# NMR and X-ray analyses of triethyl 3,7,11-triphenyl-cyclonona[1,2-*b*;4,5-*b'*;7,8-*b''*]tripyrrole-2,6,10-tricarboxylate: reinvestigation of crown vs saddle conformation of cyclononatripyrroles

Hidemitsu Uno,[a],* Yumiko Fumoto,[b] Kentarou Inoue[b] and Noboru Ono[b],*

[a]*Advanced Instrumentation Center for Chemical Analysis, Ehime University, Bunkyotyo 2-5, Matsuyama 790-8577, Japan*
[b]*Department of Chemistry, Faculty of Science, Ehime University, Matsuyama 790-8577, Japan*

**Abstract**—From X-ray analyses of 3,7,11-triphenylcyclonona[1,2-*b*;4,5-*b'*;7,8-*b''*]tripyrrole-2,6,10-tricarboxylate (CNTP **1**), the molecules existed as saddle forms in both crystals of **1**·3ClPh and **1**·1/2CHCl₃. In the former crystal, hydrogen bonds between pyrrolic hydrogen and ester carbonyl oxygen spread two-dimensionally, forming molecular sheets, between which the solvent molecules were included, while two independent molecules were bounded three-dimensionally by the hydrogen bonds in the latter. In CDCl₃, CNTP was observed to adopt a crown form, while interconversion of the conformers was observed in C₅D₅N. © 2003 Elsevier Science Ltd. All rights reserved.

## 1. Introduction

Construction of highly ordered supramolecular systems from small molecules attracts considerable attention, and the design of such small molecular units is of great interest. The molecular units are assembled by various kinds of intermolecular interactions such as coordination with metals, $\pi$–$\pi$ stacking, van der Waals, hydrophobic interaction, and hydrogen bonding.[1] The conformational structures of the units are successfully elucidated by calculation (gas phase), NMR (in solution), and X-ray (solid phase) studies. However, the conformations of the molecules expected by these methods are sometimes different each other. The different surroundings of molecules cause such problems. The conformations of representative host compounds such as calixarenes,[2] calixpyrroles,[3] and cyclotriveratrylenes (CTVs)[4] were fully studied by NMR and X-ray experiments, and various kinds of conformations were reported for the host molecules. As far as CTVs and their analogs, the crown-type conformation was commonly observed both in solid and in solution, and the saddle-type conformation was only reported in very exceptional cases such as an oxidized CTV bearing carbonyls instead of methylenes[5] and a cyclonona[1,2-*c*;4,5-*c'*;7,8-*c''*]trithiophene derivative.[6] In the latter cases, unfavorable steric interactions between substituents were presumed to disfavor the crown-type conformation.

Contrary to CTVs, structures of cyclononatripyrroles (CNTPs), pyrrole version of CTV, have not been studied due to the synthetic difficulty. We have reported the preparation of structurally pure CNTP **1** from the acid-catalyzed condensation of ethyl 3-phenyl-4-(hydroxy-methyl)pyrrole-2-carboxylate (Fig. 1).[7] The conformation of **1** in CDCl₃ was studied by ¹H NMR at various temperatures, and we presumed that the macrocycle was in the crown conformation with *C*3 symmetry,[7] and that $\Delta H$ value for the ring flipping was calculated to be over 63 kJ mol⁻¹.[7] In this paper, we would like to discuss the conformations of CNTP **1** in detail based on calculation, ¹H NMR, and X-ray analyses.
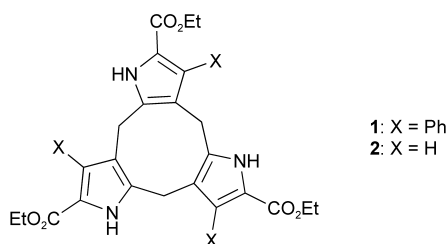


