The Crystal and Molecular Structure of (±)-2-Methylamino-4,5-bis(*p*-chlorophenyl)-4-hydroxy-4*H*-imidazole

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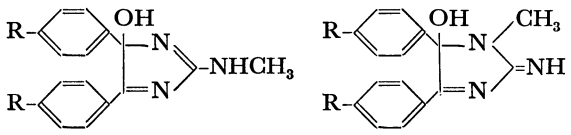
The crystal and molecular structure of (±)-2-methylamino-4,5-bis(*p*-chlorophenyl)-4-hydroxy-4*H*-imidazole has been determined by the single-crystal X-ray diffraction method. The crystals are monoclinic with space group $P2_1/c$, cell dimensions: $a=14.872(5)$, $b=9.216(7)$, $c=12.945(11)$ Å, $\beta=99.53(5)°$, and $Z=4$. The structure was determined by the symbolic addition method and refined by the least-squares method to give the final R factor of 0.072 for 1616 non-zero reflections.

In conection with the development of the new synthetic method of 2-aminoimidazoles,[1-3] 4,5-diaryl-4-hydroxy-4*H*-imidazoles (**1**) were prepared by the reaction of the corresponding benzils with methylguanidine.[4] The NMR spectra of these compounds (**1**) show a slightly broad singlet for the *N*-methyl protons indicating the structure of 4,5-diaryl-4-hydroxy-2-imino-1-methyl-5-imidazoline (**1b**).[4] On the other hand, the fact that hydrogenation of **1** produced 4,5-diaryl-2-methylaminoimidazoles suggests isomeric 4,5-diaryl-4-hydroxy-2-methylamino-4*H*-imidazoles (**1a**) as the structure of **1**.[4] Since structural interconversion between **1a** and **1b** in solution is possible,[2] it is difficult



1a

1b

to determine which isomeric structure **1a** or **1b** corresponds to compounds (**1**). Thus, an X-ray crystallographic analysis of the bis(*p*-chlorophenyl) derivative (**1**, R=Cl) was undertaken to determine the position of the methyl group and the conformation of the molecule.

Experimental

Preparation of 2-Methylamino-4,5-bis(p-chlorophenyl)-4-hydroxy-4H-imidazole (1). A mixture of 4,4′-dichlorobenzil (2.70 g) and methylguanidine (0.73 g) in 16 ml of methanol was stirred at room temperature for 30 min. The presipitate was filtered, washed with methanol, chloroform, and then ether and air-dried at room temperature. Colorless powder, mp *ca.* 295 °C dec (gradual darkening ≳125 °C), yield 3.03 g (91%). Recrystallization of **1** with methanol gave pale yellowish crystals; mp >280 °C (gradual darkning ≳126 °C); NMR (DMSO-d_6) $\delta=2.87$ (3H, s, NCH_3), 3.19 (3H, s, OCH_3), *ca.* 4.1 (2H, broad, disappeared on addition of D_2O, OH), *ca.* 7.1 (1H, broad, disappeared on addition of D_2O, NH), 7.30 (4H, s, 4-C_6H_4Cl), 7.50 (2H, d, $J=9.3$ Hz, $H_{3,5}$ of 5-C_6H_4Cl), 7.97 (2H, d, $J=9.3$ Hz, $H_{2,6}$ of 5-C_6H_4Cl). The NMR spectrum was recorded with a Hitachi R-24 (60 MHz) spectrometer. The size of crystal used for obtaining X-ray data was $0.3\times0.2\times0.4$ mm. The data are given in Table 1. The cell constants were determined by the least-squares procedure from the 2θ values of 25 reflections measured on a diffractometer using monochromated Mo $K\alpha$ radiation. The density was determined by the flotation method. The integrated intensities of the reflections were collected on a Rigaku automatic four circle diffractometer with Mo $K\alpha$ radiation monochromatized by a graphite plate. Background was counted for 10 s at both sides of each peak. Three standard reflections were measured every 50 reflections during the couse of collection. The intensities of unique reflections with 2θ values than 69° were collected, a total of 1616 reflections with $|F|>3\sigma(|F|)$ being obtained. The data were corrected for Lorentz and polarization factors, but not for absorption. The atomic scattering factors for C, O, N, and Cl were given by Cromer and Mann,[5] and that for H by Stewart *et al.*[6]

