DAEHAN HWAHAK HWOEJEE
(*Journal of the Korean Chemical Society*)
Vol. 22, No. 2, 1978
Printed in Republic of Korea

Theophylline 鹽酸鹽의 結晶 및 分子構造

具廷會 · 申鉉昭* · 吳善淑

서울大學校 自然科學大學 化學科

(1978. 2. 21 接受)

The Crystal and Molecular Structure of Theophylline Hydrochloride

Chung Hoe Koo, Hyun So Shin* and Sun Suk Oh

Department of Chemistry, College of Natural Sciences,
Seoul National University, Seoul, Korea

(Received Feb. 28, 1978)

要約. Theophylline 鹽酸鹽의 結晶 및 分子 構造를 3次元的인 X-線 回折 data로부터 Patterson 法에 의하여 決定하였고, Block-diagonal least square와 Fourier 法으로서 座標를 精密化 하였다. 이 化合物은 $a=14.01$, $b=11.49$, $c=6.77$Å의 單位格子를 갖이는 斜方晶系에 屬하는 結晶이며 空間群은 P_{na2_1}이다. 743개의 觀測된 data에 대한 최종 R값은 12.2%이다.

Theophylline 分子內 原子間 距離는 유사化合物에서 얻은 값과 거의 일치한다. 이들 原子는 同一平面을 이루고 있으며 HCl의 鹽素原子는 theophylline의 N(1) 原子와 3.06Å 距離의 Cl···N(1), 水素結合을 이루고 있다. 모든 分子는 대략 (001)과 (002)面上에 배열되어 있고 各分子間은 van der Waals force에 의해 三次元的 構造를 이루고 있다.

ABSTRACTS. The crystal and molecular structure of theophylline hydrochloride has been determined from X-ray data by Patterson techniques. The structure has been refined by block-diagonal least-squares and Fourier synthesis on three dimensional data. The unit cell is orthorhombic, space group P_{na2_1}, with $a=14.01$, $b=11.49$, $c=6.77$Å, and contains four molecules. The final R value based on 743 observed reflexions is 12.2%.

The intramolecular distances are similar to those in other compounds containing a purine or pyrimidine group. The molecules are nearly planar and are stacked in layers parallel to the (001) plane. The chlorine atom is coordinated to N(1) atom at a distance of 3.06Å. The structure is stabilized mainly by van der Waals interactions; however, a short N···Cl contact of length 3.06Å, which is slightly less than the expected van der Waals separation, suggest that weak charge transfer interaction may be present. The relationship between this structure and the known structures of theophylline monohydrate and caffeine monohydrate are discussed.

INTRODUCTION

Theophylline is a component of a aminophylline drug. Aminophylline is well known and widely used diuretic and asthma medicines[1]. Many of these diuretic and asthma agent have

*Department of Chemical Engineering, College of Engineering, Dongguk University, Seoul, Korea

been in use for several decades and a great deal of research has been carried out in their pharmalogical properties when administered individually and in combination. However, the molecular basis their interactions and thier mode of action are yet to be elucidated. Therefore a detail knowledge of the structure and the possible modes of theophylline is important in elucidating the molecular mechanism of the action of diuretic and asthma medicines.

The crystal and molecular structure of theophylline monohydrate[2] was reported in a previous investigation.

The structure of theophylline hydrochloride is of interest for the comparision of its hydrogen bonding scheme with those of the related compounds. This investigation was undertaken as a part of a research on the structures of components related to purine and pyrimidines, and with a particular aim towards furnishing accurate details of the molecular geometry and obtaining futher information concerning intermolecular forces such as hydrogen bonding and base stacking.

EXPERIMENTAL

Crystals of theophylline hydrochloride suitable for X-ray analysis were obtained by slow evaporation of an aqueous solution containing theophylline and hydrochloric acid. Because the compound is unstable in air, crystals for X-ray examination were coated by halocarbon grease.