**1**: X = Ph
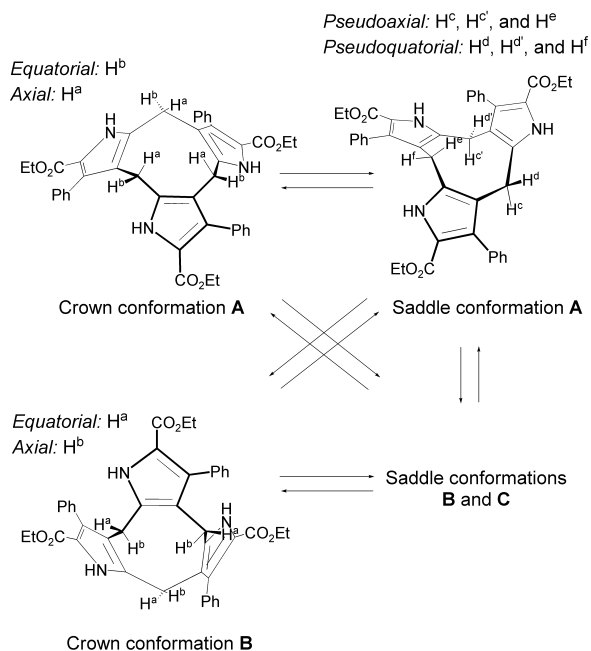**2**: X = H

**Figure 1.**

**Figure 2.** Conformations of CNTP **1b**.

## 2. Results and discussion

### 2.1. NMR

When we measured the NMR spectra of **1** in pyridine-$d_5$, the methylene protons appeared at $\delta$ 4.12 as a broad singlet signal, which did not change between −40 and 110°C. This fact suggests that **1** in pyridine-$d_5$ flips between the crown and saddle conformations (Fig. 2) and our previous consideration concerning with the conformation in CDCl$_3$ might be erroneous. If the chemical shifts of the pseudoaxial and pseudoequatorial methylene protons (pseudoaxial: H$^c$, H$^{c'}$, and H$^e$; pseudoequatorial: H$^d$, H$^{d'}$, and H$^f$) in saddle conformations are accidentally similar, the methylene protons would appear as one kind of AB quartet absorption. In this case, the methylene protons appear as the AB quartet signal, even when rapid pyrrole ring flipping causing the interconversion between saddle conformations **A**, **B**, and **C** occurs.
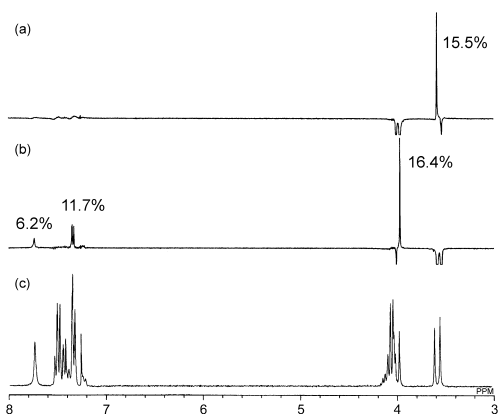


**Figure 3.** Differential NOE spectra of CNTP **1**. (a) irradiation at $\delta$ 3.98. (b) irradiation at $\delta$ 3.61. (c) basic spectrum.



