

The *O, O'*-Dibenzoyl Derivative of (*R, R*)-Tartaric Acid as a Host Compound for Simple Organic Ethers

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Abstract. The *O, O'*-dibenzoyl derivative of (*R, R*)-tartaric acid shows a good inclusion ability for diethyl and di-*n*-propyl ethers. The two crystalline inclusion compounds have 1 : 1 stoichiometry and reveal isomorphous structures. Hydrogen bonded host molecules form chains running along the *z* axis of the unit cell and guest molecules join to these chains by short O—H · · · O hydrogen bonds. Hydrogen bonding in the crystals is characterized by a C(7)D first-order network. The ether molecules are in a fully extended conformation. They are accommodated in channel-like voids running along the *x* axis. Atomic displacement parameters are significantly larger for diethyl ether than for the di-*n*-propyl ether molecule reflecting less dense packing for this inclusion compound.

Key words: (*R, R*)-Tartaric acid derivatives, host–guest compounds, crystal structure.

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1. Introduction

Optically active tartaric acid and its acyl derivatives (e.g. dibenzoyl and di-*p*-toluoyl acids) continue to be widely used in the resolution of racemates [1]. Several crystal structures with optically active dibenzoyl and di-*p*-toluoyl tartaric acids have been published, the vast majority of them containing ionized carboxylate groups [3–19]. (*R, R*)-Di-*O*-benzoyltartaric acid exists as the monohydrate with m.p. 89–90 °C, and as an anhydrous compound with m.p. 138–139 °C prepared by drying the hydrate under vacuum at 80–100 °C [2]. In the process of recrystallization of (*R, R*)-di-*O*-benzoyltartaric acid we have noticed its inherent tendency to co-crystallize with solvent molecules and decided to perform single crystal analysis of some of these compounds to reveal the mode of inclusion formation. The characteristic of the crystals obtained was their instability in air. So far we have

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not been able to obtain crystals of a good quality from simple organic alcohols, but recrystallization from diethyl and di-*n*-propyl ethers gave satisfactory results.

2. Experimental

Single crystals of (*R,R*)-di-*O*-benzoyltartaric acid–diethyl ether (1/1) (**I**) and (*R,R*)-di-*O*-benzoyltartaric acid–di-*n*-propyl ether (1/1) (**II**) were obtained by slow evaporation from diethyl and di-*n*-propyl ethers, respectively. The crystals were plate shaped and slowly decomposed when exposed to air, which was noticed after collecting intensities for **I**. The crystal of **II** was therefore sealed in a glass capillary. Unit-cell parameters were determined on a Syntex P2₁ diffractometer by a least-squares fitting of the setting angles of 15 reflections. Crystal data and some details concerning data collection and structure refinement are given in Table I. Intensities of reflections were measured using the θ – 2θ scan technique on a Syntex P2₁ diffractometer, with the scan rate depending directly on the net count obtained on a rapid pre-scan for each reflection. Two standard reflections were monitored after collection of every 100 reflections as a check of electronic reliability and crystal stability, and the intensity fluctuations of these reflections were not greater than $\pm 3\%$ and $\pm 5\%$ for **I** and **II**, respectively. Integrated intensities were obtained by peak profile analysis according to Lehmann and Larsen [20]. Data were corrected for Lorentz and polarization effects but not for absorption.

The structures were solved by direct methods with the program SHELXS-86 [21] and refined by a full-matrix least-squares method with the program SHELX-76 [22]. The function minimized was $\sum (w|F_o| - |F_c|)^2$. Data with $I \geq 2\sigma(I)$ were used in the refinement, except for five poorly determined I_{\max} reflections (002, 004, 022, 110 and 122) in **I**, the intensities of which, originally measured at lower current, were subsequently multiplied by an estimated common factor. All non-hydrogen atoms were refined anisotropically. The H atoms were placed in calculated positions, with the exception of the carboxyl hydrogens which were located from a difference Fourier map. In the refinement, H atoms were following the shifts of ('riding' on) the atoms to which they were attached.