The unit cell dimensions were obtained from their least-squares fit to 14 measurements of high angle reflexions on Weissenberg [$\lambda(CuK\alpha_1)=1.5405$, $\lambda(CuK\alpha_2)=1.5443$Å] photographs. Powder lines from a thin aluminium foil were superimposed on the Weissenberg photographs used for the determination of the cell constants.

The density was measured by floatation in a mixture of benzene and carbontetrachloride. The crystallographic data are as follows.

Molecular formular	$C_7H_9N_4O_2Cl$
Unit cell	orthorhombic
	$a=14.01$, $b=11.49$, $c=6.77$ Å
V	1089.84 Å^3
Molecular weight	216.67
Z	4
D_c	1.321 g/cm^3
D_m	1.330 g/cm^3
Space group	P_{na2_1}
Systematically absent reflexions	
	$0kl$; k, $l=2n+1$,
	$h0l$; $h=2n+1$, $h00$; $h=2n+1$,
	$0k0$; $h=2n+1$, $00l$; $l=2n+1$.

Three dimensional intensities were collected by the multiple-film equi-inclination Weissenberg technique with nickel-filtered Cu$K\alpha$ radiation. The intensities were collected for $h0l$ to $h1l$ and $hk0$ to $hk5$ from approximately crystals having diameters 0.3 and 0.5 mm respectively. The intensities of 743 independent reflexions were estimated visually by comparison with a standard scale. Correction for Lorentz-polarization factors and spot shape were made in the usual way. No absorption correction was considered necessary. Interlayer scaling was achieved using cross-layer and corrected data were placed on an absolute scale by Wilson's method.[3]

STRUCTURE DETERMINATION AND REFINMENT

The reflexions from the Layers with $l=2n$ ($n=0$, 1) show approximately the same intensity distributions of the odd layers are similar to each other, but different from those of even layers. This feature suggests that most atoms should be on the planes at $z=0$ and 1/2.

The heavy-atom method was employed for the crystal structure determination. From the

Harker lines at $u=1/2$, $w=0$ and $v=1/2$, $w=1/2$ of a sharpened three-dimensional Patterson map, it was possible to locate the position of only one of the chlorine atoms. The positions of the remaining non-hydrogen atoms were obtained from a Fourier map phased with planes for which $|F_c|\geq 0.6|F_0|$. The conventional R $(=\Sigma||F_0|-|F_c||/\Sigma|F_0|)$ value at this stage for the 743 reflexions was 0.26 for all non-hydrogen atoms included in the structure factor calculation with on overall isotropic temperature factor of 3.5Å. The function minimized in the least-squares program, adapted to the IBM 360/44 computer, was $\Sigma w(|F_0|-|F_c|)^2$. The weighting function (Cruickshank, Bujosa, Lovell and Truter)[4] was $w=1/(a+bF_0+c|F_0|)^2$, with $a=4.58$, $b=1.00$ and $c=0.018$.

Refinement reduced R to 0.18. All parameters were refined together by successive block-diagonal least-squares calculations[5]. The final R for the observed reflexions was 0.12. Atomic scattering factors for C, N, O and Cl atoms from international tables for X-ray crystallography (1968)[6] were used. The final coordinate of all non-hydrogen atoms and the thermal parameters are given in *Table* 1. Observed and calculated structure factors are given in *Table* 2.

Table 1. Fractional coordinates and thermal parameters with standard deviations.

