Pergamon

Tetrahedron: Asymmetry, Vol. 7, No. 3, pp. 843-850, 1996

0957-4166/96 $15.00 + 0.00

S0957-4166(96)00082-1

New Enantiomerically Pure Aminoalcohols from (*R*)-α-Methylbenzylamine and Cyclohexene Oxide

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Abstract: The new chiral aminoalcohols *N*-{(*S*)-[cyclohexan-(*S*)-2-ol]}-(*R*)-α-methylbenzyl amine **1** and *N*-{(*R*)-[cyclohexan-(*R*)-2-ol]}-(*R*)-α-methylbenzyl amine **2** were prepared by reaction of (*R*)-α-methylbenzylamine with cyclohexene oxide at 160 °C. The diastereoisomers were separated by fractional crystallization of the corresponding ammonium chlorides *N*-{(*S*)-[cyclohexan-(*S*)-2-ol]}-(*R*)-α-methylbenzyl ammonium chloride **1**·HCl and *N*-{(*R*)-[cyclohexan-(*R*)-2-ol]}-(*R*)-α-methylbenzyl ammonium chloride **2**·HCl. The absolute configuration of all stereocenters in **1**·HCl and **2**·HCl was determined by X-ray diffraction analyses.

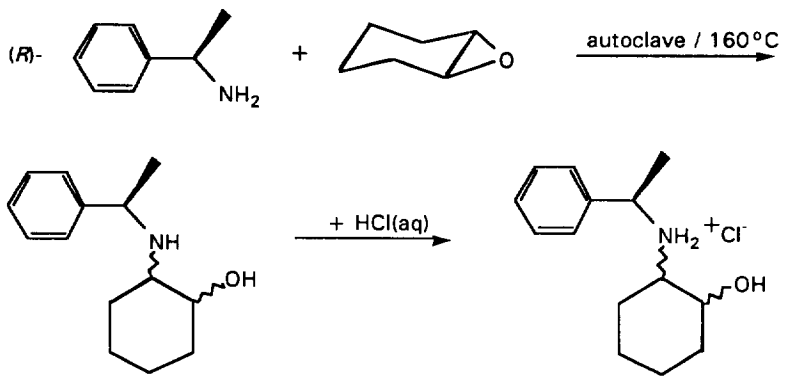
Enantiomerically pure aminoalcohols are attracting considerable interest as ligands in conjuction with Lewis-acid metal ions to generate metal complexes with potential in asymmetric catalysis, particularly for those reactions which require an electrophilic metal system to activate a substrate (e.g. Diels-Alder reactions).[1] Furthermore they are useful chiral building blocks for the preparation of a variety of chiral ligands with different number and/or nature of donor atoms: tridentate N,O_2 ligands may be obtained by further reaction with another epoxide molecule;[2, 3a] bidentate N,P- or NS-ligands or tridentate N,P_2- or NS_2-ligands may readily be prepared by standard procedures.[3]

In this paper, we describe the synthesis and characterization of the new aminoalcohols *N*-{(*S*)-[cyclohexan-(*S*)-2-ol]}-(*R*)-α-methylbenzyl amine **1** and *N*-{(*R*)-[cyclohexan-(*R*)-2-ol]}-(*R*)-α-methylbenzyl amine **2** by reaction of (*R*)-α-methylbenzylamine with cyclohexene oxide. The use of these reagents has led to the isolation of enantiomerically pure aminoalcohols with three stereocenters, all proximal to the N and O donor atoms. Also, due to the cyclohexane moiety, **1** and **2** are stereochemically rigid in solution (on the NMR timescale). Both these features generally characterize chiral ligands that are capable of efficiently transfer the chiral information to substrates.