TABLE 1. CRYSTAL DATA

$C_{16}H_{13}ON_3Cl_2\cdot CH_3OH$	
Monoclinic	Space group $P2_1/c$
$a=$ 14.872(5) Å	$D_m=1.39$ g·cm^{-3}
$b=$ 9.216(7) Å	$D_c=1.391$ g·cm^{-3}
$c=$ 12.945(11) Å	$Z=4$
$\beta=$ 99.53(5)°	
$V=$ 1749.7 Å^3	

Determination of Structure

The structure was determined by the symbolic addition method.[7] The distribution and statistics of $|E|^s$ agree with the theoretical values for the centrosymmetric case. The resulting E map revealed the location of all the 24 non-hydrogen atoms including methanol molecule. Several cycles of least-squares refinement of the coordinates with isotropic temperature factors gave an R value of 0.15. Anisotropic thermal parameters were introduced for all non-hydrogen atoms, the R value being reduced to 0.11. Of seventeen hydrogen atoms, the two hydrogen atoms of the hydroxyl group of compound **1** and the methylamino group were located on the difference map, but the other hydrogen atoms could not be identified. Refinement of the coordinates with anisotropic temperature factors for non-hydrogen atoms and isotropic thermal factors for hydrogen atoms gave the final R value 0.072. At the final stage of the refinement the difference electron density map showed only featureless peaks, which were about half of those of the two hydrogen atoms H(1) and H(2). The complete F_o-F_c data are deposited as Document No. 7932 at the Chemical Society of Japan.

TABLE 2. FINAL ATOMIC PARAMETERS ($\times 10^4$), WITH THEIR STANDARD DEVIATIONS IN PARENTHESES

(a) Fractional atomic coordinates and anisotropic temperature factors[a] for non-hydrogen atoms.

Atom	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
Cl(1)	175(2)	−230(2)	3129(2)	703(15)	559(15)	1195(20)	217(11)	272(14)	103(13)
Cl(2)	809(2)	8649(2)	−435(2)	747(15)	732(14)	767(16)	−205(12)	−29(12)	−243(12)
C(1)	5142(5)	7836(8)	4830(6)	684(54)	550(45)	564(53)	229(40)	−41(39)	4(39)
C(2)	3981(4)	6011(7)	4170(5)	423(41)	355(36)	476(45)	−11(30)	78(31)	29(32)
C(3)	3004(4)	4414(7)	3529(5)	437(42)	350(35)	453(47)	−14(29)	0(31)	−5(31)
C(4)	3390(4)	5109(7)	2632(5)	461(42)	454(38)	352(44)	9(31)	79(30)	70(32)
C(5)	2315(4)	3266(7)	3417(6)	407(42)	356(35)	588(50)	0(30)	62(33)	−19(33)
C(6)	1944(5)	2834(8)	4304(6)	613(53)	582(48)	736(58)	128(41)	169(43)	−19(43)
C(7)	1274(6)	1745(9)	4231(7)	744(59)	530(49)	828(65)	171(44)	137(47)	64(44)
C(8)	999(5)	1127(7)	3244(7)	393(44)	372(39)	989(66)	31(32)	89(41)	−2(40)
C(9)	1349(5)	1515(8)	2345(6)	534(50)	477(44)	806(61)	98(37)	56(41)	−24(41)
C(10)	2014(5)	2612(7)	2434(6)	519(46)	417(38)	538(48)	38(33)	46(35)	−5(35)
C(11)	2686(4)	5896(7)	1829(5)	367(40)	408(36)	418(44)	41(29)	26(30)	−10(31)
C(12)	1986(5)	6638(8)	2170(6)	452(45)	524(42)	526(51)	−76(35)	75(34)	87(36)
C(13)	1388(5)	485(8)	1452(6)	546(48)	574(46)	541(50)	−58(37)	35(36)	−3(38)
C(14)	1528(5)	7539(8)	432(6)	465(45)	516(42)	504(47)	−2(33)	−72(34)	−110(36)
C(15)	2213(5)	6762(9)	63(6)	538(51)	722(52)	556(54)	−146(41)	58(38)	−103(42)
C(16)	2805(5)	5926(8)	788(6)	591(48)	641(48)	401(48)	−64(40)	73(35)	−74(38)
C(17)	6286(6)	4735(9)	2661(7)	805(63)	587(51)	822(67)	−110(46)	154(49)	16(46)
O(1)	3849(3)	4064(5)	2105(4)	465(30)	517(28)	541(32)	−87(24)	67(23)	167(25)
O(2)	5644(3)	3633(5)	2840(4)	495(30)	556(30)	482(32)	75(24)	28(23)	−34(24)
N(1)	4446(4)	6733(6)	4981(4)	592(39)	473(33)	436(39)	54(30)	−42(28)	51(29)
N(2)	3351(4)	4943(6)	4420(4)	519(37)	444(32)	403(38)	28(28)	50(27)	2(28)
N(3)	4037(4)	6176(6)	3197(4)	455(34)	473(32)	331(34)	27(27)	24(25)	47(27)