	x	y	z	β
C (1)	0.1089 (8)	0.334 (1)	0.500 (2)	2.2 (2)
C (2)	0.1979 (7)	0.487 (1)	0.500 (1)	1.3 (2)
C (3)	0.3278 (8)	0.620 (1)	0.500 (4)	2.0 (2)
C (4)	0.3619 (7)	0.407 (1)	0.500 (1)	1.5 (2)
C (5)	0.2595 (7)	0.393 (1)	0.500 (1)	1.6 (2)
C (6)	0.4922 (8)	0.556 (1)	0.500 (3)	2.2 (2)
C (7)	0.1599(13)	0.694 (2)	0.500 (2)	4.0 (3)
N (1)	0.2016 (7)	0.296 (1)	0.500 (2)	1.9 (2)
N (2)	0.1056 (6)	0.451 (1)	0.500 (2)	2.0 (2)
N (3)	0.2318 (6)	0.600 (1)	0.500 (2)	1.5 (1)
N (4)	0.3901 (7)	0.524 (1)	0.500 (1)	2.1 (2)
O (1)	0.3629 (7)	0.719 (1)	0.500 (2)	3.1 (2)
O (2)	0.4164 (7)	0.324 (1)	0.500 (1)	3.9 (2)
Cl	0.2315 (2)	0.0394 (2)	0.500 (3)	2.07(4)

Table 2. Observed and calculated structure factors (×10).

K	F_0	F_c	K	F_0	F_c	K	F_0	F_c	K	F_0	F_c
$H=0$,		$L=0$	6	133	114	1	279	286	13	93	−84
2	680	651	7	301	−260	2	635	630	14	60	−29
4	280	252	8	135	−112	3	187	−140	$H=6$,		$L=0$
8	270	−236	9	299	−311	4	85	− 55	0	492	−438
12	333	−248	10	158	−136	6	194	−167	2	424	−385
14	222	−238	12	83	182	7	170	170	3	101	−89
$H=1$,		$L=0$	13	125	70	9	110	90	5	125	−105
2	104	−131	14	160	141	10	60	−45	6	120	−115
4	445	−452	$H=3$,		$L=0$	11	120	104	7	147	−130
6	294	−276	2	638	581	12	162	−131	8	114	104
7	106	−93	3	69	−45	14	112	−82	10	170	135
8	161	−136	4	377	317	$H=5$,		$L=0$	$H=7$,		$L=0$
10	279	−239	5	317	284	1	147	121	2	156	−167
14	79	74	6	197	169	2	98	−39	3	82	− 70
$H=2$,		$L=0$	8	336	310	3	304	272	4	259	244
0	1144	−1257	9	122	−104	4	506	−615	5	131	−107
1	353	−323	10	131	− 93	5	341	−300	6	305	280
2	362	−388	11	125	95	6	123	−122	7	160	−130
3	170	−105	13	56	43	8	244	−211	8	120	102
4	89	−68	$H=4$,		$L=0$	9	282	−274	9	228	240
5	501	−455	0	97	−114	11	258	−216	10	168	158