**Figure 4.** **1**·3ClPh.
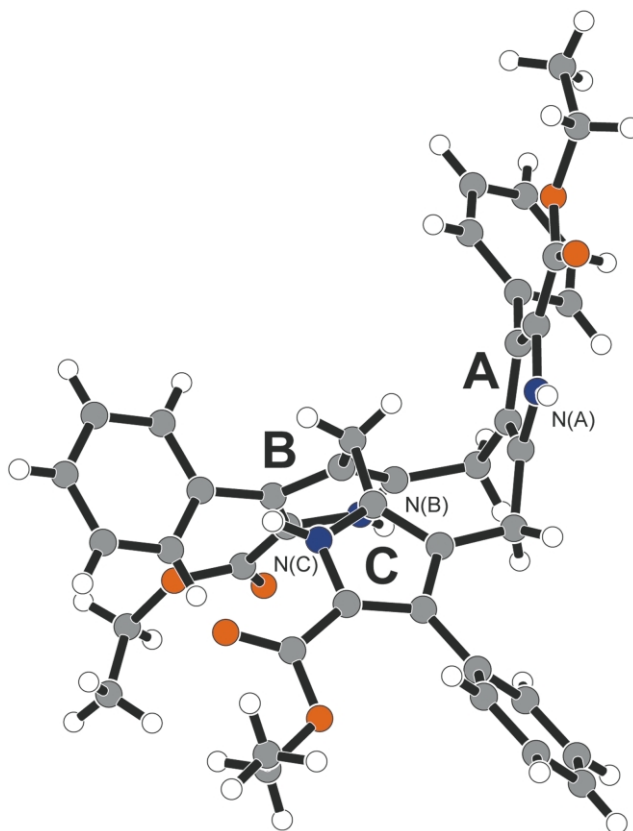
In order to examine the possibility, differential NOE experiments of CNTP **1** were carried out in CDCl$_3$ at ambient temperature, and the results are shown in Figure 3. Irradiation of the equatorial protons at $\delta$ 3.61 caused significant enhancement of aromatic *ortho* protons at $\delta$ 7.32 (11.7%) and pyrrolic NH protons at $\delta$ 7.73 (6.2%) in addition to the axial methylene protons (16.4%) and no excitation transfer between the methylene protons was observed, while no such enhancement except for the equatorial methylene protons (15.5%) was observed in irradiation of the axial protons. This fact denies both possibilities of the saddle conformation and rapid interconversion between the saddle conformations.

In pyridine-$d_5$, the NH signal of **1** was observed in very lower field ($\delta$ 12.36) than in chloroform-$d$ ($\delta$ 7.73) and toluene-$d_8$ ($\delta$ 7.88) due to the hydrogen bonding with the solvent. The MM2 (MM$^+$) calculations[8] of conformations show that the crown form is more stable than saddle one (35.06 vs 42.68 for **1** and 52.76 vs 57.36 kcal mol$^{-1}$ for **2**). Since the energy of hydrogen bonds, however, is known to be ca. 5 kcal mol$^{-1}$, it is possible to change the conformation by the hydrogen bonds depending on the conditions.

