is 2·93 Å. Within each sub-layer molecules related by the c-glide planes are held together by much weaker hydrogen bonds, denoted by dotted lines in the figure, and of average length 3·30 Å. The layers themselves are held together by van der Waals forces and this presumably accounts for the pronounced (010) cleavage plane in the crystal.

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The Crystal and Molecular Structure of Guanosine 3′, 5′-Cyclic Monophosphate (Cyclic GMP) Sodium Tetrahydrate

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(*Received* 29 *November* 1973; *accepted* 24 *January* 1974)

The crystal structure and conformation of cyclic GMP (as sodium guanosine 3′,5′-cyclic monophosphate tetrahydrate) has been determined by the single-crystal X-ray diffraction technique. The crystals are orthorhombic, space group $P2_12_12_1$ with unit-cell constants $a=18{\cdot}664$ (3), $b=7{\cdot}384$ (2) and $c=12{\cdot}706$ (3) Å; $Z=4$, $D_o=1{\cdot}66$, $D_c=1{\cdot}665$ g cm^{-3} assuming one sodium ion and four molecules of water per nucleotide. The structure was solved by direct methods using the program *MULTAN* and refined by least-squares methods to a final R value of 0·034 based on 1637 diffractometer intensities. The base displays the *syn* conformation with a glycosyl torsion angle χ[C(8)–N(9)–C(1′)–O(1′)] of 258°. The cyclization of the phosphate group forces the ribose to the $_4T^3$ [C(4′)*exo*, C(3′)*endo*] conformation which is characteristic of the cyclic nucleotides. The bond distances and angles in the ribose ring show significant differences from those of the common nucleotides. The phosphate ring is locked into a chair conformation, being puckered most about the C(3′)–C(4′) bond and flattened at the phosphate end. The sodium ion is not directly attached to the phosphate oxygen atoms but is coordinated to six water molecules at distances ranging from 2·32 to 2·68 Å. Adjacent sodium octahedra share edges to form an infinite column parallel to **b**. The crystal packing consists of alternating layers of stacked nucleotides with the interstitial holes filled by the sodium-water octahedra.

Introduction

Cyclic AMP has been known for some time to mediate a large number of hormonal and regulatory mechanisms (Sutherland & Rall, 1960), but only recently has it come to light that cyclic GMP is also involved in metabolic control and regulatory functions (Hardman, 1971). In continuation of the studies on the structure of cyclic nucleotides in this laboratory (Sundaralingam & Abola, 1972*a,b*), we have now carried out the structure determination of guanosine 3′,5′-cyclic monophosphate (cyclic GMP). Cyclic GMP has been found in a number of mammalian tissues and body fluids (Hardman, 1971). A number of studies have suggested separate roles for cyclic GMP and cyclic AMP in hormonal or metabolic control and regulatory functions (Hardman, 1971; Kuo, Lee, Reyes, Walton, Donnelly & Greengard, 1972). The recognition of the biological importance of cyclic GMP made it highly desirable that a detailed crystal-structural study of its molecular conformation be undertaken. In addition to the present work on cyclic GMP (see also preliminary communication; Chwang & Sundaralingam, 1973), the crystal structures of cyclic *C*-AMP (5′-methylene adenosine 3′,5′-cyclic monophosphate) (Sundaralingam & Abola 1972*a,b*), cyclic UMP (Coulter, 1969) and cyclic AMP (Watenpaugh, Dow, Jensen & Furberg, 1968) have been reported.

Experimental

Single crystals of cyclic GMP suitable for the structure determination were found in a sample of 'salt-free' cyclic GMP purchased from Nutritional Biochemicals, Cleveland, Ohio. (Note: on completing the X-ray structure analysis we found that the sample also contains a sodium ion and four molecules of water of crystallization.) The crystals were elongated along the *b* axis. Preliminary photographic investigations revealed that the crystals belonged to the orthorhombic system. The systematic absences $h00$, $h=2n+1$; $0k0$, $k=2n+1$; $00l$, $l=2n+1$ indicated that the space group is $P2_12_12_1$. A crystal measuring 0·15 × 0·15 × 0·2 mm was mounted on a Picker FACS-1 X-ray diffractometer with the *b* axis coincident with the φ axis of the goniostat. The unit-cell dimensions were determined by a least-squares fit of the 2θ values of 12 accurately centered high-angle reflections. They are $a=18·664\pm0·003$, $b=7·384\pm0·001$ and $c=12·706\pm0·003$ Å. The observed crystal density of 1·66 g cm^{-3}, measured by the flotation technique in a mixture of bromoform and cyclohexane, is in agreement with the calculated density of 1·650 g cm^{-3} assuming four formula units of cyclic GMP pentahydrate, $C_{10}H_{12}N_5O_7P.5H_2O$, (formula weight 435·3) in the unit cell. However, it became clear from the structure analysis that the correct composition included one sodium ion and four water molecules per nucleotide $C_{10}H_{11}N_5O_7PNa.4H_2O$ yielding a calculated density of 1·665 g cm^{-3}.

The intensity data were measured on a Picker FACS-1 diffractometer by use of nickel-filtered Cu radiation ($\lambda=1·5418$ Å) and a θ–2θ scan technique with a scan range of 1·5°, a scan rate of 2° min^{-1} and background counts of 10 s at each scan limit. Intensities of all nonequivalent reflections below 127° in 2θ were recorded. Of the 1693 recorded reflections, 1637 had intensities greater than 1·5 times their standard deviations and were used in the structure analysis after correcting for the usual Lorentz and polarization effects.

Table 1. *Starting phase set*

Other phase angles used for the reflection 11,1,7 in the multisolution are 45, 135 and 315° while for 141, 135°.

H	*K*	*L*	$\|E\|$	Phase angle	
15	5	0	3·54	90°	Origin fixing reflections
0	6	1	3·19	0	
0	3	11	3·00	90	
11	1	7	2·66	225	Other reflections in starting set
1	4	1	2·44	45	Enantiomorph fixing reflection

Structure determination and refinement

The structure was solved by direct methods (Main, Germain & Woolfson, 1970) which combines the application of the tangent formula (Karle & Hauptman, 1956) with multisolution techniques (Germain & Woolfson, 1968). The computer program *MULTAN* was used for this purpose (Main, Germain & Woolfson, 1970). The starting phase set shown in Table 1 was chosen automatically by the program. This set is one of the 8 phase sets resulting from different combinations of the starting phases and showed a figure of merit of 1·24, and an *R* index of 36·3. Next, the phases of 336 reflections with *E*'s greater than 1·3 were generated from the starting set by the application of the tangent formula (Karle & Hauptman, 1956). The *E* map revealed the positions of the atoms of the pyrimidine ring, the phosphorus atom and an attached oxygen atom. The phases of 202 reflections with $|E|>1·5$ from the structure-factor calculation on these atoms were then refined by the tangent formula. The refinement converged after 5 cycles and the *R* value, where $R=\sum||E_o|-|E_c||/\sum|E_o|$, for the 202 reflections was 0·22. The *E* map generated from these reflections and the refined phases revealed the remaining atoms of the cyclic nucleotide molecule and five other peaks which were attributed to water molecules. A structure-factor calculation based on 28 atoms gave an *R* value, where $R=\sum||F_o|-|F_c||/\sum|F_o|$, of 0·29. Two cycles of full-matrix least-squares refinement of all 28 atoms using isotropic temperature factors first and then one cycle of anisotropic refinement lowered the *R* value to 0·11 for the 1637 reflections. A difference electron-density map was computed at this stage and ten hydrogen atoms were located. Further cycles of refinement did not improve the *R* value, and it was found that the temperature factor of one of the water oxygen atoms turned to a negative value. This suggested to us that the oxygen atom should perhaps be substituted by a heavier element. We also noticed that the O···O distances between this oxygen atom and the neighboring water oxygen atoms were shorter than the usual O···O hydrogen-bond distances. We immediately suspected the presence of a Na$^+$ ion. This was also consistent with the observation that the two P–O bond distances involving the non-ester oxygens had nearly