K	F_0	F_c	K	F_0	F_c	K	F_0	F_c	K	F_0	F_c
H=8,		L=0	3	98	−144	13	119	−119	3	321	−290
0	499	529	5	143	−156	H=4,		L=1	5	58	40
2	362	333	H=15,		L=0	0	689	620	6	129	−119
3	149	140	1	149	−129	1	161	−140	10	91	−79
5	315	337	3	159	−147	2	101	79	12	111	−111
6	199	−212	5	101	−113	3	228	208	H=9,		L=1
7	373	400	H=16,		L=0	4	346	346	1	127	−130
9	148	151	3	155	149	5	414	−363	2	80	−62
10	131	−135	5	86	78	6	232	233	3	90	−128
11	79	69	H=17,		L=0	7	187	−168	4	190	−200
12	104	−75	1	151	157	8	182	−166	5	277	−305
H=9,		L=0	2	81	76	9	223	−253	6	190	155
1	201	184	3	122	129	11	246	−248	7	134	−114
2	219	−191	4	59	52	13	91	59	9	142	148
3	335	310	H=0,		L=1	H=5,		L=1	10	128	−105
4	114	110	1	253	−274	1	478	−428	12	77	−72
5	173	150	3	834	−856	3	242	−201	H=10,		L=1
6	436	−401	7	582	−543	4	315	−362	0	296	−259
7	102	−86	9	105	−97	5	300	−296	1	209	−202
8	160	−132	13	108	−104	6	160	−173	2	179	−172
9	134	−117	H=1,		L=1	7	151	118	3	203	260
11	146	−142	1	796	834	8	184	−198	4	54	42
H=10,		L=0	3	834	−856	9	117	67	5	82	116
1	141	−145	4	275	270	10	133	−100	7	84	−58
3	83	63	5	54	31	11	253	205	9	78	66
4	141	149	6	265	269	13	110	86	10	128	112
5	271	−274	7	89	−118	H=6,		L=1	H=11,		L=1
6	271	214	8	114	120	0	669	−686	1	250	205
7	379	−448	9	418	377	1	589	521	2	268	324
9	185	−156	10	149	135	2	135	−185	3	241	218
H=11,		L=0	11	275	249	3	146	193	4	397	429
1	183	−214	13	64	49	4	368	−334	5	208	216
3	186	−189	H=2,		L=1	5	126	146	6	103	105
4	81	−69	0	125	102	7	291	312	8	106	104
5	135	−131	1	77	55	8	122	−22	9	160	−121
6	126	127	2	156	−174	9	130	116	10	98	103
7	79	74	3	437	380	10	114	−95	11	87	−84
11	130	105	4	222	−173	12	95	91	H=12,		L=1
H=12,		L=0	5	627	588	13	82	−79	0	96	85
0	76	58	6	217	−184	H=7,		L=1	2	221	235
1	126	−133	7	406	370	1	79	−60	H=13,		L=1
3	100	−137	8	140	145	2	315	285	1	87	81
4	136	−143	9	158	207	3	138	163	2	298	−312
5	137	115	11	94	119	4	250	204	4	141	−135
7	129	115	H=3,		L=1	5	176	136	5	70	−64
9	143	114	1	609	743	6	161	162	6	214	−218
H=13,		L=0	3	280	292	8	171	148	8	161	−134
1	278	300	4	342	357	10	100	75	9	94	−37
4	110	−74	5	528	486	11	120	−111	H=14,		L=1
5	150	138	6	64	−44	13	56	−50	0	113	−99
9	105	−117	9	362	−424	H=8,		L=1	2	147	−135
H=14,		L=0	10	141	−149	0	591	556	4	75	−62
1	114	106	11	245	−252	2	274	301	5	47	25

