Syntheses and molecular self-assembly of chiral phosphoramidates

DU, Da-Ming*,[a](杜大明) HUA, Wen-Ting[a](花文廷) WANG, Jian-Wu[b](王建武)
JIN, Xiang-Lin[a](金祥林)
[a] *College of Chemistry and Molecular Engineering, Peking University, Beijing 100871, China*
[b] *College of Chemistry, Shandong University, Jinan, Shandong 250100, China*

Two chiral phosphoramidates, (*R*)-(−)-1,1′-binaphthyl-2,2′-dihydroxy-*N*-[α-(*S*)-methylbenzyl] phosphoramidate and (−)-1,1′-biphenyl-2,2′-dihydroxy-*N*-[α-(*S*)-methylbenzyl]-phosphoramidate were synthesized. Their crystal structures were determined by X-ray single crystal diffraction analysis. The phosphoramidate molecules are self-associated by intermolecular N—H···O=P hydrogen bonds and aromatic edge to face interactions.

Keywords Phosphoramidate, hydrogen bond, crystal structure

Introduction

In the past few years, much attention was focused on the studies of the molecular recognition properties of chiral hosts.[1,2] Intermolecular interactions between molecules are the basis for molecular recognition. Most intermolecular forces such as van der Waals' interactions are weak and nondirectional. A strong directional hydrogen bond can determine the configuration of pair or set of molecules. This hydrogen bond set can result in new molecular recognition properties and new chemical properties of its own.[3,4] Hydrogen bond interactions may also be used as the key stabilizing interactions in the host structure itself. The host could be composed of multiple hydrogen-bonded subunits that aggregate to creat pockets to trape guest molecules.[5,6]

It was reported that triphenylphosphine oxide (TPPO) induced many organic compounds to crystallize readily as large blocky crystals that have sharp edges and well-defined crystal faces, and TPPO formed 1:1 complexes through strong directed hydrogen bonds between the phosphoryl oxygen and the proton donor groups.[7,8] In the present work, we have purposely chosen system of chiral phosphoramidate, which has aromatic ring and P=O and N-H polar groups. These chiral phosphoramidates can serve as excellent host for guest molecules. In order to explore the inclusion behavior of chiral phosphoramidates, we undertook the crystal structure studies of two chiral phosphoramidates.

Experimental

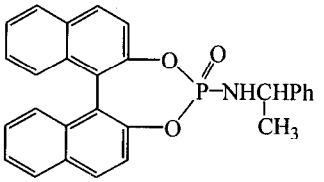
Melting points were measured on an XT-4 melting point apparatus and uncorrected. ^{1}H NMR spectra were recorded on a Varian 200 MHz spectrometer, tetramethylsilane (TMS) serving as internal standard, and ^{31}P NMR spectra were recorded using 85% H_3PO_4 as external standard. Infrared spectra were obtained on a Bruker Vector 22 spectrometer. Mass spectra were obtained on a VG-ZAB-HS mass spectrometer. Optical rotations were measured on a Perkin-Elmer 241 MC spectrometer. Elemental analyses were carried out on an Elementar Vario EL instrument. Solvents used were purified and dried by standard procedures.

Preparation of (R)-(−)-1,1′-binaphthyl-2,2′-dihydroxy-N-(α-(S)-methylbenzyl) phosphoramidate (**1**)

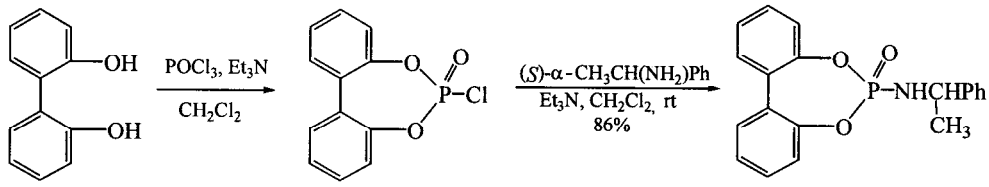
(*R*)-(−)-1,1′-*Binaphthyl*-2,2′-*dihydroxy*-*N*-

* Received February 29, 2000; accepted April 19, 2000.
Project supported by the National Natural Science Foundation of China (Grant No. 29872023), the Ministry of Education of China (Research Funds for Chinese Scholars returning from abroad) and China Postdoctoral Science Foundation.

