The Crystal Structure of Methylene Blue Pentahydrate

By Harold E. Marr III* and James M. Stewart

Department of Chemistry, University of Maryland, College Park, Maryland 20740, *U.S.A.*

and M. F. Chiu

The Atlas Computer Laboratory, Chilton, Didcot, Berkshire, England

The crystal structure of methylene blue, 3,7-bisdimethylaminophenazothionium chloride pentahydrate, was determined by direct methods from single-crystal X-ray diffraction data. $C_{16}H_{18}N_3SCl.5H_2O$ crystallizes in the monoclinic system, space group $P2_1/c$, with $a=9.646$ (9), $b=31.106$ (17), $c=6.992$ (2) Å, $\beta=96.70$ (6). The structure was refined by full-matrix least-squares calculations to $R=0.057$. The dye molecules are essentially planar, with twenty molecules of water of hydration per unit cell, forming an interesting hydrogen-bonding network through the lattice. Positions for C, N, S, O, and Cl atoms were determined from Fourier electron-density maps. Hydrogen atom positions were refined from a clathrate ice-like model.

Introduction

The molecular structure of methylene blue has been investigated in the liquid and crystalline states by numerous physical methods. X-ray diffraction studies have been attempted, but the successful refinement of the crystal structure determination has not been reported. There has also been considerable reference in the literature to the proper placement of the formal charge on the cation, $C_{16}H_{18}N_3S^+$. An X-ray diffraction study (Zhadanov, Zvonkova & Vorontsova, 1956) led to the conclusion that the sulfur atom of the methylene blue cation is closest to the chloride ion and this is possibly explained by placement of the positive charge on the sulfur as in structure (I). An observation that the chloride ion is closest to the methyl groups (Taylor, 1935) would suggest distribution of the charge between the terminal amine groups resulting from contributions to the stable structure by forms represented as structure (II). A recent report stated, from observations of X-ray line shifts of sulfur, that structure (I) is not a probable representation (Takahashi, Yabe & Sato, 1969).

(I)

(II)

---
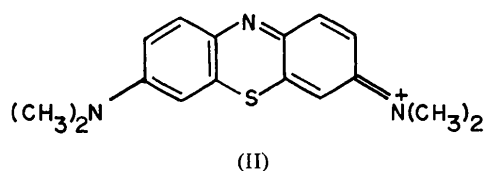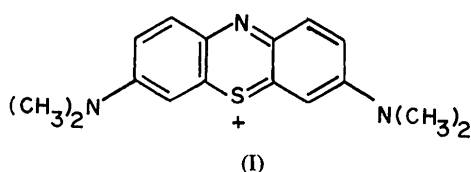
* Present address: U.S. Bureau of Mines, College Park Metallurgy Research Center, College Park, Maryland 20740, U.S.A.

A preferable description of the charge distribution is that the charge is delocalized over the whole π-orbital system of this molecule rather than being extremely localized. This belief is based upon the application of an LCAO MO calculation in contrast to the valence bond structures (I) and (II).

A study of hydrate crystals of a clathrate type found in several biologically active compounds has given rise to a molecular theory of general anesthesia (Pauling, 1961). The existence of the extensive hydrogen-bonding network in methylene blue suggested that the structure might have additional interest beyond the antimalarial studies. In the investigations of crystalline methylene blue, however, it was the instability of the hydration level (Warwicker, 1955), as well as the propensity for twinning, that probably frustrated previous attempts at the crystal structure determination. The present study was initiated in cooperation with the Walter Reed Army Institute of Research to determine the crystal structures of compounds exhibiting antimalarial activity and to clarify the molecular structure of this compound.

Crystal data

$C_{16}H_{18}N_3S^+Cl^-.5H_2O$, F. W. 410,
Monoclinic, $P2_1/c$
At 21 °C:
$a=9.646(9)$, $b=31.106(17)$, $c=6.992(2)$ Å
$\beta=96.70(6)°$, $Z=4$, $V=2083$ Å^3
$D_m=1.31$ $D_x=1.307$ g cm^{-3}
Nb filtered Mo radiation
$F(000)=216$.

Experimental

Large tabular crystals were obtained for single-crystal studies. The opaque greenish-blue plates were easily cleaved along the axes defined by the crystal edges. Several crystals, each approximately $0.5 \times 0.04 \times 0.3$ mm, were mounted on pin mountings and examined on

Table 1. *Observed and calculated structure factors*

The columns are k, $10F_o$ and $10F_c$. Unobserved data are marked with an asterisk (*).