K	F_0	F_c	K	F_0	F_c	K	F_0	F_c	K	F_0	F_c
6	109	76	6	147	−140	8	132	−126	H=17,		L=2
8	61	58	7	141	152	9	120	−110	1	151	148
H=15,		L=1	9	125	86	10	90	− 75	2	80	72
1	54	−69	11	122	99	11	111	−134	H=0,		L=3
6	143	181	12	143	−124	H=10,		L=2	1	225	−178
7	78	−62	H=5,		L=2	1	118	−123	3	224	−274
H=16,		L=1	1	116	102	3	58	52	5	83	−101
0	214	188	2	58	−44	4	130	137	7	404	−423
5	66	57	3	233	225	5	248	−253	9	101	− 89
H=0,		L=2	4	413	−516	6	186	196	13	68	− 90
0	2942	3026	5	268	−249	7	340	−415	H=1,		L=3
2	565	506	6	96	−121	8	90	− 82	1	407	453
4	244	211	8	203	−191	9	139	−148	3	538	−553
8	242	−204	9	260	−253	10	83	− 66	6	158	194
12	238	−232	11	255	−201	11	46	23	8	89	100
14	201	−224	12	62	−26	H=11,		L=2	9	329	319
H=1,		L=2	13	72	−80	1	164	−200	10	140	106
1	259	297	H=6,		L=2	3	164	−174	11	248	221
2	130	−111	0	441	−371	4	78	− 62	H=2,		L=3
4	343	−378	2	270	−324	5	111	−120	0	77	67
6	264	−241	3	77	−80	6	110	118	1	74	44
8	159	−130	5	132	−101	7	99	67	3	281	256
10	191	−217	6	93	−97	11	81	97	4	150	−120
H=2,		L=2	7	126	−120	H=12,		L=2	5	424	434
0	897	−956	8	110	94	0	63	51	6	137	−142
1	290	−252	10	159	125	1	121	−123	7	339	304
2	300	−316	H=7,		L=2	3	94	−123	8	106	117
3	89	−78	1	97	54	4	111	−131	9	150	176
4	76	−63	2	129	−123	5	124	108	11	114	105
5	438	−373	4	220	214	6	46	− 30	H=3,		L=3
6	93	94	5	95	−95	7	94	110	1	389	487
7	283	−233	6	251	256	9	101	107	2	68	13
8	117	−98	7	128	−113	H=13,		L=2	3	212	219
9	269	−279	8	126	98	1	253	260	4	220	255
11	108	−85	10	147	146	2	83	− 48	5	373	346
12	213	170	11	90	87	3	83	93	6	60	− 25
13	77	65	H=8,		L=2	4	81	− 68	9	378	−356
14	176	134	0	347	458	5	104	128	10	100	−123
H=3,		L=2	2	276	290	9	85	−108	11	243	−222
2	527	459	3	115	125	H=14,		L=2	13	95	−104
3	52	−36	5	271	303	1	122	95	H=4,		L=3
4	317	272	6	144	−190	2	91	− 73	0	457	405
5	276	232	9	153	141	3	107	−132	1	92	− 92
6	203	155	10	110	−126	4	48	42	2	87	71
7	48	−31	11	65	63	5	125	−146	3	83	120
8	332	278	12	87	−69	7	74	−111	4	243	251
9	101	−91	H=9,		L=2	H=15,		L=2	5	274	−277
10	84	−81	1	179	168	1	143	−122	6	161	173
11	118	86	2	197	−163	2	37	− 29	7	180	−148
H=4,		L=2	3	291	280	3	129	−138	8	137	−128
1	207	231	5	129	134	4	36	− 32	9	226	−218
2	505	503	6	328	−363	H=16,		L=2	11	253	−209
3	145	−111	7	103	− 79	3	110	139	13	67	51

K	F_0	F_c	K	F_0	F_c	K	F_0	F_c	K	F_0	F_c
H=5,		L=3	1	134	−149	8	78	−70	11	70	81
2	80	− 69	2	135	−146	9	206	−213	H=8,		L=4
3	195	−160	3	207	212	10	117	−76	0	304	329
4	256	−264	5	92	99	11	75	−68	2	166	212
5	195	−220	6	95	− 72	12	164	137	3	69	95
6	132	−139	9	80	54	H=3,		L=4	5	197	233
7	116	89	10	129	99	1	29	−19	6	141	−145
8	164	−169	H=11,		L=3	2	268	275	7	273	296
9	89	67	1	190	172	3	27	−22	9	101	116
10	91	− 80	2	273	281	4	236	199	10	83	−101
11	207	175	3	213	181	5	171	156	11	52	50
13	97	75	4	371	361	6	146	129	H=9,		L=4
H=6,		L=3	5	189	190	8	247	210	1	120	133
0	469	−494	6	116	96	11	93	67	2	94	−107
1	334	352	8	96	88	H=4,		L=4	3	197	218
2	142	−150	9	132	−106	0	28	13	5	119	101
3	122	157	10	83	91	1	124	135	6	262	−282
4	295	−251	H=12,		L=3	2	286	316	7	82	−63
5	99	126	0	87	77	3	66	−57	8	149	−110
7	234	253	2	156	199	5	41	30	9	88	−92
9	134	106	H=13,		L=3	6	100	−94	H=10,		L=4
10	99	− 83	1	70	69	7	103	117	1	71	−79
12	97	78	2	260	−267	9	108	75	3	55	31
H=7,		L=3	4	111	−124	11	96	95	4	108	114
1	50	− 25	6	200	−189	12	118	−105	5	199	−205
2	240	211	8	113	−117	H=5,		L=4	6	171	157
3	107	135	H=14,		L=3	1	78	79	7	318	−335
4	224	171	0	95	− 86	3	126	138	9	93	−126
5	135	116	2	134	−118	4	347	−346	H=11		L=4
6	152	134	6	68	67	5	137	−158	1	160	168
8	160	129	H=16,		L=3	6	122	−115	2	94	85
10	79	66	0	147	161	8	143	−148	3	121	−139
13	129	114	H=0,		L=4	9	217	−205	4	58	−47
H=8,		L=3	0	1441	1615	11	189	−165	5	89	−96
0	453	442	2	372	329	H=6,		L=4	6	92	96
2	214	241	4	149	135	0	323	−254	H=12,		L=4
3	255	−228	8	146	−141	2	204	−222	1	106	−101
5	41	26	12	164	−187	3	80	−65	3	96	−96
6	115	− 89	H=1,		L=4	5	114	−94	4	79	−104
10	69	− 67	2	55	− 76	7	88	−97	5	76	886
12	81	− 97	4	223	−255	8	75	71	6	39	−31
H=9,		L=3	6	165	−180	10	145	100	7	75	96
1	102	−106	8	141	−118	H=7,		L=4	H=13,		L=4
3	88	−114	10	215	−167	1	46	27	1	185	231
4	160	−170	H=2,		L=4	2	77	−82	3	75	82
5	248	−257	0	453	−562	3	66	−62	4	72	−53
6	131	120	1	172	−146	4	126	157	5	90	106
7	115	− 95	2	179	−216	5	77	−71	H=14,		L=4
9	143	124	3	58	−46	6	199	206	1	77	71
10	110	− 93	4	71	−51	7	106	−80	3	99	−105
11	64	62	5	236	−231	8	113	85	5	102	−119
H=10,		L=3	6	65	57	9	152	173	H=15,		L=4
0	260	−218	7	210	−184	10	112	117	1	79	−103