(α-(*S*)-*methylbenzyl*)*phosphoramidate* (**1**) was prepared according to the known procedure.[9] Colorless prisms were obtained upon evaporation of the ethanol solution of compound **1** at room temperature. A crystal suitable for data analysis was cut from a larger crystal.



1



2

Preparation of (−)-1,1′-*biphenyl*-2,2′-*dihydroxy*-*N*-(α-(*S*)-*methylbenzyl*)*phosphoramidate* (**2**)

1,1′-Biphenol (1.9 g, 10 mmol) was slurried with 20 mL of dichloromethane, and phosphorus oxychloride (2.2 g, 14 mmol) was added under N_2, followed by the slow addition of triethylamine (2.5 g, 25 mmol) with stirring so as to maintain gentle reflux. After 1 h of additional stirring, the reaction mixture was washed with water, and the organic layer was dried and concentrated to give the crude acid chloride. A solution of (*S*)-(−)-α-*methylbenzylamine* (1.2 g, 10 mmol) and triethylamine (1.2 g, 12 mmol) in dichloromethane (10 mL) was added dropwise with constant stirring into crude acid chloride (from 10 mmol of 1,1′-biphenol), cooled in an ice-salt bath. After the addition (0.5 h), the mixture was stirred at room temperature for 12 h. The reaction mixture was washed with brine, dried with anhydrous magnesium sulfate. Upon removal of solvent under reduced pressure, the crude product was purified by column chromatography on silica gel (elution with ethyl acetate-petroleum ether 2∶1 *V*/*V*), a colorless solid was obtained (3.0 g, 86%). mp 204—206℃. $[\alpha]_D^{20} = -7.6°$ (*c* = 1, $CHCl_3$). δ_H($CDCl_3$): 1.55 (d, *J* = 7.0 Hz, 3H, CH_3), 3.47(t, *J* = 10.8 Hz, 1H, NH), 4.40—4.62(m, 1H, CH), 6.96—7.53 (m, 13H, ArH). δ_P($CDCl_3$): 11.99. FABMS *m*/*z*: 352(M + 1). Anal. $C_{20}H_{18}NO_3P$. Calcd.: C, 68.37; H, 5.16; N, 3.99. Found: C, 68.25; H, 5.36; N, 3.78. A colorless crystal suitable for data analysis was obtained upon evaporation of the ethanol solution of compound **2** at room temperature.

Crystal data

1 $C_{28}H_{22}NO_3P$, *M* = 451.44, orthorhombic, space group *P*2(1)2(1)2(1), *a* = 1.9973(4), *b* = 2.0084(4), *c* = 1.1436(2) nm; α = 90°, β = 90°, γ = 90°, *V* = 4.5874(15) nm^3, *Z* = 8, *F*(000) = 1888, D_c = 1.307 g/cm^3, μ = 0.150 mm^{-1}. The final *R* indices [$I > 2\sigma(I)$] R_1 = 0.0463, wR_2 = 0.0996 for 4501 Mo K_α observed data.

2 $C_{20}H_{18}NO_3P$, *M* = 351.32, monoclinic, space group *P*2(1), *a* = 0.8785(2), *b* = 1.0296(2), *c* = 1.0061(2) nm; α = 90°, β = 97.18(3)°, γ = 90°, *V* = 0.9029(3) nm^3, *Z* = 2, *F*(000) = 368, D_c = 1.292 g/cm^3, μ = 0.170 mm^{-1}. The final *R* indices [$I > 2\sigma(I)$] R_1 = 0.0347, wR_2 = 0.1019 for 3382 Mo K_α observed data.