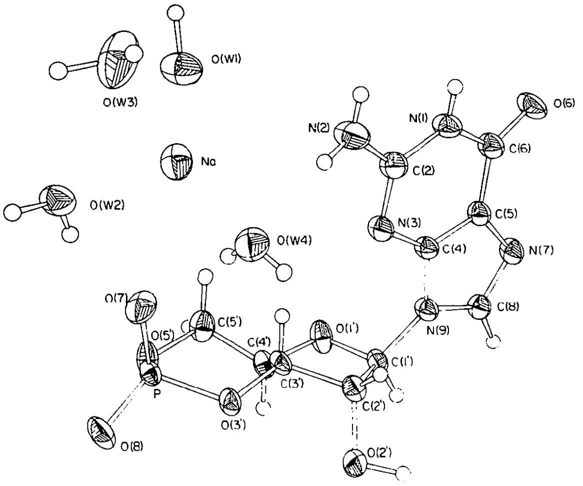

Fig. 1. The molecular conformation and atom numbering system in cyclic GMP. The sodium and the four independent water molecules in the structure are also shown. The thermal ellipsoids are drawn at 50% probability level (Johnson, 1965).

equal values suggesting that the phosphate is anionic (Sundaralingam & Jensen, 1965; Sundaralingam & Putkey, 1970). We continued the refinement using a Na^+ ion instead of the water oxygen atom. There was a large drop in the R (0·054) value. A difference electron-density map computed at this stage clearly revealed all the remaining hydrogen atoms. Two cycles of isotropic refinement of the hydrogen atoms followed by two additional cycles of refinement of the nonhydrogen atoms with anisotropic temperature factors reduced R to the final value of 0·034. The average ratios of the shifts to the estimated standard deviations were 0·067 for nonhydrogen parameters and 0·49 for hydrogen parameters.

The weighting scheme used in the refinement was $1/\sqrt{w}=1\cdot05$ for $|F_o|\le 14\cdot68$ and $1/\sqrt{w}=0\cdot54+0\cdot035|F_o|$ for $|F_o|>14\cdot68$. The reflections 002, 020, 122, 121, 120, 211, 400, 420, 504 and 600 were given zero weight because they were suspected to be suffering from secondary extinction. The scattering factors for Na

Table 2. *The observed and calculated structure amplitudes* (× 10) *for cyclic* GMP

Reflections marked with an E appeared to be suffering from secondary extinction, and were given zero weight during the refinement. Reflections marked with asterisks were less than $1\cdot5\sigma(I)$ (see text).