Isotropic temperature factors for H atoms were treated as follows. All H atoms of the guest molecule were assigned a common isotropic temperature factor of the value $U = 0.27$ and 0.14 \AA^2 for **I** and **II**, respectively. H atoms of the host molecule were given a common isotropic temperature factor of 0.11 and 0.09 \AA^2 for **I** and **II**, respectively, except for the benzene hydrogen atoms near the *para* position, where the effect of librational rigid body motion was clearly visible. For H(23), H(24) and H(25) in both crystal structures and for H(33), H(34), H(35) in **II** the U value of 0.13 \AA^2 was chosen, while for the latter three atoms in **I** the U value was 0.016 \AA^2 . At the end of the refinement an empirical isotropic extinction parameter x was introduced to correct the calculated structure factors by multiplying them by a factor $1 - xF_c^2/\sin \theta$. Atomic scattering factors used were those included in SHELX-76 [22]. Tables of anisotropic displacement parameters, bond lengths

TABLE I. Crystal data for inclusion compounds of (R, R)-di-O-benzoyltartaric acid.

	I	II
Empirical formula	C ₁₈ H ₁₄ O ₈ ·C ₄ H ₁₀ O	C ₁₈ H ₁₄ O ₈ ·C ₆ H ₁₄ O
Formula weight	432.43	460.49
m.p.	75–76 °C	77–80 °C
Temperature	293 K	293 K
Wavelength	Cu K _α (1.54178 Å)	Cu K _α (1.54178 Å)
Crystal system	orthorhombic	orthorhombic
Space group	P2 ₁ 2 ₁ 2 ₁	P2 ₁ 2 ₁ 2 ₁
Unit cell dimensions	<i>a</i> = 11.806(3) (Å) <i>b</i> = 13.152(3) <i>c</i> = 15.236(1)	<i>a</i> = 11.607(2) (Å) <i>b</i> = 13.964(4) <i>c</i> = 15.298(5)
Volume	2365.7(8) Å ³	2479.5(1.1) Å ³
<i>Z</i>	4	4
Density (calculated)	1.214 g cm ⁻¹	1.234 g cm ⁻¹
Absorption coefficient	0.076 mm ⁻¹	0.075 mm ⁻¹
Crystal size	0.4 × 0.35 × 0.2 mm	0.6 × 0.35 × 0.2 mm
2θ _{max} for data collection	115°	120°
Index ranges	0 ≤ <i>h</i> ≤ 12, 0 ≤ <i>k</i> ≤ 14, 0 ≤ <i>l</i> ≤ 16	0 ≤ <i>h</i> ≤ 12, 0 ≤ <i>k</i> ≤ 15, 0 ≤ <i>l</i> ≤ 16
Reflections collected	1907	1999
Observed reflections [<i>F</i> > 4σ(<i>F</i>)]	1381	1546
Extinction parameter	1(2) × 10 ⁻⁵	7(1) × 10 ⁻⁶
Weighting scheme	<i>w</i> = <i>k</i> /[σ ² (<i>F</i>) + 0.00025 <i>F</i> ²]	<i>w</i> = <i>k</i> /[σ ² (<i>F</i>) + 0.0002 <i>F</i> ²]
Goodness-of-fit	2.4	2.5
Final <i>R</i> indices	<i>R</i> ₁ = 0.041, <i>wR</i> ₂ = 0.056	<i>R</i> ₁ = 0.040, <i>wR</i> ₂ = 0.054
Largest diff. peak and hole	0.10 and -0.12 e Å ⁻³	0.12 and -0.13 e Å ⁻³

and angles, H-atom coordinates and lists of structure factors have been deposited. The final atomic coordinates with equivalent isotropic temperature factors for both crystal structures are given in Table II. Pertinent torsion angles are compared in Table III. The atom numbering scheme is displayed in Figure 1 [23].

3. Discussion

3.1. CONFORMATION OF THE HOST MOLECULE

As observed in the vast majority of (R, R)-tartaric acid derivatives, the conformation around the C*—C* bond, linking the two chiral centers, is staggered such that the two carboxyl groups are *anti* and the two adjacent C—OBz bonds are *minus synclinal* (*-sc*). The values of the torsion angles differ in both structures from the ideal values of 180 and -60° and amount to 173.5(4) and -68.5(4)°; 170.4(4) and -73.6(4)° in **I** and **II**, respectively. The corresponding values for 17 other crystal structures (18 independent measurements) listed in the Cambridge

TABLE II. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement coefficients ($\text{\AA}^2 \times 10^3$) for (I).