0,K,0		
8	171	-172
10	509	513
12	78*	-58
14	727	705
16	441	-411
18	465	453
20	171	-173
22	35*	-97
24	293	-259
26	140	-118
28	0*	-31
30	232	-178
32	102	-74
1,K,0		
0	1475	-1410
1	798	757
2	729	682
3	188	183
4	520	535
5	27*	22
6	148	141
7	578	-578
8	498	-506
9	0*	10
10	164	-163
11	183	-193
12	552	-529
13	322	-326
14	417	408
15	632	-613
16	85	-24
17	334	-331
18	0*	36
19	285	251
20	239	235
21	273	-258
22	71*	-95
23	231	230
25	552	-508
26	0*	-6
27	0*	-42
28	72*	-102
29	190	-183
30	38*	-6
31	131	-96
32	49*	12
33	3*	20
2,K,0		
1	840	-802
2	750	-759
3	487	-476
4	589	-589
5	355	-358
6	150	139
7	211	-217
8	635	-630
9	0*	9
10	417	-397
11	294	-301
12	135	115
13	353	-333
14	483	-452
15	83	-92
16	183	-183
17	129	-119
18	188	-190
19	171	-146
20	343	340
21	0*	-31
22	263	-245
23	58*	-115
24	416	399
25	65*	99
26	0*	-36
27	229	-219
28	85	99
29	0*	52
30	314	29
31	0*	22
32	0*	6
3,K,0		
0	473	456
1	1174	-1147
2	943	-946
3	663	641
4	77	73
5	65	-74
6	423	436
7	178	182
8	110	-118
9	212	229
10	178	-176
11	138	150
12	717	-664
13	890	846
14	236	296
15	105	-81
16	150	-158
17	633	597
18	204	198
19	79	60
20	45*	48
21	246	228
22	43*	28
23	0*	-28
24	143	-119
25	79	68
26	0*	28
27	233	220
28	0*	11
29	0*	-49
30	117	101
31	0*	9
4,K,0		
0	71*	93
1	382	372
3	149	-112
4	323	322
5	227	223
6	0*	4
7	158	-143
8	244	239
9	83	-77
10	0*	7
11	94	81
12	263	254
13	194	139
14	120	135
15	291	295
16	154	-158
17	303	277
18	201	179
19	201	187
20	86	-37
21	139	-113
22	134	127
23	287	284
24	115	-135
25	0*	23
26	124	129
27	69*	-124
28	0*	-13
29	72*	64
30	95	-69
5,K,0		
0	623	637
1	229	-223
2	189	184
3	315	-301
4	0*	-14
5	0*	23
6	395	374
7	421	-413
8	294	282
9	184	-175
10	198	192
11	25*	22
12	124	115
13	293	-276
14	61*	-36
15	372	352
16	89	-82
17	283	-266
18	69	31
19	40*	49
20	0*	33
21	319	-297
22	232	-217
23	91	-88
24	108	95
25	127	-118
26	51*	-69
27	70*	75
28	87	-109
29	0*	18
6,K,0		
0	228	-209
1	88	-103
2	237	240
3	46*	-15
4	230	-244
5	227	-212
6	0*	-64
6,K,0		
7	307	-287
8	416	-393
9	173	-160
10	0*	9
11	146	142
12	129	126
13	345	326
14	84	-77
15	555	-528
16	291	288
17	32*	30
18	305	-281
19	187	-175
20	171	162
21	33*	9
22	93	-62
23	137	-123
24	93	45
25	78*	-57
26	34*	-50
7,K,0		
0	57*	1
1	217	-217
2	392	-370
3	48*	-12
4	0*	-33
5	132	-93
6	209	-200
7	276	258
8	38*	-35
9	70*	-73
10	354	-337
11	58*	-29
12	99	-73
13	346	-349
14	242	250
15	161	152
16	234	-235
17	191	172
18	189	175
19	64*	-89
20	190	-100
21	123	94
22	87	77
23	97	-71
24	52*	-28
8,K,0		
0	199	212
1	172	170
2	243	-234
3	181	-175
4	153	137
5	306	288
6	67*	-56
7	111	-166
8	71*	65
9	166	146
10	314	309
11	175	174
12	109	-131
13	114	72
14	33*	-55
15	67*	69
16	101	-93
17	0*	-18
18	105	103
19	240	222
20	128	-101
9,K,0		
0	166	-171
1	69*	57
2	157	150
3	0*	-22
4	0*	-4
5	65*	45
6	218	222
7	37*	-14
8	37*	-3
9	55*	-41
10	78*	65
11	107	99
12	73*	95
13	14*	-3
14	0*	-18
15	115	101
10,K,0		
0	88*	83
1	115	-113
2	26*	1
3	91	62
4	43*	-7
5	95	-86
6	77*	44
7	34*	16
1,K,1		
1	148	-154
2	289	282
3	80	77
4	293	289
5	92	93
6	42*	-96
8	172	-159
9	379	-393
10	59	-65
11	675	-684
12	387	389
13	112	102
14	95	-76
15	115	-124
16	0*	-21
17	114	107
18	169	-167
19	0*	-29
20	173	-171
21	15*	18
22	17*	-45
23	223	234
24	279	273
25	281	-273
26	319	-321
27	0*	28
28	39*	-47
29	74*	66
30	0*	50
31	195	193
32	0*	-9
-1,K,1		
1	38*	-25
2	83	88
3	427	469
4	57	58
6	449	475
7	544	574
8	55	98
9	697	745
10	519	554
11	414	444
12	362	353
13	581	-606
14	291	-298
15	276	275
16	85	-92
17	0*	-54
18	120	-130
19	64	88
20	0*	8
21	0*	-7
24	484	467
25	298	309
26	469	-451
27	126	-140
28	47*	-48
29	0*	18
30	0*	24
31	277	-261
32	0*	42
2,K,1		
1	41*	-61
2	517	544
3	0*	-18
4	240	248
5	651	-668
6	608	653
7	657	-683
8	44*	19
9	101	-125
10	391	397
11	449	-456
12	800	-766
13	159	-169
14	644	683
15	146	143
16	226	235
17	92	86
18	314	311
19	106	-109
20	108	111
22	0*	-6
23	61*	78
24	192	189
25	128	134
2,K,1		
26	80	75
27	159	167
28	203	204
29	70*	-110
30	116	-121
31	0*	23
32	121	135
-2,K,1		
1	267	272
2	196	215
3	291	328
4	34*	35
5	530	564
7	335	-375
8	126	139
9	328	346
10	667	685
11	265	248
12	656	-646
13	0*	-10
14	234	252
15	56*	79
16	133	133
17	113	-115
18	236	240
19	0*	-5
20	308	311
21	112	-129
22	54*	65
23	151	132
24	196	199
25	307	-336
26	173	178
27	115	-95
28	68*	86
29	144	123
30	61*	-61
31	0*	-23
32	133	133
3,K,1		
1	370	415
2	112	-99
3	1271	1331
4	412	-413
5	273	-281
6	365	370
7	325	319
8	136	142
9	377	-361
10	202	230
11	866	872
12	463	456
13	405	-397
14	202	-181
15	39*	74
16	59*	63
17	0*	20
18	0*	32
19	102	-114
20	207	213
21	100	85
22	161	163
23	75	-103
24	10*	-5
25	96	92
26	152	176
27	318	-317
28	0*	1
29	113	126
30	0*	26
31	224	-210
-3,K,1		
1	180	-213
2	58	30
3	770	-833
4	141	-138
5	284	-292
6	686	719
7	929	-1013
8	245	-232
9	327	324
10	296	309
11	793	-789
12	532	522
13	449	435
14	548	-552
15	70	69
16	103	105
17	66	-68
18	146	-132
19	119	-108
20	163	160
21	45*	1
22	110	117
23	219	222
24	0*	28
25	57*	-41
26	114	123
27	288	291
28	0*	-24
29	152	-155
30	110	108
31	147	158
4,K,1		
1	715	739
2	24*	26
3	191	214
4	69	62
5	47*	-16
6	108	-110
7	24*	15
8	122	136
9	254	256
10	252	-244
11	133	-149
12	67*	62
13	161	143
14	194	-192
15	67	62
16	152	157
17	140	166
18	291	-289
19	0*	9
20	45*	35
21	44*	6
22	12*	-10
23	0*	12
24	87	-57
25	202	-219
26	57*	-66
27	113	110
28	225	-215
29	17*	-71
30	124	125
-4,K,1		
1	989	-942
2	158	166
3	177	177
4	497	514
5	184	-197
6	161	163
7	82	-115
8	263	-286
9	280	-289
10	377	-393
11	443	438
12	35*	22
13	379	-389
14	255	-254
15	70	35
16	167	172
17	70	-50
18	292	-290
19	91	-71
20	92	-131
21	31*	40
22	147	-137
23	46*	-44
24	80*	-45
25	191	191
26	0*	0
27	185	-182
28	235	-222
29	76	123
30	176	152
5,K,1		
1	495	-510
2	303	332
3	51*	14
4	465	-474
5	206	190
6	0*	-5
7	218	-230
8	283	-274
9	256	250
10	38*	34
11	538	-551
12	359	-367
13	53*	34
14	179	-172
15	87	-75
16	324	-323
17	140	158
5,K,1		
18	107	-85
19	152	-154
20	77	69
21	62*	60
22	116	-107
23	121	111
24	164	-168
25	0*	28
26	58*	-72
27	131	105
28	79	-58
-5,K,1		
1	390	403
2	392	385
3	195	220
4	291	-280
5	187	-162
6	248	247
7	347	354
8	594	-605
9	59*	-19
10	123	132
11	356	361
12	307	-304
13	51*	-50
14	221	-205
15	160	159
16	236	-230
17	67	-35
18	86	-68
19	91	94
20	0*	-1
21	0*	-13
22	176	-166
23	121	-118
24	23*	-42
25	172	-172
26	50*	-75
27	85	-32
28	0*	16
6,K,1		
1	268	-240
2	64*	85
3	106	-86
4	361	-376
5	114	-119
6	333	336
7	0*	3
8	410	-417
9	344	-334
10	327	324
11	329	336
12	74	-134
13	366	-365
14	164	164
15	120	-114
16	330	317
17	111	-138
18	103	-85
19	76	73
20	28*	-6
21	29*	34
22	149	-134
23	62*	57
24	76*	100
25	0*	18
26	46*	-58
-6,K,1		
1	0*	-42
2	198	-189
3	129	129
4	170	-192
5	214	224
6	389	383
7	159	151
8	355	-369
9	379	380
10	438	441
11	353	-367
12	42*	-28
13	259	268
14	79	78
15	24*	6
16	291	294
17	275	279
18	0*	0
19	119	-129
20	53*	-59
21	41*	-42
22	86	-80
23	86	-72
24	175	170
25	68*	-40
