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The Crystal and Molecular Structure of Thiethylperazine, a Derivative of Phenothiazine

BY J. J. H. MCDOWELL

Department of Physics, University of Cape Town, Republic of South Africa

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The crystal structure of an important phenothiazine derivative, thiethylperazine (2-ethylthio-10-[3-(4-methylpiperazin-1-yl)propyl]phenothiazine), has been determined from diffractometer data and refined with individual anisotropic thermal parameters by least-squares methods to a final residual of 10·5%. The space group is $P2_12_12_1$ with $a=12{\cdot}057\pm0{\cdot}01$, $b=19{\cdot}953\pm0{\cdot}01$, $c=9{\cdot}215\pm0{\cdot}01$ Å. The tricyclic group has a C–S–C angle of $99{\cdot}0\pm0{\cdot}7$° and C–S bonds of $1{\cdot}78\pm0{\cdot}02$ Å, indicating the participation of *d* orbitals in the bonding of S. The dihedral angle between the two planes of the benzene rings is 139·0°. The piperazine ring has the chair configuration. A theory of charge transfer is discussed in connexion with the action mechanism of the phenothiazines.

Introduction

Thiethylperazine (trade name Torecan) is 2-ethylthio-10-[3-(4-methylpiperazin-1-yl)propyl]phenothiazine. It is valued mainly for its anti-emetic properties and is used for the control of post-operative vomiting, vomiting associated with malignant disease, radiation therapy, *etc.* It is the second of the series of phenothiazine derivatives to have been studied in this laboratory, with the eventual hope of correlating molecular structure with psychopharmacological properties.

Certain of the phenothiazine derivatives form a very important group termed the major tranquillizers, widely used for the treatment of psychoses such as schizophrenia, mania and senile dementia. They have a depressant action on the brain stem, with little or no action on the cerebral cortex or the spinal cord. The phenothiazines are divided into three groups according to the chemical nature of the side chain attached to the nitrogen atom: (1) dimethylaminopropyl, (2) piperidine, (3) piperazine radical. Chlorpromazine (McDowell, 1969), which is psychotropically potent and one of the most widely used, belongs to the first group; thiethylperazine, which has relatively little tranquillizing or sedative action, belongs to the third. (*Progress in Drug Research*, 1963; *Extra Pharmacopoeia*, 1967).

Although the phenothiazines have been subjected to extensive clinical tests, their chemical structural features have not so far been found to have a sufficiently constant association with pharmacological, psychological and clinical effects to develop a theory of their mode of action. It seems likely that in seeking the precise mechanism of action of the drugs, the problems must be 'viewed through the glasses of the submolecular' (Szent-Györgyi, 1960).

Solution and refinement of the structure

Colourless transparent prismatic crystals were prepared by evaporation from a warmed solution of thiethylperazine in petroleum spirit. X-ray oscillation and Weissenberg photographs, with the use of Ni-filtered Cu $K\alpha$ radiation, taken about the x and y axes, gave an orthorhombic system with $a=12{\cdot}056\pm0{\cdot}02$, $b=19{\cdot}952\pm0{\cdot}03$, $c=9{\cdot}204\pm0{\cdot}01$ Å, in close agreement with the diffractometer values obtained subsequently; $a=12{\cdot}057\pm0{\cdot}01$, $b=19{\cdot}953\pm0{\cdot}01$, $c=9{\cdot}215\pm0{\cdot}01$ Å. The latter values were considered more accurate and were used in all calculations. The conditions for non-extinction were found to be $h00$, $h=2n$; $0k0$, $k=2n$; $00l$, $l=2n$, which uniquely determined the space group as $P2_12_12_1$. $D_m=1{\cdot}187$ g.cm^{-3}, $D_c=1{\cdot}198$ g.cm^{-3} for 4 molecules per unit cell.

Using specially devised apparatus, cubic-cut crystals were ground into near-perfect spheres of 0·04 cm diameter and mounted on glass rods along one of their axes, the directions of which were located as the directions of extinction under a polarizing microscope. As crystals exposed to air turned yellow within a few hours, it was found necessary to immediately coat selected crystals with a thin layer of low-absorbent polyvinylacetate.

The most suitable crystal was mounted on a Hilger & Watts automatic diffractometer and exposed to Zr-filtered Mo $K\alpha$ radiation. The measured data extended to $h, k, l(\max)=14,23,10$ respectively; however it was found that over 98% of the reflexions with $h,k,l>12,17,8$ respectively, were below the measurable threshold, therefore of the 2200 reflexions originally recorded about 800 were immediately withdrawn, *i.e.* about 56% of the Cu $K\alpha$ sphere was utilized.

The integrated intensities were collected over 120 seconds involving 60 steps of 0·02° in ω. Individual background intensities left and right were measured, but as they were subject to random fluctuations a more accurate estimate of the background correction was obtained and applied as follows: for several different values of ω the background radiation was measured for values of θ from 0·05° up to about 20° in steps of 0·05°, each measurement occupying 4 seconds. Each set of values of I plotted against θ gave erratic curves as shown in Fig. 1. The full curve suitably scaled gave the best average background intensity for any particular θ. The standard deviation was calculated and $I_{\min}$ was estimated to be approximately $3\times\sqrt{\frac{\sum\sigma^2}{n(n-1)}}$. Peak intensities which were less than $I_{\min}$ were recorded as $\frac{1}{2}I_{\min}$ and the corresponding F values are listed in the structure factor Table (Table 1) as F_{unobs}.

At this stage a correction for peak spread was applied to Lp-corrected data. On Fig. 1 can be seen the graph of the peak 520 which was scanned in steps of 0·05° in θ in a similar manner. From the shape of the peak profile it is clear that the 520 peak may overlap certain other peaks with θ values between approximately 2 and 12°, thus altering the peak intensities. This overlap is subtracted by the following procedure. A generalized peak profile common to any selected peak must be obtained by calculating normalized values of I as a function of λ, and not θ. The direct readings obtained from the graph are values of I and θ. The interplanar spacing of the (520) planes, d, is calculated from

$$2d=\frac{\lambda_{Mo}\,(\text{at }\theta_{max})}{\sin\theta_{max}}=5{\cdot}4\text{Å}\,,$$

and this value of d is re-substituted into Bragg's equation to give $\lambda=5{\cdot}4\sin\theta$, from which the λ values corresponding to each reading of θ may be calculated. Normalized values of I are calculated from

$$I_{norm}=\frac{I_L}{I_{L(max)}}\,,$$

where $I_{L(max)}$ is the Lp-corrected value of the peak intensity. The graph of the (520) peak if plotted for values of I_{norm} against λ would now be the same as the graph of any other peak, because at the maximum point the ordinate has the value 1 and the abscissa has the value

$$\lambda=0{\cdot}70926\ (=\lambda_{Mo})\,,$$

i.e. a generalized peak profile has been obtained.

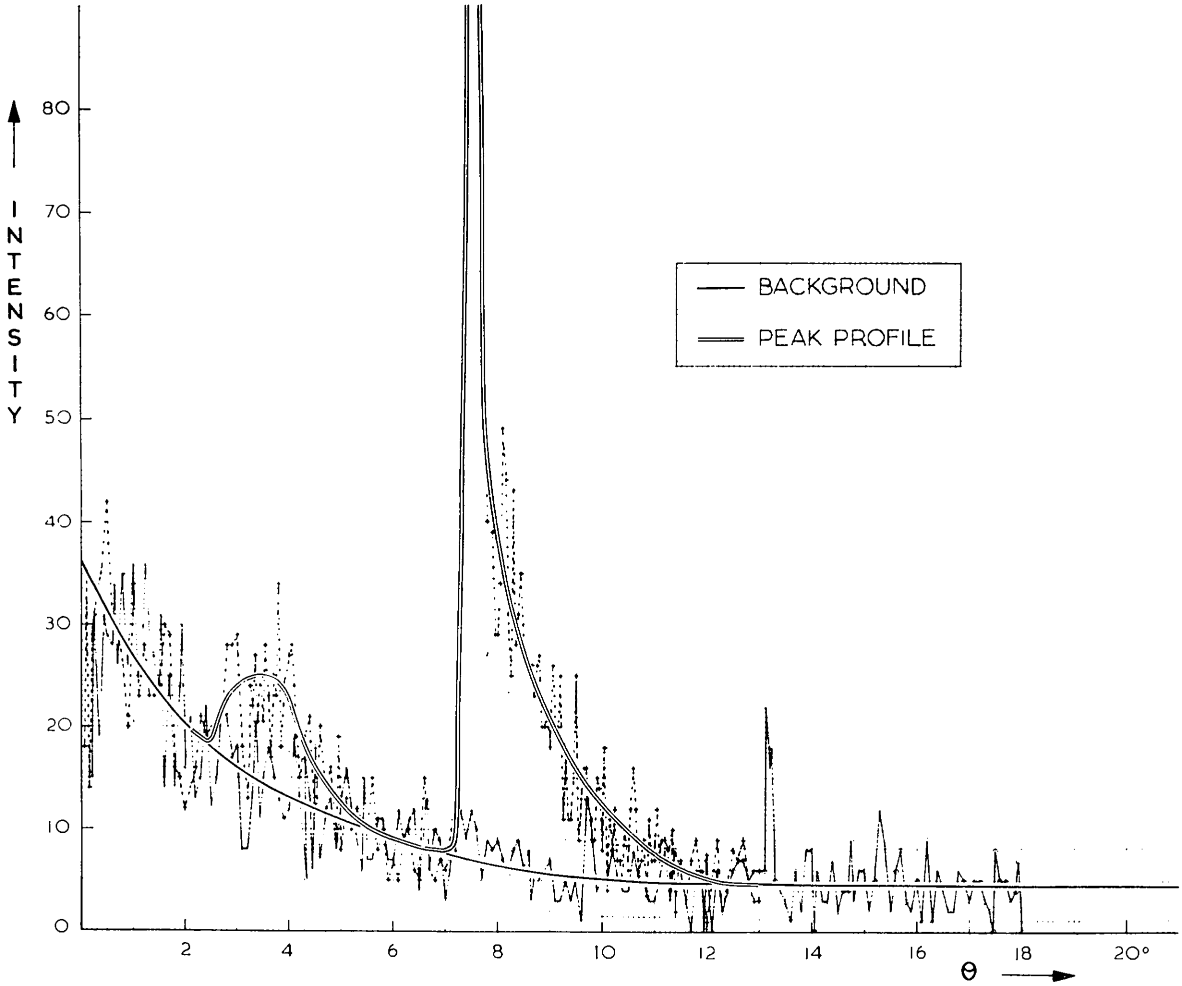


Fig. 1. Graph from which background and streak corrections were determined.

Using the program *STREACOR* the overlap of peaks occurring as a result of peak spread was corrected by searching the intensity data so that all peaks affected by any particular peak were reduced by a factor which is dependent on the relative positions of the peaks concerned.

Preliminary scale and temperature factors were estimated by Wilson's method. Absorption corrections were not applied since the value of μR for Mo $K\alpha = 0{\cdot}05$.