### 2.2. X-Ray

A few rods and many thin plate crystals were formed by slow evaporation (over three months) of a saturated chlorobenzene solution of **1**. Although the thin plate crystals were not suitable for X-ray analysis, one of the delicate rod
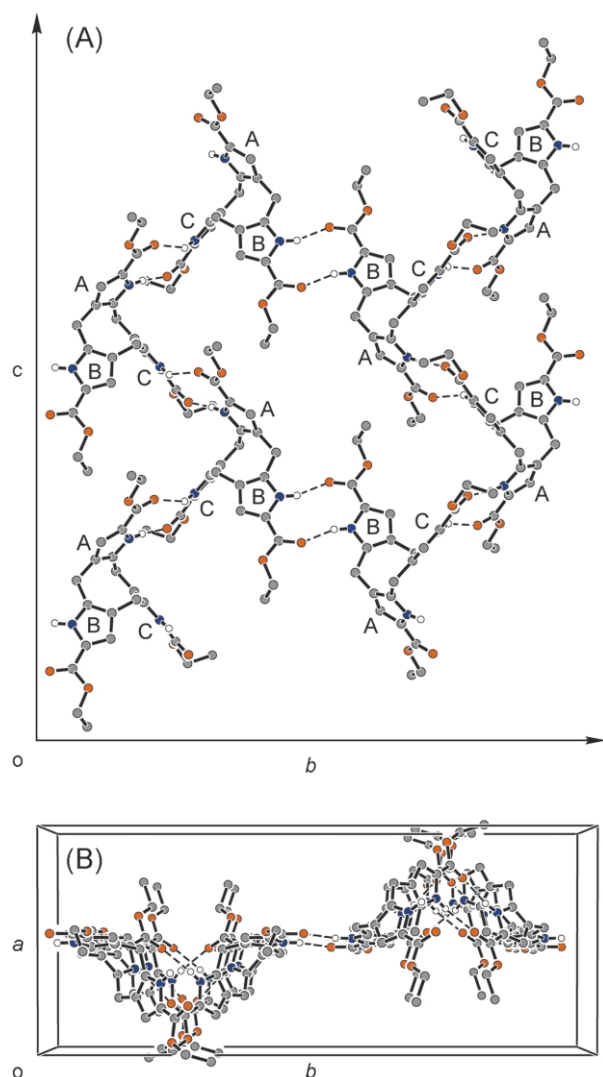
**Figure 5.** The crystal structure of **1**·3ClPh; phenyl groups and hydrogen atoms except for pyrrolic hydrogen are omitted for clarity. (A) Along *A* axis. (B) Along *C* axis.
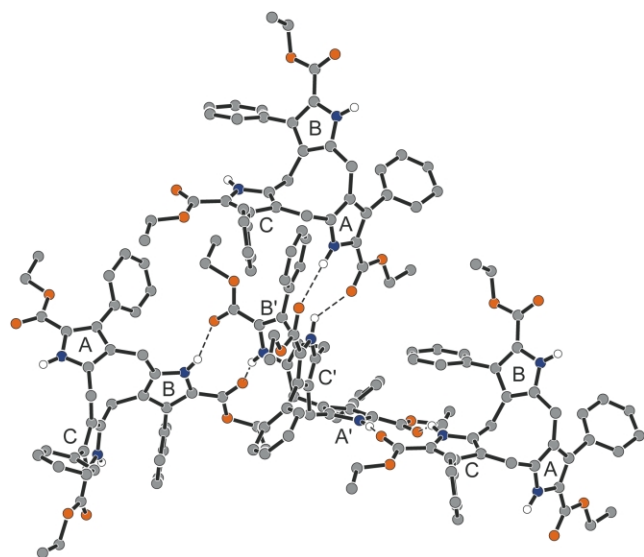


**Figure 6.** **1**·0.5CHCl₃: A, B, C and A′, B′, C′ denote the pyrrole rings of molecular 1 and 2, respectively.

crystals in air was subject to X-ray analysis at −100°C. This crystal was revealed to contain three molecules of chlorobenzene per **1**. The molecular structure of **1** adopts a saddle conformation as shown in Figure 4. Three plane angles between pyrrole rings (A–B, B–C and C–A) are 76.6(1)°, 84.8(1)° and 89.0(1)°, respectively. In this crystal system, the molecules of **1** are connected by two pairs of intermolecular hydrogen bonds between pyrrolic protons and carbonyl oxygen atoms on pyrrole rings A and C [NH(A)···O(C′), 2.869(3) and NH(C)···O(A′), 2.878(3) Å] along the *c* axis forming a molecular column, and the columns are connected anti-parallel to each other by the similar hydrogen bonds [NH(B)···O(B′), 2.825(3) Å] along the *b* axis (Fig. 5). The two-dimensional sheets are formed on the *b*–*c* plane. One phenyl group on the pyrrole B moiety stacks over the plane formed by the hydrogen bonds between the pyrrole C and the neighboring pyrrole A′ moieties. Voids between the sheets are filled with chlorobenzenes.

