On the Study of the Copper Chelates of Ephedrine and Related Compounds. II. The Crystal Structure of the Bis-l-ephedrine Copper(II) Chelate Benzene Clathlate

By Yoshiharu AMANO, Kenji OSAKI* and Tokunosuké WATANABÉ**

(Received April 23, 1964)

As is well known, when a copper(II) salt is added to an aqueous solution of *l*-ephedrine in the presence of alkali hydroxide, the color of the solution changes to blue-violet. If the mixture is extracted with *n*-hexane or benzene, a reddish-violet solution is obtained; from it well-defined crystals can be obtained. In a previous paper,[1] it was concluded that the crystal consisted of bis-*l*-ephedrine copper(II) chelate (abbreviated as ephedrine copper chelate in the following), and that the copper atom had a square-planar coordination.

Ephedrine copper chelate exhibits peculiar properties. It reacts at room temperature with carbon tetrachloride of other halogenated hydrocarbons, yielding chloride ions and the oxidation products of ephedrine.[2] It dissolves easily in non-polar solvents such as *n*-hexane in spite of having hydrophillic groups in its molecule.

In order to clarify the above-mentioned peculiar properties of the ephedrine copper chelate, a crystal structure analysis of this compound was conducted; the experimental results obtained and a discussion based on the structure will be presented below.

Experimental

Efforts were made to prepare single crystals of the ephedrine copper chelate, crystals suitable for X-ray crystal structure analysis. From a benzene solution, hexagonal plates or prisms a deep violet in color were obtained. These crystals have a cleavage plane parallel to the hexagonal basal plane. The examination, by means of ultraviolet absorption, of the volatile components of the solution obtained by dissolving these crystals in *n*-hexane showed the presence of a benzene molecule in the crystal. The results of the elemental analysis also suggest that the crystal contained two benzene

* Present address: Faculty of Pharmaceutical Sciences, Kyoto University, Kyoto.
** Present address: College of General Education, Osaka University, Toyonaka, Osaka.

1) T. Uno and Y. Amano, *Yakugaku Zasshi*, **82**, 1176 (1962).
2) Y. Amano and T. Uno, to be published.

TABLE I. ELEMENTAL ANALYSIS

	C, %	H, %	N, %	Cu, %
Found	65.11	7.232	6.287	14.34
Calcd.(1)	61.28	7.200	7.146	16.21
Calcd.(2)	64.91	7.256	6.310	14.31

(1) $(C_{10}H_{14}ON)_2 \cdot Cu$
(2) $(C_{10}H_{14}ON)_2 \cdot Cu \cdot 2/3C_6H_6$

molecules per three chelate molecules. The results of the elemental analysis are shown in Table I.

The unit cell dimensions were determined by precession photographs. These photographs show that the Laue symmetry of the crystal is $\bar{3}$m. There remain two possible space groups, P312 and P321, on the basis of the extinction rules and the Laue symmetry. In these two space groups, the mirror planes of the reciprocal lattice have different orientations with respect to the crystal axes. From the examination of the symmetry of the reciprocal lattice, it was found that there are mirror planes parallel to the a*c* planes. Therefore, it was concluded that the space group is P321-D_3^2 and that the a-axis is a two-fold axis. The density as calculated from the composition, $(C_{10}H_{14}ON)_2 \cdot Cu \cdot 2/3C_6H_6$, as was suggested by the elemental analysis, agreed with the observed value.

The specimens for the intensity measurements were cut out along the a- and c-axes from hexagonal plates or prisms. The sets of intensities were obtained from equi-inclination Weissenberg photographs using both multiple-films and varying exposures, with copper $K\alpha$ radiation filtered through nickel foil. The zeroth to third layers about the a-axis and the zeroth layer about the c-axis were recorded.

The intensities were estimated by visual comparison with a calibrated intensity scale prepared with the same specimen and reduced to the same scale.

Corrections for Lorentz and polarization factors were applied in the usual way, but none were made for absorptions since μr is 0.37 for the a-axis specimen and 0.47 for the c-axis specimen. The preliminary scale factor and temperature factors were determined by Wilson's method and were further improved during the later stages of the refinements. The crystallographic data are shown in Table II.

TABLE II. CRYSTALLOGRAPHIC DATA

$a=11.89$ Å $c=15.32$ Å
Laue symmetry : $\bar{3}$m
Space group : P321-D_3^2
Three formula units per unit cell
Volume of unit cell : 1875.7 Å^3
Linear absorption coefficient for Cu$K\alpha$ rapiation : 14.78 cm^{-1}
Density
observed : 1.20 g./cm^3
calculated : 1.18 g./cm^3

TABLE III. COMPARISON OF STATISTICALLY DISTRIBUTED BENZENE MOLECULE AND FOUR SETS OF FIXED BENZENE MOLECULE

	Coordinates x	y	z	Corresponding R value %
1	Statistically distributed			16.3
2	0.3333	0.5482	0.3650	16.3
	0.2149	0.5482	0.3650	
3	0.2967	0.5343	0.3650	15.9
	0.2011	0.5699	0.3650	
4	0.2636	0.5302	0.3650	16.5
	0.1968	0.5985	0.3650	
5	0.2365	0.5343	0.3650	16.2
	0.2011	0.6305	0.3650	