RESULTS AND DISCUSSION

The nucleophilic attack by primary or secondary amines on epoxides is a common procedure for the preparation of β-aminoalcohols.[4] When (*R*)-α-methylbenzylamine is reacted with a stoichiometric amount of

cyclohexene oxide, drastic conditions are required to accomplish the 1:1 condensation (Scheme 1). Initially, both components were heated at 100°C for 4 days to give, after distillation of the crude product, the desired β-aminoalcohols (*vide infra*) only in very low yield. Soon we realized that the reaction had occurred during the distillation as the crude mixture did not contain an appreciable amount of ring-opening products (GC-MS). Thus, the reaction was carried out in an autoclave at 160°C. In these conditions, complete transformation of the starting amine occurs in 48 h with clean and quantitative formation of the two diastereoisomers *N*-{(*S*)-[cyclohexan-(*S*)-2-ol]}-(*R*)-α-methylbenzyl amine **1** and *N*-{(*R*)-[cyclohexan-(*R*)-2-ol]}-(*R*)-α-methylbenzyl amine **2** in a 1:1 ratio (GC/MS). The crude mixture can be purified from residual cyclohexene oxide by distillation; however, a much better method of purification has been achieved by dissolving the mixture in ethanol, followed by addition of an excess of concentrated $HCl_{(aq)}$. After the solvents were removed under reduced pressure, the residue was dissolved in boiling ethanol. Work-up as described in the experimental section gave *N*-{(*S*)-[cyclohexan-(*S*)-2-ol]}-(*R*)-α-methylbenzyl ammonium chloride **1**·HCl and *N*-{(*R*)-[cyclohexan-(*R*)-2-ol]}-(*R*)-α-methylbenzyl ammonium chloride **2**·HCl by fractional crystallization in excellent yields and diastereomeric excesses (> 98%).



Scheme 1

The free aminoalcohols **1** and **2** were obtained by treatment of either **1**·HCl or **2**·HCl in diethyl ether with an aqueous solution of NaOH. After phase separation, **1** and **2** were quantitatively obtained by removing the organic solvent under reduced pressure. The absolute configuration of each stereocenter in **1**·HCl and **2**·HCl was determined by single-crystal X-ray diffraction analyses. ZORTEP drawings for both compounds are shown in Figure 1, while selected bond distances and angles are collected in Table 1. In light of the crystallographic analysis, **1**·HCl and **2**·HCl can unambiguously be assigned the absolute configurations C1(*R*)-C3(*S*)-C4(*S*) (Flack's parameter -0.06(6)) and C1(*R*)-C3(*R*)-C4(*R*) (Flack's parameter 0.0(2)), respectively. All bond lengths and angles in the two compounds are normal and do not deserve a comment. The phenyl ring in **2**·HCl is located away from the cyclohexyl moiety in a *pseudo anti*-conformation with respect to the N1-C1 bond (torsion angle C9-C1-N1-C3 = 160.4(4)°). The α-methyl group is bent toward the axial hydrogen (H3a) bound to C3 (torsion angle C1-N1-C3-C4 = 162.8(4)°; C2 - H3a separation 2.8 Å). Unlike **2**·HCl, the torsion angles C9-C1-N1-C3 = 54.1(3)° and C1-N1-C3-C4 = -166.0(4)° in **1**·HCl indicates that the cyclohexane and phenyl

rings are oriented in such a way to force H3a near to the phenyl ring (distance from the center of the phenyl ring to H3a = 3.4 Å).

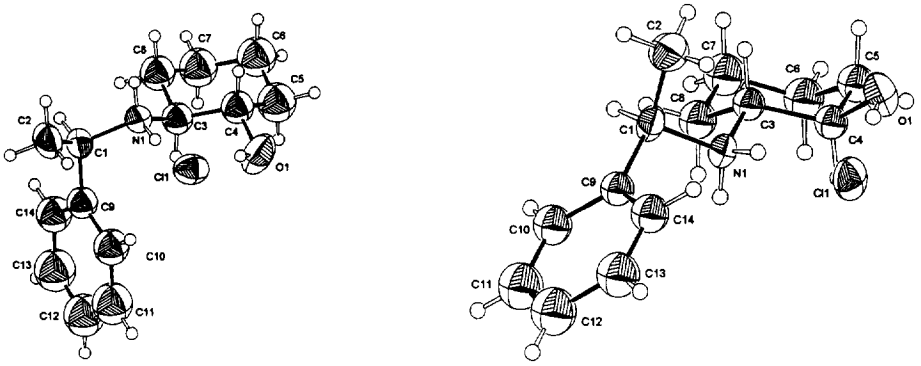


Figure 1. ZORTEP drawings of Compounds **1**·HCl (left) and **2**·HCl (right).