A three-dimensional unsharpened Patterson function was computed and gave 30 possible Harker vectors in $\frac{1}{8}$th unit-cell. A more useful sharpened Patterson function, $P'(uvw)$, was also calculated which, by a considerably improved resolution of closely neighbouring peaks, provided 63 vectors. The sharpened Patterson function was developed by Jacobson, Wunderlich & Lipscomb (1961) and Spencer & Lipscomb (1961) and may be expressed as

$$P'(uvw) = Q(uvw) + KP(uvw)\,, \qquad (1)$$

where P is the usual sharpened Patterson function and Q is a 'gradient' sharpened Patterson function, given by

$$Q(uvw) = V \int_0^1 \int_0^1 \int_0^1 \nabla \varrho(xyz) \,.\, \nabla\, \varrho(x+u, y+v, z+w) \times \mathrm{d}x\mathrm{d}y\mathrm{d}z \propto \frac{1}{V} \sum_h \sum_k \sum_l \frac{\sin^2\theta}{\lambda^2} \times |F_{hkl}|^2 \cos 2\pi(hu+kv+lw)\,. \qquad (2)$$

The value empirically chosen for K was 1/6, as it was found that a small contribution of the function P added to the gradient function decreased the negative regions around the sharpened peaks. In both functions Q and P, the $|F_{hkl}|^2$ were the usual sharpened coefficients,

$$|F_{hkl}|^2 = F_o^2 \exp{(B \sin^2\theta/\lambda^2)}/(\sum_i f_i)^2\,. \qquad (3)$$

Equations 1, 2 and 3, together with the value of 1/6 for K, lead to the relation

$$|F|^2 = (\sin^2\theta/\lambda^2 + 1/6) F_o^2 \exp{(B \sin^2\theta/\lambda^2)}/(\sum f_i)^2$$

for the sharpened Patterson coefficients, which was the formula used for thiethylperazine.

The combination of the Harker vectors of the sharpened function led to 34 possible sets of coordinates, of which two were eventually correctly assigned to the two sulphur atoms. Six successive three-dimensional Fourier and difference Fourier syntheses gave the locations of the 3 nitrogen and 22 carbon atoms. The Fourier synthesis gave evidence of considerable thermal motion among some of the atoms, notably C(22), C(21), C(18), C(10) and C(11), as well as of the anisotropic character of the S atoms. At this stage the value of R for observed reflexions was 18·7%.

The structure was refined by four least-squares cycles with the use of the Busing, Martin & Levy (1962) program *ORFLS*. The function minimized was $R_1 = \sum W(hkl)\,\{|F_o(hkl)| - |F_c(hkl)|\}^2$ with equal weight given to each term. Individual isotropic temperature factors were assigned and $F_{\rm unobs}$ were included. The number of $F_{\rm obs}$ was only 892, which was unfortunately insufficient to carry out a meaningful anisotropic cycle in which there were 244 parameters to be varied. From this point therefore the refinement was continued along two separate lines: six cycles were carried out using 1418 F values (including about 500 $F_{\rm unobs}$) and anisotropic temperature factors, resulting in a final R index for all reflexions of 0·113; six cycles were carried out using 892 $F_{\rm obs}$ and isotropic temperature factors, resulting in a final R index of 0·105. The refinement was terminated when the average parameter shifts were approximately 10% of the estimated standard deviations. Observed and calculated structure factors are listed in Table 1. The analytical f values used in all calculations are those given by Hanson, Herman, Lea & Skillman (1964). Table 2 gives the final atomic positional parameters and anisotropic thermal-motion parameters with their standard deviations which were obtained in the final cycle. The last column of Table 2 lists the isotropic temperature factors obtained at the end of the 13th cycle.

Patterson and Fourier syntheses were carried out on an ICT 1301 computer. An IBM 360/65 computer was used for the correction calculations and the least-squares refinements.

Discussion

The structure of the molecule and bond lengths and angles are shown in Fig. 2. Table 3 lists the interatomic distances and angles with associated e.s.d.'s, which were calculated from the results of the last refinement cycle using the Busing, Martin & Levy (1964) program *ORFFE.*

The tricyclic group

All C–C distances are between 1·37 and 1·42 Å, and the mean length of the C–C bonds within the first benzene ring, C(1)–C(6), which is 1·396 Å, and that of the second ring, C(7)–C(12), 1·393 Å, compare favourably with accepted values for benzene (1·397 Å, Pauling, 1960; 1·394 Å, Sutton, 1965).

Applying Cruickshank's (1949) criterion to the two C–N(1) bonds of 1·39, 1·46 ± 0·015 Å which should be expected to be chemically equivalent, the value obtained for $(l_1 - l_2)/(\sigma_1^2 + \sigma_2^2)^{1/2}$ is 3·5, which is in the zone of probable significance. However, no explanation for a significant difference in the two bonds can be suggested, as the N(1) atom is in a symmetrical environment and secluded from short intermolecular contacts. It appears more likely that the discrepancy would be reduced if the following factors, *inter alia*, were taken into consideration: (1) the bonds are not independent since a change in the position of N(1) would affect both lengths; (2) corrections for temperature librations, which could amount to as much as 0·02 Å (Cruickshank, 1960), have not been applied; and (3) as discussed above, the number of measurable reflexions was unfortunately limited by the nature of the compound.

Abrahams (1956) has calculated a value of 1·82 Å for a C–S single-bond distance. which is close to the sum

Table 1. *Observed and calculated structure factors*

Within each group the columns, reading from left to right, contain the values of l, $K|F_o|$, F_c, A_c and B_c. * indicates F_{unobs}.