26	53*	-25
7,K,1		
1	0*	-5
2	59*	35
3	95	76
4	91	-68
5	125	-149
6	44*	-46
7	51*	42
8	225	238
9	37*	12
10	82	-131
11	226	-229
12	315	316
13	0*	-6
14	271	263
15	235	229
16	161	121
17	0*	19
18	0*	7
19	23*	26
20	112	114
21	38*	49
22	35*	39
23	79	-69
-7,K,1		
2	137	-126
3	86	-94
4	62*	55
5	87	83
6	68	-66
7	0*	-37
8	344	341
9	0*	21
10	170	-170
11	238	245
12	435	435
13	49*	-51
14	47*	62
15	162	-163
16	0*	3
17	99	-106
18	78	62
19	53*	-66
20	138	131
21	14*	-39
22	126	110
23	99	81
24	30*	32
8,K,1		
1	290	292
2	17*	12
3	22*	12
4	19*	49
5	179	178
6	79	-96
7	128	-131
8	32*	-24
9	135	134
10	0*	-18
11	160	140
12	0*	13
13	46*	48
14	153	-154
15	34*	-19
16	132	142
17	38*	50
18	44*	-14
19	0*	4
-8,K,1		
1	235	-242
2	65	-61
3	54*	-39
4	97	102
5	263	-260
6	53*	-62
7	130	145
8	95	-96
9	149	-160
10	99	111
11	83	-63
12	109	-109
13	6*	-2
14	264	-258
15	57*	34
16	87	108
17	78	-70
18	0*	26
19	50*	-36
20	0*	2
9,K,1		
1	0*	7
2	117	143
3	41*	-14
4	231	-225
5	178	173
6	96	86
7	99	-115
8	131	-112
9	195	191
10	65*	58
11	109	-120
12	158	-144
13	95	104
14	17*	55
-9,K,1		
1	63*	66
2	106	102
3	30*	-10
4	161	-138
5	138	-139
6	65*	46
7	52*	23
8	150	-157
9	93	-81
10	0*	-14
11	167	161
12	105	-97
13	51*	-67
14	74*	70
15	65*	38
16	119	-130
-10,K,1		
1	105	100
2	102	-113
3	40*	-47
4	55*	55
5	248	232
6	0*	-7
7	68*	-82
8	63*	-88
1,K,2		
0	719	728
1	400	-412
2	236	-224
3	174	-185
4	734	-774
5	157	-159
6	111	111
7	591	622
8	91	96
9	419	435
10	344	-362
11	18*	47
12	565	574
13	207	170
14	483	-491
15	121	107
16	0*	-14
17	117	113
18	44*	-56
19	156	-160
20	40*	-42
21	326	334
23	124	-122
24	0*	-54
25	395	398
26	114	130
27	0*	-34
28	0*	-12
29	163	150
30	0*	10
31	98	75
-1,K,2		
2	659	-673
3	524	558
4	503	-511
5	153	131
6	72	-65
7	215	-227
8	108	115
9	102	-134
10	83	94
11	449	-463
12	404	430
13	235	-236
14	67	103
15	244	-254
16	190	-206
17	399	-430
18	45*	104
19	93	97
20	144	-148
21	240	-236
22	0*	-11
23	35*	128
24	113	-156
25	333	-328
26	0*	-6
27	0*	-4
28	0*	35
29	102	-98
30	60*	-43
31	93	-103
2,K,2		
0	442	463
1	0*	25
2	63	48
3	237	237
4	279	287
5	157	166
6	444	469
7	328	351
8	415	434
9	250	259
10	221	-221
11	320	350
12	196	-196
13	221	214
14	314	317
15	10*	-62
16	30*	-55
17	141	155
18	345	348
19	119	142
20	129	-134
21	116	127
22	147	162
23	103	127
24	343	-349
25	38*	-52
26	31*	13
27	188	195
28	0*	-61
29	56*	-56
30	36*	1
31	43*	4
-2,K,2		
0	90	-97
1	611	-646
2	466	474
3	146	139
4	391	421
5	98	-94
6	201	220
7	156	162
8	373	391
9	58	-66
10	163	182
11	320	-306
12	0*	-36
13	196	-186
14	358	370
15	198	198
16	71	66
17	20*	-39
18	235	252
19	273	-282
21	30*	30
22	0*	57
23	184	-201
24	315	-318
25	215	210
26	48*	65
27	0*	-17
28	178	-198
29	63*	64
30	53*	-21
31	58*	13
3,K,2		
0	437	-427
1	677	691
2	728	755
3	327	-336
4	28*	8
5	273	262
6	217	224
7	226	-249
8	260	273
9	243	-268
10	283	-273
11	127	-130
3,K,2		
12	483	487
13	414	-423
14	242	-242
15	99	111
16	74	83
17	346	-344
18	86	88
19	53*	-28
20	65*	53
21	279	-275
22	0*	-36
23	66*	88
24	59*	-32
25	47*	-61
26	97	102
27	137	-144
28	93	-100
29	62*	67
30	90	-65
-3,K,2		
0	411	-423
1	172	-180
2	25*	25
3	540	563
4	48*	-67
5	105	-101
6	277	282
7	329	343
8	125	119
9	202	215
10	26*	-21
11	17*	65
12	364	375
13	688	714
14	131	-150
15	164	36
16	0*	8
17	352	346
18	58*	-66
19	154	-9
20	124	106
21	271	266
22	211	-208
23	41*	-49
24	157	154
25	85	101
26	105	-130
27	232	216
28	27*	66
29	0*	-34
30	0*	-32
4,K,2		
0	262	255
1	40*	-33
2	82	86
3	40*	22
4	382	-387
5	0*	-8
6	204	202
7	116	-106
8	157	-159
9	239	-235
10	239	-239
11	38*	27
12	0*	24
13	259	-257
14	232	-243
15	47*	38
16	111	99
17	259	-262
18	37*	-63
19	150	-162
20	152	150
21	71*	-61
22	129	-138
23	286	-284
24	90	86
25	38*	2
26	48*	-81
27	50*	72
28	22*	-27
-4,K,2		
0	407	-416
1	770	776
2	269	-255
3	448	-462
4	341	-345
5	66	-75
6	200	210
7	134	132
8	112	-115
9	141	137
10	34*	-77
11	176	201
12	168	-178
13	267	-243
14	80	-69
15	312	318
16	82	78
18	196	-198
19	179	103
20	63*	55
21	69*	27
22	166	-154
23	187	191
24	0*	29
25	0*	-2
26	31*	-1
27	112	-121
28	63*	-14
29	0*	39
5,K,2		
0	212	-209
1	0*	6
2	0*	19
3	229	235
4	213	-209
5	67	63
6	304	-304
7	147	158
8	445	-443
9	120	-121
10	287	-292
11	101	101
12	0*	-3
13	275	283
14	155	155
15	365	-360
16	0*	6
17	299	298
18	77	-73
19	128	-147
20	0*	31
21	215	201
22	129	134
23	16*	7
24	5*	2
25	123	94
26	71*	84
27	89	-88
-5,K,2		
0	331	-332
1	113	-135
2	243	-247
3	303	-333
4	67	-58
5	143	-142
6	322	-309
7	142	-158
8	62	-55
9	66	-52
10	96	-89
11	45*	-53
12	146	166
13	296	-263
14	16*	17
15	196	159
16	0*	-20
17	340	-340
18	18*	-12
19	12*	9
20	122	-141
21	85	-91
22	208	212
23	145	-147
24	132	-107
25	132	-123
26	121	98
27	35*	68
28	102	99
6,K,2		
0	387	394
1	65*	49
2	191	-187
4	101	104
5	159	163
6	32*	-91
7	291	248
8	212	214
9	120	110
10	146	-140
11	49*	6
12	0*	30
13	357	-370
6,K,2		
14	0*	47
15	420	422
16	249	-264
17	0*	26
18	238	245
19	172	162
20	131	-131
21	44*	55
22	83*	84
23	75*	85
24	52*	-47
-6,K,2		
0	186	181
1	164	167
2	50*	-36
3	35*	38
4	77	68
5	277	-282
6	0*	42
7	39*	-47
8	346	347
9	97	-98
10	116	101
11	32*	-18
12	70*	79
13	191	178
14	117	133
15	320	-328
16	294	-299
17	15*	-10
18	148	150
19	138	-129
20	177	-184
21	115	134
22	0*	27
23	165	-156
24	0*	12
25	13*	3
26	99	71
7,K,2		
0	136	155
1	136	145
2	194	181
3	188	-193
4	33*	46
5	166	175
6	225	220
7	205	-209
8	14*	3
9	45*	52
10	289	290
11	212	222
12	0*	-13
13	174	174
14	91	-105
15	111	-100
16	54*	61
17	112	-98
18	73*	-72
19	147	151
20	52*	64
21	75*	-62
-7,K,2		
0	141	-153
1	55*	-47
2	422	424
3	93	84
4	74	-75
5	4*	-32
6	118	118
7	242	243
8	39*	34
9	137	-120
10	235	232
11	99	-118
12	243	236
13	252	-255
14	349	-350
15	286	287
16	301	308
17	171	164
18	221	-222
19	74*	-50
20	93	98
21	94	81
22	0*	-57
23	23*	-45
8,K,2		
0	200	-193
1	185	-185
2	166	161
3	67*	72
4	83*	-53
5	195	-237
6	140	149
7	0*	10
8	54*	-28
9	113	-129
10	188	-188
11	93	-80
12	75*	92
13	58*	-25
14	0*	-15
15	96	-77
16	132	126
17	23*	29
-8,K,2		
0	291	-282
1	212	214
2	118	124
3	132	-135
4	122	-108
5	154	167
6	40*	72
7	121	-144
8	34*	-34
9	167	162
10	323	-330
11	48*	43
12	44*	55
13	157	171
14	122	115
15	144	122
16	27*	28
17	66*	-86
18	20*	-38
19	212	214
20	61*	29
9,K,2		
0	143	124
1	86*	-91
2	143	-135
3	53*	39
4	0*	-1
5	53*	-59
6	122	-112
7	0*	-35
8	33*	25
9	0*	-18
10	101	-72
-9,K,2		
0	57*	80
1	0*	30
2	185	-183
3	50*	-13
4	79	70
5	62*	-84
6	208	-255
7	22*	2
8	51*	46
9	70*	-57
10	26*	0
11	48*	62
12	111	-108
13	54*	10
14	72*	-66
15	73*	71
-10,K,2		
0	125	-130
1	167	-155
2	73	52
3	0*	41
4	0*	-9
5	151	-138
6	0*	10
1,K,3		
1	113	-82
2	182	157
3	321	319
4	310	303
5	235	-224
6	204	192
7	436	431
8	18*	-37
9	253	234
10	132	124
11	470	470
1,K,3		
12	372	-366
13	221	-235
14	206	177
15	158	168
16	116	86
17	0*	22
18	225	227
19	102	-112
20	68*	-6
21	98	96
22	0*	18
23	127	-120
24	0*	-26
25	94*	83
26	199	189
27	0*	26
28	163	154
29	62*	-41
30	40*	-72