Table 1. Selected bond lengths [Å] and angles [deg] for **1**·HCl and **2**·HCl.

Bond lengths	1·HCl	2·HCl	Bond angles	1·HCl	2·HCl
N(1) - C(1)	1.505(8)	1.521(4)	C(1) - N(1) - C(3)	116.6(5)	115.9(3)
N(1) - C(3)	1.512(8)	1.509(5)	C(9) - C(1) - N(1)	111.4(5)	109.3(3)
O(1) - C(4)	1.437(9)	1.438(5)	C(9) - C(1) - C(2)	113.3(5)	113.7(3)
C(1) - C(9)	1.492(8)	1.512(5)	N(1) - C(1) - C(2)	108.2(5)	108.9(3)
C(1) - C(2)	1.523(10)	1.530(7)	N(1) - C(3) - C(4)	109.6(6)	110.0(3)
C(3) - C(4)	1.509(10)	1.525(5)	N(1) - C(3) - C(8)	109.6(6)	109.5(3)
C(3) - C(8)	1.513(11)	1.522(5)	C(3) - C(4) - C(5)	110.9(7)	111.1(3)
C(4) - C(5)	1.511(12)	1.513(6)	C(3) - C(8) - C(7)	111.3(8)	110.3(4)
C(5) - C(6)	1.505(14)	1.523(6)	C(4) - C(3) - C(8)	111.2(6)	111.7(3)
C(6) - C(7)	1.475(13)	1.505(6)	C(4) - C(5) - C(6)	110.8(9)	113.6(4)
C(7) - C(8)	1.524(12)	1.520(6)	C(6) - C(7) - C(8)	111.0(8)	110.2(4)
			C(5) - C(6) - C(7)	112.1(7)	109.4(4)
			O(1) - C(4) - C(3)	111.3(6)	111.9(3)
			O(1) - C(4) - C(5)	106.0(7)	105.9(4)
			C(1) - C(9) - C(10)	120.6(5)	118.4(2)
			C(1) - C(9) - C(14)	119.4(5)	121.6(2)

Selected ^{1}H and ^{13}C NMR data for the aminoalcohols and their ammonium chlorides are reported in Table 2 and Table 3, respectively. Sketches of the structures of **1**·HCl and **2**·HCl are shown in Chart 1 together with the labelling scheme used for the NMR assignments. All the resonances have been assigned unambiguously by 2D NMR spectroscopy. In the ^{1}H NMR spectra of all compounds quite sharp cyclohexane ring proton resonances are shown which can readily be attributed to the four axial protons (identified by the characteristic

quartet pattern) and to the four equatorial protons. The H3 and H4 protons adopt an axial conformation as shown by their *td* ^{1}H NMR pattern. These features indicate that in solution at 294 K the cyclohexane ring assumes a "rigid" (on the NMR time scale) chair conformation in all compounds, most likely due to the bulkiness of the α-methylbenzylamino substituent at the C3 carbon atom.

Table 2. Selected ^{1}H-NMR data for compounds **1**, **2**, **1**·HCl and **2**·HCl.[a]

compound		H1	H2	H3a	H4a	H5a	H5e	H6a	H6e	H7a	H7e	H8a	H8e
1[b]	δ	3.94	1.30	1.97	3.10	1.05*	1.92	1.18	1.61#	1.04*	1.60#	0.87	2.11
(*R*)-(*S*)-(*S*)	multipl	q	d	t d	t d	q d	m	q t	m	q t	m	q d	m
	J	6.5	6.5	10/4	10/4			10/3				12/3	
2[b]	δ	3.90	1.32*	2.32	3.09	1.28*	2.04	1.24	1.68	1.18	1.64	0.83	1.91
(*R*)-(*R*)-(*R*)	multipl	q	d	d d d	t d		m	q t	m	q t	m	q d	m
	J	6.5	6.5	12/10/3	10/4			12/3		12/3		12/3	
1·HCl[c]	δ	4.61	1.66*	2.46	3.51	1.12	1.95	1.25	1.64*	1.05	1.72	1.41	2.16
(*R*)-(*S*)-(*S*)	multipl	q	d	t d	t d	q d	m	q t		q t	m	q d	m
	J	7	7	11/4	11/5	11/2		13/3		13/4		13/4	
2·HCl[c]	δ	4.69	1.65#	2.74	3.56	1.24*	1.98	1.10	1.65#	1.22*	1.63#	1.36	1.86
(*R*)-(*R*)-(*R*)	multipl	q	d	t d	t d		m	q t				q d	m
	J	7	7	10/4	10/5			13/3				12/3	