00l	-8*	7	5	-5	0
	-6	50	46	46	0
	-4	68	69	-69	0
	-2	95	95	-95	0
01l	-8*	7	3	0	3
	-7	14	14	0	-14
	-6	10	11	0	-11
	-5	24	21	0	-21
	-4	23	23	0	-23
	-3	12	8	0	8
	-2	113	112	0	112
	-1	27	15	0	-15
02l	-9*	10	11	-11	0
	-8*	6	2	2	0
	-7	23	24	24	0
	-6	25	24	24	0
	-5	24	26	-26	0
	-4	42	41	-41	0
	-3	37	34	-34	0
	-2	165	178	-178	0
	-1	19	22	22	0
	0	108	115	115	0
03l	-8*	7	5	0	5
	-7*	6	3	0	3
	-6	11	6	0	6
	-5	18	23	0	23
	-4	27	29	0	-29
	-3	16	16	0	16
	-2	42	40	0	-40
	-1	49	42	0	-42
04l	-9	11	11	-11	0
	-8	11	15	15	0
	-7	16	16	16	0
	-6	19	19	-19	0
	-5	5	5	-5	0
	-4	10	10	10	0
	-3	28	27	27	0
	-2	61	55	55	0
	-1	62	60	60	0
	0	8	4	4	0
05l	-8*	7	6	0	-6
	-7*	6	7	0	7
	-6*	13	12	0	12
	-5*	5	8	0	8
	-4	5	3	0	3
	-3	8	6	0	-6
	-2	42	42	0	42
	-1	9	8	0	8
06l	-8	15	17	17	0
	-7	10	8	8	0
	-6	15	14	-14	0
	-5*	25	25	-25	0
	-4	5	2	2	0
	-3	28	31	-31	0
	-2	22	25	25	0
	-1	12	10	-10	0
	0	53	53	-53	0
07l	-8*	7	2	0	2
	-7*	6	1	0	-1
	-6	30	28	0	28
	5	27	26	0	-26
	4	55	52	0	-52
	3	20	19	0	19
	2	7	7	0	-7
	1	9	8	0	8
08l	-8*	7	3	3	0
	-7*	7	7	-7	0
	-6*	6	4	4	0
	-5*	5	2	2	0
	-4	28	27	27	0
	-3	22	21	21	0
	-2	18	16	-16	0
	-1	6	5	5	0
	0	44	41	-41	0
09l	-8*	7	3	0	-3
	-7	12	13	0	13
	-6*	10	9	0	9
	-5*	6	8	0	-8
	-4	19	19	0	-19
	-3	16	18	0	18
	-2	34	30	0	30
	-1	49	47	0	-47
0,10,l	-7*	7	9	-9	0
	-6*	6	6	-6	0
	-5*	6	3	3	0
	-4	6	8	-8	0
	-3	11	10	10	0
	-2	22	21	-21	0
	-1	20	17	17	0
	0	42	42	42	0
0,11,l	-7*	10	7	0	7
	-6*	7	8	0	-8
	-5	14	17	0	-17
	-4	18	19	0	19
	-3*	12	14	0	14
	-2*	5	4	0	-4
	-1	23	24	0	24
0,12,l	-7*	7	4	-4	0
	-6*	25	25	25	0
	-5	6	5	-5	0
	-4	15	15	15	0
	-3	15	15	-15	0
	-2	21	20	-20	0
	-1	20	20	20	0
	0	8	5	5	0
0,13,l	-7*	7	2	0	2
	-6*	7	4	0	-4
	-5	6	6	0	-6
	-4*	10	11	0	11
	-3	6	1	0	-1
	-2*	44	46	0	-46
	-1	6	1	0	-1
0,14,l	-6*	7	8	8	0
	-5	7	9	9	0
	-4*	13	15	-15	0
	-3*	6	4	4	0
	-2	6	6	-6	0
	-1	30	29	29	0
	0	30	30	30	0
0,15,l	-6*	7	7	0	-7
	-5*	7	2	0	-2
	-4	7	5	0	5
	-3	14	13	0	-13
	-2*	28	28	0	28
	-1	6	3	0	-3
0,16,l	-6*	7	4	-4	0
	-5	7	6	-6	0
	-4	23	21	-21	0
	-3*	24	19	-19	0
	-2*	6	5	-5	0
	-1	6	5	5	0
	0	29	31	31	0
0,17,l	-5*	7	3	0	3
	-4*	16	16	0	-16
	-3	7	4	0	-4
	-2	17	18	0	18
	-1	23	23	0	23
10l	-8*	7	5	-5	0
	-7	6	3	0	-3
	-6	19	17	-17	0
	-5	13	10	0	-10
	-4	7	1	1	0
	-3	39	31	0	31
	-2	153	161	161	0
	-1	71	83	0	-83
11l	-8*	6	6	-6	-3
	-7	13	15	-14	-7
	-6	12	12	11	5
	-5	44	44	37	23
	-4	25	25	-24	6
	-3	43	43	-18	39
	-2	44	42	35	-23
	-1	32	29	-26	-12
	0	59	66	0	-66
12l	-8*	12	12	4	-11
	-7	6	7	-6	-3
	-6	24	22	-4	21
	-5	24	26	-14	-21
	-4	24	23	-19	-12
	-3	62	57	-19	54
	-2	23	18	6	17
	-1	29	19	15	12
	0	19	22	0	22
13l	-8*	7	5	1	5
	-7	6	6	-2	-6
	6	22	21	21	-4
	5	16	11	7	9
	4	55	55	-55	-5
	3	39	38	-20	-32
	2	97	95	82	48
	1	98	95	49	-82
	0	98	94	0	94
14l	-8*	12	15	0	-15
	-7	6	7	3	6
	-6	10	6	2	5
	-5	31	29	20	-21
	-4	25	23	15	-17
	-3	27	26	25	8
	-2	33	30	-30	0
	-1	51	49	-29	39
	0	35	27	0	-27
15l	-8*	7	8	1	8
	-7*	6	5	2	-5
	-6*	6	6	2	6
	-5	18	18	-15	9
	-4	24	25	-22	-12
	-3	27	29	28	2
	-2	52	54	41	-35
	-1	61	61	-60	-15
	0	45	45	0	-45
16l	-8*	6	5	3	-4
	-7	13	13	-12	7
	-6	15	15	6	14
	-5	16	15	-15	-3
	-4	7	6	4	4
	-3*	8	8	5	-6
	-2	4	9	-7	6
	-1	29	28	26	12
	0	6	4	0	4
17l	-8*	7	6	-2	6
	-7	7	4	-1	-3
	-6	14	16	-8	-14
	-5	32	33	-32	8
	-4	39	43	35	-25
	-3	51	52	50	15
	-2	35	32	-14	29
	-1	16	16	1	16
	0	35	36	0	36
18l	-8*	7	6	5	3
	-7	7	3	-2	1
	-6	12	10	9	-5
	-5	10	9	5	-7
	-4*	23	22	-21	-5
	-3	5	5	-1	5
	-2	37	33	-31	10
	-1	16	18	-17	6
	0	35	28	0	-28
19l	-8*	7	8	-2	8
	-7	7	10	0	10
	-6	11	8	-8	3
	-5	13	13	-1	-12
	-4	13	14	14	-3
	-3	32	33	4	-33
	-2	38	39	-37	15
	-1	22	22	-22	-1
	0	17	15	0	-15
1,10,l	-7*	7	9	5	7
	-6*	18	19	9	-17
	-5	6	7	5	-5
	-4	8	10	7	8
	-3	9	9	0	-9
	-2	35	35	3	35
	-1	18	19	-12	-15
	0	49	45	0	-45
1,11,l	-7*	7	7	-2	6
	-6	14	15	13	7
	-5	15	19	15	-12
	-4	13	10	0	-10
	-3*	21	22	-10	20
	-2	5	5	-3	-4
	-1	44	43	18	33
	0	9	9	0	9
1,12,l	-7*	7	9	3	-8
	-6*	19	19	11	-15
	-5	6	7	4	-6
	-4	15	16	-13	10
	-3	17	19	-2	19
	-2	24	24	-23	6
	-1	27	24	-24	1
	0	39	41	0	-41
1,13,l	-7*	7	2	1	2
	-6	12	13	12	-4
	-5	14	15	-5	-14
	-4	31	33	-24	-23
	-3*	23	19	-19	0
	-2	6	3	3	-1
	-1	10	11	6	9
	0	32	32	0	31
1,14,l	-6*	7	6	-1	-6
	-5	7	7	7	1
	-4	14	14	-3	14
	-3	18	23	-21	11
	-2	11	9	9	-2
	-1	25	27	-16	-21
	0	16	16	0	16
1,15,l	-6*	7	8	7	4
	-5	7	2	-2	-1
	-4	16	15	-9	12
	-3*	19	20	19	4
	-2	6	7	6	3
	-1	10	10	-10	2
	0	25	25	0	-25
1,16,l	-6*	11	8	-4	7
	-5*	7	7	-6	4
	-4*	7	4	2	3
	-3	7	6	-4	4
	-2	30	30	21	-21
	-1	29	29	20	-21
	0	13	13	0	13
1,17,l	-5*	11	12	-12	-1
	-4*	7	8	3	8
	-3	16	15	12	8
	-2	11	10	-3	10
	-1	11	9	-6	7
	0	11	14	0	-14
20l	-8*	14	14	-14	0
	-7*	6	6	0	6
	-6*	6	3	3	0
	-5	5	0	0	0
	-4	50	50	50	0
	-3	33	35	0	-35
	-2	113	111	-111	0
	-1	64	74	0	74
	0	31	32	32	0
21l	-8*	7	7	1	-7
	-7	6	4	-3	-1
	-6	23	23	13	19
	-5	42	46	41	21
	-4	38	36	36	0
	-3	30	28	-26	-11
	-2	85	77	45	-62
	-1	135	141	-137	-32
	0	9	1	1	0
22l	-9*	12	12	-12	-3
	-8	7	3	-2	2
	-7	28	27	26	4
	-6	15	14	-14	0
	-5	36	37	-29	22
	-4	34	33	33	-4
	-3	33	30	12	-27
	-2	34	31	-29	-12
	-1	99	96	93	-26
	0	55	52	52	0
23l	-8	13	13	-2	-13
	-7	9	8	-7	-3
	-6	15	14	-9	10
	-5	19	17	6	16
	-4	34	34	-5	34
	-3	36	37	24	-28
	-2	70	56	-17	-53
	-1	62	62	-27	56
	0	77	68	-68	0
24l	-9	12	12	-11	-2
	-8	16	16	16	-4
	-7	25	25	22	-10
	-6	13	13	-12	3
	-5	24	24	-19	15
	-4	16	16	9	13
	-3	35	38	-37	-7
	-2	35	33	29	15
	-1	8	8	7	-2
	0	9	8	-8	0
25l	-9*	11	11	0	-11
	-8*	7	3	-2	-2
	-7*	6	8	7	3
	-6*	6	10	4	9
	-5	5	8	-6	5
	-4	25	26	22	-14
	-3	35	34	0	-34
	-2	7	9	-6	-7
	-1	27	29	-24	-15
	0	6	1	-1	0
26l	-8*	7	9	9	2
	-7	7	5	-3	-4
	-6	15	17	-12	12
	-5	12	13	6	12
	-4	29	30	-14	-26
	-3	29	31	27	-16
	-2	34	32	-4	-31
	-1	23	26	16	21
	0	48	45	-45	0
27l	-8	10	5	-1	-5
	-7	13	16	-3	16
	-6*	14	16	12	10
	-5*	6	5	5	0
	-4	31	31	17	-26
	-3	25	25	18	18
	-2	64	60	-34	49
	-1	15	16	-15	-6
	0	8	7	-7	0
28l	-8*	7	2	-1	-2
	-7	12	11	-10	5
	-6*	11	10	-1	10
	-5*	6	8	3	7
	-4*	5	3	1	-3
	-3	23	24	-7	-23
	-2	21	22	5	21
	-1	36	35	-34	8
	0	61	48	48	0
29l	-8*	7	2	-2	1
	-7*	13	13	6	11
	-6*	8	8	-2	8
	-5	34	35	4	-35
	-4	14	18	-11	-12
	-3	16	14	-8	11
	-2	24	23	-2	23
	-1	38	30	-22	20
	0	64	59	59	0
2,10,l	-7	12	10	-10	0
	-6	15	14	14	1
	-5*	22	26	15	-21
	-4	6	5	-4	-3
	-3	8	10	4	-9
	-2	23	23	-23	-1
	-1	40	38	-26	29
	0	31	27	27	0
2,11,l	-7*	7	2	2	0
	-6	11	10	3	-9
	-5*	12	12	4	-12
	-4	6	9	-9	2
	-3	16	17	-1	17
	-2	12	12	-11	-5
	-1*	29	27	-12	-24
	0	5	1	1	0
2,12,l	-7*	7	7	-5	5
	-6*	7	5	-3	4
	-5*	6	6	4	5
	-4*	6	9	-9	0
	-3*	6	7	-3	7
	-2	6	8	-1	-8
	-1	24	23	15	-17
	0	17	17	17	0
2,13,l	-7*	7	9	-8	-4
	-6*	7	8	-3	-7
	-5	7	7	7	-1
	-4	27	27	-11	24
	-3	13	13	13	0
	-2*	10	10	7	-7
	-1	6	11	-9	7
	0	26	28	28	0
2,14,l	-6*	7	1	-1	0
	-5*	7	5	-3	4
	-4	6	6	6	-1
	-3	16	18	-18	-3
	-2	17	16	0	16
	-1	26	27	25	12
	0	15	13	-13	0
2,15,l	-6*	7	4	4	1
	-5*	13	11	6	9
	-4	7	6	-4	4
	-3	12	13	-11	-7
	-2	23	26	-5	-26
	-1	25	25	-23	10
	0	16	17	17	0
2,16,l	-5*	7	9	-9	-4
	-4	18	17	12	-11
	-3*	18	19	5	-18
	-2	7	4	2	-3
	-1	28	28	27	4
	0	11	11	-11	0
2,17,l	-5*	7	6	6	3
	-4*	7	3	-1	3
	-3	7	7	1	-7
	-2	11	13	-9	-10
	-1*	11	9	-4	-8
	0	7	0	0	0
30l	-8*	7	1	-1	0
	-7*	22	22	0	-22
	-6	6	3	-3	0
	-5	8	8	0	-8
	-4	8	8	8	0
	-3	56	56	0	56
	-2	18	13	13	0
	-1	84	76	0	-76
31l	-8*	7	7	-1	7
	-7*	6	4	-4	2
	-6	16	12	11	-3
	-5	21	21	20	-6
	-4	35	36	-33	-17
	-3	46	48	-47	-3
	-2	62	50	-42	26
	-1	46	53	52	7
	0	9	5	0	5
32l	-8*	7	9	-1	-9
	-7	10	11	5	10
	-6	11	13	-13	0
	-5*	5	3	2	-2
	-4	30	28	9	-28
	-3	8	8	0	8
	-2	6	4	3	-2
	-1	38	38	2	-38
	0	8	3	0	-3
33l	-8*	7	5	0	-5
	-7	10	8	-8	6
	-6	23	22	19	10
	-5	26	28	25	-13
	-4	32	31	-21	-23
	-3	13	10	-9	-3
	-2	62	57	51	-26
	-1	47	45	-42	15
	0	60	61	0	61
34l	-9*	14	15	-4	-14
	-8	7	6	4	-4
	-7	17	16	2	16
	-6	20	19	-11	16
	-5	8	7	5	-4
	-4	22	26	19	15
	-3	42	40	-27	-29
	-2	20	18	-1	18
	-1	38	38	30	23
	0	22	25	0	-25
35l	-8	10	10	8	-5
	-7	15	16	-12	11
	-6	13	13	7	11
	-5	15	15	-11	-10
	-4	38	39	-38	-10
	-3	47	46	45	-12
	-2	24	21	1	-21
	-1	16	18	-10	14
	0	36	39	0	39
36l	-9*	13	12	-2	-12
	-8	7	7	6	3
	-7	19	19	-6	18
	-6	12	14	-8	-12
	-5	10	11	11	1
	-4	35	36	-10	-35
	-3	33	32	-28	-16
	-2	25	20	-8	19
	-1	38	39	-3	39
	0	47	45	0	45
37l	-8*	7	8	7	-2
	-7*	11	11	8	7
	-6	6	8	6	6
	-5	9	7	-7	-4
	-4	16	15	6	13
	-3	34	34	32	-11
	-2	49	48	-43	20
	-1	38	35	-32	15
	0	32	27	0	-27
38l	-8*	7	7	5	4
	-7*	16	15	-8	13
	-6	6	4	2	3
	-5	20	21	10	-18
	-4	20	20	-20	-5
	-3	21	18	15	-10
	-2	34	33	33	-1
	-1	29	28	12	25
	0	33	32	0	-32
39l	-8*	11	11	-11	-3
	-7	7	6	-2	-5
	-6	11	10	-10	1
	-5	9	9	-9	0
	-4*	32	32	30	-10
	-3*	5	6	-1	6
	-2	5	4	1	4
	-1	15	14	7	12
	0	49	47	0	-47
3,10,l	-7*	7	7	-7	-3
	-6*	6	4	-2	4
	-5	6	3	2	-3
	-4	12	9	-9	3
	-3	23	23	0	23
	-2	12	14	8	11
	-1	22	20	-17	11
	0	8	7	0	-7
3,11,l	-7*	7	7	-6	-3
	-6*	7	9	4	8
	-5*	15	15	15	0
	-4	6	4	1	-4
	-3	17	20	-20	2
	-2*	26	26	-22	14
	-1*	5	5	5	2
	0*	5	3	0	-3
3,12,l	-7*	7	3	-3	-1
	-6	7	4	-2	-3
	-5	9	5	3	4
	-4	9	9	9	-3
	-3*	9	9	2	-9
	-2	6	5	-5	-2
	-1	26	27	0	-27
	0	8	9	0	9
3,13,l	-6*	7	5	5	-1
	-5*	27	24	24	-2
	-4	6	6	5	-3
	-3	11	13	-12	5
	-2*	20	19	18	5
	-1	8	10	3	9
	0	9	9	0	-9
3,14,l	-6*	7	3	3	0
	-5	7	7	3	7
	-4*	17	17	-3	17
	-3	6	8	7	4
	-2	15	15	-6	-14
	-1	12	11	-3	-11
	0	15	15	0	-15
3,15,l	-6	4	4	3	-3
	-5	14	12	-12	-1
	-4*	12	12	-10	-6
	-3*	7	5	-4	2
	-2	6	9	6	7
	-1*	12	10	9	3
	0	6	2	0	-2
3,16,l	-5*	7	6	4	-4
	-4*	7	7	-7	-3
	-3*	7	10	6	8
	-2*	7	8	7	-5
	-1	6	6	-6	3
	0	23	24	0	24
40l	-8	12	10	-10	0
	-7	19	19	0	-19
	-6	14	17	12	0
	-5	39	42	0	42
	-4	24	23	23	0
	-3	23	21	0	21
	-2	68	71	-71	0
	-1	52	55	0	-55
	0	25	23	23	0
41l	-8*	7	6	-6	-1
	-7*	6	9	0	-9
	-6	6	6	-1	-6
	-5	24	23	-20	13
	-4	35	38	-29	24
	-3	26	26	25	-4
	-2	42	38	-15	-35
	-1	29	25	7	-24
	0	47	50	50	0
42l	-8*	7	7	-7	0
	-7*	27	29	18	-22
	-6	6	7	-1	-7
	-5	19	19	-19	2
	-4	26	28	23	16
	-3	23	23	15	18
	-2	21	17	-8	16
	-1	28	33	28	-18
	0	30	31	31	0
43l	-8*	7	8	-6	-5
	-7	21	22	17	-14
	-6	20	20	19	-3
	-5	15	14	-10	9
	-4	11	12	-5	11
	-3	20	22	-8	-21
	-2	34	31	-30	6
	-1	43	41	-22	34
	0	31	29	29	0
44l	-8	10	8	8	-1
	-7	19	19	17	-9
	-6	13	13	-13	-3
	-5*	22	24	-23	8
	-4	5	6	-5	-4
	-3	38	39	-15	36
	-2	11	12	4	-11
	-1	16	14	9	-11
	0	44	44	-44	0
45l	-8*	7	4	4	-1
	-7*	7	3	2	3
	-6*	6	6	0	6
	-5	6	9	-9	1
	-4	18	17	6	-16
	-3	29	25	18	-18
	-2	15	15	0	15
	-1	21	19	-8	17
	0	52	55	55	0
46l	-8	20	18	12	-13
	-7	10	10	2	-10
	-6*	12	14	-14	0
	-5	6	1	1	1
	-4	18	19	7	18
	-3	22	23	20	-12
	-2	55	55	36	42
	-1	27	25	20	-14
	0	37	37	-37	0
47l	-8*	7	9	3	-8
	-7	10	10	3	10
	-6	19	22	-16	16
	-5	9	9	1	-9
	-4	18	16	-13	-10
	-3	19	19	8	18
	-2	28	23	-19	-13
	-1	37	38	-37	-9
	0	27	26	26	0
48l	-7	12	10	-9	-6
	-6*	23	23	-21	10
	-5*	6	7	6	3
	-4	26	26	11	-23
	-3	11	8	-4	-7
	-2	28	28	26	-10
	-1	36	36	-29	20
	0	47	43	-43	0
49l	-7*	7	5	-4	1
	-6	11	9	4	9
	-5	20	19	-2	-19
	-4	18	16	15	5
	-3	19	18	16	8
	-2	19	15	-6	-13
	-1	16	15	-14	-6
	0	13	15	-15	0
4,10,l	-7*	7	7	-7	1
	-6	16	17	-1	17
	-5*	17	15	11	10
	-4	6	9	4	-8
	-3*	12	13	4	13
	-2	6	4	4	-1
	-1	31	31	-25	-17
	0	16	15	-15	0
4,11,l	-7*	7	7	7	-2
	-6*	14	13	-7	-11
	-5*	7	11	-4	10
	-4	6	6	2	6
	-3	12	14	4	13
	-2	16	18	12	-13
	-1*	8	9	8	-5
	-0	6	4	4	0
4,12,l	-6*	7	6	6	1
	-5*	13	14	2	-14
	-4*	6	3	-3	-1
	-3*	6	5	4	3
	-2*	6	8	-3	-8
	-1	6	7	3	7
	0	27	27	27	0
4,13,l	-6*	7	6	4	-5
	-5	7	10	-8	5
	-4	21	22	4	22
	-3	11	11	-8	-8
	-2*	10	10	-10	-3
	-1	6	6	1	-5
	0	14	10	-10	0
4,14,l	-6*	7	7	2	7
	-5*	7	6	6	0
	-4	7	6	-6	-2
	-3	14	14	-12	7
	-2	21	21	-5	-20
	-1	13	15	4	-14
	0	12	11	11	0
4,15,l	-5*	7	10	-6	9
	-4	7	5	-5	-1
	-3	18	19	18	-7
	-2	13	12	-9	-7
	-1	13	14	13	6
	0	16	16	16	0
4,16,l	-5*	7	7	2	7
	-4	7	6	6	2
	-3*	17	21	-3	21
	-2	7	6	-1	6
	-1	15	15	12	-9
	0	11	10	-10	0
50l	-8*	7	6	6	0
	-7*	7	6	0	6
	-6*	6	5	5	0
	-5*	5	5	0	-5
	-4	5	3	-3	0
	-3	8	8	0	-8
	-2	35	32	-32	0
	-1	73	71	0	-71
51l	-8*	7	6	-5	4
	-7*	7	7	3	-6
	-6	6	6	5	-3
	-5	8	8	4	-7
	-4	24	23	-5	-22
	-3	31	31	-12	-29
	-2	24	24	21	10
	-1	22	22	0	-22
	-0	41	36	0	36