TABLE IV. THE FINAL ATOMIC COORDINATES AND THE THERMAL PARAMETERS

Atom	Coordinates x	y	z	Thermal parameter
Cu	0.0000	0.1977	0.0000	7.3
O	−0.1084	0.1260	0.0980	6.7
N	0.1446	0.2910	0.0906	6.2
C(1)	−0.2444	0.1517	0.2403	7.3
C(2)	−0.3169	0.1552	0.3141	8.2
C(3)	−0.2766	0.1541	0.4025	10.1
C(4)	−0.1637	0.1497	0.4096	10.3
C(5)	−0.0855	0.1552	0.3368	8.2
C(6)	−0.1184	0.1504	0.2501	7.9
C(7)	−0.0355	0.1498	0.1761	6.5
C(8)	0.0782	0.2982	0.1707	8.1
C(9)	0.0337	0.3986	0.1593	8.0
C(10)	0.2561	0.4170	0.0633	7.8
C(B1)	0.3333	0.5482	0.3655	9.6
C(B2)	0.2967	0.5343	0.3655	9.6
C(B3)	0.2636	0.5302	0.3655	9.6
C(B4)	0.2365	0.5343	0.3655	9.6
C(B5)	0.2149	0.5482	0.3660	9.3
C(B6)	0.2011	0.5699	0.3660	9.3
C(B7)	0.1968	0.5985	0.3660	9.3
C(B8)	0.2011	0.6305	0.3660	9.3

The Determination of the Structure

The number of atoms in the unit cell gives the following information. The copper atoms must lie on the two-fold symmetry axis, so that the chelate molecule has the two-fold rotational symmetry. The center of the solvated benzene molecule lies on the three-fold axis.

Because the a-axis is shorter than the c-axis, we first attempted to proceed with a projection corresponding to the $(h0l)$ reflections and to use the other layer-line spectra to confirm the structure. The sharpened Patterson synthesis using the $(h0l)$ reflections showed that the copper atom was located at a position with $x=0$, $y=0.1935$, and $z=0$. This conclusion agreed with the results of the vector analysis.

A trial model was set up from this Patterson map using the vector convergence diagram method and also on the basis of the molecular packing. The solvated benzene molecules were disregarded at this stage.

On the basis of this trial model, the values of the $F(h0l)$ were calculated. From a comparison of these with the observed structure amplitudes, it was possible to deduce the signs of about one-third of all the $F(h0l)$ reflections obtained. Using these signs, the first Fourier synthesis was calculated. In this projection, there appeared, in addition to the expected peaks of the atoms of the copper chelate, an extended hill-like cluster almost perpendicular to the z-axis and symmetrically situated with respect to the three-fold axis. It was suggested that this hill-like cluster be the projected structure of the solvated benzene molecule. This was thought admissible because the space which the benzene molecule is to occupy corresponds to quite a large hole between the copper chelates. It was further suggested that the six carbon atoms of the benzene molecule are statistically distributed along the ring which has a radius of 1.39Å. Therefore, the effect of the benzene molecule was added in the following computations of the structure factor, where each carbon atom was assumed to lie at four equally-spaced positions with a weight of 1/4.

After several successive Fourier and difference Fourier refinements, the R values for 259 $F(h0l)$ and 49 $F(hk0)$ reflections became 26.5% and 18.8% respectively.

The Refinement of the Structure

The positional and thermal parameters were refined by the three-dimensional least-squares method using the $(h0l)$, $(h1l)$, $(h2l)$ and $(h3l)$ structure factors. The positional and isotropic individual thermal parameters were refined by disregarding the off-diagonal terms other than the x, y-interaction terms, to minimize the value of $\sum w||F_o|^2-|F_c|^2|^2$. The weights applied to the terms were:

TABLE V

h	k	l	$\|F_o\|$	F_c	h	k	l	$\|F_o\|$	F_c	h	k	l	$\|F_o\|$	F_c
0	0	2	4.77	−12.78	1	0	−3	34.87	32.73	2	0	−7	28.71	36.31
		3	74.97	82.79			−4	39.29	40.97			−8	7.53	−6.11
		4	62.25	−67.84			−5	10.84	−11.99			−9	11.80	−18.63
		5	50.11	58.71			−6	33.37	37.50			−10	12.88	−18.52
		6	17.90	19.72			−7	18.50	25.38			−11	20.13	−6.32
		7	4.77	4.72			−8	0.00	3.47			−12	12.94	−9.83
		8	29.72	30.92			−9	25.79	31.44	3	0	0	81.71	−84.56
		9	15.27	15.93			−10	5.08	3.67			1	9.74	8.64
		10	21.07	22.31			−11	14.44	16.32			2	1.80	6.62
		11	29.96	32.04			−12	18.59	22.46			3	11.24	−15.69
		12	34.70	41.05			−13	3.44	−3.62			4	27.29	25.70
		13	12.54	17.27	2	0	0	119.84	−113.35			5	8.63	6.85
		14	0.00	−1.93			1	51.79	55.98			6	12.57	15.77
		15	0.00	−2.19			2	98.67	−94.17			7	8.02	8.95
		16	0.00	2.92			3	34.52	−36.30			8	16.38	−16.55
		17	6.37	4.42			4	11.40	−5.70			9	10.28	−14.33
1	0	1	92.99	88.76			5	3.47	−3.52			10	9.82	−12.56
		2	16.90	16.48			6	22.61	28.43			11	6.94	−9.75
		3	45.75	−43.55			7	23.67	−21.09			−1	40.54	−41.80
		4	10.40	12.80			8	10.50	−11.99			−2	28.38	−29.00
		5	38.09	37.37			9	5.58	3.55			−3	47.93	−47.97
		6	11.68	−8.72			10	3.66	5.63			−4	22.17	−23.45
		7	14.16	16.90			11	6.73	−6.85			−5	0.00	6.45
		8	17.36	17.89			12	5.78	−8.58			−6	15.99	19.63
		9	10.91	10.64			13	7.33	2.91			−7	0.00	6.97
		10	26.84	33.88			−1	78.20	−87.20			−8	0.00	5.22
		11	7.78	18.65			−2	68.01	79.66			−9	9.64	−11.39
		12	14.05	13.06			−3	12.06	−12.34			−10	10.72	−8.84
		13	8.42	9.74			−4	15.74	20.31			−11	5.65	−2.80
		−1	88.87	85.50			−5	8.84	−8.52			−12	12.94	−12.58
		−2	35.13	34.46			−6	14.08	11.20	4	0	0	12.45	−10.64