[a] 500.13 MHz, 294 K. Chemical shifts in ppm, coupling constants in Hz.[b] In $CDCl_3$. [c] In MeOH-d_4.* Partially overlapped. # Partially overlapped.

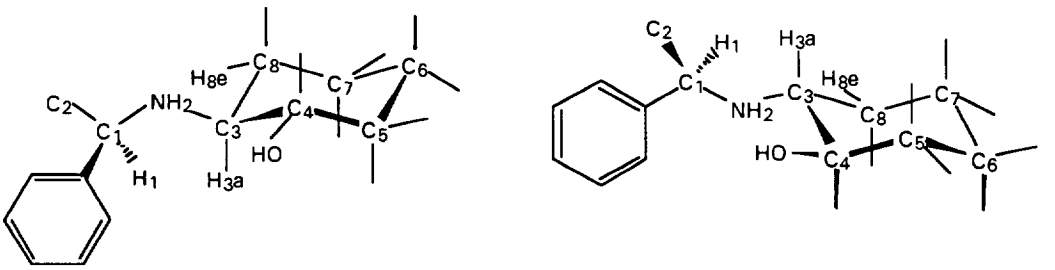
Table 3. ^{13}C-NMR data for compounds **1**, **2**, **1**·HCl and **2**·HCl.[a]

compound		C1	C2	C3	C4	C5	C6	C7	C8	C-o	C-m	C-p	C-i
1[b]	δ	54.8	24.9	60.8	74.7	33.7	25.7	26.3	31.0	127.4	129.3	127.8	145.7
(*R*)-(*S*)-(*S*)	multipl	d	q	d	d	t	t	t	t	d	d	d	s
	$^1J_{CH}$	130	132	131	142	131	140	129	125	152	161	163	--
2[b]	δ	55.7	24.0	62.0	74.5	33.5	24.7	25.8	31.8	126.8	128.7	127.5	147.3
(*R*)-(*R*)-(*R*)	multipl	d	q	d	d	t	t	t	t	d	d	d	s
	$^1J_{CH}$	134	126	133	140	129	131	128	124	157	160	160	--
1·HCl[c]	δ	57.1	21.0	62.7	71.7	35.6	24.9	25.3	27.9	128.8	130.8	130.8	138.1
(*R*)-(*S*)-(*S*)	multipl	d	q	d	d	t	t	t	t	d	d	d	s
	$^1J_{CH}$	146	129	143	142	130	125	125	127	158	162	162	--
2·HCl[c]	δ	58.5	19.0	62.1	71.3	34.6	23.6	24.2	28.7	128.0	129.4	129.4	137.3
(*R*)-(*R*)-(*R*)	multipl	d	q	d	d	t	t	t	t	d	d	d	s
	$^1J_{CH}$	146	129	146	142	128	126	126	129	163	162	162	--

[a] 125.77 MHz, 294 K. Chemical shifts in ppm, coupling constants in Hz.[b] In $CDCl_3$. [c] In MeOH-d_4.