-1,K,3		
1	443	-418
2	482	-469
3	186	-183
4	148	134
5	126	-148
6	353	-351
7	205	-199
8	78	75
9	84	-94
10	250	-273
11	323	-333
12	117	128
13	50*	59
14	127	-120
15	73	-64
16	151	-168
17	133	130
18	109	105
19	67*	-87
20	114	-109
21	0*	23
22	0*	-42
25	361	-397
26	367	327
27	169	186
28	0*	-5
29	0*	45
30	0*	22
2,K,3		
1	121	86
2	256	-241
3	536	514
4	119	84
5	81	-67
6	136	-128
7	232	241
8	43*	33
9	2*	15
10	379	-368
11	534	544
12	492	509
13	103	82
14	475	-475
15	45*	-64
16	152	-129
17	0*	-23
18	194	-184
19	140	-135
20	68*	-65
21	65*	-67
22	24*	8
23	47*	-9
24	120	-116
25	25*	-63
26	48*	81
27	151	-151
28	161	-166
29	62*	73
-2,K,3		
1	314	-289
2	492	-476
3	113	-73
4	163	142
5	215	-234
6	649	-645
7	283	253
8	196	31
9	111	85
10	217	-228
11	222	152
12	389	394
13	85	-73
14	400	-394
15	68	68
16	230	-229
17	0*	17
18	84	-69
19	44*	-57
20	257	-251
21	0*	17
22	0*	51
23	159	-153
24	0*	-38
25	370	377
26	264	-253
28	50*	-72
29	57*	-37
30	34*	48
3,K,3		
1	105	-46
2	88	97
3	417	-439
4	137	139
5	49*	3
6	88	-80
7	400	-396
8	56*	-32
9	321	318
10	101	-61
11	374	-383
12	280	-294
13	236	213
14	111	-121
15	0*	-31
16	93	-91
17	56*	78
18	177	-156
19	68*	-53
20	86	-78
21	0*	-16
22	81	-72
23	143	124
24	65*	28
25	95	-109
26	163	-166
27	229	233
28	85	-53
-3,K,3		
1	164	157
2	284	-281
3	395	366
4	143	152
5	119	136
6	75	-62
7	295	321
8	85	40
9	91	92
10	116	-91
11	708	715
12	317	-319
13	217	-212
14	256	219
15	23*	70
16	108	-106
17	120	-122
18	213	227
19	0*	-21
20	68*	-64
21	44*	-45
22	46*	-50
23	57*	-72
24	51*	61
25	67*	-46
26	71*	-78
27	168	-174
28	61*	-30
29	134	139
4,K,3		
1	960	-953
2	91	-28
3	65	21
4	246	-220
5	0*	-16
6	192	206
7	169	-150
8	59*	-42
9	0*	-2
10	315	303
12	209	-193
13	164	-159
14	48*	10
15	56*	17
16	219	-218
17	31*	-45
4,K,3		
18	158	147
19	96	-88
20	48*	44
21	58*	51
22	36*	18
23	79	78
24	0*	8
25	77*	75
26	0*	28
-4,K,3		
1	298	290
2	61*	-45
3	249	-238
4	79	-88
5	71	47
6	77	87
7	193	-181
8	169	-171
9	338	337
10	283	289
11	325	-307
12	110	76
13	467	476
14	91	83
15	0*	-25
16	51*	64
17	87	-97
18	267	251
19	62*	-55
20	22*	23
21	44*	-52
22	102	80
23	112	108
24	80	94
25	133	-126
26	64*	-10
27	187	161
28	192	179
5,K,3		
1	103	114
2	75	-54
3	63*	74
5	84	-101
6	126	122
7	158	159
8	147	133
9	243	-243
10	78	41
11	345	346
12	276	268
13	272	-267
14	129	109
15	24*	27
16	261	257
17	75	-10
18	0*	-16
19	131	126
20	27*	-6
21	0*	-10
22	39*	43
23	86	-60
24	152	134
-5,K,3		
1	410	-379
2	270	-270
3	202	-207
4	379	355
5	143	147
6	155	-150
7	197	-185
8	138	147
9	0*	13
10	241	-225
12	337	338
13	77	-75
14	40*	42
15	101	-105
16	231	229
17	35*	33
18	97	76
19	58*	-34
20	51*	-54
21	31*	-3
22	63*	59
23	61*	42
24	0*	4
25	147	143
26	103	102
6,K,3		
1	153	151
2	29*	17
3	151	154
4	254	240
5	118	126
6	231	-226
7	93	-74
8	300	284
9	285	291
10	213	-205
11	328	-333
12	108	64
13	143	125
14	0*	-20
15	224	216
16	119	-104
17	93	94
18	47*	35
19	32*	-13
20	19*	-5
21	7*	9
22	81	80
-6,K,3		
1	43*	-18
2	225	229
5	166	-175
6	212	-208
7	70	74
8	66*	-27
9	255	-249
10	227	-216
11	208	186
12	130	58
13	238	-213
14	143	-126
15	85	57
16	153	-146
17	171	-170
18	47*	-21
19	112	129
20	34*	16
21	0*	32
22	0*	-1
23	22*	0
24	77*	-77
7,K,3		
1	124	124
2	99	73
3	44*	-16
4	101	80
5	153	142
6	23*	-9
7	140	-129
8	132	-133
9	56*	33
10	74*	-47
11	148	142
12	176	-159
13	0*	10
14	149	-149
15	131	-145
16	79*	-56
17	13*	25
18	68*	-17
-7,K,3		
1	109	99
2	101	-111
3	89	69
4	172	-158
5	18*	-17
6	130	105
7	167	168
8	343	-330
9	109	-41
10	308	314
11	217	-193
12	313	-305
13	32*	79
14	79	-45
15	93	36
16	34*	20
17	192	185
18	35*	6
19	0*	31
20	114	-107
21	0*	6
8,K,3		
1	138	-158
2	47*	45
3	38*	27
4	84*	-102
8,K,3		
5	121	-113
6	84	69
7	52*	-34
8	63*	-27
9	30*	-38
10	66*	59
11	89	-82
12	74*	-100
13	45*	-39
-8,K,3		
1	174	160
2	62*	-68
3	28*	22
4	93	-87
5	106	157
6	0*	23
7	114	-106
8	108	103
9	133	135
10	116	-114
11	57*	38
12	240	224
13	32*	52
14	154	146
15	74*	-48
16	78	-76
17	45*	0
18	0*	10
-9,K,3		
1	72*	-46
2	122	-108
3	58*	-3
4	141	138
5	0*	5
6	94	-101
7	51*	52
8	95	84
9	52*	-55
10	74*	65
11	38*	-60
12	51*	23
1,K,4		
1	216	213
2	78	-74
3	108	-72
4	300	308
5	45*	-7
6	156	152
7	113	-96
8	88	123
9	25*	-56
10	77	84
11	44*	25
12	187	-191
14	356	355
15	71	-18
16	59*	-83
17	152	-153
18	130	122
19	126	127
20	33*	-16
21	98	-102
22	0*	-3
23	91	105
24	0*	-37
25	251	-246
26	38*	-43
27	0*	32
-1,K,4		
0	1351	-1361
1	857	-859
2	321	309
3	86	79
4	79	-86
5	148	-165
6	47*	-8
7	126	123
8	79	-83
9	144	147
10	55*	-20
11	49*	27
12	56*	69
13	196	178
15	113	108
16	34*	41
17	226	243
18	211	-236
19	0*	-31
20	63*	74
21	159	147
22	34*	-17
23	0*	-68
24	206	210
25	104	110
26	0*	42
27	89	95
28	0*	-33
2,K,4		
0	509	-456
1	122	125
2	46*	44
3	144	-151
4	217	-202
5	10*	-19
6	68	51
7	131	-132
8	59*	-55
9	105	-115
10	46*	-41
12	152	149
13	156	-154
14	214	-219
15	0*	12
16	45*	49
17	199	-196
18	88	-99
19	60*	-73
20	128	122
21	74*	-65
22	188	-174
23	0*	-63
24	128	134
25	0*	0
26	51*	55
-2,K,4		
1	844	831
2	321	-329
3	113	99
4	303	-289
5	78	-75
6	35*	-39
7	179	-172
8	121	-114
9	0*	5
10	33*	-28
11	142	-134
12	66	57
13	166	163
14	127	-124
15	48*	29
16	97	-73
17	84	-89
18	139	-143
19	153	159
20	75	68
21	86	-84
22	0*	-65
23	117	119
24	189	169
25	195	-186
26	71*	-67
27	10*	25
3,K,4		
0	258	259
1	123	-107
2	468	-463
3	242	241
4	137	-132
5	89	-112
6	38*	24
7	130	149
8	147	-135
9	31*	-16
10	0*	15
11	23*	44
12	189	-185
13	131	129
14	0*	50
15	34*	25
16	46*	-41
17	107	98
18	32*	-24
19	33*	-53
20	37*	29
21	176	164
22	52*	-65
23	143	-140
24	0*	19
25	111	66
-3,K,4		
0	167	140
1	105	-95
2	32*	-71
3	127	-143
4	111	99
5	90	-100
6	79	-87
7	164	-181
8	56*	35
9	80	-87
10	31*	51
11	188	-187
12	205	-228
13	293	-290
14	0*	69
15	95	91
16	0*	40
17	197	-189
18	113	117
19	32*	-40
20	105	-84
21	154	-152
22	100	107
23	0*	-8
24	200	-191
25	92	-82
26	95	113
27	66*	-54
4,K,4		
0	0*	28
1	0*	12
2	134	-125
3	172	159
4	113	115
5	104	97
6	112	-104
7	119	113
8	0*	-3
9	0*	23
10	71*	67
11	36*	-26
12	42*	-24
13	189	185
14	310	318
15	63*	-68
16	181	-170
17	228	229
18	56*	48
19	52*	11
20	73*	-83
21	94	76
22	31*	55
23	164	151
-4,K,4		
0	210	187
1	411	-414
2	86	-46
3	227	233
4	307	318
5	220	-206
6	52*	46
7	23*	18
8	83	89
9	49*	40
10	67*	77
11	223	-214
12	45*	-27
13	336	363
14	107	84
15	180	-170
16	55*	-40
17	94	98
18	120	112
19	110	-122
20	0*	7
21	68*	94
22	0*	6
23	145	-133
24	0*	12
25	58*	4
5,K,4		
0	332	316
1	85	94
2	35*	-60
3	143	-133
4	94	83
5	77	40
6	113	108
7	51*	-18
8	240	242
9	139	138
10	293	251
11	67*	-77
12	127	124
13	231	-235
14	103	-104
15	257	263
16	71*	-78
17	203	-205
18	84	-56
19	139	137
20	0*	-29
21	105	-96
-5,K,4		
0	0*	12
1	165	174
2	174	170
3	17*	-27
4	22*	26
5	107	-130
6	122	139
7	157	158
8	75	-79
9	149	136
10	88	98
11	81	72
12	96	-114
13	45*	63
14	0*	-2
15	0*	3
16	52*	34
17	139	140
18	61*	-63
19	35*	39
20	101	107
21	122	119
22	162	-165
23	107	99
24	111	101
6,K,4		