Another type of crystal was obtained by slow diffusion of hexane into a saturated chloroform solution of **1**. The platelet crystals were stable in the air. Although X-ray measurements were carried out at various temperatures (rt, −70, −100, and −150°C), the measurements above −100°C only gave meaningless solutions in spite of all our efforts. From the measurement at −150°C, the structures were successfully solved and refined. In this crystal, two independent molecules of **1** exist, one of the molecules is heavily disordered in the cyclononatriene ring, and they are hydrogen-bonded each other, forming a three-dimensional network (Fig. 6). The hydrogen-bonding pairs are observed between the pyrrole moieties of B and B′, A and C′, and C and A′.

Distortion of the nonatriene rings is illustrated in Figure 7. Distance of the ring atoms is calculated from the plane of methylene carbon atoms at 1, 4 and 7 positions in the cyclononatriene ring. From Figure 7, the distortion is very similar in all four crystal structures of CNTP **1**.

These saddle structures of CNTP in crystalline state are quite different from that of CTV which is known to exist as
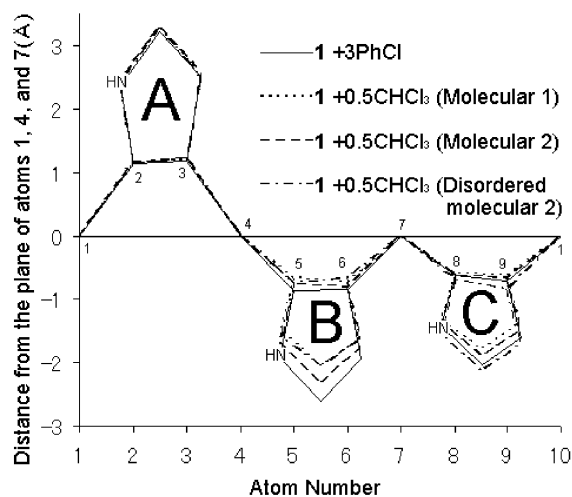


**Figure 7.** Distortion of nonatriene rings.

a rigid crown conformation both in crystalline (X-ray)[4,9] and solution (NMR).[10] These facts suggest that sterical requirement of phenyl groups at pyrrolic β-positions and the intermolecular hydrogen bonds between pyrrolic NH and ester C=O help to form the saddle conformation in the crystalline state.

In conclusion, we have succeeded in the first X-ray structural analyses of CNTP which adopted the saddle conformation. In solution, contrarily, CNTP adopted the crown conformation or underwent interconversion between several conformations depending on the solvent employed. Hydrogen bonding plays an important role for the structures.

## 3. Experimental

NMR spectra were obtained with a JNM-400 spectrometer and TMS was used as internal standard for $^1$H and $^{13}$C. Deuterated solvents were used without further purification. Chlorobenzene and hexane were distilled prior to use. Chloroform was successively treated with sulfuric acid, water, saturated sodium hydrogencarbonate, and calcium chloride; passed through an alumina column; and distilled. Other commercially available materials were used without further purification. CNTP **1** was prepared by the reported method.[7]

### 3.1. Differential NOE measurement of CNTP 1

CNTP **1** (10 mg) was dissolved in CDCl$_3$ (0.5 ml) and the solution was degassed by bubbling with argon for ca. 10 min. The pulse sequence of the differential NOE measurement supplied by JEOL was used, and pulse delay time (15 s) was determined by the measurement of T1.