In order to obtain information on the solution structure of the compounds, ^{1}H NOESY experiments were carried out. The ^{1}H NOESY spectra confirmed the chair conformation of the cyclohexane rings and allowed us to identify the *ortho* protons resonances by their strong NOEs to the H1 proton. Also, the preferred time-averaged conformations of **1**·HCl and **2**·HCl in solution appear analogous to those adopted in the solid state: for **2**·HCl this is shown by the NOEs from H1 to H3a and to H8e and by the the NOE from H2 to H3a, while for **1**·HCl this is shown by the NOEs from H3a and H8e to both H1 and the *ortho* protons. Interestingly, the ^{1}H NOESY spectra of **1** and **2** are quite similar to those of **1**·HCl and **2**·HCl, thus suggesting that the aminoalcohols essentially retain the solution structure of the corresponding ammonium chlorides.

Furthermore, the NOESY spectra, showing that the phenyl ring in the (*R*)-(*S*)-(*S*)-isomers is close to the H3a proton (as occurs in the solid state), account for the ^{1}H NMR chemical shift of this hydrogen which, in fact, resonates at higher field by ca. 0.3 ppm as compared to the (*R*)-(*R*)-(*R*)-isomers.



(R)-(S)-(S)-**1**·HCl *(R)-(R)-(R)*-**2**HCl

Chart 1. Labelling scheme adopted for NMR assignments of **1**·HCl and **2**·HCl.

EXPERIMENTAL

General Procedures. Diethyl ether and tetrahydrofuran (THF) were distilled from $LiAlH_4$ prior to use. All the other reagents and chemicals were reagent grade and were used as received by commercial suppliers. Deuterated solvents for NMR measurements (Merck) were dried over molecular sieves. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance DRX-500 spectrometer operating at 500.132 and 125.77 MHz, respectively. Peak positions are relative to tetramethylsilane and were calibrated against the residual solvent resonance (^{1}H) or against the deuterated solvent multiplet (^{13}C). The assignment of the signals resulted from 2D ^{1}H COSY, 2D ^{1}H NOESY and proton detected 2D ^{1}H,^{13}C correlations using degassed non-spinning samples. ^{1}H COSY experiments[5] were recorded with 512 increments of size 1K (with 8 scans each) covering the full range (*ca.* 4000 Hz) in both dimensions. ^{1}H NOESY measurements[6] were recorded with pulse sequences suitable for phase-sensitive representations using TPPI; 512 increments of size 1K (with 8 scans each) covering the full range (*ca.* 4000 Hz) in both dimensions were collected using a mixing time of 0.35 s. ^{1}H,^{13}C correlations[7] were recorded using the standard HMQC sequence ; 512 increments of size 1K (with 16 scans each) were collected covering the full range in both dimensions. Infrared spectra were recorded as Nujol

mulls on a Perkin-Elmer 1600 series FT-IR spectrometer between KBr plates. High-pressure reactions were performed with a Parr 4565 reactor equipped with a Parr 4842 temperature and pressure controller. GC/MS analyses were performed on a Shimadzu QP 2000 apparatus equipped with a 30 m (0.25-mm i.d., 0.25-μm FT) SPB-1 Supelco fused silica capillary column. Elemental analyses (C, H, N) were performed with a Carlo Erba model 1106 elemental analyzer. Optical rotations were measured with a Perkin-Elmer 341 polarimeter using 10 cm cells.