TABLE V (continued)

h k	l	$\|F_o\|$	F_c	h k	l	$\|F_o\|$	F_c	h k	l	$\|F_o\|$	F_c
4 0	1	30.20	26.80	6 0	1	10.67	−12.88	8 0	−8	4.25	−1.86
	2	35.37	32.21		2	3.34	2.73	9 0	0	3.47	0.21
	3	45.83	46.67		3	11.93	11.49		1	6.00	4.05
	4	44.12	45.45		4	19.73	16.02		2	0.00	2.56
	5	16.27	15.30		5	19.26	18.90		3	0.00	−0.52
	6	35.13	33.59		6	16.20	16.49		4	0.00	−5.94
	7	15.67	14.17		7	19.82	18.23		5	0.00	1.40
	8	4.59	−2.70		8	8.38	4.33		6	7.33	4.93
	9	0.00	−0.28		9	10.18	6.03		7	0.00	1.27
	10	0.00	−1.00		10	12.06	10.74		8	7.47	6.48
	11	10.63	8.17		11	8.17	5.50		9	7.85	5.71
	12	3.44	4.32		−1	33.83	33.78		−1	4.89	3.76
	13	3.47	4.93		−2	29.52	27.74		−2	10.67	10.04
	14	8.34	7.08		−3	27.19	19.32		−3	11.51	11.55
	−1	2.05	−6.67		−4	5.24	10.85		−4	5.50	9.87
	−2	17.36	13.88		−5	10.67	10.67		−5	0.00	−0.31
	−3	8.70	13.00		−6	7.50	11.36		−6	0.00	0.62
	−4	7.82	6.90		−7	8.42	11.54		−7	2.41	3.02
	−5	38.81	38.86		−8	4.03	1.08	10 0	0	8.76	1.92
	−6	27.49	31.64		−9	0.00	4.68		1	11.41	7.54
	−7	9.64	13.18		−10	7.33	8.40		2	10.28	8.96
	−8	19.45	23.96		−11	3.47	2.11		3	5.90	2.47
	−9	10.55	13.33		−12	7.67	5.93		4	8.93	5.59
	−10	8.24	10.15		−13	7.75	7.25		5	9.96	6.38
5 0	0	32.80	31.61		−14	4.89	3.19		6	7.96	5.82
	1	10.28	2.53	7 0	0	16.45	19.32		7	6.29	5.58
	2	53.92	55.73		1	5.21	1.57		8	4.25	3.80
	3	30.15	27.39		2	0.00	−4.69		9	2.80	2.84
	4	38.09	32.15		3	0.00	−5.80		10	2.60	1.73
	5	55.25	54.04		4	6.29	−6.00		−1	10.01	3.93
	6	44.27	36.07		5	8.51	−5.94		−2	9.08	3.94
	7	27.40	25.27		6	13.40	−16.67		−3	7.62	6.76
	8	17.19	17.24		−1	0.00	0.87		−4	5.33	4.96
	9	9.69	5.13		−2	0.00	4.00		−5	5.26	4.02
	10	8.56	1.52		−3	0.00	4.40		−6	9.47	5.63
	11	11.51	9.28		−4	0.00	−4.40		−7	7.72	3.80
	12	6.52	6.19		−5	8.51	−6.61		−8	4.25	3.15
	13	0.00	3.79		−6	19.23	−18.64		−9	2.80	2.28
	14	6.62	6.53		−7	10.92	−8.42		−10	4.49	2.98
	15	5.31	5.23		−8	4.21	−2.26		−11	3.98	2.44
	16	4.28	4.08	8 0	0	0.00	3.51	11 0	0	0.00	−0.66
	−1	65.56	69.61		1	8.38	12.20		1	0.00	0.71
	−2	10.90	10.13		2	0.00	−7.37		2	7.96	6.36
	−3	24.23	25.07		3	0.00	−3.74		3	8.71	6.44
	−4	33.91	36.41		4	9.84	−7.46		4	7.35	4.48
	−5	35.60	37.59		5	15.27	−15.58		−1	0.00	0.87
	−6	34.00	35.42		6	8.80	−8.32		−2	0.00	−1.14
	−7	18.91	20.17		7	0.00	−0.51		−3	0.00	−0.56
	−8	17.89	19.03		8	8.17	5.61		−4	0.00	1.04
	−9	11.44	9.45		−1	10.63	−5.80		−5	5.50	2.75
	−10	9.50	8.71		−2	7.01	−1.46		−6	4.84	3.67
	−11	8.46	7.46		−3	4.72	−5.24		−7	4.21	3.01
	−12	9.19	5.89		−4	0.00	3.54		−8	4.28	2.62
	−13	11.39	9.54		−5	4.18	−3.02		−9	3.47	2.03
	−14	6.17	5.54		−6	13.57	−11.54				
6 0	0	15.40	18.18		−7	9.84	−8.96				