### 3.2. X-Ray analysis

To a saturated chlorobenzene solution (ca. 1.5 ml) of CNTP **1** in a vial were added a few drops of chlorobenzene and then this vial was closed by a cap with a pin whole. When the volume became ca. 0.5 ml (3 months), a few rods and many thin platelet crystals were formed. One of the pale yellow rod (0.50×0.15×0.15 mm$^3$) was put in a Lindeman capillary tube (0.3 mmφ) and measured by Rigaku RAXIS IV imaging plate with graphite monochromated Mo Kα radiation and a rotating anode generator (50 kV, 100 mA). The diameter of the incident beam collimator was 0.5 mm and the crystal to IP detector distance was 120 mm. The data were collected at −100°C. No absorption correction was applied. The structure was solved by the SIR92 method,[11] expanded using the DIRDIF techniques,[12] and refined by the teXsan program[13] on an SGI O$_2$ computer. The crystal consisted of **1** and three molecules of chlorobenzene, one chlorine atom of which was disordered. Crystallographic summary for **1**·3ClPh: C$_{60}$H$_{54}$Cl$_3$N$_3$O$_6$, FW 1019.46, monoclinic, $P2_1/c$, $Z$=4 in a cell of dimensions of $a$=12.484(2) Å, $b$=30.13(2) Å, $c$=13.837(2) Å, $\beta$=91.75(2)°, $V$=5202(3) Å$^3$, $D_{calc}$=1.301 g cm$^{-3}$, $F(000)$=2136, collected reflections, 13776 (3.70°<2$\theta$<51.36°), unique reflections, 8414 with $F^2$>−10$\sigma$($F^2$), $R_{int}$=4.0. The structure

was refined on $F^2$. The final $R_1$=0.070 [7002 reflections with $F^2$>2$\sigma$($F^2$)]. $R$=0.096 (all), $R_w$=0.161 (all), goodness-of-fit=1.32 for 672 parameters. $\Delta\rho_{max}$=0.32 e$^-$/Å$^3$, $\Delta\rho_{min}$=−0.27 e$^-$/Å$^3$. CCDC 177654.

To a saturated chloroform solution (ca. 3 ml) of CNTP **1** in a vial were added two drops of chloroform. This vial was placed in a jar containing a small amount of hexane and the jar was tightly closed. After ca. 2 weeks, a few prismatic crystals were formed. One of the platelet crystal (0.70×0.20×0.08 mm$^3$) was mounted on a glass fiber and measured by Rigaku AFC7R Mercury CCD diffractometer with graphite monochromated Mo Kα radiation and a rotating anode generator (50 kV, 100 mA). The diameter of the incident beam collimator was 1.0 mm and the crystal to CCD detector distance was 35 mm. The data were collected at −150°C. Empirical absorption correction was applied. The structure was solved by the SIR92 method,[11] expanded using the DIRDIF techniques,[12] and refined by the teXsan program[13] on an SGI O$_2$ computer. The crystal consisted of one chloroform molecule and two molecules of **1**. Both of the CNTP molecules were disordered and the coordinates of the disordered non-hydrogen atoms were refined isotropically. Occupancies of these disordered atom groups were determined by the $R$ and $B_{eq}$ values when the ratios were put as 0.5:0.5, 0.55:0.45, 0.6:0.4, and 0.65:0.35. One of the CNTP molecules was heavily disordered in the cyclononatriene ring. In this highly disordered molecule, one of the phenyl groups with smaller occupancy was refined as a rigid group and the hydrogen atoms on one ethyl group were calculated from the atoms with the higher populations. The C–C bond lengths of this disordered ethyl group were restrained (bond length: 1.54, Sigma value 0.002). In the less disordered molecule, one of the phenyl groups with smaller occupancy was refined as a rigid group and the hydrogen atoms on one disordered ethyl group were calculated from the atoms with the highest populations. The C–C bond lengths of this disordered ethyl group were restrained (bond length: 1.54, Sigma value 0.002). Crystallographic summary for **1**·1/2CHCl$_3$: C$_{42.5}$H$_{39.5}$Cl$_{1.5}$N$_3$O$_6$, FW 741.48, monoclinic, $C2/c$, $Z$=16 in a cell of dimensions of $a$=47.581(5) Å, $b$=14.4761(7) Å, $c$=29.122(3) Å, $\beta$=129.367(3)°, $V$=15507(2) Å$^3$, $D_{calc}$=1.270 g cm$^{-3}$, $F(000)$=6224, collected reflections, 34359 (1.98°<2$\theta$<54.97°), unique reflections, 17680 with $F^2$>−10$\sigma$($F^2$), $R_{int}$=4.3. The structure was refined on $F^2$. The final $R_1$=0.088 [9664 reflections with $F^2$>2$\sigma$($F^2$)]. $R$=0.133 (all), $R_w$=0.198 (all), goodness-of-fit=1.48 for 1048 parameters. $\Delta\rho_{max}$=0.32 e$^-$/Å$^3$, $\Delta\rho_{min}$=−0.27 e$^-$/Å$^3$. CCDC 194423.