X-Ray data collection and structure analysis

Computing data collection: MSC/AFC Diffractometer Control Software MSC (Molecular Structure Corporation 1994). Cell refinement: MSC/AFC Diffractometer Control Software. Data reduction: SHELXS97 (Sheldrick, G. M., 1997). Molecular graphics: Interactive Molecular Graphics XP, Virsion 5.1 for MSDOS (1998).

A colorless crystal was selected and mounted on a glass fiber in a random orientation. Preliminary exami-

nation and data collection were performed with Mo K_α radiation ($\lambda = 0.071073$ nm) on a Rigaku AFC6S diffractometer equipped with a graphite crystal incident beam monochromator. The determination of the crystal class, orientation matrix, and accurate unit-cell parameters was performed according to established procedures.[10] Unit-cell and intensity data were measured at 293 K using the ω-2θ variable-scan mode,[11] the intensity data obtained were corrected for Lorentz and polarization effects and empirical absorption correction based on ψ-scan data was applied.[12] The crystal structure was solved by the direct method using SHELXS-97, and full-matrix least-squares refinement on F^2 was performed with SHELXL-97 program. All the non-hydrogen atoms were deduced from an E-map and refined anisotropically. The positions of hydrogen atoms were generated geometrically and included in structure factor calculations with assigned isotropic thermal parameters. All computations were performed on a FOUNDER FP$^+$ 5-166 586 personal computer.

Results and discussion

The fractional atomic coordinates and equivalent isotropic temperature factors for the crystal structures of compounds **1** and **2**, along with their estimated standard deviations, are presented in Tables **1** and **2**, respectively.

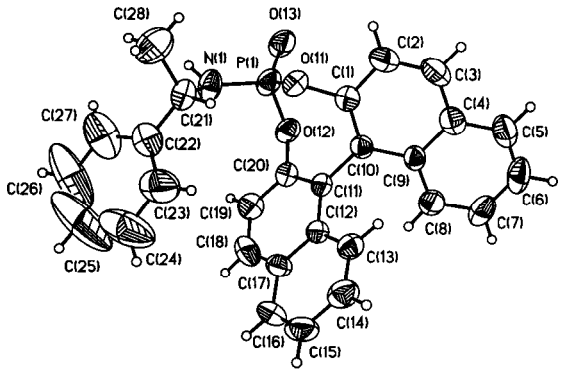
Table 1 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($nm^2 \times 10$) for compound **1**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor

Atom	x	y	z	U(eq)	Atom	x	y	z	U(eq)
P(1)	1293(1)	1112(1)	1978(1)	52(1)	C(24)	2039(8)	1303(6)	6759(10)	165(7)
P(2)	4074(1)	4006(1)	7418(2)	58(1)	C(25)	1526(12)	1088(8)	7456(12)	217(13)
O(11)	1774(2)	1736(2)	1795(3)	52(1)	C(26)	901(9)	1090(7)	7050(10)	187(8)
O(12)	1801(2)	502(2)	2089(3)	49(1)	C(27)	746(5)	1329(4)	5955(8)	112(3)
O(13)	835(2)	947(2)	1030(3)	68(1)	C(28)	529(3)	2319(3)	4040(7)	92(3)
O(21)	3443(2)	4496(2)	7476(4)	57(1)	C(31)	2853(3)	4289(3)	8031(5)	49(2)
O(22)	3722(2)	3298(2)	7163(4)	59(1)	C(32)	2697(3)	4594(3)	9099(6)	61(2)
O(23)	4545(2)	4234(2)	6534(4)	69(1)	C(33)	2126(3)	4414(3)	9667(5)	62(2)
N(1)	942(2)	1279(2)	3207(4)	54(1)	C(34)	1695(3)	3921(3)	9226(5)	49(2)
N(2)	4405(2)	3919(3)	8686(5)	67(2)	C(35)	1109(3)	3730(3)	9798(5)	60(2)
C(1)	2322(3)	1677(3)	1034(5)	45(2)	C(36)	704(3)	3250(4)	9366(7)	70(2)
C(2)	2299(3)	2074(3)	5(5)	64(2)	C(37)	885(3)	2924(3)	8328(6)	63(2)
C(3)	2808(3)	2020(3)	-770(5)	66(2)	C(38)	1438(3)	3100(3)	7731(5)	51(2)
C(4)	3341(3)	1573(3)	-611(5)	51(2)	C(39)	1855(3)	3616(3)	8138(5)	44(2)
C(5)	3823(3)	1458(4)	-1476(6)	67(2)	C(40)	2451(2)	3825(3)	7511(5)	42(1)
C(6)	4312(3)	994(4)	-1329(6)	70(2)	C(41)	2644(3)	3548(3)	6356(5)	47(2)
C(7)	4342(3)	624(3)	-306(6)	63(2)	C(42)	2220(3)	3579(3)	5351(5)	43(1)
C(8)	3883(3)	724(3)	570(5)	52(2)	C(43)	1612(3)	3934(3)	5342(5)	51(2)
C(9)	3371(2)	1199(3)	452(4)	41(1)	C(44)	1243(3)	3995(4)	4340(6)	66(2)
C(10)	2864(3)	1296(3)	1314(4)	40(1)	C(45)	1463(4)	3707(4)	3309(7)	83(2)
C(11)	2886(2)	959(3)	2473(5)	37(1)	C(46)	2042(4)	3354(4)	3271(6)	77(2)
C(12)	3428(2)	1055(3)	3276(4)	39(1)	C(47)	2442(3)	3285(3)	4283(5)	57(2)
C(13)	3959(2)	1504(3)	3062(5)	45(2)	C(48)	3060(3)	2964(4)	4262(6)	71(2)
C(14)	4442(3)	1601(3)	3888(6)	58(2)	C(49)	3480(3)	2959(3)	5199(6)	71(2)
C(15)	4426(3)	1250(4)	4965(6)	65(2)	C(50)	3261(3)	3274(3)	6232(6)	52(2)
C(16)	3932(3)	819(4)	5180(5)	61(2)	C(51)	4107(3)	3633(3)	9742(6)	62(2)
C(17)	3417(3)	707(3)	4347(5)	47(2)	C(52)	4136(3)	4109(3)	10769(6)	56(2)
C(18)	2875(3)	273(3)	4604(5)	61(2)	C(53)	4618(3)	4596(3)	10868(6)	66(2)
C(19)	2344(3)	214(3)	3866(5)	50(2)	C(54)	4656(4)	4994(4)	11864(7)	81(2)
C(20)	2363(2)	571(3)	2820(5)	39(1)	C(55)	4215(4)	4890(4)	12753(7)	94(3)
C(21)	1099(3)	1827(3)	4029(5)	51(2)	C(56)	3718(5)	4426(5)	12653(8)	106(3)
C(22)	1246(4)	1558(3)	5235(6)	64(2)	C(57)	3683(4)	4035(4)	11671(7)	91(2)
C(23)	1884(5)	1548(4)	5650(7)	99(3)	C(58)	4468(4)	2994(3)	10053(7)	91(3)

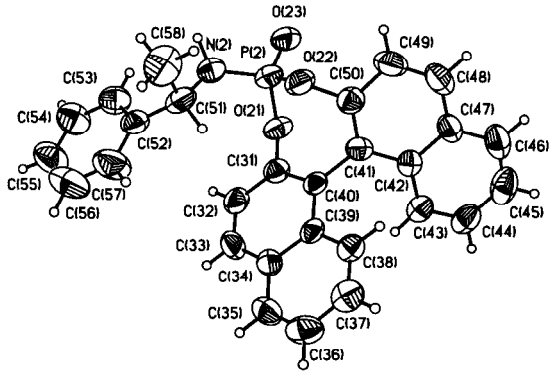
Table 2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($nm^2 \times 10$) for compound **2**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor

Atom	x	y	z	U(eq)
P(1)	4315(1)	3055(1)	4258(1)	41(1)
O(1)	5149(2)	3017(2)	2936(2)	51(1)
O(2)	2770(2)	2283(2)	3792(2)	43(1)
O(3)	4143(2)	4402(2)	4657(2)	57(1)
N(1)	5128(2)	2132(2)	5419(2)	48(1)
C(1)	5192(3)	1886(2)	2173(3)	50(1)
C(2)	6584(4)	1271(4)	2164(3)	69(1)
C(3)	6703(6)	226(4)	1329(4)	88(1)
C(4)	5434(6)	-211(4)	542(4)	87(1)
C(5)	4038(5)	389(3)	567(3)	75(1)
C(6)	3874(3)	1474(3)	1385(2)	53(1)
C(7)	2400(3)	2146(3)	1390(3)	58(1)
C(8)	1420(4)	2378(4)	203(3)	84(1)
C(9)	42(5)	2994(6)	229(4)	105(2)
C(10)	-418(4)	3397(5)	1414(5)	101(2)
C(11)	525(3)	3203(4)	2604(3)	71(1)
C(12)	1887(3)	2582(3)	2570(3)	51(1)
C(13)	5751(4)	1769(3)	7820(3)	65(1)
C(14)	6004(3)	2648(2)	6653(2)	45(1)
C(15)	7680(3)	2833(2)	6516(2)	44(1)
C(16)	8658(4)	1803(3)	6399(4)	69(1)
C(17)	10194(4)	2000(5)	6315(4)	87(1)
C(18)	10774(4)	3239(5)	6335(3)	86(1)
C(19)	9807(5)	4271(4)	6437(4)	80(1)
C(20)	8287(4)	4073(3)	6514(3)	61(1)

As shown by X-ray analysis, there are two independent molecules in the asymmetric unit of the compound **1**: molecule **I** is composed of atoms C(1) to C(28), and the molecule **II** is composed of atoms C(31) to C(58) (see Fig. 1). The dihedral angles between two naphthylene rings of binaphthyl are 63.1° and 61.1° for molecules **I** and **II** respectively. The difference between molecules **I** and **II** are the dihedral angles of naphthylene rings to the benzene rings of α-methylbenzylamine. The dihedral angles between naphthylene and benzene rings are 41.2° and 23.8° in molecule **I**, whereas in molecule **II**, the corresponding dihedral angles are 6.8° and 66.3°, respectively. The torsion angles of binaphthyl and heterocyclic ring within the two molecules are similar, C(1)-C(10)-C(11)-C(20) 52.7°, C(9)-C(10)-C(11)-C(12) 60.0°, O(11)-P(1)-O(12)-C(20) 46.2° and P(1)-N(1)-C(21)-C(22) - 124.9° in molecule **I**, and C(31)-C(40)-C(41)-C(50) 54.1°, C(39)-C(40)-C(41)-C(42) 58.0°, O(21)-P(2)-O(22)-C(50) 50.5° and P(2)-N(2)-C(51)-C(52) - 124.8° in molecule **II**. The main difference between molecules **I** and **II** is the torsion angles of O-P-N-C, the corresponding torsion angles within the two molecules are O(11)-P(1)-N(1)-C(21) - 7.5° and O(21)-P(2)-N(2)-C(51) 62.9°, respectively. The O = P bond is 0.1455(4) nm, which is the same as the O = P bond length in TPPO molecule. The molecular packing of compound **1** in unit cell is given in Fig. 2. Two independent molecules are disposed alternatively. The two kinds of molecules are connected by intermolecular N—H···O = P hydrogen bond [N(1)—H(61)···O(23), $x - 1/2$, $-y + 1/2$, $-z + 1$; 0.2987(6) nm, 170.1(3)°; N(2)—H(62)···O(13), $x + 1/2$, $-y + 1/2$, $-z + 1$; 0.2888(5) nm, 166.9(3)°] interaction between pairs of related molecules. The layer structure was thus formed through the intermolecular hydrogen bond interaction.