Table 1 (*cont.*)

52l

-8*	13	11	-4	-10
-7*	7	5	-3	-3
-6*	32	34	-13	32
-5*	6	7	7	2
-4	12	13	13	0
-3	24	22	-7	21
-2	25	24	2	-24
-1	18	21	-4	-21
0	58	56	0	56

53l

-8*	7	7	2	-6
-7	7	6	5	-4
-6	20	18	11	14
-5	17	17	-10	15
-4	30	28	-27	8
-3	27	27	-12	24
-2	26	24	11	-21
-1	36	36	33	13
0	16	15	0	-15

54l

-8*	22	18	5	-17
-7	7	9	-9	-1
-6	23	23	-14	18
-5	9	8	-5	6
-4	18	18	14	-11
-3	24	23	-13	-19
-2	36	33	11	-31
-1	34	30	30	-6
0	25	23	0	23

55l

-8*	15	14	2	-14
-7*	7	4	4	1
-6	6	5	0	5
-5*	11	10	-4	-10
-4	6	2	-2	0
-3	18	20	20	0
-2	12	9	9	0
-1	21	21	-19	9
0	31	35	0	35

56l

-7*	7	4	1	3
-6	19	20	-12	17
-5	18	19	19	4
-4	10	12	-11	5
-3	9	5	-3	-4
-2	13	14	9	-11
-1	25	30	-16	26
0	24	19	0	-19

57l

-7	10	8	5	6
-6	21	21	-14	16
-5	26	26	-26	-2
-4	17	16	14	-7
-3	10	11	0	-11
-2	12	8	-3	-7
-1	8	6	1	-6
0	12	13	0	-13

58l

-7*	7	11	-9	-6
-6	7	6	2	-5
-5*	13	13	-3	-12
-4	6	8	8	0
-3	15	15	5	15
-2	32	32	19	26
-1	28	26	0	26
0	8	5	0	-5

59l

-7	12	14	12	-6
-6*	16	16	-11	11
-5	6	9	1	9
-4	20	20	12	-16
-3	10	12	2	11
-2	21	18	-17	7
-1*	11	12	5	11
0	5	5	0	5

5,10,l

-7*	8	10	-9	-2
-6*	19	19	-2	-19
-5*	7	3	0	3
-4*	8	5	2	-5
-3	6	7	7	0
-2	22	25	-22	11
-1	11	10	0	-10
0	27	27	0	-27

5,11,l

-6*	10	10	-4	9
-5	7	6	3	-5
-4	14	14	13	-4
-3*	16	17	-5	-16
-2*	6	7	-4	6
-1*	6	8	4	8
0	6	4	0	4

5,12,l

-7	13	11	-4	-10
-6	12	12	-8	-10
-5	12	16	16	1
-4	16	15	13	6
-3*	12	10	-2	10
-2	6	9	9	-1
-1*	11	12	-10	6
0	6	4	0	4

5,13,l

-6*	7	6	1	6
-5	7	4	1	-4
-4	13	13	-12	5
-3*	18	18	-18	2
-2	6	6	4	-4
-1	17	15	5	15
0	26	29	0	-29

5,14,l

-6*	8	5	-1	-5
-5*	7	4	4	2
-4	7	5	-2	4
-3*	13	10	-7	-7
-2*	7	10	9	-5
-1	6	8	7	-3
0	24	25	0	25

5,15,l

-5	11	13	13	-3
-4*	14	14	-13	-5
-3	7	5	5	0
-2*	22	25	20	15
-1*	7	4	-4	-1
0	7	4	0	4

5,16,l

-5*	8	9	6	7
-4*	7	9	-9	2
-3	7	8	2	-7
-2	11	11	-6	-10
-1*	11	11	-7	-8
0	7	4	0	4

60l

-7*	7	5	0	-5
-6*	6	4	4	0
-5	6	8	0	8
-4	25	25	-25	0
-3*	9	8	0	-8
-2	5	1	1	0
-1	25	28	0	28
0	102	105	105	0

61l

-7	16	14	-10	-10
-6	34	36	10	-34
-5	17	18	17	6
-4	28	29	5	29
-3	20	17	9	-15
-2	33	33	0	33
-1	73	70	-65	26
0	15	10	10	0

62l

-7*	7	5	2	-4
-6	18	17	16	2
-5	12	13	-13	3
-4	11	15	-2	-15
-3	15	14	1	-14
-2	35	34	-28	18
-1	9	5	-5	-1
0	9	10	-10	0

63l

-8*	11	10	-1	10
-7	7	6	3	-5
-6	9	11	9	-6
-5	26	29	2	28
-4	15	14	-5	-13
-3	32	32	3	-32
-2	10	12	-10	-5
-1	10	6	-5	3
0	29	29	29	0

64l

-7*	7	4	4	-2
-6*	7	3	2	-3
-5	9	7	4	-6
-4	13	12	-5	-11
-3	31	31	31	-1
-2	15	14	14	0
-1*	19	15	13	7
0	5	3	-3	0

65l

-7*	13	14	14	0
-6	6	6	-6	2
-5	14	14	-12	8
-4	13	15	-2	-15
-3	15	13	-9	-9
-2	47	50	-17	47
-1	13	14	13	7
0	9	4	4	0

66l

-7*	7	7	6	-5
-6	12	12	-7	9
-5	13	14	-11	7
-4	9	9	-7	6
-3	13	18	-16	7
-2	30	30	27	-14
-1	15	18	-13	-12
0	19	23	-23	0