H, 0, 0		
2	565	625
4	1474E	1987
6	1587E	1996
8	362	324
10	667	669
12	416	401
14	215	211
16	275	267
18	167	171
20	101	106
H, 0, 1		
1	410	474
2	150	161
3	335	322
4	36	45
5	547	558
6	210	211
7	458	469
8	258	252
9	62	68
10	232	235
11	574	538
12	149	151
13	100	99
14	28	17
15	29	22
16	221	229
17	296	246
18	29	39
19	108	113
20	58	56
21	63	59
H, 0, 2		
0	691E	769
1	429	433
2	609	638
3	177	184
4	181	199
5	559	563
6	659	647
7	133	99
8	468	451
9	500	496
10	529	536
11	152	145
12	372	352
13	417	420
14	456	473
15	332	336
16	42	36
17	222	218
18	285	285
19	298	259
20	109	107
21	77	76
H, 0, 3		
1	318	318
2	209	205
3	378	378
4	165	186
5	271	289
6	253	260
7	562	558
8	22	9
9	291	282
10	26	18
11	66	66
12	0*	11
13	35	38
14	88	90
15	185	181
16	366	375
17	283	276
18	80	72
19	118	129
20	0*	8
21	69	69
H, 0, 4		
0	595	607
1	515	547
2	139	152
3	238	247
4	239	221
5	1219E	1324
6	46	37
7	36	41
8	127	118
9	381	382
10	428	423
11	434	439
12	16*	1
13	296	296
14	504	516
15	189	187
16	89	87
17	35	35
18	156	155
19	84	93
20	169	163
H, 0, 5		
1	482	474
2	669	686
3	679	705
4	38	40
5	404	398
6	275	286
7	949	964
8	406	389
9	125	127
10	112	105
11	117	126
12	24	10
13	326	321
14	269	267
15	72	76
16	320	316
17	87	93
18	159	161
19	51	59
20	96	93
H, 0, 6		
0	27	32
1	130	133
2	210	202
3	258	239
4	488	511
5	135	118
6	228	220
7	148	122
8	317	371
9	18*	4
10	240	246
11	13*	7
12	29	22
13	217	238
14	163	163
15	119	128
16	27	6
17	32	9
18	37	35
19	39	39
H, 0, 7		
1	236	233
2	57	69
3	115	105
4	145	152
5	80	90
6	181	180
7	280	271
8	309	309
9	84	89
10	206	199
11	267	261
12	364	355
13	248	250
14	78	79
15	117	117
16	57	53
17	19*	2
18	36	26
19	98	105
H, 0, 8		
0	230	233
1	125	115
2	98	104
3	78	95
4	327	336
5	430	431
6	71	67
7	214	207
8	278	290
9	134	136
10	130	134
11	315	322
12	116	112
13	0*	8
14	395	405
15	263	254
16	48	52
17	53	62
18	13*	10
H, 0, 9		
1	161	159
2	134	121
3	44	35
4	223	239
5	49	49
6	24	9
7	219	212
8	22*	18
9	61	63
10	12*	5
11	152	150
12	328	317
13	63	58
14	111	105
15	46	43
16	25	33
17	18*	3
H, 0,10		
0	74	76
1	185	179
2	85	50
3	183	180
4	401	394
5	117	119
6	320	315
7	264	280
8	96	102
9	369	358
10	279	281
11	60	59
12	107	100
13	67	63
14	154	155
15	197	184
16	159	159
H, 0,11		
1	161	174
2	157	166
3	268	264
4	80	86
5	57	68
6	30	11
7	134	150
8	54	58
9	105	106
10	172	174
11	21*	19
12	68	71
13	50	80
14	50	56
H, 0,12		
0	296	311
1	291	293
2	282	287
3	172	170
4	156	162
5	527	536
6	68	66
7	227	226
8	96	97
9	287	297
10	62	60
11	197	203
12	33	26
H, 0,13		
1	43	39
2	105	106
3	70	72
4	0*	3
5	159	169
6	61	70
7	12*	28
8	200	201
9	32	29
10	17*	20
H, 0,14		
0	135	135
1	198	208
2	119	124
3	45	52
4	188	187
5	201	206
6	34	38
7	147	154
H, 1, 0		
1	26	43
2	510	535
3	488	510
4	706	764
5	67	45
6	125	121
7	282	286
8	263	276
9	394	390
10	165	172
11	111	121
12	744	736
13	546	549
14	22*	2
15	117	107
16	34	34
17	114	112
18	0*	15
19	0*	2
20	29	38
21	19*	27
H, 1, 1		
0	476	503
1	99	109
2	1009E	1156
3	261	270
4	1150E	1345
5	250	274
6	261	259
7	320	333
8	379	367
9	189	188
10	364	371
11	303	318
12	302	294
13	251	242
14	397	387
15	437	436
16	389	394
17	130	136
18	17*	27
19	121	123
20	172	182
21	39	40
H, 1, 2		
0	304	306
1	440	467
2	333	346
3	544	569
4	152	152
5	258	253
6	120	107
7	290	267
8	425	415
9	438	427
10	222	224
11	26	26
12	270	259
13	237	247
14	41	33
15	81	88
16	139	134
17	175	171
18	196	199
19	163	167
20	88	83
21	95	85
H, 1, 3		
0	390	387
1	619	680
2	182	183
3	470	485
4	499	525
5	761	804
6	427	446
7	276	289
8	318	304
9	285	303
10	251	236
11	228	236
12	209	210
13	389	390
14	27	30
15	145	155
16	193	201
17	119	118
18	113	116
19	122	123
20	69	62
21	68	66
H, 1, 4		
0	329	339
1	409	408
2	190	187
3	142	160
4	159	151
5	301	314
6	145	148
7	451	456
8	467	471
9	69	66
10	48	49
11	266	251
12	140	140
13	256	250
14	105	99
15	283	281
16	35	32
17	92	84
18	116	134
19	185	194
20	70	73
H, 1, 5		
0	395	411
1	109	98
2	446	470
3	518	524
4	260	271
5	327	314
6	642	648
7	524	528
8	220	216
9	132	120
10	376	383
11	336	324
12	311	305
13	22*	32
14	25	37
15	188	183
16	259	265
17	62	59
18	92	94
19	151	153
20	62	73
H, 1, 6		
0	354	350
1	515	504
2	293	276
3	472	464
4	554	527
5	550	526
6	85	76
7	170	157
8	243	253
9	285	285
10	264	256
11	220	217
12	186	178
13	205	208
14	85	76
15	151	143
16	94	86
17	131	139
18	65	62
19	29	40
H, 1, 7		
0	65	72
1	433	456
2	388	371
3	389	358
4	345	347
5	152	152
6	202	191
7	226	225
8	212	206
9	321	313
10	228	232
11	552	555
12	250	250
13	23	27
14	148	155
15	317	308
16	90	95
17	85	92
18	74	86
19	164	162
H, 1, 8		
0	462	472
1	219	208
2	172	168
3	196	186
4	362	360
5	101	98
6	58	52
7	116	117
8	166	168
9	202	191
10	185	174
11	155	154
12	296	292
13	140	142
14	241	232
15	115	111
16	68	75
17	86	85
18	156	155
H, 1, 9		
0	324	315
1	252	251
2	302	288
3	60	61
4	119	119
5	357	345
6	249	231
7	327	328
8	559	574
9	149	134
10	238	239
11	70	68
12	359	358
13	212	216
14	77	66
15	27	39
16	63	63
17	184	184
H, 1,10		
0	209	207
1	451	451
2	220	223
3	271	270
4	445	450
5	360	348
6	163	162
7	216	217
8	211	207
9	19*	29
10	209	207
11	65	54
12	103	109
13	74	74
14	67	69
16	29	32
H, 1,11		
0	439	451
1	131	136
2	111	113
3	323	329
4	299	296
5	137	136
6	351	357
7	259	267
8	14*	34
9	340	323
10	208	203
11	32	37
12	91	90
13	27	24
14	100	101
H, 1,12		
0	239	244
1	352	355
2	192	192
3	131	125
4	324	323
5	164	160
6	26	38
7	51	57
8	177	181
9	52	51
10	124	120
11	30	20
12	102	107
H, 1,13		
0	158	149
1	220	217
2	103	90
3	257	261
4	114	121
5	256	259
6	32	31
7	223	216
8	62	58
9	227	236
10	12*	15
H, 1,14		
0	24	21
1	46	42
2	86	85
3	109	97
4	129	132
5	68	68
6	69	77
H, 2, 0		
0	1798E	2337
1	1026E	1123
2	701	729
3	219	209
5	357	366
6	251	221
7	95	114
8	311	318
9	357	360
10	332	314
11	269	258
12	251	254
14	253	232
15	65	65
16	193	194
17	113	117
18	317	322
19	103	115
20	168	169
21	17*	23
H, 2, 1		
0	502	527
1	999E	1163
2	142	128
3	383	368
4	426	412
5	339	320
6	249	257
7	516	497
8	647	660
9	355	340
10	409	419
11	248	237
12	23	35
13	190	184
14	154	156
15	204	202
16	161	158
17	137	130
18	64	64
19	147	147
20	40	35
21	54	54
H, 2, 2		
0	410	401
1	881E	985
2	689	716
3	616	630
4	877	924
5	302	290
6	166	154
7	454	461
8	192	178
9	405	393
10	219	208
11	169	178
12	247	235
13	265	253
14	130	113
15	149	143
16	179	185
17	213	217
18	193	192
19	160	163
20	24	18
H, 2, 3		
0	528	564
1	484	481
2	325	329
3	975E	1038
4	696	687
5	238	226
6	344	351
7	191	191
8	465	462
9	593	587
10	130	136
11	16*	13
12	123	123
13	365	366
14	136	110
15	79	84
16	208	198
17	231	235
18	67	70
19	118	121
20	15*	34
H, 2, 4		
0	397	413
1	494	520
2	399	400
3	293	282
4	343	348
5	355	339
6	310	303
7	162	162
8	361	348
9	565	553
10	251	247
11	485	481
12	31	46
13	194	193
14	445	438
15	435	432
16	64	76
17	142	139
18	142	149
19	169	168
20	110	116
H, 2, 5		
0	348	360
1	243	237
2	409	402
3	233	217
4	321	317
5	448	451
6	250	237
7	326	311
8	239	231
9	303	285
10	107	112
11	429	428
12	175	173
13	198	190
14	195	186
15	404	401
16	214	216
17	99	104
18	71	65
19	192	200
H, 2, 6		
0	330	338
1	362	368
2	292	293
3	369	348
4	427	434
5	199	210
6	416	426
7	58	62
8	253	249
9	314	302
10	172	174
11	225	220
12	196	214
13	143	150
14	46	52
15	251	251
16	117	122
17	47	58
18	28	34
19	31	27
H, 2, 7		
0	420	409
1	177	180
2	355	360
3	141	126
4	76	74
5	199	194
6	96	93
7	219	205
8	183	182
9	166	162
10	126	121
11	294	291
12	68	48
13	173	174
14	330	327
15	183	189
16	60	60
17	88	97
18	61	60
H, 2, 8		
0	129	125
1	42	40
2	310	301
3	428	438
4	388	383
5	339	347
6	179	167
7	318	316
8	126	119
9	357	351
10	166	173
11	238	245
12	91	77
13	236	229
14	209	204
15	155	151
16	95	101
17	57	58
H, 2, 9		
0	374	378
1	180	178
2	159	163
3	112	113
4	336	325
5	300	332
6	225	222
7	90	85
8	346	344
9	95	93
10	79	80
11	101	99
12	126	116
13	69	67
14	99	96
15	10*	17
16	50	54
H, 2,10		
0	285	284
1	275	275
2	164	167
3	229	236
4	478	476
5	139	133
6	335	339
7	187	190
8	399	402
9	253	245
10	248	252
11	44	40
12	115	119
13	30	44
14	107	107
15	54	54
H, 2,11		
0	149	154
1	215	225
2	173	172
3	184	176
4	146	154
5	156	162
6	181	182
7	79	74
8	94	98
9	67	67
10	80	70
11	65	56
12	40	35
13	92	96
H, 2,12		
0	62	64
1	154	146
2	214	223
3	65	71
4	141	149
5	265	270
6	41	41
7	120	111
8	196	206
9	76	69
10	76	75
11	71	75
H, 2,13		
0	138	141
1	34	41
2	47	43
3	39	44
4	138	132
5	126	134
6	111	118
7	109	107
8	64	80
9	17*	5
H, 2,14		
0	44	39
1	165	167
2	55	56
3	38	42
4	96	98
5	164	164
H, 3, 0		
1	49	42
2	128	145
3	78	70
4	33	8
5	240	253
6	353	354
7	84	81
8	195	195
9	100	107
10	68	56
11	176	169
12	0*	18
14	145	145
15	192	191
17	91	87
18	123	124
19	93	98
20	22	11
H, 3, 1		
0	308	320
1	438	424
2	855	906
3	370	362
4	188	184
5	348	338
6	350	348
7	178	163
8	211	219
9	107	107
10	51	47
11	68	68
12	46	42
13	228	224
14	232	235
15	86	95
16	187	174
17	141	143
18	64	68
19	82	83
20	91	91
H, 3, 2		