	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> (eq)
O(1)	7726(3)	5819(3)	5976(2)	95(1)
O(10)	6143(3)	6238(3)	6680(2)	114(2)
O(4)	7503(4)	3239(3)	8700(2)	110(2)
O(40)	7235(3)	4757(3)	9288(2)	93(1)
O(2)	8708(2)	5167(2)	7497(2)	73(1)
O(20)	9257(3)	6798(3)	7448(3)	106(2)
O(3)	6864(3)	3903(3)	7089(2)	77(1)
O(30)	5191(3)	3299(3)	7527(3)	118(2)
C(1)	7166(4)	5881(4)	6622(3)	81(2)
C(2)	7555(4)	5502(3)	7526(3)	72(2)
C(20)	9502(4)	5912(4)	7452(3)	77(2)
C(21)	10656(4)	5496(3)	7436(3)	71(2)
C(22)	11542(5)	6166(4)	7313(4)	96(2)
C(23)	12648(5)	5802(5)	7294(4)	110(3)
C(24)	12854(5)	4791(5)	7403(4)	109(3)
C(25)	11983(5)	4130(4)	7508(4)	98(2)
C(26)	10877(4)	4467(3)	7520(3)	82(2)
C(3)	6840(4)	4609(3)	7792(3)	72(2)
C(4)	7249(4)	4103(4)	8638(3)	77(2)
C(30)	5956(4)	3278(4)	7004(3)	82(2)
C(31)	6002(5)	2630(4)	6221(3)	85(2)
C(32)	5130(6)	1993(5)	6071(5)	117(3)
C(33)	5140(9)	1366(7)	5341(7)	167(5)
C(34)	6017(12)	1413(9)	4758(6)	210(6)
C(35)	6893(10)	2065(8)	4915(5)	195(5)
C(36)	6901(7)	2681(5)	5649(4)	127(3)
C(1A)	5982(16)	8309(9)	5280(9)	243(11)
C(2A)	5162(12)	7706(12)	4945(8)	220(9)
O(3A)	5224(4)	6684(6)	5214(3)	150(3)
C(4A)	4433(13)	6085(17)	4877(10)	277(13)
C(5A)	4562(16)	5020(13)	5046(12)	303(13)

*Equivalent isotropic *U* defined as one third of the trace of the orthogonalized U_{ij} tensor.

Structural Database [24] give average torsion angle moduli of 172(2) and 65(10)°. It is worth mentioning the presence of the unusual *plus synclinal* conformer in the (*R, R*)-hydrogen-di-*O*-benzoyltartrate anion [19] and in *N, N'*-tetramethyl-di-*O*-benzoyltartramide [25].

The conformation around the C—C* bond in both crystal forms, and at both ends of the molecule is the same, i.e. the C—OBz bond always eclipses the carbonyl

TABLE II. Continued. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement coefficients ($\text{\AA}^2 \times 10^3$) for (II).