TABLE V (continued)

h k	*l*	$\|F_o\|$	$\|F_c\|$	A_c	B_c	*h k*	*l*	$\|F_o\|$	$\|F_c\|$	A_c	B_c
0 1	2	29.45	34.46	34.46	0.00	3 1	4	30.84	33.73	−0.83	33.72
	3	35.55	32.73	32.73	0.00		5	25.54	24.34	−11.12	21.66
	4	40.38	40.97	40.97	0.00		6	20.93	18.90	−15.21	11.21
	5	10.18	11.99	−11.99	0.00		7	14.64	13.94	1.41	13.87
	6	35.02	37.50	37.50	0.00		8	9.36	2.05	−1.88	0.81
	7	20.02	25.38	25.38	0.00		−1	41.56	43.02	−34.70	25.42
	8	0.00	3.47	3.47	0.00		−2	38.01	37.66	−27.97	25.20
	9	22.58	31.44	31.44	0.00		−3	17.51	18.06	−0.29	18.06
	10	9.74	3.67	3.67	0.00		−4	7.26	11.05	−9.42	−5.79
	11	10.38	16.32	16.32	0.00		−5	20.01	21.83	3.33	21.57
	−2	13.34	16.48	16.48	0.00		−6	14.41	18.89	3.89	18.48
	−3	40.60	43.55	−43.55	0.00		−7	0.00	15.17	−10.32	11.11
	−4	7.20	12.80	12.80	0.00		−8	13.23	12.51	4.15	11.80
	−5	35.82	37.37	37.37	0.00	4 1	0	26.41	21.45	20.17	7.30
	−6	9.71	8.72	−8.72	0.00		1	35.82	35.93	28.25	22.20
	−7	13.64	16.90	16.90	0.00		2	30.67	31.74	28.10	−14.77
	−8	15.96	17.89	17.89	0.00		3	24.71	23.00	20.38	−10.66
	−9	0.00	10.64	10.64	0.00		4	12.98	17.62	17.61	0.59
	−10	32.33	33.88	33.88	0.00		5	11.29	9.37	7.83	5.14
	−11	16.42	18.65	18.65	0.00		6	17.41	17.62	16.22	−6.88
1 1	0	71.53	61.74	−41.37	45.15		7	12.57	17.68	15.76	−8.01
	1	67.23	67.09	−37.12	55.87		−1	30.91	27.10	21.08	−17.03
	2	4.59	7.46	2.54	7.01		−2	16.20	22.73	7.85	21.33
	3	38.69	36.46	30.81	−19.49		−3	23.45	22.72	21.47	7.41
	4	7.66	11.86	−10.57	5.38		−4	28.45	35.36	35.15	3.81
	5	28.65	30.42	2.92	30.28		−5	19.55	17.07	15.96	6.05
	6	45.04	52.04	12.89	50.42		−6	21.57	17.13	16.02	−6.06
	7	21.80	27.81	−12.46	25.01		−7	13.44	17.01	15.39	7.24
2 1	0	92.15	93.63	−30.60	88.49	5 1	0	32.58	32.70	6.62	−32.02
	1	17.83	24.70	−22.64	9.87		1	0.00	12.26	10.46	6.40
	2	41.49	41.88	−14.54	39.27		2	0.00	6.55	2.80	5.92
	3	51.24	50.35	−8.10	49.70		3	8.34	12.07	10.30	−6.28
	4	45.25	45.52	−9.07	44.61		4	19.53	16.49	16.48	−0.57
	5	44.24	43.21	−6.30	42.74		5	22.91	21.05	21.03	−0.79
	6	49.64	48.13	−28.18	39.02		6	20.35	22.49	22.35	2.56
	7	27.23	27.98	−18.65	20.86		7	14.50	17.81	17.78	1.10
	8	0.00	16.48	−15.80	4.70		8	10.70	15.54	15.54	−0.26
	9	21.23	20.99	−12.12	17.14		−1	35.11	26.11	20.56	−16.10
	10	22.66	14.49	−9.28	11.13		−2	36.02	30.58	29.45	8.20
	11	17.02	22.16	−18.53	12.16		−3	15.94	10.59	10.13	3.09
	12	11.23	15.83	−5.83	14.71		−4	20.36	20.17	18.41	8.23
	−1	93.90	96.34	−57.19	77.52		−5	23.58	26.60	26.57	1.22
	−2	24.58	23.52	−22.29	7.49		−6	16.52	17.22	17.16	−1.43
	−3	36.75	33.35	−10.50	31.65	6 1	0	0.00	4.57	−1.99	−4.11
	−4	13.71	16.61	−5.91	15.52		1	0.00	9.02	−1.73	8.85
	−5	25.70	27.07	−13.50	23.46		2	14.52	20.21	−6.82	19.02
	−6	42.49	41.54	−27.24	31.36		3	9.85	13.69	−9.54	9.81
	−7	13.73	21.43	−7.51	20.08		−1	0.00	4.76	1.01	4.65
	−8	19.32	22.30	−12.17	18.69		−2	19.36	11.33	9.20	6.62
	−9	20.38	23.15	−18.32	14.16	7 1	0	15.94	6.29	−0.16	6.29
	−10	17.55	21.76	−12.51	17.80		1	0.00	4.70	0.60	4.67
	−11	16.15	17.89	−12.64	12.65		2	10.64	14.56	−0.11	14.56
3 1	0	78.35	72.69	−8.75	72.16		3	20.85	14.56	−4.74	13.77
	1	32.75	32.07	7.99	31.06		4	15.44	15.33	−5.25	14.40
	2	18.58	22.80	22.76	−1.38		−1	24.58	21.99	−8.23	20.40
	3	23.79	22.54	7.26	21.34		−2	23.79	21.73	−16.33	14.33