0	126	120
1	668	689
2	93	88
3	304	294
4	457	465
5	458	435
6	218	224
7	161	150
8	266	270
9	240	234
10	158	160
11	85	70
12	231	235
13	135	124
14	372	361
15	261	261
16	161	168
17	174	174
18	32	34
19	156	151
20	86	87
H, 3, 3		
0	341	329
1	107	101
2	449	455
3	371	372
4	421	410
5	80	76
6	110	96
7	362	357
8	242	251
9	74	72
10	150	153
11	230	215
12	257	243
13	290	289
14	136	137
15	207	205
16	153	153
17	98	90
18	70	67
19	240	254
H, 3, 4		
0	585	593
1	606	630
2	329	320
3	388	382
4	368	377
5	320	309
6	284	286
7	453	456
8	79	78
9	44	51
10	108	102
11	450	438
12	147	132
13	226	218
14	97	102
15	291	290
16	68	74
17	94	100
18	93	89
19	148	161
H, 3, 5		
0	275	269
1	276	272
2	441	438
3	349	345
4	296	301
5	43	39
6	305	284
7	265	256
8	332	348
9	139	138
10	197	192
11	113	113
12	237	233
13	89	88
14	115	114
15	104	104
16	192	194
17	78	83
18	42	43
19	25	25
H, 3, 6		
0	693	704
1	90	81
2	317	304
3	245	244
4	516	531
5	362	352
6	182	176
7	352	351
8	35	42
9	348	338
10	305	298
11	281	283
12	240	244
13	267	276
14	185	188
15	165	169
16	102	98
17	172	174
18	27	13
H, 3, 7		
0	12*	19
1	439	452
2	382	373
3	177	167
4	243	228
5	353	336
6	196	152
7	239	236
8	214	208
9	289	287
10	303	303
11	297	286
12	313	310
13	94	93
14	185	172
15	114	120
16	47	44
17	71	73
H, 3, 8		
0	223	213
1	259	258
2	482	487
3	56	61
4	227	221
5	89	85
6	359	349
7	70	66
8	231	226
9	170	160
10	361	353
11	157	150
12	173	180
13	63	74
14	134	129
15	60	58
16	130	135
H, 3, 9		
0	182	183
1	52	48
2	110	113
3	299	291
4	187	179
5	15*	18
6	221	210
7	371	375
8	128	135
9	153	150
10	115	117
11	50	55
12	211	216
13	178	178
14	76	74
15	50	50
H, 3,10		
0	350	356
1	234	218
2	28	22
3	122	122
4	411	421
5	60	54
6	185	183
7	247	232
8	138	135
9	233	228
10	33	29
11	163	159
12	55	51
13	89	100
14	66	67
H, 3,11		
0	482	482
1	161	172
2	23*	17
3	217	223
4	366	361
5	103	105
6	212	214
7	278	287
8	96	102
9	180	184
10	101	102
11	108	117
12	52	61
H, 3,12		
1	54	44
2	126	118
3	61	59
4	216	213
5	167	160
6	173	172
7	43	41
8	205	198
9	49	44
10	91	95
H, 3,13		
0	36	116
1	87	84
2	84	83
3	195	194
4	48	43
5	81	81
6	47	49
7	59	54
H, 4, 0		
0	134	145
1	613	611
2	174	178
3	272	276
4	34	27
5	248	259
6	70	73
7	173	169
8	292	243
9	179	185
10	64	59
11	102	100
12	130	136
13	41	42
14	174	172
15	160	160
16	40	42
17	173	174
18	85	86
19	37	40
H, 4, 1		
0	781	788
1	868	911
2	39	15
3	485	472
4	168	171
5	217	205
6	160	152
7	90	102
8	174	160
9	265	256
10	302	287
11	379	348
12	58	64
13	173	179
14	83	82
15	141	140
16	89	91
17	238	237
18	38	36
19	150	153
H, 4, 2		
0	339	338
1	247	235
2	160	169
3	281	276
4	208	214
5	214	209
6	161	156
7	51	37
8	227	220
9	116	121
10	255	240
11	70	77
12	128	125
13	149	150
14	109	115
15	75	77
16	197	203
17	211	217
18	103	107
19	32	38
H, 4, 3		
0	332	324
1	299	267
2	134	139
3	388	389
4	361	348
5	54	57
6	88	79
7	367	363
8	219	218
9	220	209
10	297	289
11	216	209
12	228	214
13	158	152
14	208	206
15	197	197
16	75	68
17	68	71
18	156	152
H, 4, 4		
0	347	355
1	132	123
2	160	151
3	229	222
4	568	567
5	77	74
6	235	227
7	153	150
8	410	402
9	211	191
10	224	222
11	163	154
12	120	114
13	110	105
14	198	192
15	144	141
16	84	89
17	157	160
18	87	97
H, 4, 5		
0	0*	20
1	294	288
2	129	126
3	214	227
4	363	357
5	408	394
6	192	188
7	143	149
8	247	242
9	319	316
10	100	95
11	329	317
12	88	85
13	197	196
14	109	118
15	377	384
16	80	72
17	95	96
H, 4, 6		
0	78	79
1	109	107
2	241	233
3	188	176
4	90	94
5	320	324
6	458	452
7	196	201
8	180	176
9	155	157
10	369	366
11	237	240
12	225	229
13	96	94
14	232	229
15	184	179
16	163	162
17	98	94
H, 4, 7		
0	196	189
1	100	102
2	323	327
3	213	208
4	336	329
5	139	132
6	272	249
7	295	301
8	120	120
9	176	178
10	117	116
11	41	39
12	109	109
13	138	133
14	239	236
15	21*	26
16	72	66
H, 4, 8		
0	353	366
1	82	74
2	300	303
3	122	121
4	267	262
5	109	100
6	124	123
7	247	246
8	202	198
9	250	248
10	196	195
11	74	80
12	166	166
13	164	165
14	30	24
15	44	47
H, 4, 9		
0	408	416
1	114	108
2	100	104
3	210	201
4	257	254
5	257	240
6	290	290
7	128	123
8	151	157
9	44	51
10	197	199
11	0*	12
12	111	120
13	128	127
14	33	31
H, 4,10		
0	103	104
1	120	114
2	55	63
3	112	102
4	136	145
5	138	132
6	37	28
7	139	143
8	122	121
9	70	68
10	119	120
11	51	47
12	53	50
H, 4,11		
0	189	177
1	29	24
2	116	119
3	22*	28
4	136	134
5	124	125
6	266	251
7	116	115
8	135	147
9	180	171
10	39	38
H, 4,12		
0	37	31
1	75	74
2	89	86
3	103	105
4	100	98
5	72	74
6	98	95
7	124	121
H, 4,13		
0	184	186
1	51	52
2	101	104
H, 5, 0		
1	180	183
2	342	329
3	341	333
4	22*	33
5	377	378
6	162	160
7	245	231
8	70	70
9	344	325
10	138	137
11	337	351
12	212	202
13	315	299
14	55	55
15	475	473
16	27	21
17	128	131
H, 5, 1		
0	29	9
1	450	455
2	328	329
3	194	180
4	153	150
5	229	225
6	122	134
7	61	62
8	117	123
9	200	199
10	198	196
11	150	146
12	206	213
13	69	61
14	140	138
15	62	53
16	12*	13
17	28	35
H, 5, 2		
0	297	295
1	287	289
2	276	263
3	372	361
4	364	350
5	439	439
6	151	143
7	131	127
8	173	161
9	226	217
10	212	199
11	70	67
12	173	176
13	77	73
14	265	246
15	63	58
16	157	162
17	22	23
H, 5, 3		
0	151	156
1	95	96
2	134	140
3	193	195
4	169	166
5	154	154
6	124	121
7	214	214
8	128	122
9	72	67
10	60	58
11	169	168
12	87	90
13	51	54
14	42	41
15	105	111
16	112	118
17	64	66
H, 5, 4		
0	216	220
1	265	268
2	194	194
3	66	69
4	114	110
5	342	340
6	329	316
7	62	55
8	309	300
9	154	156
10	168	168
11	157	165
12	179	187
13	112	105
14	0*	3
15	72	73
16	73	71
H, 5, 5		
0	40	34
1	89	93
2	47	46
3	126	118
4	139	140
5	169	159
6	45	33
7	94	85
8	246	235
9	93	101
10	82	77
11	97	88
12	89	81
13	86	97
14	80	81
15	159	169
16	118	119
H, 5, 6		
0	61	61
1	155	154
2	266	247
3	58	51
4	116	118
5	282	279
6	166	156
7	171	170
8	252	246
9	204	200
10	166	167
11	323	324
12	195	192
13	86	81
14	40	36
15	213	214
H, 5, 7		
0	21*	3
1	43	36
2	211	196
3	40	44
4	213	222
5	243	251
6	150	151
7	24	35
8	114	124
9	75	70
10	209	201
11	84	85
12	63	55
13	101	98
14	118	120
H, 5, 8		
0	312	308
1	132	113
2	107	101
3	196	203
4	203	211
5	118	114
6	195	196
7	169	173
8	121	124
9	53	51
10	197	189
11	189	188
12	122	130
13	89	90
H, 5, 9		
0	309	310
1	138	145
2	52	43
3	207	206
4	116	123
5	106	102
6	92	88
7	79	84
8	42	43
9	13*	22
10	43	49
11	63	57
H, 5,10		
0	124	111
1	105	100
2	161	163
3	221	212
4	52	53
5	94	82
6	128	125
7	192	185
8	181	177
9	233	231
H, 5,11		
0	250	247
1	168	171
2	103	116
3	79	81
4	169	174
5	102	95
6	70	72
7	57	52
H, 5,12		
0	187	190
1	51	57
H, 6, 0		
0	244	243
1	270	261
2	318	307
3	127	124
4	64	69
5	82	81
6	59	59
7	435	442
8	291	280
9	49	41
10	92	97
11	327	325
12	105	107
13	124	133
14	12*	22
15	51	49
H, 6, 1		
0	663	676
1	370	374
2	89	96
3	99	90
4	399	387
5	307	304
6	69	76
7	195	189
8	158	147
9	162	157
10	121	123
11	298	250
12	132	131
13	200	196
14	31	24
16	75	76
H, 6, 2		
0	34	19
1	[illegible]	[illegible]
2	142	[illegible]
3	[illegible]	[illegible]
4	154	150
5	151	137
6	[illegible]	[illegible]
7	229	222
8	193	[illegible]
9	56	[illegible]
10	66	[illegible]
11	85	[illegible]
12	96	90
13	41	[illegible]
14	56	[illegible]
15	80	[illegible]
H, 6, 3		
0	193	195
1	64	[illegible]
2	347	[illegible]
3	76	[illegible]
4	160	157
5	114	112
6	263	261
7	55	[illegible]
8	160	158
9	64	61
10	311	310
11	62	[illegible]
12	123	122
13	69	[illegible]
14	264	[illegible]
H, 6, 4		
0	128	123
1	78	74
2	135	[illegible]
3	196	[illegible]
4	121	126
5	103	101
6	139	137
7	207	202
8	142	139
9	36	33
10	30	33
11	31	[illegible]
12	128	137
13	98	[illegible]
14	74	72
H, 6, 5		
0	282	291
1	[illegible]	[illegible]
2	96	103
3	143	144
4	197	203
5	201	201
6	123	125
7	67	76
8	70	65
9	233	227
10	38	36
11	85	84
12	55	55
13	100	102
H, 6, 6		
0	0*	3
1	130	132
2	150	162
3	128	130
4	118	124
5	27	9
6	70	61
7	100	108
8	36	36
9	50	45
10	111	106
11	70	70
12	84	83
H, 6, 7		
0	226	225
1	64	66
2	183	187
3	64	56
4	248	249
5	68	72
6	122	120
7	143	138
8	106	109
9	88	90
10	132	132
11	93	89
H, 6, 8		
0	28	29
1	133	139
2	94	108
3	83	72
4	78	84
5	97	102
6	39	37
7	22	22
8	78	80
9	96	97
10	100	111
H, 6, 9		
0	27	18
1	99	93
2	13*	16
3	174	167
4	62	60
5	130	129
6	122	118
7	155	156
8	48	44
H, 6,10		
0	8*	1
1	132	138
2	87	83
3	78	74
4	24	22
5	123	121
H, 7, 0		
[illegible]	[illegible]	[illegible]
8	51	59
9	87	81
10	95	97
11	80	83
H, 7, 4		
0	22*	17
1	65	58
2	198	206
3	82	92
4	103	111
5	63	67
6	135	136
7	46	52
8	101	102
9	52	51
10	83	89
11	45	46
H, 7, 5		
0	210	209
1	81	86
2	112	108
3	104	109
4	77	78
5	74	74
6	33	38
7	68	78
8	133	135
9	104	99
10	38	38
H, 7, 6		
0	31	35
1	69	65
2	180	190
3	20*	23
4	3*	23
5	100	105
6	135	141
7	97	93
8	22	33
9	26	26
H, 7, 7		
0	77	67
1	34	24
2	26	38
3	61	66
4	51	55
5	83	89
6	50	57
7	92	80
H, 7, 8		
0	136	139
1	111	112
2	118	125
3	17*	16
4	159	161
H, 8, 0		
0	86	89
1	87	99
2	98	103
3	152	155
4	83	79
5	73	74
6	42	37
7	6*	17
8	50	43
H, 8, 1		
[illegible]	[illegible]	[illegible]