Synthesis of *N*-{(*S*)-[cyclohexan-(*S*)-2-ol]}-(*R*)-α-methylbenzyl ammonium chloride 1·HCl and *N*-{(*R*)-[cyclohexan-(*R*)-2-ol]}-(*R*)-α-methylbenzyl ammonium chloride 2·HCl. Enantiopure (*R*)-α-methylbenzylamine (15.3 g, 126 mmol) was mixed with a slight excess of cyclohexene oxide (13 g, 130 mmol) into the Parr reactor. The mixture was heated at 160°C for 48 h (internal pressure *ca.* 3 atm.). After cooling to room temperature and depressurizing, the oily product was dissolved in 30 mL of hot ethanol. The resulting solution was treated with ca. 25 mL of concentrated HCl(aq). The solvents were removed in vacuo at 70 °C and the solid residue was dissolved in hot ethanol (10 mL). After cooling to room temperature, diethyl ether (10 mL) was added and the solution was stored at 4°C. After one day, 7.9 g of the (*R*)-(*S*)-(*S*)-diastereoisomer were collected in 80 % diastereomeric excess (*de*) determined by NMR spectroscopy (^{1}H, ^{13}C). Addition of further 10 mL of diethyl ether gave a second crop of the (*R*)-(*S*)-(*S*)-diastereoisomer (ca. 5. g) with *de* ranging from 60 to 80 % (total product yield 90 %). Evaporation of the solvents in vacuo and crystallization from THF and diethyl ether gave 6 g of the homochiral (*R*)-(*R*)-*R*)-diastereoisomer in > 98% *de*. Concentration of the filtrate gave further product (total product yield ca. 50 %). The (*R*)-(*S*)-(*S*)-diastereoisomer was recrystallized twice from hot ethanol to obtain an almost diastereomerically pure product (*de* > 98%). Anal. Calcd. for $C_{14}H_{22}Cl_1N_1O_1$ (M = 255.79): C, 65.74; H, 8.67; N, 5.48. Found: C, 66.63; H, 9.11; N, 5.49. $[\alpha]_D^{25}$ = + 71 (c = 10.8, ethanol). IR: ν(NH) = 3361 (st) cm^{-1}. After recrystallization from THF/diethyl ether, the (*R*)-(*R*)-*R*)-diastereoisomer was obtained with a *de* > 98 %. $[\alpha]_D^{25}$ = + 14 (c = 10.7, ethanol).

Synthesis of *N*-{(*S*)-[cyclohexan-(*S*)-2-ol]}-(*R*)-α-methylbenzyl amine 1 and *N*-{(*R*)-[cyclohexan-(*R*)-2-ol]}-(*R*)-α-methylbenzyl amine 2. To a suspension of the enantiopure (*R*)-(*S*)-(*S*)-ammonium chloride 1·HCl (2.53 g, 10 mmol) in 20 mL of diethyl ether was added an excess of NaOH (1 g, 25 mmol) in 25 mL of H_2O. The mixture was stirred for 15 min. The organic phase was separated and the water phase was extracted four times with diethyl ether. After the combined organic phases were dried over Na_2SO_4, the solvent was removed in vacuo to give the free amine. The (*R*)-(*S*)-(*S*)-amine **1** was obtained as an off-white powder (2.10 g, 96 %). Anal. Calcd. for $C_{14}H_{21}N_1O_1$ (M = 219.33): C, 76.67; H, 9.65; N, 6.39. Found: C, 75.97; H, 9.59; N, 6.24. $[\alpha]_D^{25}$ = + 92 (c = 10.2, ethanol). IR: ν(NH) = 3463, 3310 cm^{-1}. MS (EI, m/z [%]): 219 (5 %, M^+), 204 (85 %, M^+-CH_3), 186 (10 %, M^+-CH_3-H_2O), 160 (30 %, M^+-$C_3H_7O^+$), 105 (100 %, $C_8H_9^+$). Following an identical procedure, the (*R*)-(*R*)-*R*)-amine **2** was obtained from the (*R*)-(*R*)-*R*)-ammonium chloride 2·HCl as an oil (2.05 g, 93 %). $[\alpha]_D^{25}$ = +15 (c = 12.5, ethanol).

X-Ray structural analyses of 1·HCl and 2·HCl. Diffraction data for 1·HCl were collected on an Enraf Nonius CAD-4 diffractometer with graphite monochromated Mo Ka radiation (λ = 0.71069 Å). A set of 25 carefully centered refelections having 8 < θ < 11 ° were used to determine the cell constants. The selected crystal had the dimension of 0.15 x 0.17 x 0.40 mm. Diffraction data for 2·HCl were collected on a Philipis PW1100 FEBO diffractometer with graphite monochromated Cu Kα radiation (λ = 1.54180 Å). A set of 25 carefully centered refelections having 12.5 < θ < 18 ° were used to determine the cell constants. The selected crystal had the dimension of 0.70 x 0.50 x 0.13 mm. Crystal data for 1·HCl: f. w. 255.78, orthorombic $P2_12_12_1$, a = 12.191(2), b = 17.027(3), c = 7.335(1) Å, V = 1.522.6(4) Å^3, Z = 4, D_c = 1.116 Mg/m^3, F(000) = 552.