67l

-7*	7	8	8	-1
6	10	9	-6	7
5	22	23	-17	-16
4	28	30	12	-27
3*	18	19	18	7
2	6	5	4	3
1	17	18	16	9
0	9	8	8	0

68l

-7*	7	12	-5	-11
-6	7	2	1	-1
-5*	19	22	8	20
-4	6	7	4	-6
-3	22	20	16	13
-2	10	8	7	4
-1	12	15	-11	-10
0	45	45	-45	0

69l

-7*	7	7	2	6
-6	7	5	1	-5
-5*	22	22	-21	5
-4	6	6	-2	-6
-3	15	15	13	8
-2	12	10	-6	9
-1	19	22	2	-21
0	13	14	14	0

6,10,l

-7*	13	12	-10	-7
-6*	7	5	4	3
-5	7	6	4	-4
-4	16	16	-16	-2
-3	9	8	8	-1
-2	9	10	3	9
-1	23	26	-19	-17
0	35	36	36	0

6,11,l

-7*	14	10	3	-10
-6*	7	4	2	-4
-5*	7	3	0	-3
-4	7	7	-6	3
-3	15	15	10	12
-2*	11	11	-10	5
-1*	6	5	-4	2
-0	6	5	5	0

6,12,l

-6*	17	20	20	0
-5*	7	2	-1	-2
-4	7	4	4	-2
-3	17	20	-10	18
-2*	17	17	-17	0
-1*	6	7	-7	1
0	6	3	3	0

6,13,l

-5*	7	7	5	6
-4*	7	5	-1	-5
-3	7	8	-5	6
-2	18	19	4	-18
-1*	13	15	-11	-10
0	6	10	10	0

6,14,l

-5*	7	9	4	-8
-4*	7	4	-3	3
-3*	7	3	-3	0
-2	7	7	-5	5
-1	12	12	12	1
0	12	12	12	0

6,15,l

-5*	8	6	4	4
-4*	7	7	4	6
-3	7	7	-5	-5
-2*	17	19	-1	19
-1	7	7	-7	0
0	7	3	-3	0

6,16,l

-4	12	10	-10	1
-3*	15	14	-13	-5
-2*	7	6	1	-6
-1	7	3	2	1
0	13	15	15	0

70l

-7*	7	7	0	-7
-6	7	4	-4	0
-5	9	13	0	13
-4	22	25	25	0
-3	12	12	0	12
-2	13	13	13	0
-1	52	56	0	-56

71l

-7*	7	8	6	-5
-6*	15	15	9	12
-5*	6	7	4	5
-4	6	7	-5	5
-3	26	26	-23	11
-2	16	18	10	-15
-1	22	22	20	10
0	16	15	0	-15

72l

-7*	14	14	-8	-11
-6	7	5	1	-5
-5*	10	11	11	2
-4	6	6	-5	3
-3	24	22	-18	13
-2	24	23	-22	-5
-1	22	24	11	-22
0	16	14	0	-14

73l

-7*	7	5	5	0
-6	7	4	0	-4
-5	17	19	-18	7
-4	25	29	-28	-6
-3	6	9	-4	-7
-2	21	23	20	13
-1	20	16	13	-9
0	25	27	0	27

74l

-7*	7	5	3	-3
-6	6	5	4	4
-5	20	23	23	4
-4	9	11	-3	10
-3*	13	13	-13	1
-2	6	6	6	1
-1*	17	15	-11	11
0	5	7	0	7

75l

-7*	7	8	7	-3
-6	7	5	-4	3
-5*	16	19	-18	-6
-4	6	4	-4	1
-3	18	18	17	6
-2	14	15	14	-5
-1	18	17	-16	-6
0	31	33	0	-33

76l

-7*	7	4	3	3
-6	11	11	5	9
-5*	12	10	-9	4
-4	6	8	-8	-2
-3	20	20	-7	-19
-2	12	15	14	-6
-1*	21	21	18	11
0	6	8	0	8

77l

-7*	7	3	3	1
-6	12	14	-10	-9
-5	12	8	-8	-2
-4	23	23	16	-17
-3	34	35	27	21
-2*	18	21	-5	20
-1	6	8	-4	7
0	15	13	0	13

78l

-6	10	9	8	-5
-5	11	9	-4	8
-4	14	14	-14	0
-3	15	16	10	-12
-2	12	12	-12	1
-1	15	14	-14	4
0	17	17	0	-17

79l

-6*	14	15	-13	6
-5	7	8	-1	-8
-4	13	13	8	-11
-3	21	22	13	-18
-2	10	8	-5	7
-1*	22	24	-24	-4
0	6	2	0	2

7,10,l

-6*	7	5	2	-5
-5*	7	10	1	10
-4	7	10	10	2
-3	10	10	5	-9
-2	11	9	7	6
-1*	18	19	-6	-17
0	6	4	0	4

7,11,l

-6*	7	5	-5	2
-5	7	8	8	0
-4*	14	15	12	-10
-3*	7	4	1	4
-2	6	4	-4	2
-1*	18	21	-4	20
0	6	5	0	5

7,12,l

-5*	11	9	3	9
-4	7	7	-7	3
-3	10	9	-7	4
-2	20	17	-13	-10
-1	18	19	16	-10
0	18	20	0	20

7,13,l

-5*	7	8	5	-7
-4	11	11	6	-10
-3*	16	17	-15	-7
-2	7	10	-4	9
-1*	19	19	19	2
0	7	5	0	5

7,14,l

-5*	8	6	3	5
-4*	7	4	-3	-2
-3	7	11	-11	1
-2*	12	13	5	-12
-1	7	7	-6	4
0	16	16	0	16

7,15,l

-4*	8	8	-1	8
-3*	11	11	-9	5
-2*	7	4	1	4
-1	7	4	-1	-4
0	19	22	0	-22

80l

-7*	7	7	0	-7
-6*	7	3	3	0
-5	7	4	0	-4
-4	11	15	15	0
-3*	15	15	0	-15
-2	6	8	-8	0
-1	29	26	0	26
0	33	33	-33	0

81l

-7*	7	7	-7	1
-6	12	11	5	-10
-5	19	19	3	19
-4	12	13	1	13
-3	12	12	9	-8
-2	23	24	-6	-23
-1*	16	13	-13	-4
0	6	10	10	0

82l

-7*	7	7	6	3
-6	7	4	-4	0
-5*	12	8	-5	6
-4*	6	7	7	1
-3	6	8	5	-7
-2	21	18	10	-14
-1	18	20	17	-10
0	9	10	-10	0

83l

-7*	7	8	-7	-3
-6	7	2	-1	-2
-5	11	13	4	12
-4	15	15	-6	13
-3	26	29	10	-27
-2	11	13	-13	-1
-1	22	20	8	18
0	19	19	19	0

84l

-7*	18	16	15	3
-6	7	4	2	4
-5	11	12	-12	0
-4	12	10	4	9
-3	12	14	-12	7
-2*	15	16	16	-4
-1	6	8	6	5
0	24	25	-25	0

85l

-6*	7	1	-1	-1
-5	10	7	-1	7
-4	16	18	13	-13
-3*	13	13	-12	-3
-2*	6	5	3	-4
-1*	6	5	3	-3
0	6	8	8	0

86l

-6*	7	4	-3	2
-5	10	13	-13	-3
-4	12	10	-9	-2
-3	24	25	18	-17
-2	25	25	11	-22
-1	14	15	14	7
0	29	30	-30	0

87l

-6*	7	6	-6	0
-5*	7	6	5	1
-4	7	8	7	3
-3	11	13	0	13
-2	21	21	-5	20
-1	21	21	-14	-16
0	22	24	-24	0

88l

-6*	7	5	-3	4
-5*	7	8	5	7
-4	7	10	-10	4
-3	23	24	3	-24
-2	16	17	16	-3
-1*	29	31	-29	13
0	6	4	4	0

89l

-6	12	9	-7	-6
-5*	13	11	8	-8
-4*	7	5	1	-5
-3	7	6	-5	3
-2	12	11	8	8
-1*	37	37	-35	13
0	6	1	-1	0

8,10,l

-5*	11	14	14	0
-4	7	7	-3	-7
-3	15	14	1	-13
-2	12	11	-3	10
-1*	36	38	-32	21
0	6	0	0	0

8,11,l

-5*	7	8	8	1
-4*	7	5	4	3
-3*	7	5	-5	-2
-2	7	5	-1	4
-1*	25	24	-20	-13
0	7	7	-7	0

8,12,l

-5*	8	7	7	2
-4*	12	9	-3	-9
-3	7	6	2	-6
-2*	12	11	-1	11
-1*	7	7	-4	-6
0	7	5	5	0

8,13,l

-4*	7	9	-1	9
-3*	7	6	6	-1
-2*	7	8	-6	-6
-1	7	10	4	9
0	10	10	10	0

90l

-6*	7	3	0	0
-5*	14	15	0	15
-4	7	4	4	0
-3	14	13	0	13
-2	20	20	-20	0
-1	15	18	0	-18

91l

-6*	7	10	6	-8
-5	7	9	9	-4
-4	17	17	-15	9
-3	10	8	-5	-7
-2*	14	11	-3	11
-1	6	7	0	7
0	17	19	0	-19

92l

-6*	7	6	5	4
-5*	17	16	15	6
-4	7	7	0	-7
-3*	14	15	-12	-9
-2	6	4	-3	-2
-1	23	24	2	-24
0	22	23	0	23

93l

-6*	7	10	7	-7
-5*	7	9	5	-7
-4*	7	6	-5	3
-3	6	4	4	1
-2	18	18	18	1
-1	19	17	-12	12
0	15	14	0	-14

94l

-6*	14	14	8	12
-5	7	9	4	8
-4	12	12	-12	-3
-3	11	8	-6	-4
-2	11	13	2	-13
-1	10	6	5	-3
0	11	12	0	12

95l

-6*	7	3	2	0
-5*	12	13	-13	0
-4	7	6	6	-2
-3	10	13	12	3
-2	14	14	-14	1
-1*	13	12	5	-11
0	6	5	0	5

96l

-6*	7	6	3	5
-5	7	5	-2	-4
-4	25	23	-11	-20
-3	14	12	8	-8
-2	12	16	15	-6
-1	26	26	-17	20
0	37	40	0	40

97l

-5*	7	5	-4	3
4*	15	14	12	6
3	7	5	-3	3
2	24	25	-25	2
1*	19	19	-6	-18
0	6	3	0	-3

98l

-5*	7	8	-7	-5
-4	7	4	-3	-3
-3	17	17	14	-9
-2	19	19	19	1
-1*	23	21	4	20
0	6	3	0	3

99l

-5*	7	2	1	2
-4*	12	12	12	-3
-3*	7	8	-7	4
-2	7	6	5	-4
-1*	16	17	16	-4
0	7	9	0	-9

9,10,l

-5*	8	7	-5	5
-4*	7	5	4	3
-3*	7	4	-4	2
-2*	7	6	-1	5
-1	7	7	-3	7
0	17	16	0	-16

9,11,l

-4*	7	2	-1	2
-3*	11	12	-11	-5
-2*	7	9	-8	5
-1*	7	6	6	0
0	7	2	0	-2

9,12,l

-4*	8	8	8	1
-3*	7	7	-2	-7
-2*	7	4	-4	0
-1*	7	7	5	-5
0	7	2	0	2

10,0,l

-5*	7	2	0	2
-4*	7	3	-3	0
-3	7	4	0	4
-2*	10	10	-10	0
-1	7	5	0	-5
0	14	13	13	0

10,1,l

-5*	7	3	1	3
-4*	14	14	-4	14
-3	7	4	3	-4
-2*	19	18	5	-17
-1	7	3	2	2
0	15	15	15	0

10,2,l

-5*	7	9	1	-9
-4*	7	9	1	9
-3*	7	6	-6	-2
-2*	7	5	5	1
-1*	7	7	-1	7
0	7	5	5	0

10,3,l

-5*	7	6	-3	5
-4	7	8	-3	7
-3	16	16	-8	-14
-2*	12	12	-11	-5
-1*	7	10	10	4
0	7	6	6	0

