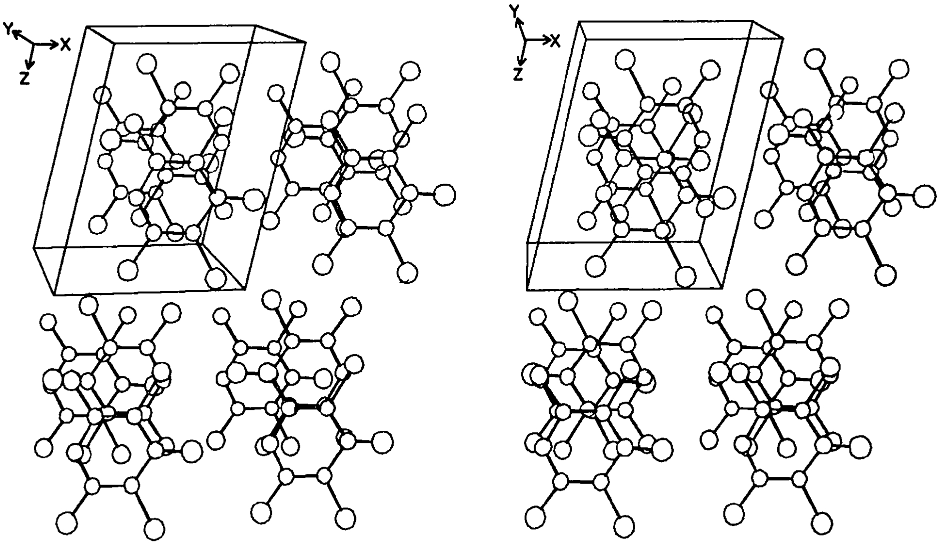

Fig. 5. Three-dimensional stereopair view of the crystal structure of clopidol as viewed down the *y* axis.

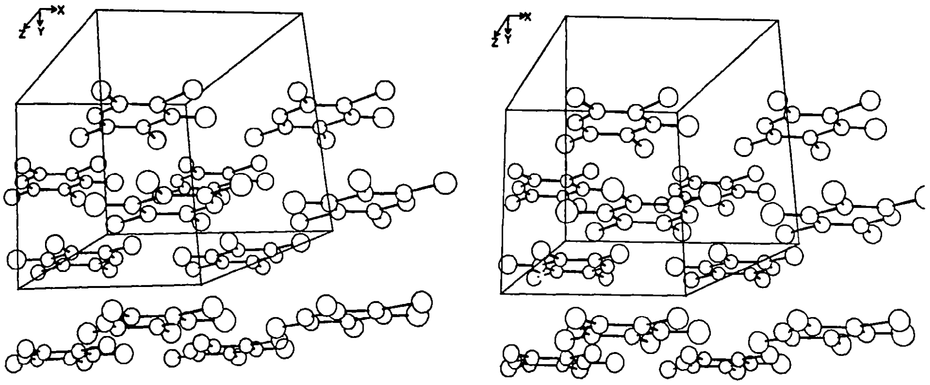

Fig. 6. The crystal structure of clopidol as viewed perpendicular to the xy plane.

Interatomic contacts below 3·7 Å are summarized in Table 5. With one exception, where a methyl–chlorine contact is generated by the double translation **a**+**c**, all interactions arise by the **a** or **c** translations or the inversion centers at $\frac{1}{2},0,\frac{1}{2}$ and $\frac{1}{2},\frac{1}{2},\frac{1}{2}$. Since adjacent layers are only 3·398 Å apart ($b/2$) the greatest number of contacts are generated by the inversion centers. Within each layer there is one unique chlorine–chlorine interaction at a distance (3·608 Å) approximately equal to the sum of two chlorine van der Waals radii, and four close chlorine–methyl contacts ranging from 3·688 to 3·769 Å (Table 5).

Table 5. *Interatomic contacts less than* 3·7 Å

Atom 1	Atom 2	Symmetry transform, Atom 2	Distance Å
Cl(1)	C(5)	$1-x,\ 1-y,\ 1-z$ (2)	3·474
Cl(1)	Cl(2)	$x,\ y,\ z-1$	3·608
Cl(1)	C(3)	$1-x,\ 1-y,\ 1-z$ (2)	3·678
Cl(1)	CH_3(7)	$x,\ y,\ z-1$	3·688
Cl(1)	CH_3(6)	$1+x,\ y,\ z$	3·718
Cl(2)	CH_3(7)	$1+x,\ y,\ z$	3·762
Cl(2)	CH_3(6)	$1+x,\ y,\ 1+z$	3·769
O	N	$1+x,\ y,\ z$	2·755
O	CH_3(7)	$1+x,\ y,\ z$	3·343
O	C(5)	$1+x,\ y,\ z$	3·522
O	C(4)	$1-x,\ 1-y,\ 1-z$ (2)	3·626
O	CH_3(6)	$1-x,\ 1-y,\ 1-z$ (2)	3·643
O	C(6)	$1+x,\ y,\ z$	3·662
O	C(4)	$1+x,\ y,\ z$	3·689
C(1)	C(4)	$1-x,\ 1-y,\ 1-z$ (2)	3·472
C(1)	C(2)	$1-x,\ 1-y,\ 1-z$ (2)	3·656
C(2)	C(2)	$1-x,\ 1-y,\ 1-z$ (2)	3·652

We thank J. J. Flynn Jr for valuable help in selecting crystals, and J. W. Turley and F. P. van Remoortere for stimulating discussions.

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