Table 3. *Positional and thermal parameters of atoms in the sodium salt of guanosine 3′,5′-cyclic monophosphate tetrahydrate*

Positional parameters of nonhydrogen atoms have been multiplied by 10^4. Positional parameters of hydrogen atoms have been multiplied by 10^3. Anisotropic thermal parameters have been multiplied by 10^4. The anisotropic temperature factor is of the form $\exp\left[-(\beta_{11}h^2+\ldots+2\beta_{12}hk+\ldots)\right]$. Standard deviations in parentheses refer to the least significant digits.

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
N(1)	5598 (1)	−2290 (4)	7661 (2)	12 (1)	164 (6)	27 (1)	6 (2)	1 (1)	5 (3)
C(2)	5134 (2)	−2143 (5)	6828 (2)	17 (1)	139 (7)	25 (2)	7 (2)	0 (1)	4 (3)
N(2)	5422 (1)	−2141 (6)	5869 (2)	16 (1)	281 (9)	27 (2)	18 (2)	2 (1)	5 (4)
N(3)	4432 (1)	−2022 (4)	6940 (2)	14 (1)	165 (1)	17 (1)	6 (2)	0 (1)	2 (3)
C(4)	4235 (1)	−1999 (5)	7961 (2)	12 (1)	102 (6)	22 (2)	4 (2)	1 (1)	6 (3)
C(5)	4651 (2)	−2128 (5)	8847 (2)	14 (1)	128 (6)	20 (2)	4 (2)	−2 (1)	0 (3)
C(6)	5406 (2)	−2371 (5)	8716 (2)	16 (1)	138 (7)	25 (2)	5 (2)	−4 (1)	4 (3)
O(6)	5867 (1)	−2640 (4)	9399 (2)	15 (1)	241 (7)	30 (1)	9 (2)	−9 (1)	0 (3)
N(7)	4237 (1)	−1993 (4)	9757 (2)	16 (1)	147 (6)	20 (1)	0 (2)	1 (1)	1 (3)
C(8)	3584 (2)	−1795 (5)	9402 (2)	16 (1)	116 (6)	20 (2)	1 (2)	0 (1)	4 (3)
N(9)	3542 (1)	−1804 (4)	8318 (2)	13 (1)	130 (6)	20 (1)	3 (2)	−2 (1)	2 (3)
C(1′)	2877 (2)	−1841 (5)	7724 (2)	11 (1)	117 (6)	25 (2)	−5 (2)	−2 (1)	−7 (3)
O(1′)	2782 (1)	−3652 (3)	7360 (2)	26 (1)	107 (4)	24 (1)	−13 (2)	−7 (1)	12 (2)
C(2′)	2842 (2)	−567 (5)	6762 (3)	15 (1)	100 (6)	28 (2)	0 (2)	−4 (1)	0 (3)
O(2′)	2178 (1)	399 (4)	6755 (2)	23 (1)	121 (5)	37 (1)	18 (2)	−12 (1)	−18 (3)
C(3′)	2848 (2)	−1923 (5)	5874 (2)	12 (1)	110 (6)	16 (1)	0 (2)	−3 (1)	7 (3)
O(3′)	2517 (1)	−1373 (3)	4911 (2)	18 (1)	88 (4)	20 (1)	4 (2)	−5 (1)	4 (2)
C(4′)	2468 (2)	−3524 (5)	6342 (2)	16 (2)	111 (6)	20 (2)	−7 (2)	−3 (1)	2 (3)
C(5′)	2581 (2)	−5164 (5)	5672 (3)	26 (1)	102 (6)	27 (2)	−2 (2)	−2 (1)	8 (3)
O(5′)	2277 (1)	−4703 (3)	4645 (2)	28 (1)	96 (4)	20 (2)	−15 (2)	−3 (1)	5 (2)
P	2511 (0)	−2928 (1)	4023 (1)	12 (0)	93 (1)	18 (0)	−2 (1)	−2 (0)	4 (1)
O(7)	3244 (1)	−3113 (4)	3587 (2)	17 (1)	193 (6)	48 (2)	−11 (2)	12 (1)	−30 (3)
O(8)	1938 (1)	−2436 (4)	3279 (2)	25 (1)	136 (5)	41 (2)	3 (2)	−18 (1)	7 (3)
O(*W*1)	5666 (1)	−4068 (4)	3451 (2)	23 (1)	196 (6)	52 (2)	10 (2)	2 (1)	30 (3)
O(*W*2)	4293 (1)	−3498 (4)	1873 (2)	20 (1)	164 (5)	40 (2)	13 (2)	−1 (1)	17 (3)
O(*W*3)	6050 (2)	−1534 (5)	1468 (2)	47 (1)	282 (9)	54 (2)	−42 (3)	22 (1)	−31 (4)
O(*W*4)	4399 (1)	−922 (4)	4180 (2)	19 (1)	180 (6)	47 (2)	−4 (2)	6 (1)	−12 (3)
Na	5140 (1)	−1320 (2)	2710 (1)	20 (0)	138 (3)	35 (1)	−11 (1)	3 (1)	1 (1)