K	F_0	F_c	K	F_0	F_c	K	F_0	F_c	K, H	F_0	F_c
3	90	−114	1	69	−51	H=7,		L=5	H=12,		L=5
H=0,		L=5	2	91	67	2	105	135	2	143	147
1	164	−112	4	165	174	3	84	104	H=13,		L=5
3	154	−174	5	172	−186	4	124	133	2	165	−204
5	139	−103	6	113	111	5	106	92	4	76	−103
7	271	−290	7	143	−120	6	102	96	H=14,		L=5
H=1,		L=5	8	101	−84	8	123	100	2	75	− 91
1	178	208	9	167	−168	10	58	50	K=0,		L=6
3	293	−322	11	155	−159	H=8,		L=5	0	898	900
6	111	122	H=5,		L=5	0	272	322	2	305	−355
8	100	80	1	213	−205	2	164	174	4	72	56
9	302	243	2	76	−52	3	156	−160	6	175	−165
10	90	72	3	131	−117	10	58	−47	8	207	223
H=2,		L=5	4	150	−165	H=9,		L=5	K=1,		L=6
1	58	43	5	132	−143	1	104	−76	2	72	− 85
4	105	−87	6	110	−98	4	129	−128	11	118	−127
5	286	293	7	81	56	5	206	−198	12	63	− 77
6	105	−105	8	125	−129	6	112	82	K=0,		L=7
7	274	228	9	85	61	9	65	90	4	116	138
8	97	84	11	125	132	H=10,		L=5	6	201	−206
9	124	133	H=6,		L=5	0	185	−163	8	222	226
11	66	84	0	268	−317	1	92	−91	K=1,		L=7
H=3,		L=5	1	166	205	2	111	−109	0	78	− 77
1	224	286	2	113	−125	3	134	152	1	96	111
3	168	159	3	109	122	H=11,		L=5	3	166	170
4	135	166	4	153	−168	1	155	130	5	100	−135
5	197	212	5	118	99	2	179	223	6	101	116
9	282	−267	6	37	27	3	134	133	K=0,		L=8
11	186	−175	7	178	179	4	263	268	0	548	539
H=4,		L=5	9	125	88	5	144	153	2	242	−232
0	261	233	10	68	−66	6	79	78			

RESULT AND DISCUSSION

The atomic labeling and interatomic distances and angles involving non-hydrogen atoms, uncorrected for thermal motion, are shown in *Fig.* 1 for the theophylline molecule. The cell parameter errors and coordinate standard deviation obtained from the least-squares refinement were used to calculate estimated standard deviations for the distance and angles.