a) The anisotropic temperature factors are expressed in the from: $\exp[-2\pi^2(U_{11}h^2a^{*2}+U_{22}l^2c^{*2}+U_{33}l^2c^{*2}+2U_{12}hka^*b^*+2U_{13}hla^*c^*+2U_{23}klb^*c^*)]$.

(b) Atomic coordinates ($\times 10^3$) and isotopic temperature factors ($\times 10^2$) for hydrogen atoms.

Atom	x	y	z	U
H(1)	459(6)	421(10)	226(7)	14(4)
H(2)	434(5)	633(9)	571(6)	11(3)

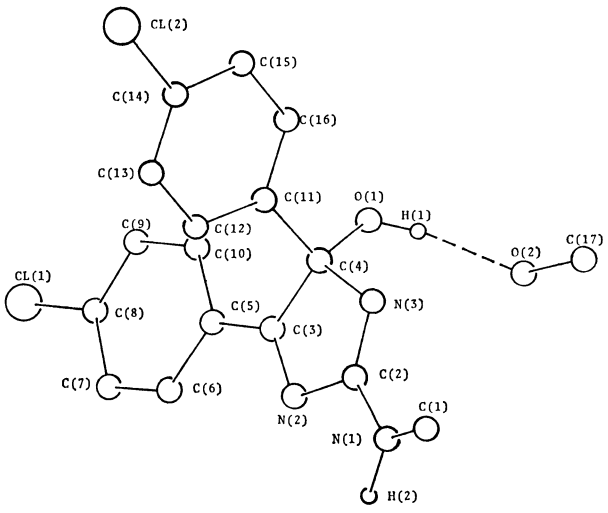


Fig. 1. The molecular structure and numbering of (±)-2-methylamino-4,5-bis(*p*-chlorophenyl)-4-hydroxy-4*H*-imidazoles.

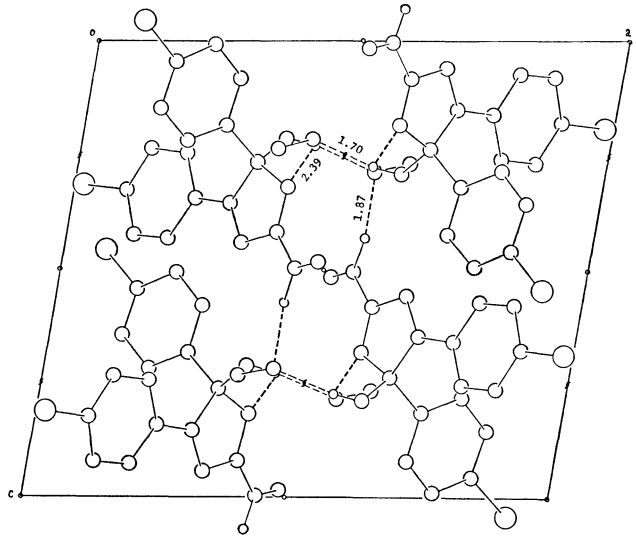


Fig. 2. The molecular arrangement in this crystal viewed along the b axis. The dotted lines show the hydrogen bonds. Their distances are given in Å.