Molecule I



Molecule II

Fig. 1 Molecular structure of compound **1**.

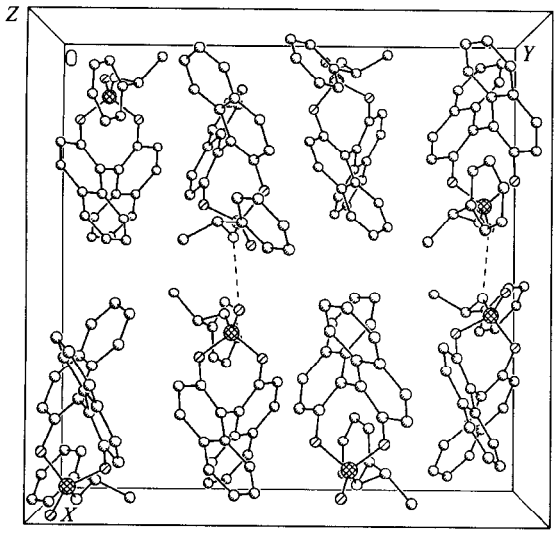


Fig. 2 Molecular packing of compound **1** in unit cell.

The molecular structure of compound **2** is given in Fig. 3, and the molecular packing of compound **2** along the *c* axis is given in Fig. 4. The two benzene rings of biphenyl are not coplanar, and the dihedral angle is 138.8°. The benzene ring of α-methylbenzylamine is perpendicular to one ring of biphenyl with dihedral angle of 96.0°. The molecules are associated by intermolecular N—H···O = P hydrogen bond interaction [N-H···O, $-x+1$, $y-1/2$, $-z+1$, 0.2886(3) nm, 159.82 (13)°]. The self-assembly layer structure is thus formed through the hydrogen bond chain N—H···O = P—N—H ···O = P—N—H···. The π-π stacking through overlapping of the edge of aromatic ring to aromatic ring may play an important role in molecular self-assembly. Theoretical modeling of the benzene dimer suggests that the face-to-face dimer have an optimum center-to-center distance of ca. 0.38 nm, whereas the edge-to-face dimer have an optimum center-to-center distance of 0.5 nm.[13,14] In the same chain, the distances of the six atoms of benzene ring (C(7) to C(12)) to the nearest mean plane of benzene ring of α-methylbenzylamine (C (15) to C(20)) are 0.299, 0.345, 0.389, 0.479, 0.524 and 0.568 nm, respectively. The dihedral angle between two interactive benzene rings is 92.0°. There is no hydrogen bonding between two layers, and the distance between the two hydrogen bond chains is about 0.786 nm. The edge to face stacking of aromatic ring to aromatic ring also plays an important role in molecular association between layers. The distances of the two atoms of the nearest edge to the nearest mean plane of benzene ring of α-methylbenzylamine (C(15) to C(20)) are 0.367 and 0.378 nm, respectively. The dihedral angle of two interactive benzene rings is 96.3°.