0	99	-68
1	66*	-37
2	123	113
3	39*	-2
4	103	-98
5	62*	-38
6	168	152
7	113	-123
8	158	-161
9	82	-60
10	110	122
11	43	76
12	0*	-20
13	196	190
14	47*	37
15	301	-301
16	89	80
17	39*	-48
18	141	-147
-6,K,4		
0	0*	-9
1	70	-69
2	25*	-53
3	89	-99
4	30*	-23
5	85	75
6	153	-148
7	45*	-5
8	221	-227
9	77	69
10	0*	-11
11	31*	-4
12	24*	-35
13	61*	-74
14	90	-82
15	212	206
16	141	155
17	0*	-30
18	106	-122
19	101	90
20	80	66
21	51*	-70
22	59*	41
7,K,4		
0	64*	-75
1	239	-198
2	125	-96
3	121	135
4	54*	-16
5	149	-149
6	67*	-72
7	115	127
8	71*	-8
7,K,4		
9	0*	6
10	222	-220
11	159	-162
12	32*	6
13	43*	-64
-7,K,4		
0	129	137
1	136	143
2	232	-221
3	68*	-37
4	78	43
5	81	-60
6	124	-127
7	139	-133
8	0*	2
9	0*	32
10	67*	-47
11	29*	35
12	179	-180
13	148	141
14	281	284
15	91	-135
16	267	-275
17	154	-129
18	136	140
19	0*	13
8,K,4		
0	131	142
1	47*	41
-8,K,4		
0	117	136
1	90	-103
2	0*	9
3	113	137
4	97	79
5	97	-92
6	24*	-61
7	95	118
8	65*	50
9	175	-175
10	223	218
11	0*	-38
12	41*	-6
13	78*	-132
14	193	-235
-9,K,4		
0	137	-131
1	0*	19
2	149	155
3	0*	-4
4	0*	-46
5	76*	57
6	172	167
7	0*	-11
0,K,5		
1	31*	27
2	97	-93
4	67*	-74
5	0*	11
6	105	-84
7	141	149
8	166	-177
9	105	105
10	67*	-81
11	173	162
12	0*	-32
13	181	-177
14	122	-135
15	65*	64
16	0*	44
17	29*	-44
18	55*	-70
19	0*	32
20	50*	-69
21	0*	25
22	49*	-59
24	251	-237
1,K,5		
1	61*	31
2	125	-122
3	85	-78
4	0*	-63
5	41*	31
6	100	-72
7	205	-193
8	105	-119
9	0*	0
10	181	-183
11	145	-130
12	281	297
13	174	178
14	160	-165
15	105	-115
16	0*	10
17	21*	-23
18	121	-122
19	0*	-15
20	67*	-24
21	61*	-64
22	66*	-64
23	63*	84
24	54*	-15
-1,K,5		
1	0*	22
2	119	120
3	141	131
5	108	106
6	211	216
7	189	201
8	169	-164
9	35*	-65
10	174	185
11	81	89
12	36*	-27
13	34*	-17
14	71*	87
15	5*	-3
16	92	98
17	49*	32
18	47*	31
19	41*	39
20	78	45
21	0*	-19
22	0*	8
23	60*	-125
2,K,5		
1	50*	-45
2	130	112
3	282	-259
4	82	-87
5	55*	32
6	101	97
7	269	-266
8	162	-153
9	133	113
10	252	249
11	179	-188
12	243	-243
13	57*	15
14	162	155
15	73*	31
16	68*	78
17	0*	-16
18	85	68
19	13*	5
20	58*	22
21	65*	-5
22	0*	-19
23	30*	51
-2,K,5		
3	0*	-18
4	93	-131
5	50*	41
6	222	217
7	115	-135
8	31*	-52
9	24*	-27
10	161	165
11	149	-157
12	51*	-70
13	0*	34
14	94	94
15	47*	-53
16	72	51
17	0*	30
18	97	97
19	38*	1
20	112	114
21	14*	14
22	0*	-26
23	135	118
24	0*	13
3,K,5		
1	72*	-94
2	166	-153
3	191	185
3,K,5		
4	98	-115
5	36*	-33
6	112	105
7	96	91
8	0*	-3
9	66*	-61
10	144	138
11	178	182
12	87	94
13	121	-135
14	0*	3
15	68*	71
16	0*	10
17	90	-99
18	131	131
19	52*	-12
20	66*	43
21	0*	2
-3,K,5		
1	66*	-55
2	97	-91
3	156	-169
4	0*	-11
5	110	-88
6	109	-116
7	135	-114
8	0*	-36
9	73	-86
10	49*	45
11	266	-249
12	208	224
13	158	153
14	190	-183
15	55*	-62
16	34*	26
17	13*	43
18	0*	-53
19	40*	-9
20	0*	-23
21	0*	8
22	66*	46
23	0*	6
4,K,5		
1	177	179
2	41*	-15
3	41*	10
4	119	106
5	49*	41
6	87	-82
7	102	103
8	76*	72
9	0*	1
10	151	-160
11	123	122
12	209	198
13	0*	-9
14	62*	-55
15	0*	8
16	121	118
17	70*	57
18	60*	-79
19	88	63
-4,K,5		
1	0*	9
2	107	-98
3	77	47
4	85	86
5	63*	-63
6	72	-74
7	34*	87
8	0*	41
9	158	-144
10	171	-167
11	267	286
12	62*	13
13	245	-262
14	39*	-33
15	0*	39
16	48*	-47
17	43*	-23
18	89	-40
19	27*	36
20	69*	-50
21	10*	37
22	68*	-66
5,K,5		
1	88	-73
2	35*	9
3	0*	-8
4	52*	43
5	125	125
6	89*	-82
7	144	-132
8	53*	-32
9	238	244
10	57*	-16
11	251	-246
12	183	-175
13	121	135
14	96	-75
15	79*	81
16	122	-122
-5,K,5		
1	231	230
2	122	131
3	58*	40
4	110	-113
5	69*	-45
6	62*	87
7	110	84
8	202	-201
9	47*	-6
10	165	154
11	12*	-7
12	197	-193
13	110	122
14	63*	42
15	57*	28
16	72*	-45
17	83	-62
18	43*	11
19	34*	30
20	48*	-31
6,K,5		
1	70*	-63
2	86	54
3	57*	-75
4	56*	-45
5	61*	-37
6	132	112
7	64*	14
8	175	-153
9	123	-106
10	0*	22
11	190	189
-6,K,5		
1	0*	4
2	111	-119
3	84	-77
4	61*	55
5	198	205
6	80	89
7	68*	-67
8	47*	7
9	113	112
10	54*	54
11	181	-156
12	77	59
13	63*	83
14	49*	56
15	67*	-62
16	78*	87
17	91	91
18	80*	67
-7,K,5		
1	37*	-45
2	45*	76
3	65*	-49
4	93	80
5	0*	32
6	92	-74
7	74*	-70
8	170	155
9	0*	-13
10	164	-180
11	64*	45
12	199	205
13	76*	-72
14	0*	-45
-8,K,5		
1	46*	-28
2	0*	-3
3	62*	-35
4	0*	-8
5	94	-82
6	24*	26
7	95	92
8	82*	-83
0,K,6		
0	363	-399
1	112	-40
2	68*	61
3	69*	-14
4	32*	-1
5	46*	35
6	57*	13
7	57*	-25
8	71*	-62
9	24*	-19
10	79	-62
11	37*	35
12	96	-90
13	182	-166
14	49*	47
15	0*	-3
16	0*	11
17	87	-71
18	38*	-38
19	34*	41
1,K,6		
0	185	-148
1	125	-68
2	32*	45
3	38*	-2
4	143	-132
5	77	-70
6	0*	-4
7	35*	40
8	52*	-50
9	37*	40
10	62*	-47
11	34*	-68
12	53*	57
13	125	105
14	193	-187
15	0*	-8
16	45*	52
17	43*	31
18	67*	-56
-1,K,6		
0	612	579
1	538	512
2	61*	-47
3	113	-135
4	65*	42
5	46*	-37
6	55*	-75
7	0*	-13
8	31*	40
9	42*	-33
10	48*	24
11	0*	-27
12	0*	15
13	0*	-35
14	47*	24
15	56*	20
16	45*	-29
17	125	-131
18	113	105
19	46*	20
2,K,6		
0	264	242
1	27*	28
2	156	-142
3	83	67
4	109	78
5	68*	-68
6	36*	18
7	106	96
8	0*	25
9	19*	6
10	17*	8
11	81	88
12	89	-101
13	97	83
14	97	87
15	73*	48
16	31*	-43
17	76*	82
-2,K,6		
0	167	-115
1	492	-489
2	174	164
3	65*	56
4	119	87
5	0*	-9
6	18*	-36
7	79	75
8	33*	46
9	58*	-10
10	63*	-1
11	0*	34
12	53*	11
13	62*	-25
14	55*	17
15	29*	42
16	39*	34
17	86	87
18	48*	21
19	95	-93
3,K,6		
0	0*	-71
1	67*	33
2	141	120
3	46*	-40
4	70*	61
5	45*	43
6	36*	7
7	56*	-61
8	80*	73
9	0*	-11
10	12*	10
11	59*	-53
12	48*	32
13	0*	-6
14	19*	62
15	38*	27
-3,K,6		
0	209	-176
1	202	242
2	77*	73
3	49*	67
4	70*	-45
5	0*	-12
6	50*	16
7	56*	54
8	0*	-19
9	64*	24
10	0*	-51
11	0*	9
12	63*	56
13	180	168
14	86	-61
15	63*	26
16	0*	3
17	48*	34
18	89	-62
4,K,6		
0	0*	50
1	0*	59
2	18*	45
3	53*	-92
4	68*	-67
5	66*	-65
6	51*	43
7	73*	-67
8	0*	53
9	59*	27
10	0*	20
11	0*	-49
-4,K,6		
0	177	-127
1	151	136
2	64*	48
3	89	-45
4	127	-94
5	61*	64
6	28*	-29
7	23*	-33
8	42*	-20
9	0*	-4
10	70*	-56
11	77*	48
12	36*	-14
13	183	-194
14	110	-99
15	99	98
16	78*	75
17	106	-87
5,K,6		
0	100*	-120
1	93	-69
2	0*	37
3	32*	55
4	72*	-89
-5,K,6		
0	51*	41
1	113	-129
2	126	-100
3	12*	18
4	87	69
5	49*	5
6	71*	-79
7	47*	-41
8	53*	41
9	0*	2
10	0*	-37
11	92	-82
12	32*	-19
13	61*	19
14	47*	26
-6,K,6		
0	65*	-53
1	98*	41
2	123	108
3	72*	39
4	0*	23
5	69*	-73
6	69*	39
7	85	54
8	72*	59
9	40*	6
10	56*	33
11	0*	7
-7,K,6		
0	52*	-20
1	91	-81
2	104	93
3	0*	21
0,K,7		
1	12*	23
2	0*	18
3	41*	-55
4	44*	48
5	0*	15
6	58*	50
7	84*	-79
8	0*	10
9	20*	-32
10	45*	-14
11	125	-119
1,K,7		
1	0*	1
2	36*	53
3	57*	10
4	0*	2
5	0*	0
6	69*	53
7	51*	4
8	0*	-24
9	0*	-14
-1,K,7		
1	27*	-6
2	55*	-68
3	59*	-39
4	48*	23
5	25*	-16
6	98	-75
7	46*	-17
8	43*	11
9	0*	23
10	39*	-57
11	0*	-22
2,K,7		
1	65*	43
2	128	-122
3	144	118
4	55*	41
5	53*	-48
-2,K,7		
1	41*	-12
2	51*	7
3	19*	40
4	0*	25
5	0*	17
6	56*	-54
7	90	85
8	0*	0
9	0*	-41
10	61*	-19
11	82	47
-3,K,7		
1	67*	55
2	30*	11
3	53*	50
4	0*	-20
5	13*	-2
6	102	91
7	52*	46
8	35*	-8
9	0*	13
10	47*	35
-4,K,7		
1	0*	18
2	43*	10
3	80*	-59
4	78*	-20
5	50*	3
6	0*	26
7	41*	-14