	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> (eq)
O(1)	7677(3)	5767(2)	5924(2)	83(1)
O(10)	6061(3)	6098(2)	6666(2)	80(1)
O(4)	7670(4)	3263(3)	8568(2)	106(2)
O(40)	7384(3)	4670(2)	9215(2)	87(1)
O(2)	8736(3)	5130(2)	7414(2)	69(1)
O(20)	9244(3)	6678(3)	7442(3)	95(1)
O(3)	6788(3)	3927(2)	7023(2)	68(1)
O(30)	5254(3)	3252(3)	7660(2)	100(2)
C(1)	7130(4)	5783(3)	6589(3)	66(2)
C(2)	7568(4)	5420(3)	7466(3)	64(1)
C(20)	9528(4)	5852(4)	7416(3)	72(2)
C(21)	10727(4)	5484(4)	7404(3)	74(2)
C(22)	11613(5)	6141(5)	7313(3)	95(2)
C(23)	12737(5)	5822(7)	7312(4)	119(3)
C(24)	12959(6)	4855(7)	7398(5)	127(4)
C(25)	12091(5)	4214(5)	7475(4)	107(3)
C(26)	10959(4)	4508(4)	7482(3)	84(2)
C(3)	6861(4)	4562(3)	7757(3)	67(2)
C(4)	7382(4)	4067(4)	8552(3)	70(2)
C(30)	5884(4)	3306(3)	7039(3)	73(2)
C(31)	5777(4)	2749(3)	6221(3)	67(2)
C(32)	6452(5)	2921(4)	5497(3)	84(2)
C(33)	6256(6)	2415(5)	4732(4)	106(3)
C(34)	5368(8)	1752(5)	4707(5)	115(3)
C(35)	4704(7)	1582(4)	5419(5)	104(3)
C(36)	4895(5)	2080(3)	6177(4)	85(2)
C(1A)	5760(6)	9167(4)	5154(5)	110(3)
C(2A)	5955(5)	8107(3)	5279(3)	90(2)
C(3A)	4948(5)	7522(4)	5008(4)	85(2)
O(4A)	5162(3)	6530(2)	5173(2)	76(1)
C(5A)	4220(5)	5922(3)	4954(4)	87(2)
C(6A)	4554(5)	4902(3)	5020(4)	103(3)
C(7A)	3588(5)	4213(4)	4840(4)	110(3)

*Equivalent isotropic *U* defined as one third of the trace of the orthogonalized U_{ij} tensor.

oxygen of the carboxyl residue, the corresponding torsion angles being in the range from $-2.7(7)$ to $5.8(7)^\circ$. This leads to the formation of planar $\text{O}=\text{C}-\text{C}^*-\text{O}$ fragments within the molecule and results in an approximate C_2 symmetry of the host molecule (Figure 1). The tendency for the benzoyloxy oxygen to eclipse one

TABLE III. Selected torsion angles ($^{\circ}$).

	I	II
C(2)—O(2)—C(20)—C(21)	179.3(4)	177.2(4)
C(2)—O(2)—C(20)—O(20)	0.9(7)	-1.6(6)
C(20)—O(2)—C(2)—C(1)	74.3(5)	77.9(5)
C(20)—O(2)—C(2)—C(3)	-166.5(4)	-161.4(4)
C(3)—O(3)—C(30)—C(31)	175.2(4)	173.3(4)
C(3)—O(3)—C(30)—O(30)	-3.0(7)	-5.6(6)
C(30)—O(3)—C(3)—C(2)	-152.8(4)	-157.5(4)
C(30)—O(3)—C(3)—C(4)	83.8(5)	79.5(5)
O(1)—C(1)—C(2)—O(2)	5.8(7)	4.6(6)
O(10)—C(1)—C(2)—O(2)	-176.1(4)	-176.5(4)
O(10)—C(1)—C(2)—C(3)	65.6(5)	63.9(5)
O(1)—C(1)—C(2)—C(3)	-112.5(5)	-115.0(5)
O(2)—C(2)—C(3)—O(3)	-68.5(4)	-73.7(4)
C(1)—C(2)—C(3)—O(3)	51.9(5)	47.9(4)
C(1)—C(2)—C(3)—C(4)	173.5(4)	170.4(4)
O(2)—C(2)—C(3)—C(4)	53.1(5)	48.8(5)
O(3)—C(3)—C(4)—O(40)	179.5(4)	-177.5(4)
O(3)—C(3)—C(4)—O(4)	-2.8(7)	-1.2(7)
C(2)—C(3)—C(4)—O(40)	59.6(5)	62.6(5)
C(2)—C(3)—C(4)—O(4)	-122.8(5)	-121.1(5)