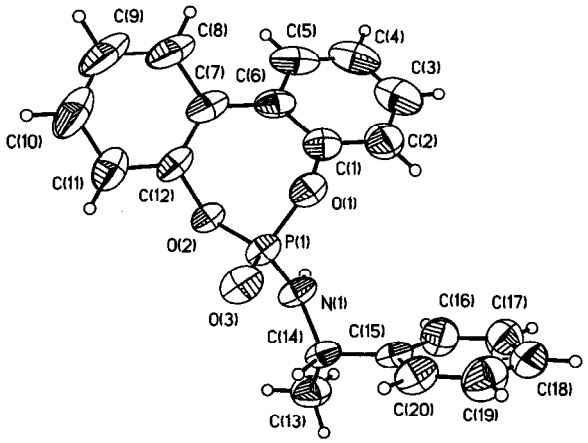


Fig. 3 Molecular structure of compound **2**.

As discussed above, the phosphoramidate molecules are self-associated by intermolecular N—H··· O = P hydrogen bonds and aromatic edge to face interactions. These chiral phosphoramidates can serve as new hosts for polar molecules, the further study of these molecules is undergoing and will be reported in forthcoming papers.

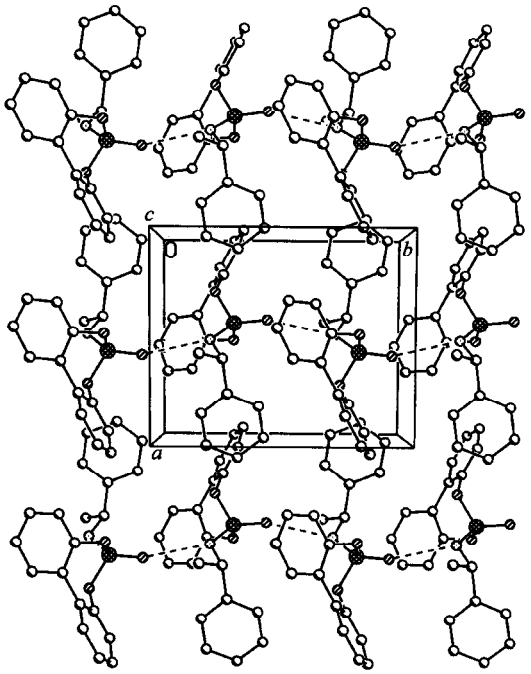


Fig. 4 Molecular packing of compound **2** along the *c* axis.

References

1. Lehn, J.M., *Angew. Chem., Int. Ed. Engl.*, **27**, 89 (1988).
2. Webb, T.H.; Wilcox, C.S., *Chem. Soc. Rev.*, **22**, 383 (1993).
3. Jeffrey, G.A.; Saenger, W., *Hydrogen Bonding in Biological Structures*, Springer-Verl, New York, 1991.
4. Kelley, T.R.; Maguire, M.P., *J. Am. Chem. Soc.*, **109**, 6549(1987).
5. Sanderson, P.E.J.; Kilburn, J.D.; Still, W.C., *J. Am. Chem. Soc.*, **111**, 8314(1989).
6. Hong, J.I.; Namgoong, S.K.; Bernard, A., *J. Am. Chem. Soc.*, **113**, 5111(1991).
7. Etter, M.C.; Baures, P.W., *J. Am. Chem. Soc.*, **110**, 639(1988).
8. Etter, M.C.; Reutzel, S.M., *J. Am. Chem. Soc.*, **113**, 2586(1991).
9. Gong, B.Q.; Chen, W.Y.; Hu, B.F., *J. Org. Chem.*, **56**, 423(1991).
10. Sparks, R.A. in "*Crystallographic Computing Techniques*", Eds. Ahmed, F.R., Munksgaard, Copenhagen, 1976, p. 452.
11. Diamond, R., *Acta Crystallogr., Sect. A*, **A25**, 43 (1969).
12. Sheldrick, G.M. in "*Computational Crystallography*", Eds. Sayre, D., Oxford University Press, New York, 1982, p.506.
13. Linse, P., *J. Am. Chem. Soc.*, **115**, 8793(1993).
14. Bartell, L.S.; Shi, X., *J. Phys. Chem.*, **92**, 5667 (1988).

(E200002043 JIANG, X.H.; LING, J.)