X-ray diffraction investigation of a number of similar compounds have been reported; theophylline monohydrate[2], purine[7], caffeine[8], and 9-methylguanine hydrobromide[9]. The C(3)-O(1) and C(4)-O(2) bonds are 1.234 and 1.221Å respectively, indicating that the bonds are predominantly double bond in character and that molecule exists in the keto form. In uracil[10], and α-pyridone[11] the average of these bonds is 1.236Å, and in xanthazol[12] the two bonds are 1.21 and 1.24Å. The distance of 1.34Å between C(1)-N(2) appears to be significantly shorter than the other bond distances C(1)-N(1), C(5)-N(1), C(2)-N(2) which are 1.37, 1.38 and 1.36Å respectively, indicating that this bond has a large amount of duoble bond character.

The structure as viewed down *c* is shown in *Fig.* 2. The sheets of planar molecules are stacked parallel to the (001) planes, with an interplanar distance is 3.38Å. This stacking distance is similar to the values observed in a wide variety of purines; *e.g.* in purine itself the

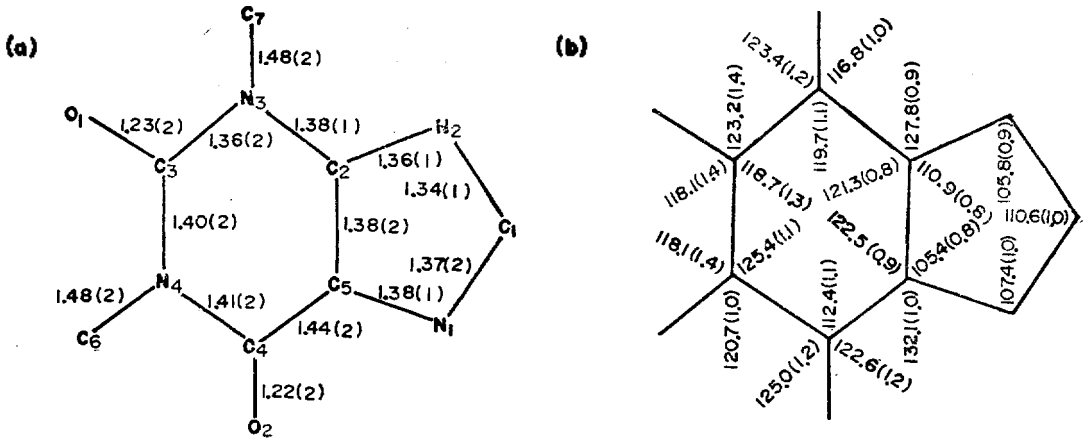

Fig. 1. (a) Interatomics distance and numbering of the atoms. (b) bond angles.