## References

1. For a review, see: Lehn, J.-M. *Supramolecular Chemistry*; VCH: Weinheim, 1995.
2. (a) Gutsche, C. D. *Calixarenes*; The Royal Society of Chemistry: Cambridge, 1989; and references cited therein. (b) Ungaro, R. *Comprehensive Supramolecular Chemistry*; Vögtle, F., Ed.; Pergamon: Tarrytown, NY, 1996; Vol. 2, p 103.
3. (a) Gale, P. A.; Sessler, J. L.; Lynch, V. *J. Am. Chem. Soc.* **1996**, *118*, 5140–5141. (b) Gale, P. A.; Sessler, J. L.; Král, V. *Chem. Commun.* **1998**, 1–8.
4. *Comprehensive Supramolecular Chemistry*; Szejtli, J., Oasa, T., Eds.; Pergamon: Tarrytown, NY, 1996; Vol. 3, and references cited therein.
5. Zheng, M.; Li, K.; Pan, Z.; Xianglin, X.; Tang, Y. *Beijing Daxue Xuebao Ziran Kexueban* **1989**, *25*, 138–145.
6. (a) Meth-Cohn, O. *Tetrahedron Lett.* **1973**, 91–94. (b) Russell, M. J. H.; White, C. A. Y.; Maitlis, P. M. *J. Chem. Soc., Dalton Trans.* **1978**, 857–861. (c) Staffilani, M.; Bonvicini, G.; Steed, J. W.; Holman, K. T.; Atwood, J. L.; Elsegood, M. R. *J. Organomet.* **1998**, *17*, 1732–1740.
7. Fumoto, Y.; Uno, H.; Ito, S.; Tsugumi, Y.; Sasaki, M.; Kitawaki, Y.; Ono, N. *J. Chem. Soc., Perkin Trans. 1* **2000**, 2977–2981.
8. For reviews, see: (a) Burkert, U.; Allinger, N. L. *Molecular Mechanism*; ACS: Washington, DC, 1982. (b) Clark, T. *Computational Chemistry*; Wiley: New York, 1985.
9. (a) Cerrini, S.; Giglio, E.; Mazza, F.; Pavel, N. V. *Acta Crystallogr.* **1979**, *B35*, 2604–2609. (b) George, I. B.; Klug, D. D.; Pigmeester, J. A.; Tse, J. S. *Can. J. Chem.* **1985**, *63*, 3258–3263.
10. Canceill, J.; Collet, A.; Gottarelli, G. *J. Am. Chem. Soc.* **1984**, *106*, 5997–6003.
11. SIR92: Altomane, A.; Burla, M. C.; Camalli, M.; Cascarano, M.; Giacovazzo, C.; Guagliardi, A.; Polidori, G. *J. Appl. Crystallogr.* **1994**, *27*, 435.
12. DIRDIF94: Beurskens, P. T.; Admiraal, G.; Beurskens, G.; Bosman, W. P.; de Gelder, R.; Israel, R.; Smitz, J. M. N. *The DIRDIF94 Program System*; Technical Report of the Crystallography Laboratory; University of Nijmegen: The Netherlands, 1994.
13. *teXsan. Single Crystal Structure Analysis Software*; version 1.11; Molecular Structure Corporation MSC, Rigaku Corporation. 3200 Research Forest Drive, The Woodlands, TX 77381, USA. Rigaku, 3-9-12 Akishima, Tokyo, Japan, 2000.