TABLE V (continued)

h	k	l	$\|F_o\|$	$\|F_c\|$	A_c	B_c
7	1	−3	18.65	11.30	−9.09	6.70
−1	2	3	37.26	36.46	30.81	19.49
		4	10.45	11.86	−10.57	−5.38
		5	29.60	30.42	−2.92	−30.28
		6	45.12	52.04	12.89	−50.42
		7	24.28	27.81	−12.16	−25.01
0	2	2	77.10	79.66	79.66	0.00
		3	15.38	12.34	−12.34	0.00
		4	17.42	20.31	20.31	0.00
		5	6.35	8.52	−8.52	0.00
		6	9.89	11.20	11.20	0.00
		7	31.32	36.31	36.31	0.00
		8	0.00	6.11	−6.11	0.00
		9	0.00	18.63	−18.63	0.00
		10	22.05	18.52	−18.52	0.00
		−2	89.19	94.17	−94.17	0.00
		−3	31.95	36.30	−36.30	0.00
		−4	11.30	5.70	−5.70	0.00
		−5	0.00	3.51	−3.52	0.00
		−6	23.72	28.43	28.43	0.00
		−7	25.57	21.09	−21.09	0.00
1	2	0	91.28	93.63	−30.60	88.49
		1	101.12	96.34	−57.19	77.52
		2	28.82	23.52	−22.29	7.49
		3	37.64	33.35	−10.50	31.65
		4	16.96	16.61	−5.91	15.52
		5	28.43	27.07	−13.50	23.46
		6	43.17	41.54	−27.24	31.36
		7	17.60	21.43	−7.51	20.08
		8	24.68	22.30	−12.17	18.69
		9	26.23	23.15	−18.32	14.16
		10	24.77	21.76	−12.51	17.80
		11	21.51	17.89	−12.64	12.65
		−1	21.62	24.70	−22.64	9.87
		−2	44.23	41.88	−14.54	39.27
		−3	54.27	50.35	−8.10	49.70
		−4	50.70	45.52	−9.07	44.61
		−5	45.16	43.21	−6.30	42.74
		−6	52.35	48.13	−28.18	39.02
		−7	25.55	27.98	−18.65	20.86
		−8	12.34	16.46	−15.80	4.70
		−9	20.57	20.99	−12.12	17.14
		−10	14.30	14.49	−9.28	11.13
		−11	22.17	22.16	−18.53	12.16
2	2	0	25.32	23.21	10.35	20.77
		1	45.90	46.60	−9.24	45.67
		2	41.26	38.32	−11.71	36.48
		3	42.58	34.56	−27.51	20.92
		4	38.88	38.04	−17.63	33.71
		5	49.47	43.87	−26.13	35.24
		6	62.56	62.59	−54.78	30.27
		7	22.86	24.81	−18.43	16.60
		8	20.33	21.33	−5.81	20.52
		9	20.25	17.10	−3.81	16.67
		10	17.35	12.47	−3.74	11.90
		11	15.56	17.70	−4.80	17.04
3	2	0	49.68	45.88	44.31	−11.91
		1	24.57	20.78	18.40	9.66
		2	15.09	17.26	−15.74	7.07
		3	9.05	6.81	−5.38	−4.16
		4	42.26	44.38	−44.37	−1.28
		5	40.20	36.21	−36.17	−1.78
		6	17.37	18.35	−11.01	14.68
		7	17.29	15.47	−14.45	5.52
		−1	9.83	13.39	−13.05	−3.00
		−2	10.06	9.52	−6.77	−6.69
		−3	0.00	10.58	−7.68	−7.28
		−4	23.34	20.49	−20.25	−3.16
		−5	22.47	18.88	−18.58	3.34
		−6	26.06	27.24	−23.16	14.34
4	2	0	24.52	21.06	12.56	−16.91
		1	0.00	12.44	−8.09	−9.45
		2	0.00	8.96	−5.88	6.76
		3	0.00	4.28	0.10	−4.28
		4	15.66	15.26	−14.28	−5.36
		5	14.42	14.65	0.95	−14.62
		−1	32.40	25.68	8.60	−24.19
		−2	31.09	26.59	−0.62	−26.58
		−3	22.17	18.14	11.62	−13.93
		−4	12.28	12.32	4.61	−11.42
		−5	16.42	15.29	−14.56	−4.67
		−6	22.81	19.47	−6.00	−18.52
		−7	19.30	20.01	−9.79	−17.45
5	2	0	15.71	15.87	−15.74	−2.01
		1	0.00	8.68	−1.87	8.48
		2	18.44	21.74	−20.39	7.53
		3	18.21	15.78	−15.20	4.27
		−1	0.00	15.43	−8.55	−12.84
6	2	0	21.50	18.19	−12.83	12.88
		1	20.33	13.14	−4.46	12.36
		2	19.86	17.84	−4.81	17.18
		3	23.25	16.68	−12.95	10.52
		−1	25.92	16.12	−11.00	11.77
		−2	26.14	20.31	−17.49	10.33
		−3	23.25	17.85	−9.98	14.80
		−4	27.01	23.02	−9.08	21.16
		−5	20.29	14.30	−5.82	13.06
7	2	0	25.92	16.17	−13.89	8.28
		1	15.64	11.80	−9.47	7.03
		2	13.62	5.51	−2.92	4.68
		−1	22.12	14.99	−10.31	10.87
		−2	21.55	15.47	−11.62	10.21
		−3	20.99	15.22	−11.18	10.32
−1	3	2	23.19	23.52	−22.29	−7.49
		3	37.62	33.35	−10.50	−31.65
		4	18.88	16.61	−5.91	−15.52
		5	29.53	27.07	−13.50	−23.46
		6	45.66	41.54	−27.24	−31.36
		7	21.68	21.43	−7.51	−20.08
		8	24.62	22.30	−12.17	−18.69
		9	28.13	23.15	−18.32	−14.16
		10	23.88	21.76	−12.51	−17.80