the optical goniometer. It was assumed that no coating was necessary, as the crystals seemed stable in air over a period of several weeks under conditions of high relative humidity. The hydration, and consequently the stability of the crystals, is dependent on the ambient humidity and during the course of this project, the humidity was maintained at a level above 60% r.h.

Initial values of cell parameters were determined from rotation photographs and zero-level Weissenberg photographs from a Weissenberg camera using Cu $K\alpha$ radiation. The absence of $h0l$ reflections with l odd and $0k0$ reflections with k odd, indicated the space group $P2_1/c$.

Settings were calculated for methylene blue for use on the General Electric XRD-6 diffractometer equipped with a molybdenum target tube and card automated Eulerian cradle.

Intensity measurements were made on all the reflections by scanning over 2θ at $2\cdot0°$ per min and integrating over the scan range. Backgrounds were measured for twenty sec at each end of the 2θ scan range by a stationary count method. Four reflections were chosen as standards and were repeatedly measured throughout the course of the collection of data. Data was automatically recorded on punched cards and subsequently processed with the use of the X-ray crystallographic computing system X-RAY67 (1967). 5594 total observations yielded an averaged asymmetric set consisting of 1506 independent observed reflections and 1018 reflections coded unobserved (Table 1). A unique set of reflections from the asymmetric unit was selected, the scan intensities were adjusted for background and $1/Lp$ corrections were applied. No absorption corrections were applied.

In the solution of the structure of methylene blue, the preliminary computations were made with all weights equal. A weighting scheme was later applied in which the weighting factor $= Q_1/J$, where J is the maximum of three functions: (1) standard deviation from counting statistics; (2) $Q_2 \cdot F_{obs}$; (3) Q_3. For methylene blue, the following values were used: $Q_1 = 0\cdot15$, $Q_2 = 0\cdot01$, $Q_3 = 0\cdot15$.

The scattering factors for C,N,O,S and Cl$^-$ were taken from International Tables for X-ray Crystallography (1962) for C, N, O, S, Cl$^-$. Hydrogen scattering factors were taken from Stewart, Davidson, & Simpson (1965).

292 phases with high E values were generated from the $\bar{1}02$, 331, and $\bar{1}12$ reflections. This process was carried out with the X-RAY67 programs DATFIX, SIGMA2 and PHASE. The signed values of these 292 quasi-normalized structure factors were used to generate a probability electron-density map with the E values as coefficients in the Fourier transform equations.

From the E map, the basic covalent bonded unit of one sulfur, three nitrogen and sixteen carbon atoms was found. Other peaks, presumably chlorine or oxygen, were noted. Structure factors calculated from the coordinates of these 20 atoms resulted in an R index of 0·48.

At this state of refinement a comparison of the calculated and observed structure factors showed that the $0kl$ reflections consistently calculated higher structure factors than observed. Reference to the original observations of scan and background intensities showed that the peaks were badly overlapping for this particular crystal mounting. Certain other reflections which showed large differences between calculated and observed structure factors were noted to have large dif-

Table 2. *Atomic positions and thermal parameters* ($\times 10^4$)

	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
S(5)	7291 (1)	2757 (1)	7740 (2)	336 (7)	328 (5)	606 (9)	7 (6)	31 (5)	−10 (7)
N(10)	4035 (4)	2827 (1)	6970 (6)	438 (23)	352 (25)	451 (27)	−16 (18)	51 (18)	−41 (21)
N(11)	6143 (4)	1177 (1)	7504 (6)	500 (27)	308 (25)	629 (33)	28 (18)	89 (21)	17 (20)
N(12)	6875 (4)	4371 (1)	7723 (6)	508 (27)	333 (25)	613 (33)	−31 (18)	− 2 (21)	24 (21)
C(1)	3716 (5)	2075 (2)	6881 (8)	384 (28)	544 (34)	557 (39)	− 7 (22)	21 (25)	2 (29)
C(2)	4197 (5)	1668 (2)	6979 (7)	518 (31)	401 (30)	435 (37)	−63 (24)	68 (25)	0 (26)
C(3)	5651 (5)	1581 (2)	7367 (7)	458 (30)	392 (30)	326 (32)	−16 (21)	59 (23)	9 (25)
C(4)	6559 (5)	1934 (2)	7586 (7)	348 (28)	446 (30)	437 (36)	−34 (22)	38 (23)	32 (25)
C(4a)	6073 (5)	2343 (2)	7461 (7)	427 (28)	367 (30)	321 (32)	12 (19)	36 (22)	−45 (24)
C(10a)	4619 (5)	2437 (2)	7102 (7)	399 (28)	377 (30)	373 (36)	−21 (21)	42 (24)	−63 (25)
C(5a)	6284 (5)	3215 (2)	7529 (7)	435 (30)	426 (34)	355 (33)	3 (22)	18 (22)	7 (26)
C(6)	6943 (5)	3597 (2)	7716 (7)	400 (30)	416 (30)	503 (35)	46 (22)	53 (24)	− 7 (27)
C(7)	6215 (4)	3995 (2)	7556 (7)	378 (28)	450 (30)	406 (35)	18 (22)	− 5 (23)	22 (25)
C(8)	4711 (5)	3967 (2)	7199 (8)	443 (30)	348 (30)	600 (41)	21 (24)	122 (26)	−28 (28)
C(9)	4063 (5)	3586 (2)	7000 (8)	336 (29)	450 (34)	606 (39)	34 (22)	66 (24)	−48 (29)
C(9a)	4787 (4)	3189 (2)	7155 (7)	333 (27)	455 (30)	476 (37)	48 (22)	81 (20)	− 7 (28)
C(13)	5243 (6)	804 (2)	7314 (11)	616 (36)	377 (34)	779 (45)	13 (25)	53 (30)	−91 (32)
C(14)	7625 (6)	1096 (2)	7864 (11)	545 (36)	455 (34)	861 (49)	113 (25)	106 (31)	54 (33)
C(15)	8387 (6)	4409 (2)	8944 (11)	506 (34)	549 (34)	971 (53)	−61 (27)	−25 (31)	0 (36)
C(16)	6134 (7)	4783 (2)	7589 (11)	663 (38)	377 (35)	756 (48)	−27 (25)	−28 (31)	− 12 (31)
Cl(1)	2186 (2)	4867 (1)	7359 (3)	650 (9)	583 (9)	977 (13)	30 (7)	− 5 (8)	−30 (10)
O(1)	516 (5)	482 (2)	8419 (8)	737 (28)	950 (34)	1074 (39)	−110 (74)	− 6 (24)	228 (30)
O(2)	11 (4)	2090 (2)	7658 (7)	664 (25)	745 (29)	922 (35)	−75 (21)	134 (22)	43 (25)
O(3)	1777 (4)	835 (1)	5453 (8)	730 (26)	700 (29)	1035 (38)	−89 (22)	114 (23)	99 (26)
O(4)	1005 (4)	2905 (1)	6550 (7)	526 (23)	705 (29)	948 (33)	15 (18)	109 (21)	−237 (24)
O(5)	295 (4)	3425 (1)	9503 (8)	716 (26)	661 (29)	998 (33)	21 (21)	103 (23)	− 2 (25)

Table 2 (*cont.*)

Hydrogen atom position and thermal parameters ($\times 10^4$)

	x	y	z	U
H(1)	2742 (44)	2147 (13)	6764 (60)	489
H(2)	3527 (40)	1422 (13)	6800 (59)	444
H(3)	7508 (40)	1903 (13)	7894 (57)	412
H(4)	7909 (40)	3572 (13)	7923 (56)	430
H(5)	4156 (40)	4224 (14)	7354 (60)	469
H(6)	3108 (43)	3550 (13)	6816 (58)	466
H(7)	4450 (47)	776 (14)	7872 (71)	557
H(8)	5742 (42)	523 (16)	7397 (63)	557
H(9)	4625 (47)	860 (14)	6261 (71)	557
H(10)	7814 (42)	765 (16)	7640 (67)	616
H(11)	8103 (44)	1226 (15)	6600 (60)	616
H(12)	8245 (46)	1216 (14)	8922 (68)	616
H(13)	8710 (46)	4380 (16)	9243 (74)	650
H(14)	8937 (47)	4217 (16)	7538 (73)	650
H(15)	8680 (43)	4756 (16)	7645 (70)	650
H(16)	6348 (43)	4887 (15)	6485 (72)	541
H(17)	5021 (47)	4799 (13)	7375 (63)	541
H(18)	6604 (45)	4954 (15)	8141 (73)	541
H(19)	1197 (55)	414 (17)	9696 (85)	916
H(20)	− 213 (55)	302 (17)	8261 (79)	916
H(21)	165 (47)	2020 (16)	9073 (81)	762
H(22)	261 (49)	2368 (17)	7396 (75)	762
H(23)	1357 (49)	712 (17)	6569 (78)	801
H(24)	1664 (47)	647 (17)	3882 (81)	801
H(25)	591 (46)	3020 (16)	7617 (77)	706
H(26)	2016 (53)	2884 (14)	6740 (70)	706
H(27)	744 (49)	3670 (17)	9798 (74)	789
H(28)	250 (46)	3318 (16)	1135 (81)	789

ferences between the two measurements of background. All such reflections were systematically eliminated.

A difference synthesis $|F_o - F_c|$ brought out several strong peaks, two of which were at the positions predicted for the possible sites of the chlorine atom (Zhdanov, Zvonkova & Vorontsova, 1956). Chlorine atoms, each with one half-site occupancy, were placed in these positions and three cycles of full-matrix least-squares were computed on positional parameters and isotropic temperature factors. The R value dropped to 0·38 but, more significantly, the temperature factor of one of the chlorine atoms became negative, indicating that more electron-density than that represented by $\frac{1}{2}$ a chlorine atom was needed at that site. The temperature factor for the atom at the other site was not unreasonable, however, and it was clear that this site was occupied, presumably by an oxygen atom of a water molecule.

A second difference map indicated possible site occupancy at several other positions. Once the chloride ions were correctly placed and the oxygen atoms at five sites included in the model, isotropic least-squares refinement reduced the R to 0·14.