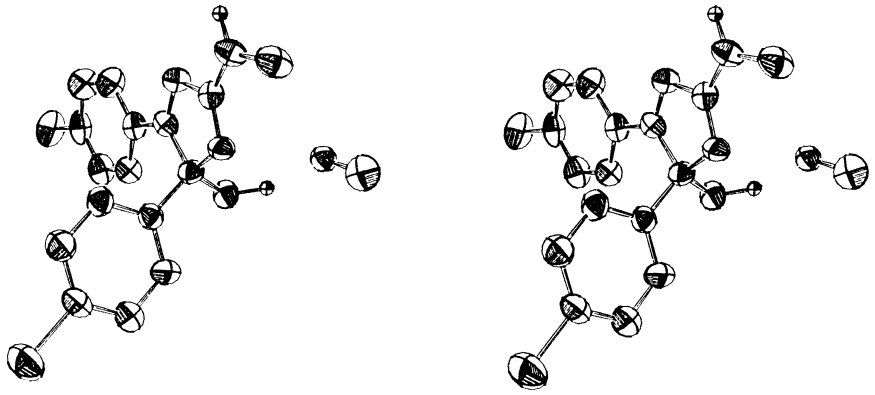


Fig. 3. Stereoscopic view of the compound **1**.

Table 3. Bond angles and their standard deviations

C(3)-C(4)-C(11)	114.6(6)°	C(1)-N(1)-C(2)	121.2(6)°
C(3)-C(5)-C(6)	119.0(6)	C(2)-N(2)-C(3)	104.0(6)
C(3)-C(5)-C(10)	120.7(7)	C(2)-N(3)-C(4)	104.6(5)
C(4)-C(11)-C(12)	119.0(6)	C(3)-C(4)-N(3)	102.3(5)
C(4)-C(11)-C(16)	119.1(6)	C(3)-C(4)-O(1)	110.7(5)
C(4)-C(3)-C(5)	125.2(6)	C(4)-C(3)-N(2)	112.4(6)
C(5)-C(6)-C(7)	121.0(7)	C(5)-C(3)-N(2)	122.5(6)
C(6)-C(7)-C(8)	116.7(8)	C(11)-C(4)-N(3)	109.2(5)
C(7)-C(8)-C(9)	124.4(7)	C(11)-C(4)-O(1)	108.9(5)
C(8)-C(9)-C(10)	118.0(7)	C(7)-C(8)-Cl(1)	117.8(7)
C(9)-C(10)-C(5)	119.6(7)	C(9)-C(8)-Cl(1)	117.8(6)
C(10)-C(5)-C(6)	120.3(6)	C(13)-C(14)-Cl(2)	117.7(6)
C(11)-C(12)-C(13)	119.4(7)	C(15)-C(14)-Cl(2)	119.1(6)
C(12)-C(13)-C(14)	118.3(7)	C(1)-N(1)-H(2)	125.1(43)
C(13)-C(14)-C(15)	123.2(7)	C(2)-N(1)-H(2)	113.1(44)
C(14)-C(15)-C(16)	117.8(7)	C(4)-O(1)-H(1)	112.1(49)
C(15)-C(16)-C(11)	119.5(7)	N(1)-C(2)-N(2)	116.0(6)
C(16)-C(11)-C(12)	121.7(6)	N(1)-C(2)-N(3)	127.2(6)
		N(2)-C(2)-N(3)	116.8(5)
		N(3)-C(4)-O(1)	110.8(5)

Table 4. Bond lengths and their standard deviations

C(3)-C(4)	1.519(10) Å	C(1)-N(1)	1.487(10) Å
C(5)-C(6)	1.412(11)	C(2)-N(1)	1.335(8)
C(6)-C(7)	1.406(11)	C(2)-N(2)	1.432(9)
C(7)-C(8)	1.397(12)	C(2)-N(3)	1.309(9)
C(8)-C(9)	1.398(12)	C(3)-N(2)	1.279(9)
C(9)-C(10)	1.406(10)	C(4)-N(3)	1.473(8)
C(11)-C(12)	1.378(10)	C(4)-O(1)	1.419(8)
C(12)-C(13)	1.411(10)	C(17)-O(2)	1.439(10)
C(13)-C(14)	1.372(11)	C(8)-Cl(1)	1.740(7)
C(14)-C(15)	1.392(11)	C(14)-Cl(2)	1.747(7)
C(15)-C(16)	1.405(11)		
C(3)-C(5)	1.463(9)	N(1)-H(2)	1.05(8)
C(4)-C(11)	1.530(9)	O(1)-H(1)	1.10(8)
C(5)-C(10)	1.412(10)		
C(11)-C(16)	1.389(10)		