TABLE V (continued)

h k	*l*	$\|F_o\|$	$\|F_c\|$	A_c	B_c
−1 3	11	17.99	17.89	−12.65	−12.65
	12	11.68	13.49	−9.69	−9.39
	−2	37.20	41.88	−14.54	−39.27
	−3	49.59	50.35	−8.10	−49.70
	−4	47.73	45.52	−9.07	−44.61
	−5	46.07	43.21	−6.30	−42.74
	−6	52.93	48.13	−28.18	−39.02
	−7	30.00	27.98	−18.65	−20.86
	−8	9.78	16.48	−15.80	−4.70
	−9	19.89	20.99	−12.12	−17.14
	−10	16.22	14.49	−9.28	−11.13
	−11	18.67	22.16	−18.53	−12.16
	−12	10.44	15.83	−5.83	−14.71
0 3	0	80.12	84.56	−84.56	0.00
	1	43.58	41.80	−41.80	0.00
	2	31.92	29.00	−29.00	0.00
	3	54.44	47.97	−47.97	0.00
	4	25.69	23.45	−23.45	0.00
	5	5.43	6.45	6.45	0.00
	6	19.52	19.63	19.63	0.00
	−1	9.85	8.64	8.64	0.00
	−2	5.02	6.62	6.62	0.00
	−3	14.13	15.69	−15.69	0.00
	−4	31.47	25.70	25.70	0.00
	−5	6.26	6.85	6.85	0.00
	−6	11.44	15.77	15.77	0.00
	−7	7.55	8.95	8.95	0.00
	−8	13.60	16.55	−16.55	0.00
1 3	0	79.88	72.69	−8.75	72.16
	1	47.11	43.02	−34.70	25.42
	2	42.00	37.65	−27.97	25.20
	3	22.02	18.06	−0.29	18.06
	4	7.02	11.05	−9.42	−5.79
	5	26.10	21.83	3.33	21.57
	6	16.85	18.89	3.89	18.48
	7	7.43	15.17	−10.32	11.11
	8	8.57	12.51	4.15	11.80
	−1	36.01	32.01	7.99	31.06
	−2	23.10	22.80	22.76	−1.38
	−3	28.87	22.54	7.26	21.34
	−4	37.44	33.73	−0.83	33.72
	−5	30.01	24.34	−11.12	21.66
	−6	23.83	18.90	−15.21	11.21
	−7	15.13	13.94	1.41	13.87
	−8	11.81	2.05	−1.88	0.81
2 3	0	41.83	45.88	44.31	−11.91
2 3	1	10.24	13.39	−13.05	−3.00
	2	0.00	9.52	−6.77	−6.69
	3	14.49	10.58	−7.68	−7.28
	4	23.35	20.49	−20.25	−3.16
	5	21.87	18.88	−18.58	3.34
	6	25.83	27.24	−23.16	14.34
	−1	26.21	20.78	18.40	9.66
	−2	12.76	17.26	−15.74	7.07
	−3	6.65	6.81	−5.38	−4.16
	−4	46.71	44.38	−44.37	−1.28
	−5	41.94	36.21	−36.17	−1.78
	−6	21.83	18.35	−11.01	14.68
	−7	10.86	15.47	−14.46	5.52
3 3	0	7.54	13.73	2.28	−13.54
	1	28.36	24.71	5.22	−24.15
	2	31.41	29.05	−10.61	−27.04
	3	28.80	27.85	−17.50	−21.66
	4	34.74	29.17	−16.13	−24.30
	5	39.13	35.63	−30.28	−18.78
	6	30.29	26.86	−24.16	−11.72
	7	22.52	18.66	−14.31	−11.97
	8	13.81	16.01	−5.14	−15.16
4 3	0	26.08	22.29	−18.91	−11.78
	1	27.16	21.74	−19.19	−10.20
	2	32.24	26.95	−14.99	−22.39
	3	26.25	20.92	−8.76	−19.00
	4	17.01	13.84	−9.88	−9.69
	5	22.64	20.08	−7.50	−18.63
	6	19.55	17.33	−5.19	−16.53
	7	11.52	11.58	−9.86	−6.06
	−1	25.58	20.40	−6.46	−19.35
	−2	29.72	25.50	−6.00	−24.78
	−3	33.54	28.09	−8.39	−26.81
	−4	27.78	23.51	−8.42	−21.95
	−5	19.74	18.44	−15.10	−10.58
	−6	20.12	18.15	−10.59	−14.74
	−7	19.66	20.91	−6.79	−19.77
5 3	0	9.15	4.98	−4.88	−0.96
	1	0.00	2.37	−2.18	−0.93
	−1	0.00	13.44	−13.01	−3.39
	−4	12.80	9.95	−8.96	4.34
	−5	0.00	3.94	−0.20	−3.94
	−6	10.19	5.47	3.03	−4.55
6 3	0	0.00	5.54	−1.48	5.34
	1	0.00	7.17	−2.83	6.59
	−1	11.29	10.78	−7.41	7.84

$w=0.25$ for $|F_o|\leq 5$

$w=|F_o|/20$ for $5\leq|F_o|\leq 20$

$w=1.0$ for $20\leq|F_o|\leq 30$

$w=30/|F_o|$ for $30\leq|F_o|$

After each cycle of the refinements, the positional and thermal parameters of the atoms of the copper chelate were improved. Those of the carbon atoms of the benzene molecule, however, showed unreasonable shifts. Therefore, no shifts were applied to the parameters of the benzene molecule. After several cycles of least-squares, the R value was reduced to 16.3% for all the reflections used, including the non-observed reflections.

At this stage, we tried to see if any model of the structure with the benzene molecule at

a definite orientation would improve the structure factors. The structure factors were calculated by using the parameters obtained for the atoms of the copper chelate, and by adding the contribution of the benzene molecule in either of the four sets of coordinates listed in Table III. No significant differences were found in the R values among the four sets of the carbon atoms and the statistical model described earlier. However, the R value increased to 23.1% if we disregarded the contributions of the benzene molecule. The final set of positional and thermal parameters corresponding to the statistical model is listed in Table IV. The observed and calculated structure factors are reproduced in Table V.

A Description and Discussion of the Structure

The intermolecular bond lengths and angles of the copper chelate molecule as calculated on the basis of the above atomic parameters are shown in Fig. 1. Although the accuracy of the results is not still adequate to enable us to discuss the bond lengths and angles quantitatively, the overall stereochemical relation of the atoms in the copper chelate molecule and the mutual disposition of the copper chelates are clear.