10,4,l

-5*	7	5	-2	-4
-4	7	9	-8	-3
-3	11	11	-10	6
-2	12	11	9	-6
-1	9	8	-7	-5
0	22	23	-23	0

10,5,l

-5*	12	10	-8	6
-4*	7	8	-8	-2
-3*	7	6	4	-5
-2	7	8	-6	4
-1	26	27	25	10
0	27	26	26	0

10,6,l

-5*	7	2	-2	-1
-4	7	7	6	3
-3	12	11	5	10
-2	32	29	23	18
-1	12	11	-8	-7
0	26	29	-29	0

10,7,l

-5*	8	9	-8	3
-4*	8	8	-8	-1
-3*	7	4	-4	-1
-2	7	5	1	-5
-1*	11	9	7	-6
0	7	6	6	0

10,8,l

-4*	8	10	9	-2
-3	7	6	6	0
-2	13	10	10	0
-1	15	14	-14	2
0	36	33	-33	0

10,9,l

-4	13	12	11	2
-3*	10	7	7	0
-2*	7	9	9	-4
-1	7	3	3	1
0	27	26	-26	0

10,10,l

-4*	8	6	4	4
-3*	7	4	4	1
-2*	7	6	-4	-4
-1*	7	9	-6	-7
0	7	7	7	0

11,0,l

-5*	8	3	0	-3
-4*	7	2	2	0
-3	7	1	0	-1
-2*	10	9	-9	0
-1	7	2	0	-2

11,1,l

-5*	6	12	11	-3
-4*	7	2	-2	1
-3*	11	12	-11	-3
-2*	7	9	9	2
-1*	7	5	4	-3
0	7	2	0	-2

11,2,l

-5*	7	6	4	-5
-4	7	3	3	-1
-3*	18	17	-15	10
-2*	7	5	0	-5
-1*	7	9	6	7
0	7	5	0	5

11,3,l

-4	15	15	-12	9
-3*	13	10	-4	9
-2*	7	10	10	-1
-1*	7	4	3	-3
0	7	8	0	-8

11,4,l

-4*	7	3	1	-3
-3*	7	4	-3	-2
-2	7	3	2	-2
-1	11	12	12	0
0	12	12	0	12

11,5,l

-4*	8	4	-4	1
-3	15	14	12	6
-2	14	14	14	-1
-1*	16	14	-7	-13
0	7	6	0	6

11,6,l

-4*	8	7	-5	5
-3*	7	10	8	-5
-2*	7	4	-2	-3
-1*	7	6	-4	3
0	7	9	0	-9

11,7,l

-4*	8	7	5	-4
-3*	7	4	-3	-2
-2	7	6	4	-4
-1*	13	13	5	-12
0	7	2	0	-2

11,8,l

-4*	8	4	1	4
-3*	7	5	5	-1
-2	7	9	0	9
-1*	15	12	-4	12
0	7	6	0	-6

12,0,l

-4*	6	9	-9	0
-3*	8	8	0	8
-2*	7	5	-5	0
-1	7	4	0	-4
0	15	16	16	0

12,1,l

-4*	6	6	2	6
-3*	8	7	-7	1
-2*	7	3	2	-3
-1*	7	6	2	6
0	7	9	-9	0

12,2,l

-3*	8	9	-4	8
-2	10	10	-4	-10
-1	10	10	10	-3
0*	7	5	5	0

12,3,l

-3*	8	7	-4	-6
-2*	7	6	4	-4
-1*	7	8	7	-4
0	7	6	-6	0

12,4,l

-3*	8	5	4	-1
-2	8	4	0	-4
-1*	11	8	6	1
0	7	7	7	0

12,5,l

-3*	8	8	-7	-5
-2	16	17	-3	17
-1*	12	11	11	0
0	7	8	-8	0

12,6,l

-3*	8	3	-3	-1
-2*	8	6	4	-4
-1*	8	7	-6	2
0	8	3	3	0

12,7,l

-3*	6	6	6	1
-2	8	8	3	7
-1*	17	17	17	4
0	8	5	-5	0

of the covalent radii for sulphur and carbon given by Pauling (1960). Using Pauling's relation $R = R_S - (R_S - R_D)3x/(2x+1)$ for the resonance–interatomic distance curve, the value of x obtained for the C–S(2) bond lengths, which are both 1·78 ± 0·015 Å, is 0·07, *i.e.* they have 7% double-bond character. (Abrahams' bond-order, bond-length curve gives a value of 25%.)

The angles of the heterocyclic ring are all approximately 118° except for the C–S–C angle which is 99·0 ± 0·7°. Table 4 lists a number of compounds of interest for comparative purposes. It can be seen that

Table 2. *Final atomic fractional coordinates* (× 10⁴) *and thermal parameters* (× 10⁴) *with estimated standard deviations*

Anisotropic temperature factor $= \exp\{-(h^2\beta_{11}+k^2\beta_{22}+l^2\beta_{33}+2hk\beta_{12}+2hl\beta_{13}+2kl\beta_{23})\}$ with $\beta_{11}=2\pi^2a^{*2}U_{11}$, $\beta_{12}=2\pi^2a^*b^*U_{12}$, *etc.*

The least-squares standard errors are given in parentheses.
Isotropic temperature factors are given in the last column.

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}	B
S(1)	1729 (4)	3003 (2)	0905 (6)	91 (4)	28 (1)	264 (10)	-9 (2)	30 (6)	8 (3)	5.83
S(2)	0079 (3)	5809 (2)	3137 (5)	73 (3)	41 (2)	138 (6)	-3 (2)	16 (4)	-24 (3)	4.93
N(1)	2181 (8)	5584 (5)	1552 (13)	45 (8)	22 (4)	145 (18)	-10 (5)	36 (10)	4 (7)	3.50
N(2)	5626 (8)	5272 (6)	2031 (13)	38 (7)	36 (5)	112 (18)	-9 (5)	-5 (9)	4 (7)	3.66
N(3)	6933 (9)	4193 (7)	3230 (15)	68 (9)	44 (5)	165 (22)	1 (6)	16 (13)	15 (9)	4.80
C(1)	1302 (12)	3823 (8)	1455 (16)	64 (11)	30 (5)	130 (24)	4 (7)	-38 (15)	-19 (9)	4.24
C(2)	1941 (10)	4380 (7)	1168 (16)	44 (9)	13 (4)	188 (25)	-14 (6)	-23 (13)	-1 (8)	2.98
C(3)	1567 (10)	4998 (7)	1689 (15)	39 (9)	26 (5)	106 (20)	-11 (6)	10 (12)	26 (8)	3.13
C(4)	0525 (12)	5030 (7)	2401 (16)	90 (13)	23 (5)	121 (23)	-11 (7)	15 (15)	10 (8)	3.79
C(5)	-0127 (14)	4449 (9)	2565 (16)	84 (14)	45 (7)	88 (20)	-5 (8)	-5 (14)	9 (9)	4.20
C(6)	0252 (13)	3837 (8)	2125 (18)	75 (14)	33 (6)	154 (26)	-6 (7)	12 (16)	-2 (10)	4.52
C(7)	0604 (11)	6354 (7)	1770 (15)	69 (11)	29 (5)	75 (18)	-1 (6)	-7 (13)	-15 (8)	3.69
C(8)	1602 (12)	6194 (7)	1106 (16)	80 (12)	25 (5)	107 (21)	9 (7)	18 (14)	3 (8)	4.13
C(9)	2024 (13)	6608 (7)	0010 (17)	91 (14)	17 (4)	163 (26)	-8 (7)	10 (16)	-9 (8)	4.10
C(10)	1440 (16)	7188 (9)	-0348 (22)	100 (17)	43 (7)	217 (34)	-8 (9)	-39 (22)	-9 (13)	6.18
C(11)	0449 (17)	7340 (9)	0313 (23)	121 (19)	36 (7)	230 (37)	-18 (10)	-17 (23)	-15 (14)	5.77
C(12)	0003 (14)	6930 (9)	1390 (21)	81 (13)	33 (6)	256 (35)	4 (8)	-65 (21)	-41 (12)	5.40
C(13)	3374 (12)	5534 (7)	1176 (19)	61 (11)	22 (5)	213 (29)	1 (6)	4 (16)	-4 (9)	3.67
C(14)	4044 (11)	6067 (7)	2007 (18)	57 (10)	29 (5)	147 (24)	-7 (6)	4 (14)	-3 (9)	4.12
C(15)	5288 (10)	5957 (7)	1690 (16)	61 (10)	23 (5)	136 (23)	-2 (6)	-11 (14)	24 (9)	3.98
C(16)	5698 (13)	5151 (8)	3652 (15)	81 (13)	36 (5)	87 (20)	8 (7)	4 (14)	9 (8)	4.84
C(17)	5934 (12)	4408 (9)	3925 (21)	65 (12)	47 (7)	223 (33)	6 (8)	46 (17)	8 (13)	5.29
C(18)	7176 (15)	3469 (9)	3484 (26)	118 (17)	38 (6)	349 (48)	25 (9)	16 (26)	77 (15)	7.66
C(19)	6923 (12)	4325 (8)	1645 (17)	79 (12)	37 (6)	130 (25)	1 (7)	-4 (15)	1 (10)	4.93
C(20)	6688 (11)	5081 (8)	1389 (15)	66 (11)	44 (6)	77 (20)	9 (7)	-1 (13)	20 (9)	3.95
C(21)	3192 (18)	3104 (9)	0453 (27)	136 (21)	33 (7)	380 (52)	9 (10)	97 (30)	21 (16)	7.71
C(22)	3673 (24)	2454 (14)	0180 (39)	207 (33)	69 (10)	559 (75)	26 (16)	210 (45)	-11 (24)	12.43

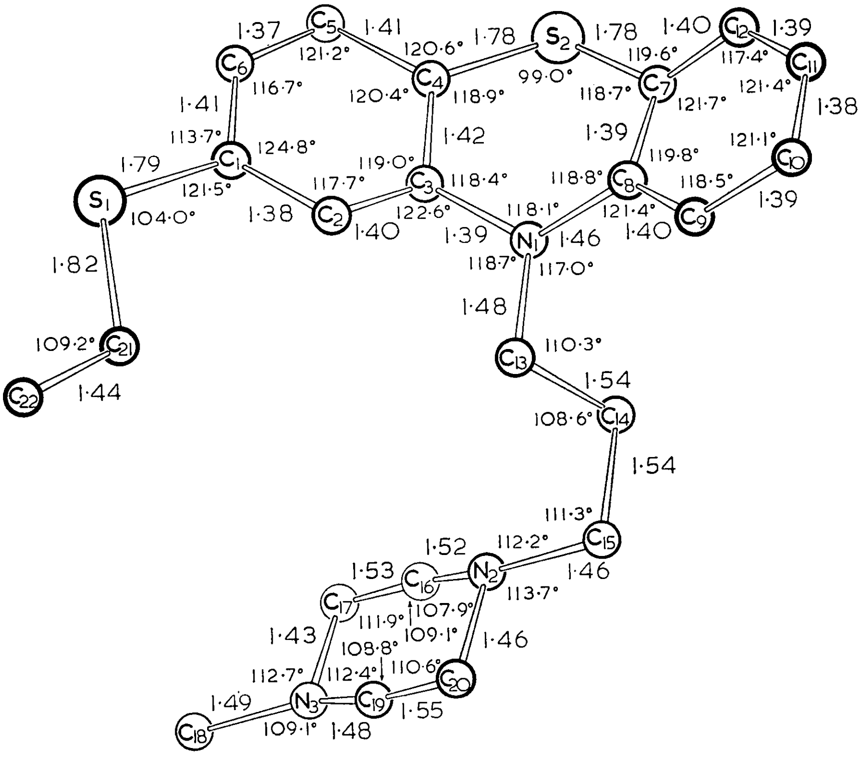


Fig. 2. Bond lengths and angles.