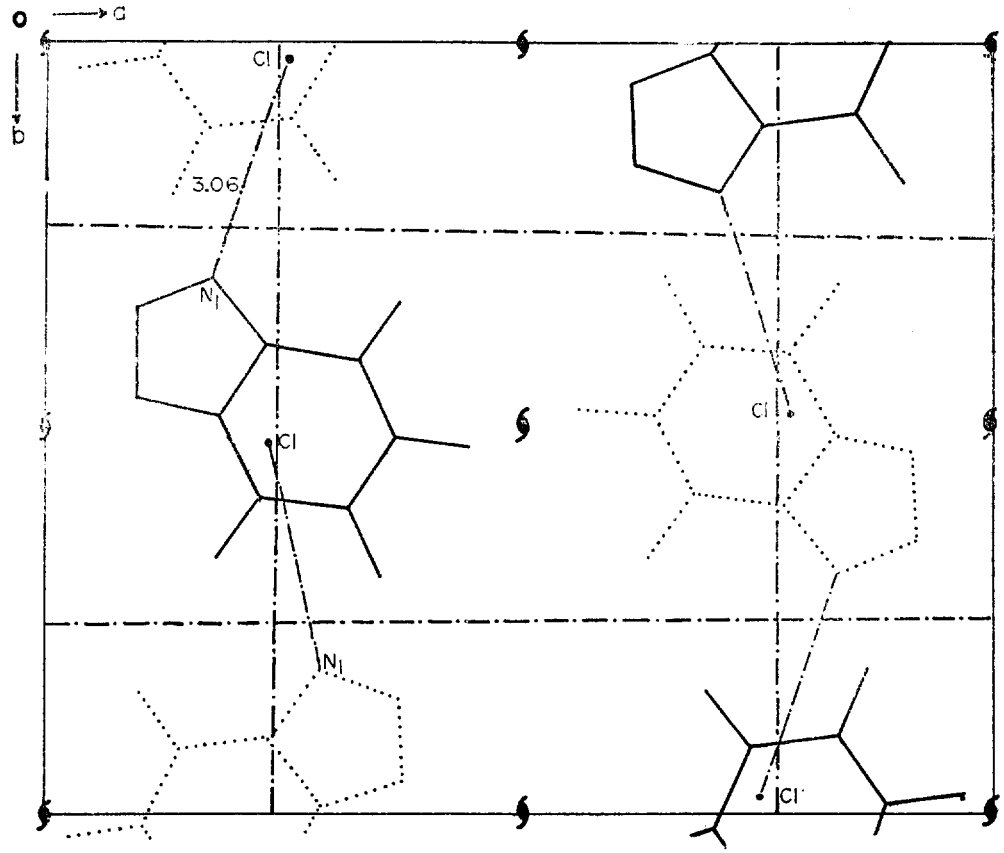

Fig. 2. Structure of theophylline hydrochloride viewed down the *c* axis.

distance is 3.39Å, within each layer of this system, there is no oppertunity for hydrogen bonding formation.

The chlorine atom is only 3.06Å from the N(1), and this immediately suggests the presence of an hydrogen bond between them. It is unfortunate that no indication of the site of the hydrogen atom of the HCl appeared in the structure analysis but it is possible that it is on the line joining N and Cl in direction.

In this crystal, the easy decomposition is explained by molecular packing and hydrogen bonding considerations.

REFERENCES

1. Martha Windholz *et al.*, "The Merck index", P. 471, Merck & Co., inc. N.J., USA, 1976.
2. D. June Sutor. *Acta cryst.*, **11**, 83 (1958).
3. A. J. C. Wilson, *Nature, Lond.* **150**, 152 (1942).
4. D. W. J. Cruickshank, "Computing Methods and the phase problem in X-ray Crystal Structure Analysis", Pergamon Press, N. Y., 1961.
5. R. Shiono, Crystallographic Computing Programs for the IBM System, Technical Report No. 49 (1971). Department of Crystallography, Univ. of Pittsburgh, Pa.
6. International Tables for X-ray Crystallography, (Kynoch Press, Birmingham 1968) Vol. 3, 202.
7. David G. Watson, Robert M. Sweet & Richard E. Marsh, *Acta. Cryst.*, **19**, 573 (1965).
8. D. June Sutor, *Acta Cryst.*, **11**, 453 (1958).
9. H. M. Sobell & Ken-Ichi Tomita, *Acta Cryst.*, **B 27**, 753 (1964).
10. G. S. Parry, *Acta Cryst.*, **4**, 313(1954).
11. B. R. Penford, *Acta Cryst.*, **6**, 591 (1956).
12. W. Nowacki &H. Burki, *Z. Kristallogr.*, **106**, 339 (1955).