Results and Discussion

The molecular structure and numbering are shown in Fig. 1. The methyl group was found to be bonded with the 2-amino group. The final atomic coordinates and thermal parameters with their standard deviations are given in Table 2, and bond distances and angles with their standard deviations in Tables 3 and 4, respectively. The sum of the bond angles around the N(1) atom is 359.4°, and the bond length of N(1)–C(2) is 1.34 Å. The values suggest that the atomic configuration of N(1) is sp^2 hybridized, and that the N(1)–C(2) bond is conjugated with the imidazole ring. The crystal structure projected along the b axis is shown in Fig. 2. The crystal of compound **1** contains four methanol molecules in an unit cell. The

Table 5. Equations of least-squares planes in the $AX+BY+CZ+D=0$[a] form displacements (1/Å) of atoms from the planes are given in square brackets

Benzene plane I

$0.690X+0.693Y+0.207Z=7.075$

[C(5) 0.002, C(6) 0.000, C(7) 0.000, C(8) 0.002, C(9) 0.004, C(10) 0.004]

Benzene plane II

$0.581X+0.788Y+0.205Z=-0.422$

[C(11) 0.012, C(12) −0.007, C(13) −0.007, C(14) 0.014, C(15) −0.008, C(16) −0.005]

Imidazole plane

$0.719X+0.689Y+0.090Z=6.626$

[C(2) 0.004, N(2) −0.001, C(3) −0.002, C(4) 0.004, N(3) −0.004]

a) X, Y, and Z are orthogonal coordinates in Å related to the crystal axes by

$$\begin{bmatrix} X \\ Y \\ Z \end{bmatrix} = \begin{bmatrix} 1 & 0 & \cos\beta \\ 0 & 1 & 0 \\ 0 & 0 & \sin\beta \end{bmatrix} \begin{bmatrix} ax \\ by \\ cz \end{bmatrix}$$

Table 6. Selected dihedral angles (°)

C(5)-C(3)-C(4)-C(11)	61.55	C(3)-C(4)-O(1)-H(1)	71.8
C(1)-N(1)-C(2)-N(2)	1.96	C(11)-C(4)-O(1)-H(1)	55.1
C(1)-N(1)-C(2)-N(3)	2.24	N(2)-C(2)-N(1)-H(2)	6.6
C(3)-N(2)-C(2)-N(1)	0.26	N(3)-C(2)-N(1)-H(2)	6.3
C(4)-N(3)-C(2)-N(1)	0.50	N(3)-C(4)-O(1)-H(1)	4.7
C(2)-N(3)-C(4)-O(1)	62.61		
N(2)-C(3)-C(4)-O(1)	62.28		

Dihedral angles between the planes (°)

Benzene plane I and benzene plane II	95.9
Benzene plane I and imidazole plane	6.9
Benzene plane II and imidazole plane	96.2

oxygen atom of the methanol molecule is hydrogen-bonded with the hydrogen atom of the hydroxy group of compound **1** and the methylamino group. The N(3) atom is also hydrogen-bonded with the H(1) atom. A stereoscopic view of compound **1** is shown in Fig. 3. The dihedral angles are given in Table 6. The dihedral angle between two phenyl groups is 95.5° and that between the imidazole ring and the phenyl group attached to C(3) and the phenyl group attached to C(4) is 6.88° and 96.2°, respectively. The least-squares planes and deviations of atoms from these planes are given in Table 5. The benzene ring attached to C(3) and the imidazole ring are nearly coplanar. C(1), N(1), and H(2) are almost of the imidazole ring plane, and H(2) is on the N(2) side and C(1) on the N(3) side of the imidazole ring.

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