Molecular Structure. — In a previously reported paper,[1] it was concluded that the hydrogen atom of the alcoholic hydroxyl group of the ephedrine molecule was replaced by the copper ion in the chelate formation, and also that the chelate ring was built by a four-coordinated square-planar configuration. The results of the X-ray crystal structure analysis not only confirmed the above prediction, but also led to useful information about the structure, as will be described below.

The copper atom lies on the two-fold rotational axis and is surrounded by two oxygen and two nitrogen atoms in a square configuration. These four atoms are almost coplanar with the copper atom, and there are no atoms

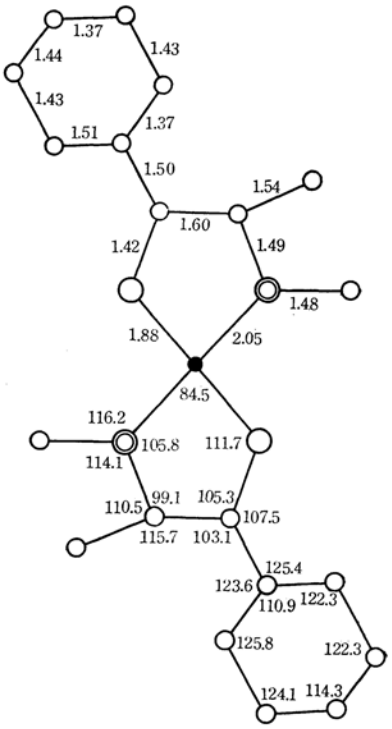

Fig. 1. Interatomic bond lengths and angles.

between the copper atoms in the adjacent unit cells in the direction perpendicular to the plane of the square. As is well known, however, the majority of cupric compounds, have distorted octahedral configurations, in agreement with the conclusions of the theory of Orgel[3] based on the Jahn-Teller effect.[4] In the ephedrine copper chelate, therefore, its configuration can be regarded as a limiting case of the usual distorted octahedral configuration with two ligands completely removed. This configuration of the copper chelate coordinated through the alcoholic hydroxyl group of the ephedrine molecule, without using two available orbitals, would be related to the peculiar property of the ephedrine copper chelate, namely, its reactivity with the halogenated hydrocarbons,[2] and also

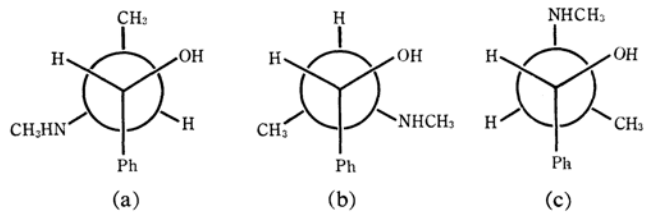

Fig. 2. Conformations of ephedrine molecule.

3) L. E. Orgel, *J. Chem. Soc.*, **1952**, 4756.

4) L. E. Orgel and J. D. Dunitz, *Nature, Lond.*, **179**, 462 (1957).

to its light absorption associated with copper-(II), which has its maximum at 518 mμ.

With respect to the ephedrine molecule, there are three possible conformations (cf. Figs. 2 (a), (b) and (c)). Conformation (a) has been proposed for the free ephedrine molecule by Close.[5] For the ephedrine molecule of the copper chelate, however, there remain two possible conformations, (b) and (c), bacause the nitrogen and oxygen atoms must be close together to form a chelate with the copper atom. The conformation of the ephedrine molecule of the copper chelate as found by present investigation is concluded to be the conformation (c), which is the same as that reported for ephedrine hydrochloride.[6]

Intermolecular Relation of the Chelate.— Although the positions of the hydrogen atoms were not determined, the existence of the hydrogen bonds can be inferred from the observed interatomic distances and from the possible distribution of the hydrogen atoms. In this crystal, three chelate molecules related by the three-fold symmetry form a trimer structure by means of six hydrogen bonds, as is shown in Fig. 3. In this trimer structure, the normals of the three square planes formed by the copper, oxygen and nitrogen atoms point to the three-fold symmetry axis. The distance between the two copper atoms in the trimer molecule is 4.07 Å, which is the shortest copper-copper atom distance in this crystal. There will be no direct coupling between these copper atoms. The main force forming the trimer structure would be the six intermolecular hydrogen bonds of the NH···O type.

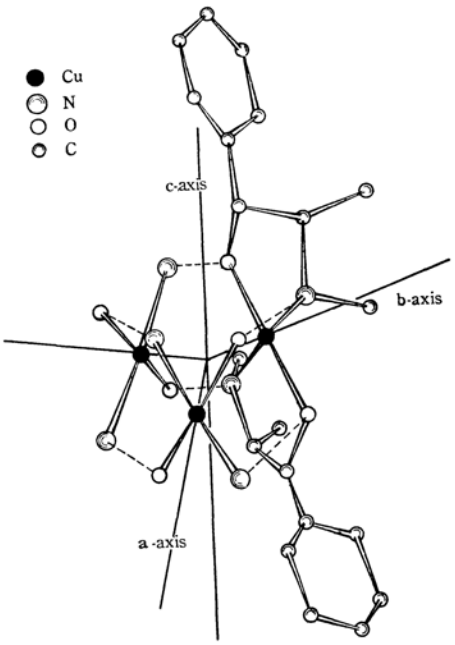

Fig. 3. Trimer structure of chelate molecule.