Since one of the more interesting aspects of this structure, from a crystallographic standpoint, was the hydrogen-bonding network, a considerable effort was made to locate the hydrogen atoms on the water mole-
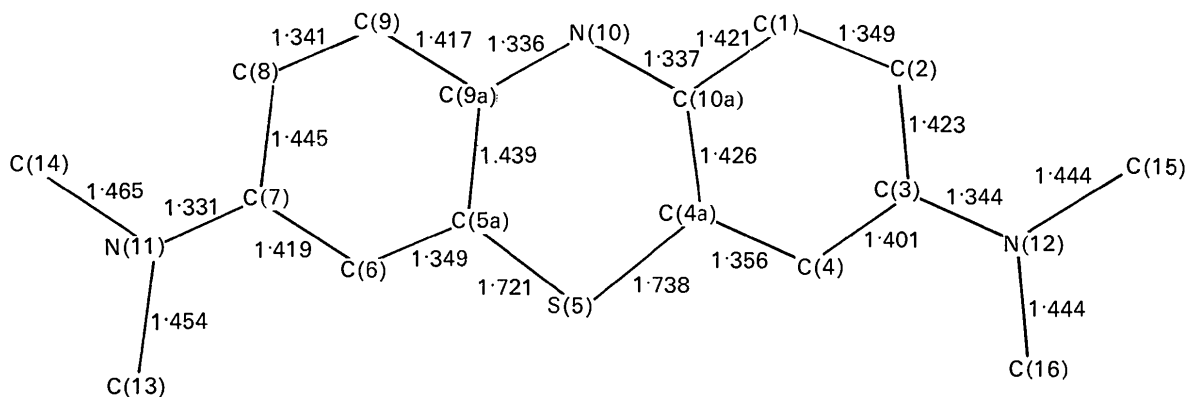

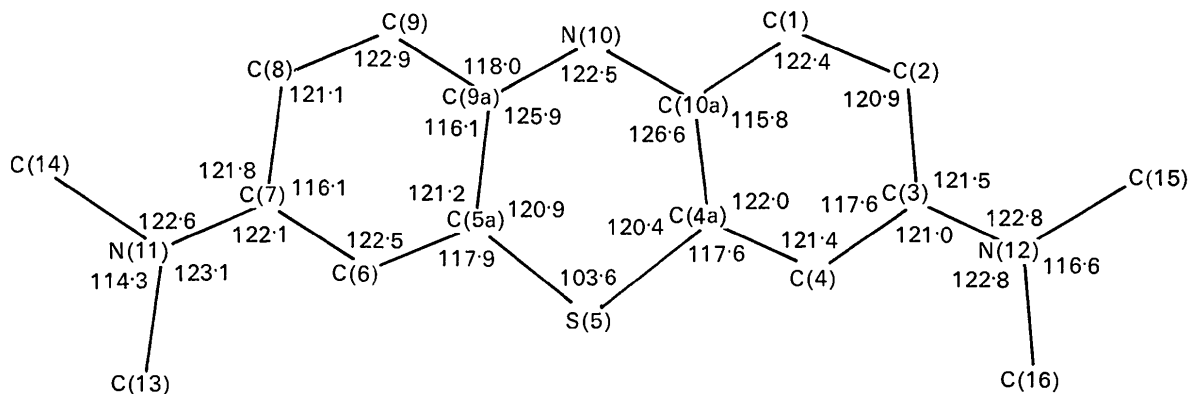Fig. 1. Bond lengths for methylene blue. E.s.d.'s are 0·007 Å.

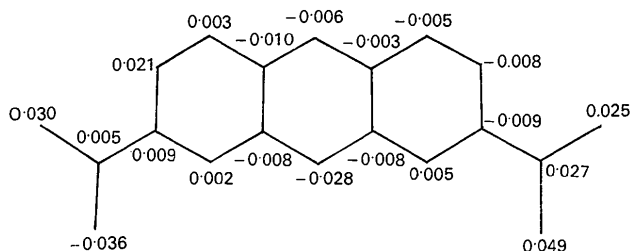Fig. 2. Bond angles for methylene blue. E.s.d.'s are 0·5°.
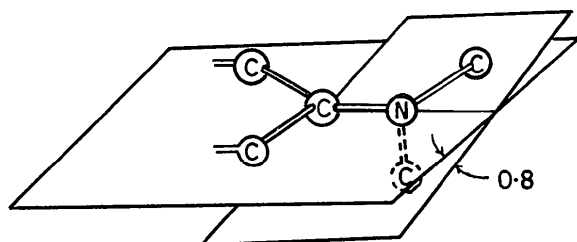
Fig. 3. Distances (Å) from least squares plane.

Fig. 4. Intersection of planes showing rotation of dimethyl-amine group around C–N bond.

cules. A tetrahedrally linked framework of hydrogen bonds was expected and a possible model was calculated which yielded hydrogen–oxygen bond distances of 0·96 Å. The proton positions were initially placed on the oxygen–oxygen center lines with the angles determined by the tetrahedral packing of the oxygen, nitrogen, and chlorine atoms. Then the hydrogen coordinates were subjected to three cycles of full matrix least-squares refinement. The final R value calculated for the structure was 0·057.

Isotropic temperature factors for the hydrogen atoms were assigned from the final isotropic temperature factor of the atom which each hydrogen was bonded.

The anisotropic temperature factors were defined by the following equation:

$$T = \exp\left[-(U_{11}h^2a^{*2} + U_{22}k^2b^{*2} + U_{33}l^2c^{*2} \right.$$
$$\left. + U_{12}hka^*b^* + U_{13}hla^*c^* + U_{23}klb^*c^*)2\pi^2 \right].$$

The final values for the atomic positional parameters and thermal parameters are shown in Table 2.

A simple Hückel MO π-electron calculation was performed to obtain eigenvalues, eigenvectors and π-bond orders for this molecule. The Hückel h_X and k_{XY} parameters for sulfur ($h_S = 1·25$, $k_{CS} = 0·57$) and nitrogen ($h_N = 0·50$, $h_{CN} = 0·80$, $h_N = 1·50$, $h_{C-N} = 0·70$) were obtained from Lamotte & Berthier (1966) and Streitwieser (1961, p. 135) respectively. The methyl groups were described by the 'conjugation model' employing the parameters of Lazdins & Karplus (1965) (N–X–Y, $h_X = -0·10$, $k_{NX} = 0·70$ $h_Y = 0·50$, $k_{XY} = 2·50$). For the purposes of this calculation the molecule was forced to have $2/m$ ($C2_v$) symmetry. LCAO MO calculated bond lengths were obtained from the Hückel bond orders using Coulson's (1939) formula with Streitwieser's parameters (1961, p. 167).

Discussion

The bond lengths and angles given by the X-ray data are shown in Figs. 1 and 2, and Table 3 gives the C–H bond lengths. Fig. 6 shows the location of the chloride ions relative to the dye and water molecules. It should be noted that the shortest Cl–N distance in each case is to the methyl substituted nitrogen and not to the intratracyclic N or S atoms as has been reported.

Table 3. *Carbon–hydrogen bond lengths*

C(1)—H(1)	0·96 (4) Å	C(9)—H(6)	0·92 (4) Å
C(2)—H(2)	1·00 (4)	C(8)—H(5)	0·98 (4)
C(4)—H(3)	0·92 (5)	C(6)—H(4)	0·93 (4)
C(13)–H(7)	0·90 (5)	C(15)–H(13)	0·87 (5)
C(13)–H(8)	1·00 (5)	C(15)–H(14)	0·90 (5)
C(13)–H(9)	0·91 (5)	C(15)–H(15)	1·16 (5)
C(14)–H(10)	1·06 (5)	C(16)–H(16)	0·88 (5)
C(14)–H(11)	1·12 (5)	C(16)–H(17)	1·07 (5)
C(14)–H(12)	0·97 (4)	C(16)–H(18)	0·77 (5)
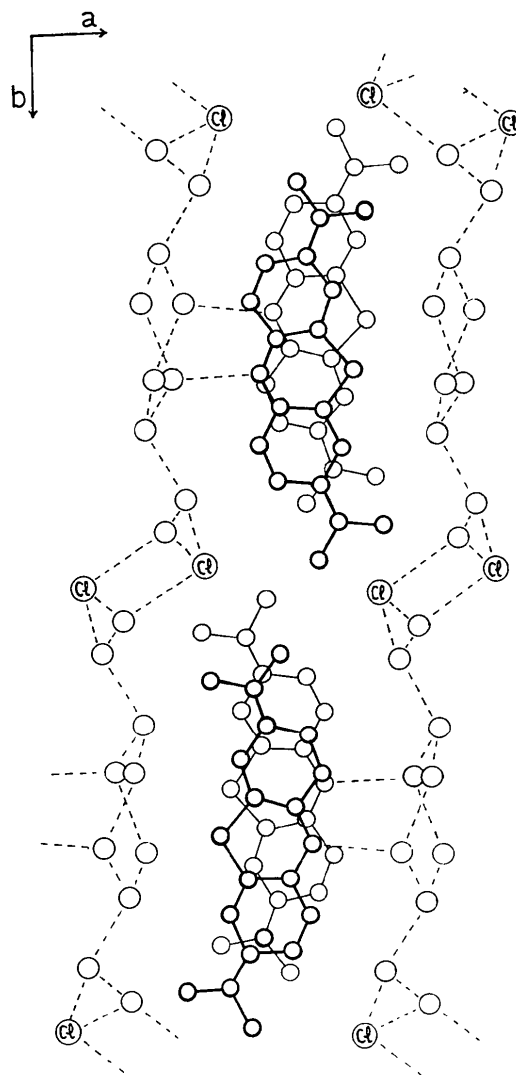
Fig. 5. Methylene blue viewed down the c^* axis of the unit cell.

The equation which describes the plane of the molecule was calculated to be: $-1.721x - 0.150y + 6.978z = 4.133$. Fig. 3 shows the molecule, and the figure in parentheses beside each atom is the distance in Å to the plane. The methyl groups were not included in the least-squares determination of the plane, but the distances from the plane were calculated. The average estimated error in each position parameter for the heavy atoms is approximately 0.005 Å, the accumulated error for three dimensions being about 0.009 Å. If the molecule were truly planar, the standard deviation of the distances of the atoms from the planes would be expected to be of this magnitude. In fact, the standard deviation is 0.013 Å.