Table 3 (*cont.*)

	x	y	z	B
H(1)	603 (3)	−234 (11)	757 (5)	5·9 (16)
H(21)	519 (2)	−166 (6)	531 (3)	2·6 (9)
H(22)	585 (3)	−225 (10)	583 (5)	5·9 (15)
H(8)	318 (2)	−162 (6)	990 (3)	2·0 (8)
H(1′)	251 (2)	−153 (6)	820 (3)	2·4 (9)
H(2′)	320 (2)	28 (7)	672 (4)	3·0 (10)
H(O2′)	222 (3)	116 (8)	736 (4)	4·6 (12)
H(3′)	334 (2)	−226 (6)	577 (3)	2·2 (9)
H(4′)	201 (2)	−311 (6)	641 (3)	2·1 (8)
H(5′1)	313 (3)	−547 (7)	557 (4)	3·5 (10)
H(5′2)	230 (2)	−640 (7)	595 (4)	3·5 (11)
H1(*W*1)	552 (3)	−461 (9)	387 (5)	6·9 (16)
H2(*W*1)	617 (4)	−456 (10)	327 (6)	7·1 (17)
H1(*W*2)	397 (4)	−334 (13)	216 (6)	9·0 (23)
H2(*W*2)	424 (3)	−301 (9)	107 (5)	5·6 (15)
H1(*W*3)	583 (4)	−191 (13)	80 (7)	10·6 (22)
H2(*W*3)	630 (4)	−27 (12)	119 (7)	1·3 (23)
H1(*W*4)	412 (3)	−163 (9)	416 (5)	5·6 (15)
H2(*W*4)	429 (4)	−4 (10)	447 (5)	5·7 (16)

were from *International Tables for X-ray Crystallography* (1962). Those for P, O, N, and C were from Cromer & Waber (1965) and those for H were from Stewart, Davidson & Simpson (1965).

Results

The observed and calculated structure amplitudes are given in Table 2. The final positional and thermal parameters together with their e.s.d.'s are given in Table 3. The thermal ellipsoids for the nonhydrogen atoms are represented in Fig. 1. The bond distances and angles are shown in Fig. 2. The average estimated standard deviations are 0·005 Å for C–C bonds, 0·004 Å for C–O and C–N bonds, 0·003 Å for P–O bonds and 0·2 to 0·3° for angles involving C, N and O atoms, and 0·1° for O–P–O angles.

Discussion

Bond distances and angles

Base: There is generally good agreement between the dimensions of the guanosine moiety in this structure and those found in guanosine dihydrate (Thewalt, Bugg & Marsh, 1970) and *N*,*N*-dimethylguanosine (Brennan, Weeks, Shefter, Rao & Sundaralingam, 1972) both of which have also been determined with high precision.

Ribose: The bond distances and bond angles of the furanose ring are in good agreement with the values found in cyclic *C*-AMP (Sundaralingam & Abola, 1972*b*) and cyclic UMP (Coulter, 1969). The ring C–O bond distances, C(1′)–O(1′) = 1·430 Å and C(4′)–O(1′) = 1·425 Å, are equal within the experimental errors and confirm the previous observation on other cyclic nucleotides (Sundaralingam & Abola, 1972*b*). This is in striking contrast to the common nucleotides which

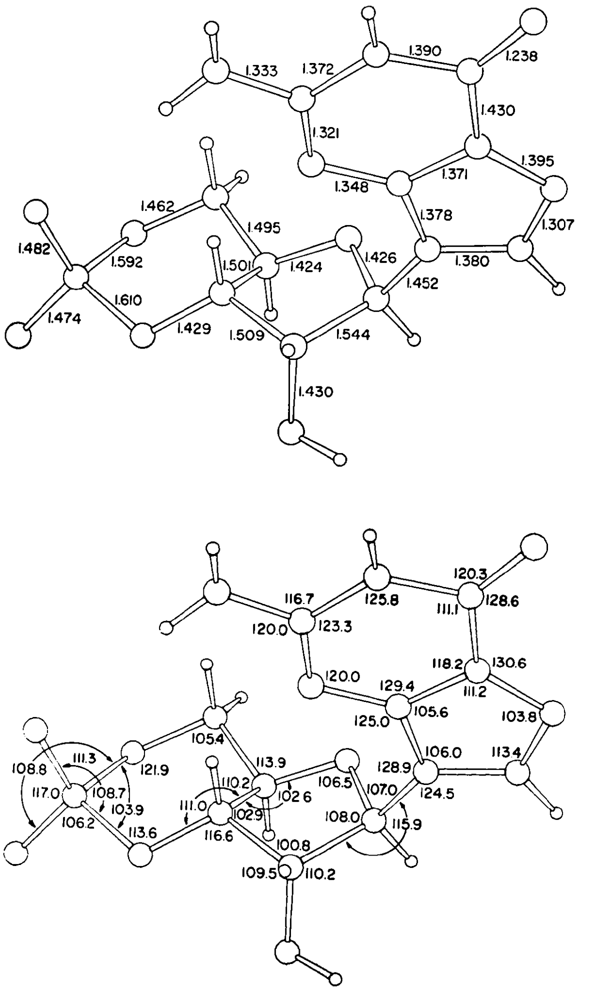

Fig. 2. Bond distances and angles in cyclic GMP. The anionic charge on the phosphate is not shown. The average estimated standard deviations are 0·005 Å for C–C bonds, 0·004 Å for C–O and C–N bonds, 0·003 Å for P–O bonds and 0·2 to 0·3° for angles involving C, N and O atoms and 0·1° for O–P–O angles.

exhibit an average intracyclic anomeric C(1′)–O(1′) bond of 1·409 Å which is significantly shorter than the average C(4′)–O(1′) bond of 1·450 (Sundaralingam, 1965).

Phosphate: The bond distances in the phosphate ring of cyclic GMP are in good agreement with the values of cyclic UMP with the exception of O(5′)–P, which is about 0·019 Å shorter. The bond angles C(5′)–O(5′)–P and O(5′)–P–O(7) of 121·9 and 111·3° respectively are about 3° greater than those found in cyclic UMP. The other angles show only small variations in the different cyclic nucleotides.

The molecular conformation

Glycosyl torsion angle: The torsion angle χ [O(1′)–C(1′)–N(9)–C(8): Sundaralingam, 1969] about the glycosyl bond is 257·6° and corresponds to the *syn* conformation for the base relative to the sugar. This value is slightly greater than the values usually found for the *syn* purine nucleosides (Rao & Sundaralingam, 1970; Sundaralingam, 1973) but is similar to the value (258°) found for one of the molecules of cyclic AMP (Waten-

Table 4. *Deviations of atoms from the least-squares plane through the base* (Å)

Equation of plane: $-0{\cdot}1078X-0{\cdot}9940Y-0{\cdot}0161Z=0{\cdot}4313$ where X,Y,Z are in Å units referred to the orthogonal axes a, b and c. Atoms marked with an asterisk were used in the fitting of the plane.