Table 3. *Bond lengths and angles and estimated standard deviations*

The e.s.d.'s in the bond lengths × 10^2 and the e.s.d.'s in the bond angles are given in parentheses.

Bond	ℓ	Angle	θ
C(1) - C(2)	1.38(2) Å	C(6) - C(1) - C(2)	124.8°(1.4°)
C(2) - C(3)	1.40(2)	C(1) - C(2) - C(3)	117.7 (1.2)
C(3) - C(4)	1.42(2)	C(2) - C(3) - C(4)	119.0 (1.2)
C(4) - C(5)	1.41(2)	C(3) - C(4) - C(5)	120.4 (1.4)
C(5) - C(6)	1.37(2)	C(4) - C(5) - C(6)	121.2 (1.4)
C(6) - C(1)	1.41(2)	C(5) - C(6) - C(1)	116.7 (1.4)
C(7) - C(8)	1.39(2)	C(12) - C(7) - C(8)	121.7 (1.5)
C(8) - C(9)	1.40(2)	C(7) - C(8) - C(9)	119.8 (1.4)
C(9) - C(10)	$1.39(2_5)$	C(8) - C(9) - C(10)	118.5 (1.6)
C(10) - C(11)	$1.38(2_5)$	C(9) - C(10) - C(11)	121.1 (1.9)
C(11) - C(12)	$1.39(2_5)$	C(10) - C(11) - C(12)	121.4 (1.9)
C(12) - C(7)	1.40(2)	C(11) - C(12) - C(7)	117.4 (1.6)
C(4) - S(2)	$1.78(1_5)$	S(2) - C(4) - C(3)	118.9 (1.1)
C(7) - S(2)	$1.78(1_5)$	C(4) - C(3) - N(1)	118.4 (1.3)
C(3) - N(1)	$1.39(1_5)$	C(3) - N(1) - C(8)	118.1 (1.0)
C(8) - N(1)	$1.46(1_5)$	N(1) - C(8) - C(7)	118.8 (1.3)
S(1) - C(1)	$1.79(1_5)$	C(8) - C(7) - S(2)	118.7 (1.2)
S(1) - C(21)	1.82(2)	C(7) - S(2) - C(4)	99.0 (0.7)
C(21) - C(22)	1.44(3)	C(6) - C(1) - S(1)	113.7 (1.2)
N(1) - C(13)	$1.48(1_5)$	C(2) - C(1) - S(1)	121.5 (1.1)
C(13) - C(14)	1.54(2)	C(1) - S(1) - C(21)	104.0 (0.8)
C(14) - C(15)	1.54(2)	S(1) - C(21) - C(22)	109.2 (1.6)
C(15) - N(2)	$1.46(1_5)$	C(3) - N(1) - C(13)	118.7 (1.1)
N(2) - C(16)	1.52(2)	C(8) - N(1) - C(13)	117.0 (1.1)
C(16) - C(17)	1.53(2)	N(1) - C(13) - C(14)	110.3 (1.2)
C(17) - N(3)	1.43(2)	C(13) - C(14) - C(15)	108.6 (1.2)
N(3) - C(19)	1.48(2)	C(14) - C(15) - N(2)	111.3 (1.1)
C(19) - C(20)	1.55(2)	C(15) - N(2) - C(16)	112.2 (1.2)
C(20) - N(2)	$1.46(1_5)$	C(15) - N(2) - C(20)	113.7 (1.1)
N(3) - C(18)	1.49(2)	C(20) - N(2) - C(16)	107.9 (1.1)
		N(2) - C(16) - C(17)	109.1 (1.3)
		C(16) - C(17) - N(3)	111.9 (1.4)
		C(17) - N(3) - C(19)	112.4 (1.3)
		N(3) - C(19) - C(20)	108.8 (1.3)
		C(19) - C(20) - N(2)	110.6 (1.2)
		C(17) - N(3) - C(18)	112.7 (1.5)
		C(19) - N(3) - C(18)	109.1 (1.5)
		C(2) - C(3) - N(1)	122.6 (1.2)
		N(1) - C(8) - C(9)	121.4 (1.4)
		C(5) - C(4) - S(2)	120.6 (1.2)
		S(2) - C(7) - C(12)	119.6 (1.3)

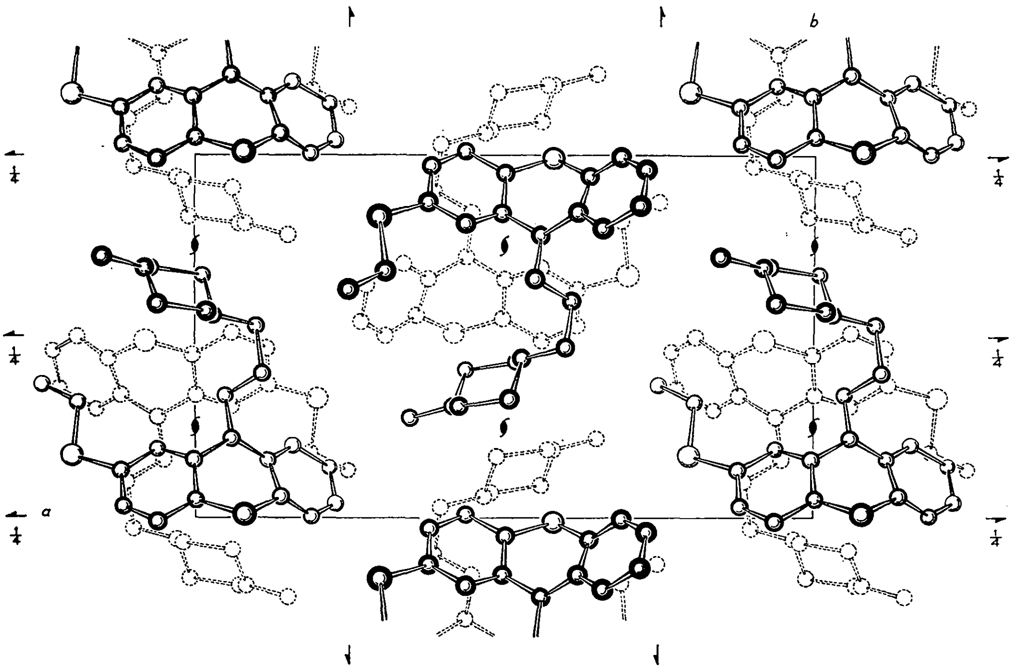


Fig. 3. The structure viewed down the *c* axis.

C–S–C angles are all in the range 93–100°, and that all C–S lengths are shorter than a C–S single-bond. Further, the tricyclic molecules which contain S are folded with a dihedral angle of approximately 140°.

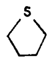
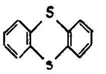
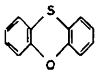
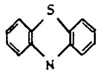
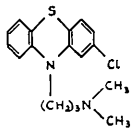
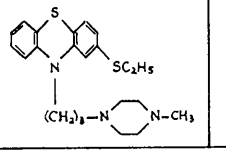
The size of the C–S–C angles, the folding of the molecules and the contraction of the C–S bonds in substituted anthracene-type molecules may possibly be explained in terms of π-bonding molecular orbitals formed by the carbon atoms with the $3d$ orbitals of the sulphur atom. The suggestion that S in heterocyclic compounds can have a decet of electrons was first made by Schomaker & Pauling (1939), and calculations of the molecular orbitals in thiophene were subsequently performed by Longuet-Higgins (1949). In thiethylperazine it is possible that the $2p_z$ atomic orbitals of the C atoms conjugate with hybrid orbitals formed from linear combinations of the $3p_z$, $3d_{yz}$ and $3d_{xz}$ atomic orbitals of the S atom.

The best planes for the two benzene rings were calculated by the method of Schomaker, Waser, Marsh & Bergman (1959), with the program *LSPLANE* and are given in Table 5, together with the individual displacements of atoms from the planes. The maximum deviation of the C atoms is 0·03 Å so that the benzene rings may be regarded as planar, within the limits of error. The S and N atoms however do not lie in both planes of the aromatic rings, as is also the case in phenothiazine and in chlorpromazine. The dihedral angle between the planes is 139·0°, in close agreement with that in chlorpromazine, but differing by 14° from that in phenothiazine.

Aliphatic chains and piperazine ring

When the C(21)–C(22) bond is compared with a C–C single bond of 1·54 Å the value obtained for $\delta l/\sigma$ is 3·3, which again is in the zone of probable significance. Double-bond character of a C–C bond in

Table 4. *Comparison of bond lengths and angles in heterocyclic compounds containing sulphur*

Compound	Chemical Formula	C–S–C (°)	$\mathrm{C}\underset{\sigma}{-}\mathrm{S}$ (Å)	$\mathrm{C}\underset{\sigma}{-}\mathrm{N}$ (Å)	Dihedral angle(°)	Reference
Thiophene		91±4 92.16±0.10	1.74 ±0.03 1.714±0.002	- -	- -	(a) (b) (c)
Thianthrene		100±0.5	1.76 ±0.015	-	128	(d) (e) (f)
Phenoxthionine		97.7±0.03	1.75±0.04	-	138	(d) (g) (h)
Phenothiazine		99.6±1.5	1.770±0.003	1.406±0.002	153.3	(d) (g) (i)
Chlorpromazine		97.3±0.3	1.75±0.01	1.41±0.01	139.4	(j)
Thiethylperazine		99.0±0.7	1.78±0.02	1.425±0.02	139.0	(k)

a) Schomaker & Pauling (1939).
b) Longuet-Higgins (1949).
c) Bak, Christensen, Hansen-Nygaard & Rastrup-Anderson (1961).
d) Cullinane & Rees (1940).
e) Lynton & Cox (1956).
f) Rowe & Post (1958)
g) Wood, McCale & Williams (1941).
h) Hosoya (1966).
i) Bell, Blount, Briscoe & Freeman (1968).
j) McDowell (1969).
k) Present work.

Table 5. *Mean plane parameters and deviations of atoms from the plane*

I Benzene ring, C(1)–C(6)

$$-0{\cdot}4453x+0{\cdot}1523y-0{\cdot}8824z=-0{\cdot}6911$$

	Deviation		Deviation
C(1)	−0·029 Å	S(2)	−0·137 Å
C(2)	0·030	N(1)	−0·045
C(3)	−0·005	S(1)	−0·061
C(4)	−0·015	C(13)	−0·395
C(5)	0·025		
C(6)	−0·006		

II Benzene ring, C(7)–C(12)

$$0{\cdot}4963x+0{\cdot}5202y+0{\cdot}6950z=8{\cdot}0889$$

	Deviation		Deviation
C(7)	0·001 Å	S(2)	−0·003 Å
C(8)	0·007	N(1)	0·006
C(9)	−0·013	C(13)	0·427
C(10)	0·010		
C(11)	−0·002		
C(12)	−0·004		

III Piperazine ring, N(2)–C(16)–C(17)–N(3)–C(19)–C(20)

$$0{\cdot}7107x+0{\cdot}6009y+0{\cdot}3657z=11{\cdot}9721$$

	Deviation		Deviation
N(2)	−0·145 Å	C(18)	−0·489 Å
C(16)	0·318	C(15)	0·272
C(17)	−0·279		
N(3)	0·085		
C(19)	−0·299		
C(20)	0·320		

such a position would be most unusual, and it does seem more likely that the standard deviations in the positions of the two atoms with high thermal motion may have been underestimated.