Crystal data for **2**·HCl: f. w. 255.78, monoclinic $P2_1$, a = 7.604(1), b = 8.143(1), c = 11.553(2), α = 90.00(1), β = 97.91(1),γ = 90.00(1) °, V = 708.5(2) Å^3, Z = 2, D_C = 1.199 Mg/m^3, F(000) = 276, RI = 0.0639. As a general procedeure three standard reflections were measured every 200 refelections for orientation and intensity control. No decay of the specimen was noticed. Intensity data were corrected for Lorentz-polarization effects. Atomic scattering factors were those reported by Cromer and Waber[8] with anomalous dispersion correction.

Table 4. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^2 x 10^3) for **1**·HCl and **2**·HCl. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x		y		z		U(eq)	
	1·HCl	**2**·HCl	**1**·HCl	**2**·HCl	**1**·HCl	**2**·HCl	**1**·HCl	**2**·HCl
Cl(1)	3542(2)	7282(1)	9545(1)	7487(2)	9671(2)	8251(1)	63(1)	50(1)
O(1)	3935(4)	6097(4)	10099(3)	6403(5)	5562(8)	10541(3)	45(1)	50(1)
N(1)	4661(6)	3355(4)	11118(3)	7988(4)	8582(8)	8761(3)	86(2)	31(1)
C(1)	4310(5)	2055(4)	9415(4)	7480(7)	4419(10)	7702(3)	51(2)	37(1)
C(2)	3594(6)	2460(7)	8710(4)	5714(7)	4879(12)	7375(4)	68(2)	57(1)
C(3)	4553(6)	3021(4)	10861(4)	7271(5)	5325(10)	9916(3)	56(2)	34(1)
C(4)	4274(8)	4680(4)	11219(5)	7442(7)	3495(11)	10813(3)	70(2)	37(1)
C(5)	4814(9)	4317(6)	12019(5)	6926(6)	3259(13)	12016(4)	84(3)	46(1)
C(6)	4528(8)	2697(6)	12548(6)	7756(7)	4780(14)	12400(4)	87(3)	53(1)
C(7)	4822(9)	1103(6)	12201(5)	7449(9)	6603(13)	11500(4)	87(3)	57(1)
C(8)	4272(7)	1429(6)	11414(4)	8119(6)	6865(10)	10320(4)	61(2)	46(1)
C(9)	5506(3)	2145(4)	9263(3)	8700(3)	4664(7)	6725(2)	55(2)	37(1)
C(10)	5934(4)	750(3)	9106(3)	9800(4)	6383(6)	6460(3)	72(2)	49(1)
C(11)	7045(5)	794(4)	8946(4)	10947(4)	6585(7)	5573(3)	95(3)	67(2)
C(12)	7729(3)	2233(5)	8943(3)	10993(4)	5069(9)	4951(3)	97(3)	69(2)
C(13)	7301(4)	3629(4)	9100(3)	9894(5)	3350(7)	5216(3)	100(3)	61(1)
C(14)	6190(4)	3585(3)	9260(3)	8747(4)	3148(6)	6103(3)	72(2)	47(1)

All the computational work was carried out on a Digital Dec 2000 AXP workstation using the programs SIR92[9] and SHELX93.[10] The program ZORTEP was also used. The structures were solved by direct methods and all the non-hydrogen atoms were found through a series of F_0 Fourier maps. The phenyl rings were treated as rigid groups with D_{6h} symmetry. Hydrogen atoms were introduced in calculated positions and refined riding to the respective carbon atom. The refinement was done by full-matrix least-squares calculations, initially with isotropic thermal parameters, then with anisotropic thermal parameters only for N, O, Cl and C1 and C2 atoms. Atomic coordinates are reported in Table 4. The final values of the residual R and w$R2$ values were 0.0654 and 0.1625 (**1**·HCl for 1032 refelections with $I>2\sigma(I)$) and 0.0639 and 0.1516 (**2**·HCl for 2145 refelections with $I>2\sigma(I)$), respectively. The highest peak in the final difference-Fourier map was 0.491 eÅ^3 for **1**·HCl, and 0.484 eÅ^3 for **2**·HCl. Flack's parameters were refined giving a value of -0.06(6) for **1**·HCl, and 0.0(2) for **2**·HCl, consistent with a very reliable determination of the absolute configuration of both compounds.