N(1)*	−0·033
C(2)*	−0·030
N(3)*	0·019
C(4)*	0·021
C(5)*	0·015
C(6)*	0·044
N(7)*	−0·020
C(8)*	−0·027
N(9)*	0·010
N(2)	−0·070
O(6)	0·135
C(1′)	0·184
O(1′)	1·540
r.m.s.	0·026

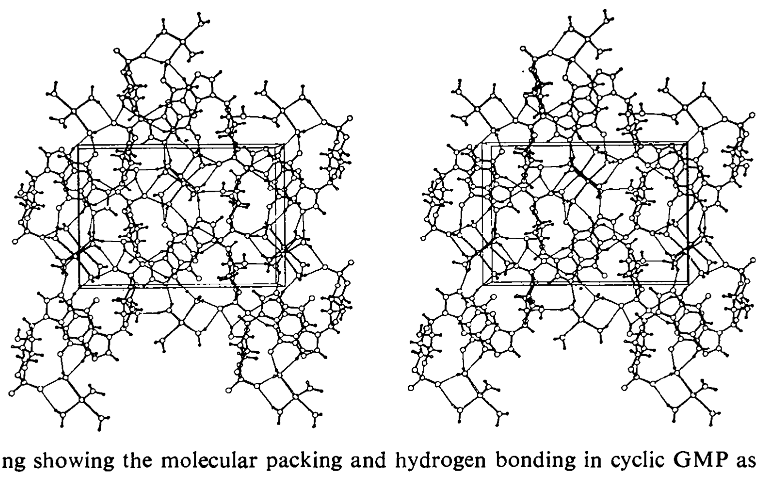

Fig. 3. Stereoscopic drawing showing the molecular packing and hydrogen bonding in cyclic GMP as viewed down the *b* axis.

paugh, Dow, Jensen & Furberg, 1968). Cyclic *C*-AMP was also found to exhibit the *syn* conformation with $\chi=234{\cdot}9°$ (Sundaralingam & Abola, 1972*a*,*b*). Theoretical potential-energy calculations also predict that the *syn* conformation is favored for cyclic GMP (Yathindra & Sundaralingam, 1974).

Planarity of the base: The least-squares plane through the nine atoms of the purine base (Table 4) indicates that atom C(6) shows the largest displacement (0·044 Å) from the plane. The exocyclic atoms O(6) and C(1′) show even greater displacements of 0·135 and 0·184 Å respectively on the same side of the plane, while N(2) is displaced 0·070 Å on the opposite side. The planes through the five atoms of the imidazole ring and the six atoms of the pyrimidine ring form a rather high dihedral angle of 2·54°.

Table 5. *Deviations of atoms from least-squares planes through the ribose* (Å)

Values marked with an asterisk are for atoms used in fitting the plane.

The equations of the planes are:

Plane I $0{\cdot}9982X-0{\cdot}0588Y-0{\cdot}0128Z=5{\cdot}2602$
Plane II $0{\cdot}9363X-0{\cdot}1678Y-0{\cdot}3884Z=2{\cdot}3281$
Plane III $0{\cdot}9886X-0{\cdot}0886Y-0{\cdot}1221Z=4{\cdot}2310$

where X,Y,Z are in Å units referred to the orthogonal axes *a*, *b* and *c*.

	Plane I	Plane II	Plane III
O(1′)	−0·037*	0·103*	−0·000*
C(1′)	0·055*	−0·098*	0·000*
C(2′)	−0·052*	0·058*	0·000*
C(3′)	0·034*	0·586	0·239
C(4′)	−0·612	−0·063*	−0·430
C(5′)	−0·320	0·599	−0·011
N(9)	1·282	0·826	1·132
O(2′)	−1·331	−1·219	−1·288
O(3′)	−0·590	0·317	−0·258
R.m.s.	0·045	0·083	0·000

Conformation of the ribose ring: The displacements of atoms from the best and next-best four-atom least-squares planes (planes I and II) for the ribose moiety are given in Table 5. Atom C(4′) is displaced 0·612 Å on the opposite side (*exo*) of N(9) (plane I) and atom C(3′) is displaced 0·586 Å on the same side (*endo*) as N(9) (plane II). [The puckerings of cyclic nucleotides are described here relative to the glycosyl nitrogen N(9) for reasons given by Sundaralingam & Abola (1972*b*).] The furanose ring pucker is best described in terms of the deviations of the atoms C(4′) and C(3′) with respect to the three-atom plane O(1′), C(1′), C(2′) (plane III), which is consistent with the pseudorotation concept (Altona & Sundaralingam, 1972). With reference to the latter plane the sugar exhibits a twist (T) conformation ${}_4T^3$ [C(4′)*exo*, C(3′)*endo*]. This mode of puckering is characteristic of the cyclic nucleotides (Sundaralingam & Abola, 1972*a*,*b*; Chwang & Sundaralingam, 1973). The pseudorotation (Altona & Sundaralingam, 1972) phase angle P and the maximum amplitude of puckering τ_m for the furanose ring are 42·6 and 44·2° respectively. These values (P, τ_m) resemble the values found for cyclic UMP (molecule 1, 42·0, 47·8; molecule 2, 47·9, 47·2) and cyclic *C*-AMP (36·8, 45·7). It may be noted that in cyclic nucleotides the P values are slightly shifted to higher values than those generally found for C(3′)-*endo* nucleosides and nucleotides (Chwang & Sundaralingam, 1973).

Conformation of the phosphate ring: The phosphate ring is constrained to the chair conformation. The greatest puckering occurs in the C(3′)–C(4′) bond which is the common linkage of the bicyclic ribophosphate system. The ester P–O bonds on the remote side of the C(3′)–C(4′) bond show the smallest ring torsion angles. Thus, the C(3′)C(4′) half of the phosphate ring is sharpened while the PO(5′) half is flattened (Table 6). A similar feature is observed in cyclic UMP and the analog cyclic *C*-AMP.

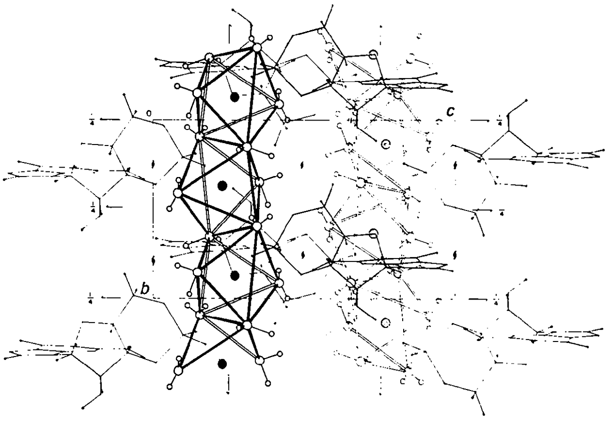

Fig. 4. Packing diagram viewed along the *a* axis showing the columns of sodium–water octahedra running parallel to the *b* axis.

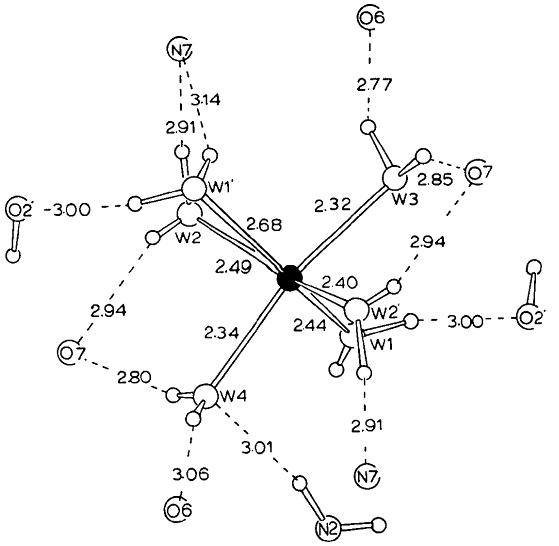

Fig. 5. The water to sodium bond distances and the water to nucleotide hydrogen bond distances.