The difference in the angles C(2)–C(1)–S(1), 121·5°, and C(6)–C(1)–S(1), 113·7°, is probably caused by steric hindrance between the hydrogen atoms attached

Table 6. *Intramolecular and intermolecular distances*

The e.s.d.'s × 10^2 are given in parentheses.

The superscripts$^{\mathrm{i}}$,$^{\mathrm{ii}}$,$^{\mathrm{iii}}$ and $^{\mathrm{iv}}$ denote the equivalent positions at $(x+1,y,z)$, $(\frac{1}{2}-x,\bar{y},\frac{1}{2}+z)$, $(\frac{1}{2}+x,\frac{1}{2}-y,\bar{z})$ and $(\bar{x},\frac{1}{2}+y,\frac{1}{2}-z)$ respectively.

C(2) – C(21)	3.03(2) Å
C(13) – C(2)	2.88(1$_5$)
C(13) – C(9)	2.90(2)
C(13) – N(2)	2.87(2)
C(22) – C(18)	5.59(4)
S(1) – S(2)	6.29(1)
S(2) – C(21$^{\mathrm{ii}}$)	3.69(2)
C(1) – C(9$^{\mathrm{ii}}$)	3.94(2)
C(4) – C(13$^{\mathrm{ii}}$)	3.89(2)
C(5) – C(13$^{\mathrm{ii}}$)	3.94(2)
C(5) – C(15$^{\mathrm{ii}}$)	3.89(2)
C(7) – C(21$^{\mathrm{ii}}$)	3.85(3)
C(11) – C(6$^{\mathrm{iv}}$)	3.90(3)
C(12) – S(1$^{\mathrm{iv}}$)	3.89(2)
C(16) – C(3$^{\mathrm{ii}}$)	3.92(2)
C(16) – C(4$^{\mathrm{ii}}$)	3.77(2)
C(16 – C(5$^{\mathrm{ii}}$)	3.76(2)
C(16) – C(6$^{\mathrm{ii}}$)	3.95(2)
C(17) – C(4$^{\mathrm{ii}}$)	3.82(2)
C(17) – C(7$^{\mathrm{ii}}$)	3.55(2)
C(17) – C(12$^{\mathrm{ii}}$)	3.68(2)
C(18) – C(6$^{\mathrm{i}}$)	3.98(2)
C(18) – C(11$^{\mathrm{ii}}$)	3.93(4)
C(18) – C(12$^{\mathrm{ii}}$)	3.84(3)
C(19) – C(5$^{\mathrm{i}}$)	3.66(2)
N(3) – C(5$^{\mathrm{i}}$)	3.63(2)
C(22) – S(1$^{\mathrm{iii}}$)	3.92(3)
C(22) – C(6$^{\mathrm{iii}}$)	3.84(3)

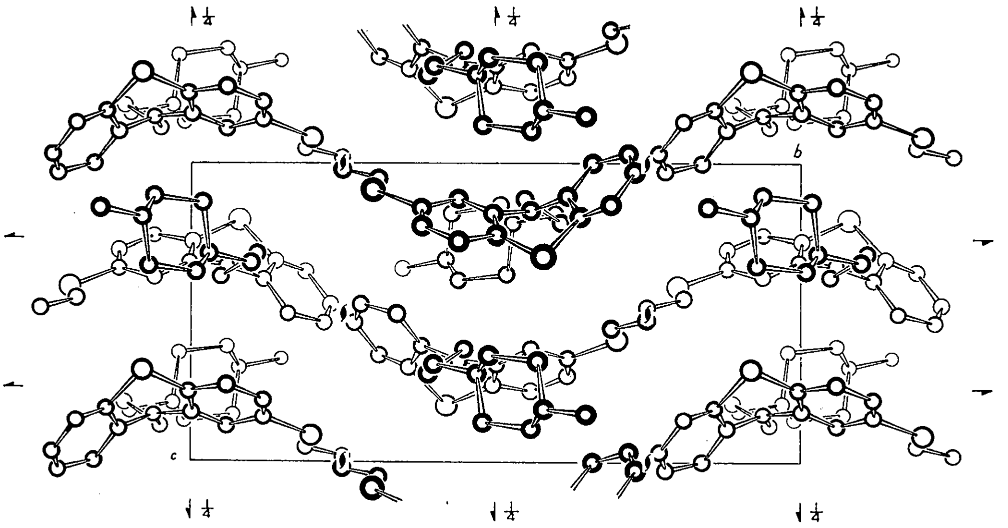


Fig. 4. The structure viewed down the *a* axis.

to C(2) and C(21). The angles centred at N(1) are nearly trigonally symmetric, and the angles between the chain carbon atoms are quite close to the tetrahedral value (109°28′).

The average value of the six C–N bonds associated with the piperazine ring is 1·47 Å, which is close to the value given by Kennard (1962) for three-covalent nitrogen (1·472 Å for sp^2–sp^3 bond type), but the individual bonds vary between 1·43 and 1·52 Å. It was shown by Kitajgorodskij (1965) that the effects of intermolecular interaction on molecular shape are generally small, but that the packing can affect the molecular geometry in some cases. The atoms of the piperazine ring have a number of contacts shorter than 3·85 Å, as shown in Table 6; also the distance between C(16) and benzene ring I of molecule (2) is 3·67 Å, and that between C(17) and benzene ring II is 3·73 Å. It seems possible that the slight distortions in the ring may be partly attributed to molecular close packing requirements.

The best plane for the piperazine ring and the deviation of the atoms are given in Table 5, from which it can be seen that the ring has the chair configuration.

Molecular packing

In Figs. 3 and 4 the packing in the crystal is viewed along the *c* and *a* axes respectively. Table 6 gives some intramolecular non-bonded distances and intermolecular contacts less than 4 Å. The molecules are arranged in parallel undulating layers perpendicular to the *yz* plane.

Unlike chlorpromazine, one enantiomorph only appears in the crystal. The molecular dissymmetry suggested the study of the optical activity of solutions of the compound. A 2½% solution of powdered thiethylperazine in absolute alcohol was tested in the polarimeter using sodium D light and, as expected, was found to be optically inactive. Further experiments are now in progress to investigate the optical activity of this material and it is hoped to establish whether the crystals exhibit enantiomorphism.

Molecular structure and mechanism of action

Although the phenothiazine derivatives form a vast class, the most useful ones have substituents at positions 2 (R_1) and 10 (R_2), and may be considered as consisting of two parts (Fig. 5):

(1) *The* R_2 *substituent*. Effects on the higher centres of the nervous system only appear in earnest when the side chain consists of three carbon atoms in a row. It could be surmised that a substance of this molecular size fits best into the biological binding site.

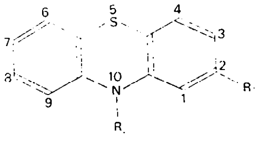


Fig. 5. The phenothiazine 'nucleus' ($R_1 = R_2 = H$).

(2) *The phenothiazine nucleus and* R_1 *substituent*. The phenothiazine nucleus consists of a system of conjugated double bonds having an extensive π pool of delocalized electrons and lone pairs of electrons on the N and S atoms. Chlorpromazine, theithylperazine and phenothiazine have closely similar structural features (Table 4) apart from the different dihedral angle in phenothiazine, which may possibly be of importance. The psychotropic potency is affected by the substituent forming all or part of R_1 in the ascending order H, S, Cl, F. It is significant to note that this is in parallel with the order of increasing electronegativity of the atoms.

Although attempts to correlate molecular structure with biochemical action must be highly tentative due, among other factors, to the complex nature of the action mechanism of the drugs (*Scientific Basis of Drug Therapy in Psychiatry*, 1964), a suggestion has been made by Szent-Györgyi (1960) which is of considerable interest and is compatible with the results of the present study. According to Szent-Györgyi there are many factors tending to suggest that charge transfer is involved in biological activity, the drugs acting as electron donors or acceptors.

Using the LCAO approximation of the molecular orbital method, the energy levels of many molecules taking part in different biological reactions have been determined (Pullman & Pullman, 1958). Chlorpromazine was found (Karreman, Isenberg & Szent-Györgyi, 1959) to have a most unusual antibonding highest-filled orbital in its normal, stable state, and is thus an exceedingly strong monovalent electron donor.

Thiethylperazine has little tranquillizing action while prochlorperazine has five times and trifluperazine ten times the potency of chlorpromazine. The determination of the *k* values of these substances would be of considerable interest as it might lead to a direct relationship between potency and electron-donating properties, and provide further support for the theory that pharmacological action is due to a charge transfer.

The *k* values of phenothiazine have been determined and are found to be quite close to those of chlorpromazine. Since phenothiazine is *not* a psychotropically potent drug it is evident therefore that the donor–acceptor properties must be combined with a suitable molecular complement, which it appears likely is provided by the R_2 substituent.

Szent-Györgyi brings forward some evidence in support of the fascinating suggestion that schizophrenia may be due to the presence of a strong electron acceptor in the blood (*e.g.* bilirubin, which inhibits production of hematoporphyrins and also inhibits oxidative phosphorylation). If such is the case, then the inactivation of this substance by a strong donor, such as chlorpromazine, affords the possible key to the mechanism of action. More exciting still, precise investigation of the nature of the electron acceptor causing the dmaage may lead eventually not only to permanent cure for the psychotically abnormal, but also to the prevention of this tragic disease.

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La Structure Cristalline du Palladocyanure de Rubidium Monohydraté

PAR LÉON DUPONT

Cristallographie Approfondie et Physique de l'Etat Solide, Université de Liège au Sart-Tilman (par Liège 1)

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$Rb_2Pd(CN)_4.H_2O$ crystallizes in space group *Pncn* with $a=10{\cdot}01$, $b=13{\cdot}74$, $c=7{\cdot}44$ Å and with four molecules in the unit cell. The structure was determined from three-dimensional film data and refined with anisotropic thermal parameters using the method of least squares. The $Pd(CN)_4^{2-}$ group is planar and square within experimental errors with average distances Pd–C 2·01, C≡N 1·13 Å, and with average angle C–Pd–C, 90°. Rb atoms coordinations are respectively 7 and 8.

Introduction

On sait que les structures des complexes tétracyanés, à base de Pt, Pd et Ni, se caractérisent par un empilement des plans $X(CN)_4^{2-}$ (X = Pt, Pd ou Ni). De nombreuses études tant spectroscopiques que structurales ont déjà été effectuées en vue d'arriver à une meilleure connaissance de la liaison inter-complexes responsable de cette propriété. On a pu ainsi observer une certaine corrélation entre la distance séparant les groupes $X(CN)_4^{2-}$ et leur angle de rotation relatif, suivant l'idée émise par Brasseur (1938). Par ailleurs, en comparant les propriétés optiques et structurales des cyanures complexes, on a pu mettre en évidence l'évolution ré-