Acknowledgements: Thanks are due to Mr. Dante Masi for technical assistance in the X-ray structure determinations. A grant to V. S. from the EC (contract CHBI CT94 1568) is also gratefully acknowledged.

REFERENCES

1. (a) *Catalytic Asymmetric Synthesis*, Ojima, I.; Ed., VCH, Weinheim, **1993**. (b) Deloux, L.; Srebnick, M. *Chem. Rev.* **1993**, *93*, 763. (c) Soai, K.; Niwa, S. *Chem. Rev.* **1992**, *92*, 833. (d) Blaser, H. U. *Chem. Rev.* **1992**, *92*, 935. (e) Togni, A.; Venanzi, L. M. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 497. (f) Kagan, H. B.; Riant, O. *Chem. Rev.* **1992**, *92*, 1007. (g) Kagan, H. B. in *Asymmetric Synthesis*, Vol. 5, Morrison, J. D.; Ed., Academic Press, Orlando, **1985**, p. 28. (h) Di Simone, B.; Savoia, D.; Tagliavini, E.; Umani-Ronchi, A. *Tetrahedron: Asymmetry* **1995**, *6*, 301. (i) Aggarwal, V. D.; Anderson, E.; Giles, R.; Zaparucha, A. *Tetrahedron: Asymmetry* **1995**, *6*, 1301. (l) Bach, T. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 417.
2. (a) Barbaro, P.; Belderrain, T. R.; Bianchini, C.; Scapacci, G.; Masi, D. *submitted for publication.* (b) Barbaro, P.; Belderrain, T. R.; Bianchini, C.; Scapacci, G. *submitted for publication.*
3. (a) Bianchini, C.; Farnetti, E.; Glendenning, L.; Graziani, M.; Nardin, G.; Peruzzini, M.; Rocchini, E.; Zanobini, F. *Organometallics* **1995**, *14*, 1489. (b) Barbaro, P.; Bianchini, C.; Scapacci, G.; Masi, D.; Zanello, P. *Inorg. Chem.* **1994**, *33*, 3180. (c) Wilson, M. E.; Nuzzo, R. G.; Whitesides, G. M. *J. Am. Chem. Soc.* **1978**, *100*, 2269. (d) Hayashi, T.; Konishi, M.; Fukushima, M.; Kanehira, K.; Hioki, T.; Kumada, M. *J. Org. Chem.* **1983**, *48*, 2195 (e) Albinati, A.; Lianza, F.; Berger, H.; Pregosin, P. S.; Rüegger, H.; Kunz, R. W. *Inorg. Chem.* **1993**, *32*, 478.
4. (a) Houben-Weyl, *Methoden der Organischen Chemie*, G. Thieme Verlag, Stuttgart, **1957**, Band XI/1, p. 311. (b) Curtin, D. Y.; Kellom, D. B. *J. Am. Chem. Soc.* **1953**, *75*, 6011.
5. Shaka, A. J.; Freeman, R. *J. Magn. Reson.* **1983**, *51*, 169.
6. Sklener, V.; Miyashiro, H.; Zon, G.; Miles, H. T.; Bax, A. *FEBS Lett.* **1986**, *208*, 94.
7. Summers, M. F.; Marzilli, L. G.; Bax, A. *J. Am. Chem. Soc.* **1986**, *108*, 4285.
8. Cromer, D. T.; Waber, J. T. *Acta Cryst.* **1965**, *18*, 104.
9. Altomare, A.; Burla, M. C.; Camalli, M.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Polidori, G. *J. Appl. Cryst.* **1994**, in preparation.
10. Sheldrick, G. M., *J. Appl. Chem.*, in preparation.
11. Zsolnai, L.; Pritzkow, H. Un. Heidelberg, **1994**.

(*Received in UK* 11 *January* 1996)