Table 6. *A comparison of the sugar phosphate ring conformations of cyclic GMP with those of cyclic* UMP

		Cyclic GMP	Cyclic UMP	
			Molecule 1	Molecule 2
Glycosyl angle	χ	257·6° (*syn*)	77° (*anti*)	58°(*anti*)
Ribose ring conformation	τ_0	−18·4	−19·3	−23·5
	τ_1	−9·3	−10·4	−5·5
	τ_2	31·7	34·6	30·8
	τ_3	−44·3	−48·1	−46·7
	τ_4	38·7	41·5	43·2
Puckering		${}_4T^3$	${}_4T^3$	${}_4T^3$
Phosphate ring conformation				
P——O(3′)		44·2	57·4	49·3
O(3′)–C(3′)		−59·8	−66·7	−61·2
C(3′)–C(4′)		68·5	69·1	67·1
C(4′)–C(5′)		−60·5	−61·4	−59·5
C(5′)–O(5′)		53·6	60·5	56·5
O(5′)–P		−44·3	−56·7	−50·5

A comparison of the dihedral angles of the ribose and phosphate rings of cyclic GMP and cyclic UMP (molecule 1 and molecule 2) is given in Table 6. The torsion angles of the furanose ring of cyclic GMP show only small differences from the corresponding angles of cyclic UMP indicating, as has been mentioned before (Sundaralingam & Abola, 1972*b*; Chwang & Sundaralingam, 1973), that the sugar ring is highly rigid in the cyclic nucleotides. However, the torsion angles of the phosphate ring in cyclic GMP and cyclic UMP show some variation, indicating that the six-membered phosphate ring is more flexible than the furanose ring. The main differences occur in the torsions about the P–O bonds, then the torsions about the C–O bonds; the torsions about the C–C bonds show the least variation. Recent ^{1}H and ^{13}C n.m.r. studies (Blackburn, Lapper & Smith, 1973; Lapper, Mantsch & Smith, 1973) on cyclic nucleotides in solution confirm the conformations found for the ribophosphate moiety in the solid state.

Molecular packing and hydrogen bonding: A stereoscopic view of the molecular packing and hydrogen bonding is shown in Fig. 3. The hydrogen-bonding distances and angles are given in Table 7. The nucleotides are packed in a 'head-to-tail' fashion with bases stacked in columns along alternate screw axes parallel to the *b* axis. The closest interbase contact of 3·53 Å involves the atoms N(1) and N(3) of screw-related molecules. With the exception of the ribose ring O(1′), all donor and acceptor atoms participate in hydrogen bonding. The N(7) and O(6) sites of the bases are involved in acceptor hydrogen bonding to different water molecules. It is of interest to note that in the DNA double helix these base sites face the broad groove and it appears likely that similar hydrogen bonding may occur for the guanine residues of DNA in solution. In the common nucleosides exhibiting the *syn* conformation the base atom N(3) is usually found to be involved in an intramolecular hydrogen bond O(5′)–H···N(3) to the ribose hydroxyl group (Rao & Sundaralingam, 1970). In the cyclic nucleotides, this hydrogen bonding is not possible. However, in cyclic GMP the N(3) atom may possibly be involved in a weak intramolecular van der Waals attractive interaction with the ribose H(3′) atom where H(3′)···N(3) = 2·54, C(3′)···N(3) = 3·25 Å, and the angle C(3′)–H(3′)···N(3) = 132°.

Phosphate–sugar hydrogen bonding: The hydroxyl group O(2′)H is involved in a bifurcated hydrogen bond to the two anionic phosphate oxygen atoms O(7) and O(8). This hydrogen bond links the sugar and the phosphate groups of adjacent nucleotides forming infinite chains parallel to the *b* axis at *a*/4 and 3*a*/4 (Fig. 3). Adjacent chains of nucleotides are crosslinked by phosphate–base hydrogen bonding.

Phosphate–base hydrogen bonding: The phosphate oxygen O(8) is simultaneously hydrogen bonded to the two base atoms N(1) and N(2) of a symmetry-related molecule, N(1)···O(8) 2·78 Å and N(2)···O(8) 3·05 Å.

Table 7. *Hydrogen-bond lengths* (Å) *and angles* (°)

Bond	Symmetry code for	Distance			Angle
A–H···B	B	A–H	H···B	A···B	A–H···B
O(*W*1)–H1(*W*1)···N(7)	I	0·72	2·51	3·14	146·8
O(*W*1)–H2(*W*1)···O(2′)	II	1·04	1·98	3·00	167·9
O(*W*2)–H1(*W*2)···O(7)	III	0·71	2·27	2·94	157·8
O(*W*2)–H2(*W*2)···N(7)	IV	1·09	1·83	2·91	172·7
O(*W*3)–H1(*W*3)···O(6)	IV	0·99	1·86	2·77	153·0
O(*W*3)–H2(*W*3)···O(7)	V	1·10	1·83	2·85	152·3
O(*W*4)–H1(*W*4)···O(7)	III	0·74	2·10	2·80	158·3
O(*W*4)–H2(*W*4)···O(6)	VI	0·78	2·30	3·06	167·0
O(2′)—H(O2′)····O(8)	VII	0·95	2·17	2·96	138·9
O(2′)—H(O2′)····O(6)	VII	0·95	2·30	3·17	151·8
N(1)—H(1)······O(8)	II	0·81	2·02	2·78	155·9
N(2)—H(21)·····*W*(4)	III	0·90	2·13	3·01	164·5
N(2)—H(22)·····O(8)	II	0·80	2·34	3·05	147·5

Symmetry code	I	$1-x,\ y-\frac{1}{2},\ 1\frac{1}{2}-z$	II	$\frac{1}{2}+x,\ -\frac{1}{2}-y,\ 1-z$
	III	$x,\ y,\ z$	IV	$x,\ y,\ z-1$
	V	$1-x,\ \frac{1}{2}+y,\ \frac{1}{2}-z$	VI	$1-x,\ \frac{1}{2}+y,\ 1\frac{1}{2}-z$
	VII	$\frac{1}{2}-x,\ \bar{y},\ \frac{1}{2}+z$		

Phosphate–base hydrogen bonding has been observed in a variety of schemes in the nucleotides and cyclic nucleotides (Sundaralingam & Abola, 1972*b*). The ester oxygen O(3′) is in close contact to the H(8) atom of an adjacent base, $H(8)\cdots O(3')=2{\cdot}56$ and $C(8)\cdots O(3')=3{\cdot}18$ Å. Similar contacts, which may represent *weak* $C\text{–}H\cdots O$ interactions are a recurring feature in the cyclic nucleotides (Sundaralingam & Abola, 1972*b*; Watenpaugh, Dow, Jensen & Furberg, 1968).

The water hole: The nucleotides are stacked in columns along alternating screw axes parallel to **b**. The space between the nucleotide columns is filled by the water and the sodium ions (Fig. 3). The sodium ions are surrounded by the water molecules thus barring them from direct contact with the anionic phosphate oxygens. This feature is similar to that encountered in the crystal structure of sodium inosine 5′-phosphate octahydrate (Rao & Sundaralingam, 1969) where each sodium was coordinated to four water molecules and the *cis* hydroxyl groups of the ribose. In cyclic GMP the water molecules form a distorted octahedron around the Na ion. Adjacent octahedra share edges to generate an infinite water hole impregnated with sodium ions (Fig. 4). The sodium ions are 3·77 Å apart. The sodium–water bond distances and the hydrogen-bond distances between the nucleotides and the sodium octahedron are shown in Fig. 5. *W*(3) and *W*(4) are involved in the shorter contacts to the Na^+ while the remaining four water molecules are at distances ranging from 2·40–2·68 Å. The water molecules around the sodium are in turn linked to the ribose 2′-hydroxyl, the base N(7), O(6) and N(2) and the phosphate oxygen O(7). Thus the nucleotide fully exploits its versatility in hydrogen bonding. Practically all of the potential hydrogen-bond donor and acceptor sites on the nucleotide are facing the water hole. The only water molecule involved in an acceptor hydrogen bond is *W*(4) which is hydrogen bonded to the amino group of the base.

We thank Dr R. K. McMullan for collecting the X-ray data. This work was supported by a research grant GM-17378 from the National Institutes of Health of the United States Public Health Service. An award of computer time by the University Graduate School is hereby acknowledged.

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