An infrared absorption spectrum of the crystal had already shown the presence of a hydrogen-bonded N–H stretching band, the type of molecular association which existed in the crystal had not yet been determined. This problem can now be interpreted, without any doubt, on the basis of the trimer structure of the chelate molecule described above. The observed absorption frequeny, 3130 cm^{-1}, in the infrared absorption spectrum agrees well with the value

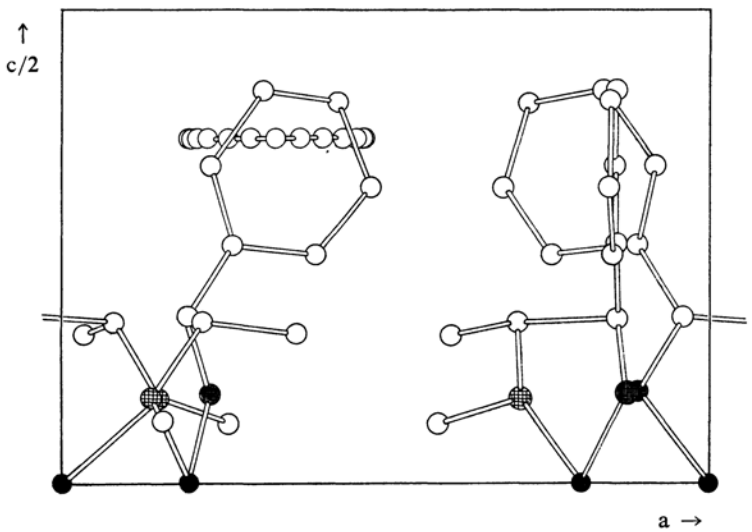

Fig. 4. Projection along b-axis.

5) W. J. Close, *J. Org. Chem.*, **15**, 1131 (1950).

6) D. C. Phillips, *Acta Cryst.*, **7**, 159 (1954).

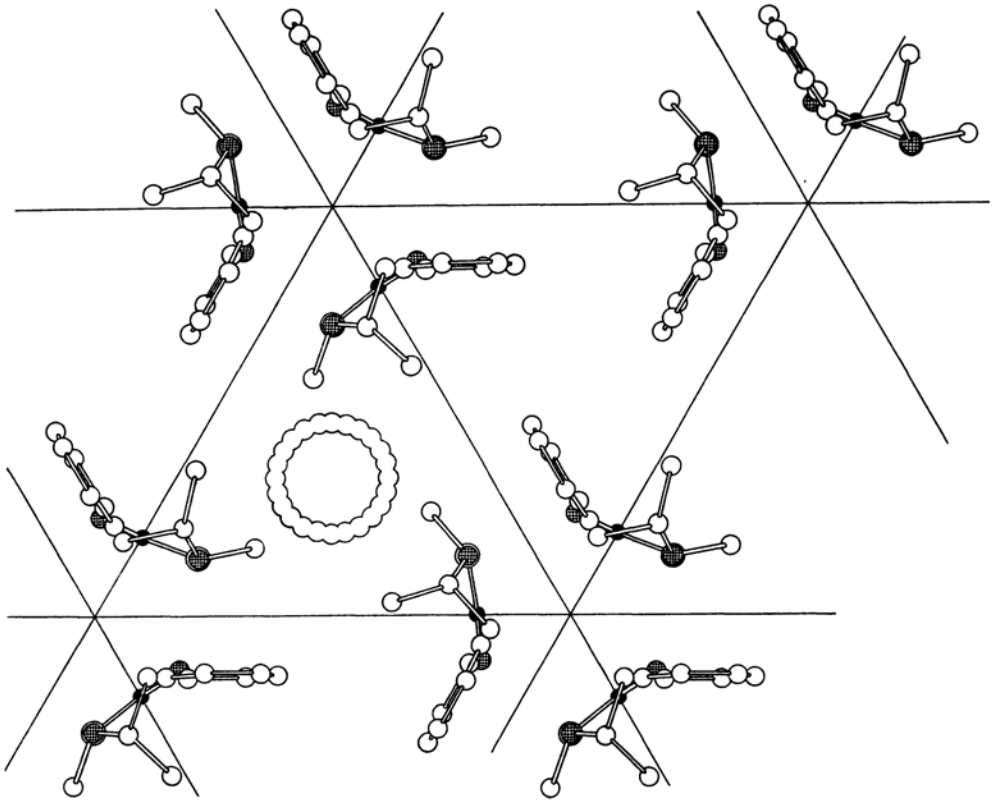

Fig. 5. Bounded projection $B(x, y;\ z=0 \rightarrow z=1/2)$.

obtained from the intermolecular N(H)–O bond length (2.87Å), using the table given by Nakamoto et al.[7]

The ephedrine copper chelate is easily soluble in non-polar solvents, such as *n*-hexane or benzene. This indicates that the ephedrine copper chelate still retains its trimer structure in these solvents, because it is hardly acceptable that the monomer chelate molecule with hydrophillic groups would dissolve in non-polar solvents. In fact, the absorption spectrum of the crystal is almost identical with the spectrum of its *n*-hexane or benzene solution in the visible region.

Molecular Packing.—The arrangement of the trimer chelate molecules in this crystal structure leaves two large cavities in the unit cell; the benzene molecules are enclosed in these cavities (Fig. 4 and Fig. 5). This crystal can, therefore, be considered to be a sort of clathlate compound. Namely, the trimer chelate is the host, and the benzene the guest molecule. It may be suggested that these benzene molecules are also responsible for holding together the trimer chelate molecules by virtue of the van der Waals attraction forces. It is highly probable that they rotate or are distributed statistically about the symmetry axis.

Throughout this study, the calculation of the structure factor, the Fourier summation and the least-squares method were carried out on the NEAC 2203 and the NEAC 2206 at the Computation Center of Osaka University, using partial modifications of programs originaly written by one of the authors (K. O.).

Faculty of Pharmaceutical Sciences
Kyoto University
Sakyo-ku, Kyoto (Y. A.)

Depertment of Physics
Faculty of Science
Osaka University
Nakanoshima, Osaka
(K. O. & T. W.)

7) K. Nakamoto, M. Margoshes and R. E. Rundle, *J. Am. Chem. Soc.*, 77, 6480 (1955).