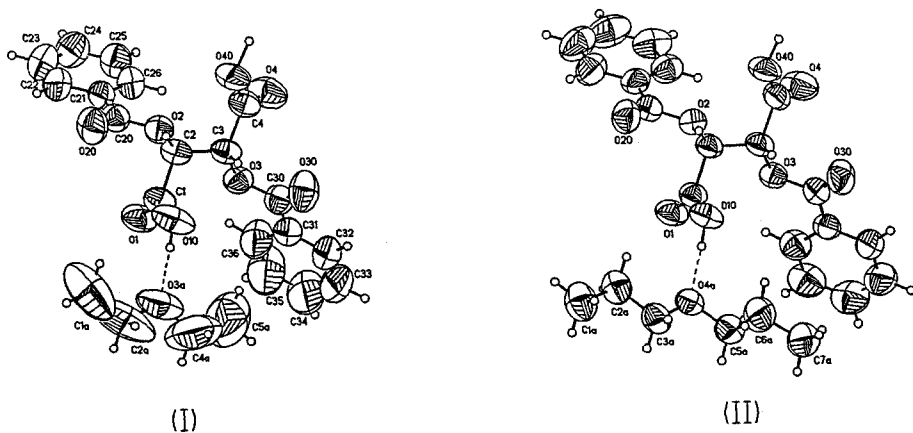


Fig. 1. Atom numbering scheme and thermal ellipsoids drawn at the 50% probability level for I and II.

of the oxygen atoms from the neighbouring carboxyl moiety is observed in the majority of the acyl derivatives mentioned above, although deviations up to 32° have also been reported.

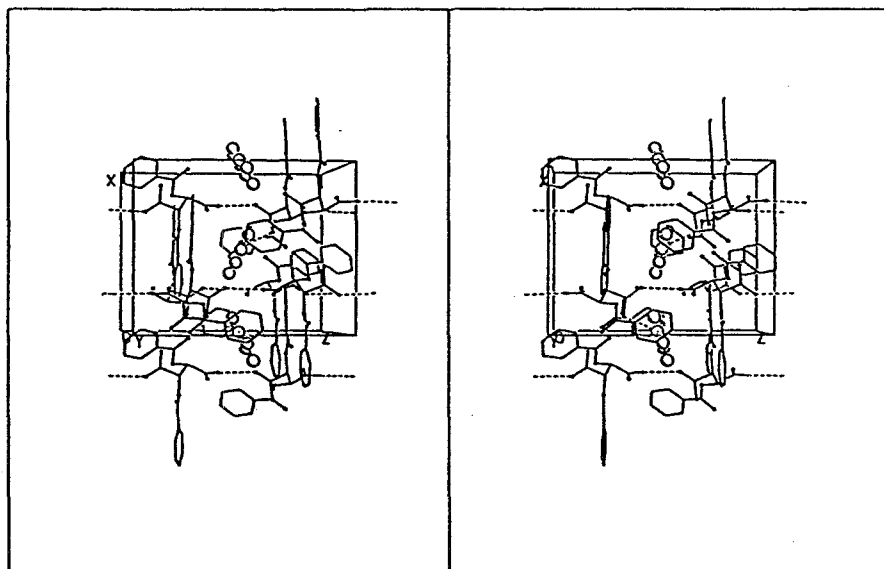


Fig. 2. Crystal packing in **II**. Atoms of the guest molecules are shown as large circles, O atoms of the host are shown as small circles, H atoms have been omitted for clarity.

3.2. CRYSTAL STRUCTURE

The two crystalline inclusion compounds have 1 : 1 stoichiometry and reveal isomorphous structures. In the crystals, host molecules are connected head to tail via hydrogen bonds between the carboxyl groups and form chains running along the z axis (Figure 2). The lattice c parameter is the least affected unit-cell parameter when diethyl ether is changed to a larger guest. Ether molecules join to the host chains via relatively short O—H \cdots O hydrogen bonds between one of the host carboxyl groups and the guest ether oxygen atom. Thus, hydrogen bonding in these crystals is characterized by a C(7)D first-order network [26]. The geometry of the hydrogen bonds is given in Table IV. The O_(carboxyl) \cdots O_(ether) distances of 2.552(6) and 2.582(4) Å in **I** and **II**, respectively, are shorter than contacts between the carboxyl group and PO groups (2.676, 2.619 Å) observed in (*S, S*)-di-*O*-benzoyltartaric acid – (–)bicyclo[2.2.1]hept-5-ene-2,3-diyl-bis(diphenylphosphane oxide) (1/1) [11].