Therefore, by a test of mathematical statistical significance, the molecule would be considered nonplanar. However, for most chemical purposes and for crystal packing considerations, the structure is essentially planar. The lack of planarity is probably due to a slight puckering of the molecule at the sulfur and nitrogen atoms which bridge the two benzene rings.

The methyl groups were not included in the fitting of the planes and an examination of the carbon atom positions yields some information about the contribution of the amine nitrogens to the π systems. The distance from the phenothiazine plane to C(15) is 0.049 Å and to C(16) is 0.025 Å, both having a positive sense relative to the origin, indicating a rotation and a bend. Atoms C(13) and C(14) are -0.036 and 0.030 Å from the plane, indicating a rotation around the bond between the nitrogen and the phenothiazine nucleus. In order to calculate the rotation around these bonds, the planes defined by the nitrogen atoms and three carbon atoms were determined. The rotations were calculated to be 0.8 and 1.1° for N(12) and N(11) respectively (Fig. 4). The fact that the methyl carbons were very close to the plane of the molecule indicated that there was a high degree of π bonding involving the amine nitrogen atoms. The contribution of structure (II) as the appropriate representation of methylene blue, with the formal charge placed on the nitrogen of the amine group, is supported by the concept of π bonding involving the amine group.

The pattern of hydrogen bonding involving the water molecules in crystalline methylene blue is shown in Figs. 5 and 6. From the tetrahedral model of the hydrogen atoms, which was constructed from peaks on an electron-density difference map, the hydrogen atomic coordinates were refined by three cycles of least-squares refinement. This type of refinement was near the limit of sensitivity of the X-ray data, but the reliability of the data was strengthened by the observation that the bond lengths and angles involving hydrogen atoms remained reasonable after three cycles of refinement. Each water molecule formed two hydrogen bonds which ranged between 1.69 and 2.33 Å. Although the possibility existed that oxygen–oxygen distances of 2.77 Å were not hydrogen bonds but simple van der Waals contacts with random packing, the general ordering of the hydrogen

atoms along the oxygen–oxygen centerlines seemed to preclude this possibility. The distances and angles which describe the water molecules and contact distances in the hydrogen bonding network are shown in Table 4.

The methylene blue cations are stacked in layers perpendicular to the c^* axis. The unit cell as viewed down this axis is represented in Fig. 5. A hydrogen-bonding network is formed by the water molecules and chloride ions. This network exists as a narrow layer which is roughly perpendicular to the planes formed by the cations, occupying a region midway between units in adjacent cells. A view of the hydrogen-bonding network down the a^* axis is shown in Fig. 6. In order to show the methylene blue structure, the cell has been rotated 20° about the b^* axis.

The bond lengths and angles calculated for methylene blue are comparable with values observed in sim-
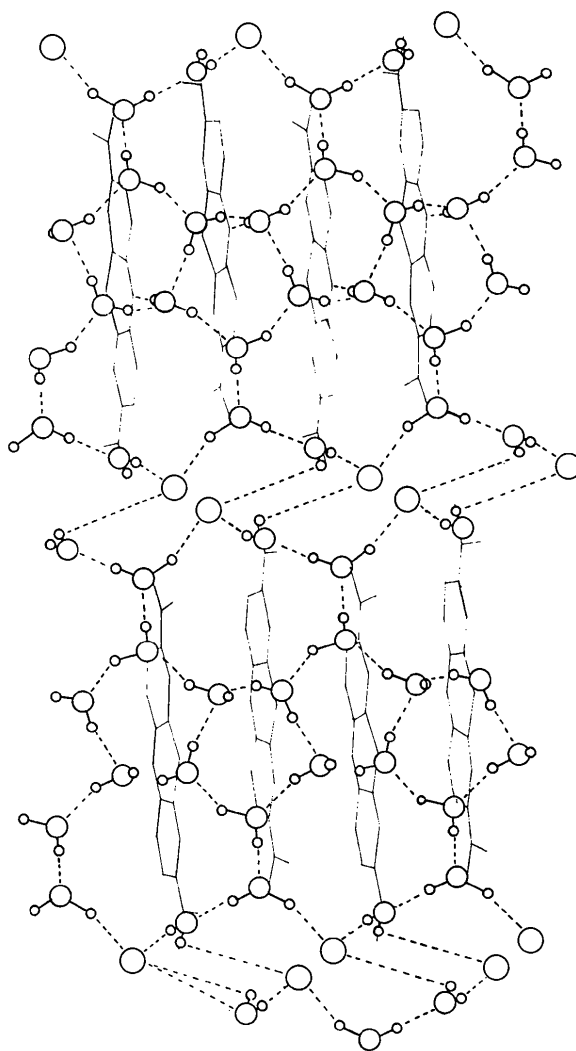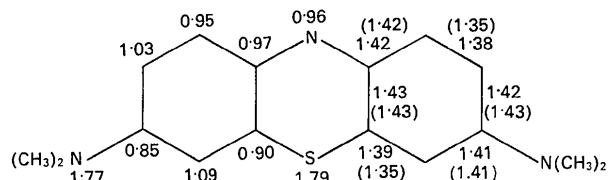

Fig. 6. Hydrogen bonding. Two unit cells of methylene blue viewed approximately down the a^* axis (rotated 20° about b^*).

Table 4. *Bond lengths and bond angles for water molecules after refinement*

O(1)–H(19)	1·025 (5) Å	O(1)–H(20)	0·90 (5) Å
O(2)–H(21)	1·01 (5)	O(2)–H(22)	0·93 (5)
O(3)–H(23)	1·24 (5)	O(3)–H(24)	1·00 (5)
O(4)–H(25)	0·96 (5)	O(4)–H(26)	0·97 (5)
O(5)–H(27)	0·89 (5)	O(5)–H(28)	1·20 (5)

H–O(1)–H	113 (5)°
H–O(2)–H	113 (5)
H–O(3)–H	121 (5)
H–O(4)–H	115 (5)
H–O(5)–H	95 (5)

Hydrogen bonds

O(1)···H	1·76 (5) Å
O(2)···H	1·69 (5)
O(3)···H	1·86 (5)
O(4)···H	1·84 (5)
O(5)···H	1·87 (5)

Oxygen–oxygen contacts

O(1)–O(3)	2·76 (1) Å
O(2)–O(4)	2·78 (1)
O(2)–O(5)	2·77 (1)
O(3)–O(5)	2·75 (1)
O(4)–O(5)	2·77 (1)

Chlorine–oxygen contacts

Cl(1)–O(1)	3·22 (1) Å
Cl(1)–O(3)	3·18 (1)
Cl(1')–O(1)	3·15 (1)

Nitrogen–oxygen contact

N(10)–O(4)	2·92 (1) Å

ilar structures. The calculated bond lengths and bond angles of the dye molecule are represented in Figs. 1 and 2 with estimated standard deviations in parentheses. Of the two valence bond representations of the charge distribution that have been considered, the bond lengths for methylene blue determined by the present study indicate that structure (II) is the more appropriate representation, the most prominent indication being the pronounced shortening of bonds C(1)–C(2) and C(4)–C(4a) compared with the other carbon–carbon bonds. If structure (I) were significant, bond C(3)–C(4)

would tend to be shorter than the normal benzene C–C bond of 1·397 Å. Bonds C(3)–C(4) and C(6)–C(7) are slightly longer than 1·397 Å, indicating a little less double-bond character than would be expected if (I) were a contributing structure. The two structures are meant to identify the two types of structures with different placements of the formal charges. There are several equivalent forms for each representation, resulting in C_{2v} symmetry of the resonance hybrid.

The conclusions drawn from the molecular-orbital description is different from that implied by the isolated valence bond structures (I) and (II). The averaged diffraction-derived C–C bond lengths are compared with those obtained from the HMO calculations in Fig. 7. As the values of the heteroatom parameters are typical of those used in a variety of other applications, our results suggest that the charge distribution around the dye molecule in the crystal is not distortingly anisotropic. The similarity of calculated π-electron charges on the centers of interest ($S, P^\pi = 1·79$: N [exocyclic] $P^\pi = 1·77$) though only a guide, suggest that the positive charge of the molecule is fairly evenly distributed over all three atoms. The diffraction evidence indicates a preponderance of positive attraction on the exocyclic nitrogen in agreement with but not strongly predicted by the HMO calculation. The π-electron charges derived from this calculation are shown in italics in Fig 7.

Fig. 7. Bond lengths and π-electron charges from molecular orbital calculations.

References

COULSON, C. A., (1939). *Proc. Roy. Soc.* A169, 413–428.
International Tables for X-ray Crystallography (1962). Vol. III. Birmingham: Kynoch Press.
LAMOTTE, B. & BERTHIER, G., (1966). *J. Chim. Phys.* 63, 369–378.
LAZDINS, D. & KARPLUS, M., (1965). *J. Amer. Chem. Soc.* 87, 920–921.
PAULING, L. (1961). *Science*, 134, 15–21.
STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* 42, 3175–3187.
STREITWIESER, A. (1961). *Molecular Orbital Theory for Organic Chemists.* New York: John Wiley.
TAKAHASHI, Y., YABE, K. & SATO, T. (1969). *Bull. Chem. Soc. Japan*, 42. 2707–2708.
TAYLOR, W. H. (1935). *Z. Kristallogr.* 91, 450–465.
WARWICKER, J. O. (1955). *J. Chem. Soc.* p. 2531.
X-RAY 67 (1967). *Program System for X-ray Crystallography.* Computer Science Center, Univ. of Maryland Technical Report 67–58, 181 pages.
ZHDANOV, G. S., ZVONKOVA, Z. V. & VORONTSOVA, L. G. (1956). *Sov. Phys. Crystallogr.* 1, 44–48.