In both crystal structures the ether molecules are in a fully extended conformation and accommodated in channel-like voids running along the x axis. The arrangement of the guest molecules in these voids is shown in Figure 3. The molecular long axis (the line joining the terminal C atoms) of the guest forms an angle of 20 and 21° with the crystal y axis, and 110 and 111° with the channel direction in **I** and **II**, respectively. This is in line with the observation that changes in lattice parameters are most prominent for b which increases by about 6% in the crystal containing the bulkier di-*n*-propyl ether molecule. However, these changes are smaller than would be expected from a change (~ 2.5 Å) of one of the molecular

TABLE IV. Geometry of the hydrogen bonds.

D—H···A	D···A (Å)	D—H (Å)	H···A (Å)	<D—H···A (°)
I				
O(10)—H(10)···O(3A)	2.552(6)	0.85	1.72	164
O(40)—H(40)···O(1 ⁱ)	2.681(4)	1.16	1.58	156
II				
O(10)—H(10)···O(4A)	2.582(4)	0.91	1.67	176
O(40)—H(40)···O(1 ⁱ)	2.686(4)	1.00	1.87	136

Symmetry code: (i) $1.5 - x, 1 - y, z + 0.5$.

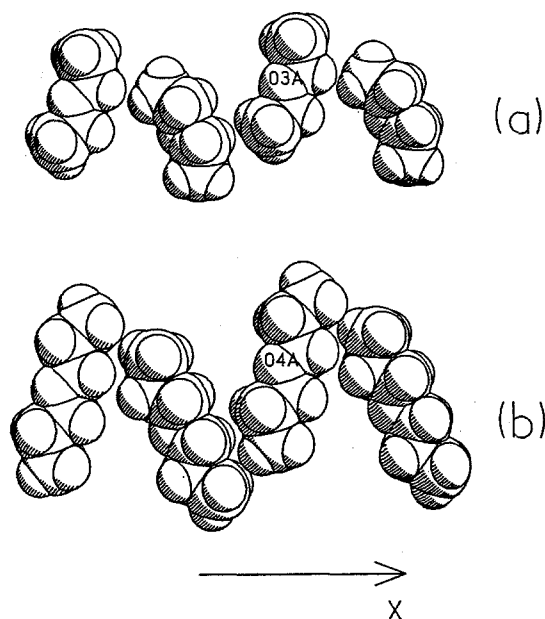


Fig. 3. Arrangement of (a) diethyl ether molecules and (b) di-*n*-propyl ether molecules along the channel.

dimensions of the guest. Significantly larger atomic displacement parameters for diethyl ether than for the di-*n*-propyl ether molecule confirm that crystal packing is relatively loose in **I**. Large atomic displacement parameters are also observed for the atoms near the *para* position in the benzoyl groups [especially that at C(3)] in both structures.

Di-*O*-acyl derivatives of (*R,R*)-tartaric acid exhibit strong conformational preferences in solution and in the solid state. A partial rigidification of a seemingly flexible molecule, an *anti* disposition of the carboxylic groups, and an approximate C_2 symmetry of the molecule may be at the root of the good inclusion ability of these compounds.

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References

1. E.L. Eliel, S.H. Wilen, and L.N. Mander: *Stereochemistry of Organic Compounds*, John Wiley & Sons, Inc., New York (1994).
2. M. Semonsky, A. Cerny, and V. Zikan: *Coll. Czech. Chem. Commun.* **21**, 382 (1956).
3. P.S. Anderson, J.J. Baldwin, D.E. McClure, G.F. Lundell, J.H. Jones, W.C. Randall, G.E. Martin, M. Williams, J.M. Hirshfield, B.V. Clineschmidt, P.K. Lumma, and D.C. Remmy: *J. Med. Chem.* **26**, 363 (1983).
4. V. Kettmann, L. Benes, and M. Tichy: *Acta Crystallogr.* **C41**, 208 (1985).
5. J.H. Jones, P.S. Anderson, J.J. Baldwin, B.V. Clineschmidt, D.E. McClure, G.F. Lundell, W.C. Randall, G.E. Martin, M. Williams, J.M. Hirshfield, G. Smith, and P.K. Lumma: *J. Med. Chem.* **27**, 1607 (1984).
6. S. Elz, M. Drager, H.J. Sattler and W. Schunack: *Z. Naturforsch.* **B42**, 617 (1987).
7. J.F. DeBernardis, D.J. Kerkman, D.L. Arendsen, S.A. Buckner, J.J. Kyncl, and A.A. Hancock: *J. Med. Chem.* **30**, 1011 (1987).
8. A.N. Chekhlov, Yu. P. Belov, J.V. Martynov, and A. Yu. Aksinenko: *Izv. Akad. Nauk SSSR, Ser. Khim.* 2821 (1986); *Chem. Abstr.* **107**, 236840c (1987).
9. X. Zhang, K. Mashima, K. Koyano, N. Sayo, H. Kumobayashi, S. Akutagawa and H. Takaya: *Tetrahedron Lett.* **32**, 7283 (1991); idem: *J. Chem. Soc., Perkin Trans. 1* 2309 (1994).
10. A. A. Freer and G.A. Sim: *J. Chem. Soc., Perkin Trans. 2*, 1717 (1990).
11. H. Brunner, W. Pieronczyk, B. Schönhammer, K. Streng, I. Bernal, and J. Korp: *Chem. Ber.* **114**, 1137 (1981).
12. C.J. Swain, R. Baker, C. Kneen, R. Herbert, J. Moseley, J. Saunders, E.M. Seward, G.I. Stevenson, M. Beer, J. Stanton, K. Watling, and R.G. Ball: *J. Med. Chem.* **35**, 1019 (1992).
13. N.C. Payne and M.E. Thachuk: *Chirality* **1**, 284 (1989).
14. G. Shapiro, P. Floersheim, J. Boelsterli, R. Amstutz, H. Gammenthaler, G. Gmelin, P. Supavilai and M. Walkinshaw: *J. Med. Chem.* **35**, 15 (1992).
15. G.A. Rogers, S.M. Parsons, D.C. Anderson, L.M. Nilsson, B.A. Bahr, W.D. Kornreich, R. Kaufman, R.S. Jacobs, and B. Kirtman: *J. Med. Chem.* **32**, 1217 (1989).
16. T.E. D'Ambra, K.G. Estep, M.R. Bell, M.A. Eissenstat, K.A. Josef, S.J. Ward, D.A. Haycock, E.R. Baizman, F.M. Casiano, N.C. Beglin, S.M. Chippari, J.D. Grego, R.K. Kullnig, and G.T. Daley: *J. Med. Chem.* **35**, 1429 (1992).
17. Y.L. Chen, J. Nielsen, K. Hedberg, A. Dunaiskis, S. Jones, L. Russo, J. Johnson, J. Ives, and D. Liston: *J. Med. Chem.* **35**, 1429 (1992).
18. P.L. Ornstein, D.D. Schoepf, M.B. Arnold, N.D. Jones, J.B. Deeter, D. Lodge, and J.D. Leander: *J. Med. Chem.* **35**, 3111 (1992).
19. S.I. Hommeltoft, A.D. Cameron, T.A. Shackleton, M.E. Fraser, S. Fortier and M.C. Baird: *Organometallics* **5**, 1380 (1986).
20. M.S. Lehmann and F.K. Larsen: *Acta Crystallogr.* **A30**, 580 (1974).
21. G.M. Sheldrick: SHELXS86. *Program for the solution of crystal structures*, Univ. of Göttingen, Germany (1986).
22. G.M. Sheldrick: SHELX76. *Program for crystal structures determination*. Univ. of Cambridge, England (1976).
23. *Stereochemical Workstation Operation Manual* (1989), Release 3.4, Siemens Analytical X-Ray Instruments, Inc., Madison, Wisconsin, USA.
24. F.H. Allen, O. Kennard, and R. Taylor: *Acc. Chem. Res.* **16**, 146 (1983).
25. U. Rychlewska: *Acta Crystallogr.* **C48**, 965 (1992).
26. M.C. Etter, J.C. MacDonald, and J. Bernstein: *Acta Crystallogr.* **B46**, 256 (1990).