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Synthesis and crystal structure of benzyl-*N*-(diphenylmethylene)-glycine ethyl ester

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Abstract

Optically active α-amino acid was asymmetrically synthesized under soluble polymer-supported quinine by homogeneous phase catalytic reaction. The precursor of L-phenylalanine, Ph_2=NCH(CH_2Ph)$CO_2C_2H_5$ ($C_{24}H_{23}NO_2$, $M_r = 364.38$) has been determined by X-ray diffraction analysis. The crystal belongs to monoclinic system with space group $P2_1/c$, $a = 10.4539(10)$, $b = 9.8315(10)$, $c = 19.8896(19)$ Å, $\alpha = 90.00$, $\beta = 93.661(2)$, $\gamma = 90.00°$, $V = 2040.0(3)$ Å^3, $Z = 4$, $D_c = 1.164$ mg mm^{-3}, $\mu = 0.074$ mm^{-1}, $F(000) = 760$. The final R and wR factors are 0.0463 and 0.1239, respectively, with 3610 ($R_{int} = 0.0291$) independent reflections.

Keywords: Benzyl-*N*-(diphenylmethylene)-glycine ethyl ester; Crystal structure; Asymmetric synthesis; Soluble polymer-supported quinine; Homogeneous phase catalyst

1. Introduction

During past 20 years, much attention has been drawn to investigate the synthesis of α-amino acid because of the wide spread use of these compounds in the physical and life sciences [1], the major advance has been realized in the asymmetric synthesis of amino acid [2], especially in the use of stoichiometric amounts of chiral auxiliaries [3]. For example, *N*-(diphenylmethylene)-glycine alkyl ester reacts with activated alkyl halides under chiral catalytic to give optically active phenylalanine. However, the precursor crystal structure of the reaction is seldom reported. Our group has been interested in the use of Schiff base for asymmetric synthesis of α-amino acid by cross-linked polymer-supported cinchonine as chiral phase transfer catalyst [4–6]. Earlier, we have reported the crystal structure of benzyl-*N*-(diphenylmethylene)-glycine *tert*-butyl ester [6], but failed to get ethyl ester. Here, we successfully get the single crystal of the precursor of L-phenylalanine using soluble polymer (polyethylene glycol)-supported quinine as homogeneous phase catalytic reaction, and study on its crystal structure by X-ray analysis.

2. Experimental

2.1. Synthesis of the title compound [7]

In a 100 ml round-bottomed flask equipped with a

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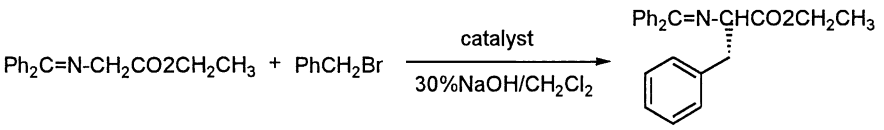

Scheme 1. Homogeneous phase catalytic reaction.

magnetic stirbar, *N*-(diphenylmethylene)-glycine ethyl ester (1.2 g, 4.49 mmol) and polyethylene glycol-2000 supported quinine (1.3 g dissolved in 20 ml dichloromethane and benzyl bromide (0.54 ml, 4.51 mmol) were added. Ten minutes later, 7.2 g of 30% aqueous solution of sodium hydroxide was added sequentially with stirring at room temperature for 5 h. Ten milliliters water and 10 ml dichloromethane were added and the aqueous phase was extracted with dichloromethane (2×10 ml) combined with the organic phase and washed with water (2×10 ml). The organic layer was dried over anhydrous sodium sulfate and concentrated. Purification of the residue by column chromatography on silica gel (only dichloromethane as eluants) gave 0.3 g of colorless oil. Several days later, the single crystal of the title compound was obtained from the oil. (yield 18.8%). The molecular structure was confirmed by ^{1}H NMR ($CDCl_3$): 7.2–7.7 (10H, m, Ph_3-H), 6.8 (5H, m, Ph_3-H), 4.3 (1H, s, CH), 4.1 (2H, m, CH_2), 3.3 (2H, d, CH_2-Ph), 1.3 (3H, t, CH_3). $[\alpha]_D^{25} = -1.67°$ ($c = 1.2$, CH_2Cl_2).

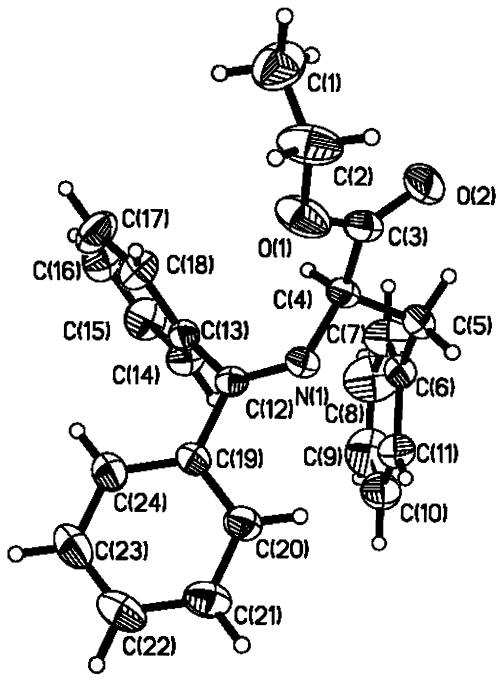

Fig. 1. Structure of the title compound.

2.2. X-ray crystallography

A colorless single crystal of the title compound obtained from oil after standing for several days with an approximate size of 0.25 mm × 0.30 mm × 0.35 mm was selected for X-ray diffraction analysis. The determination of unit cell dimensions and data collection were performed on a BRUKER SMART 1000 CCD diffractometer equipped with a graphite monochromator for data collection with Mo Kα radiation ($\lambda = 0.71073$ Å). A total of 3610 independent reflections were collected in the range of $1.95 < \theta < 25.03°$ with $R_{int} = 0.0291$ by ω–θ scan technique at 298(2) K, in which 2262 reflections with $I > 2\sigma(I)$ were observed and used in the succeeding refinements. All data were corrected using SADABS method.

The structure was solved by direct methods using SHELXL-97 program [8,9]. The non-hydrogen atoms were located in successive difference Fourier syntheses. The final refinement was reformed by full matrix least-squares method with anisotropic thermal parameters for non-hydrogen atoms on F^2. The hydrogen atoms were added theoretically, riding on the concerned atoms and refined with fixed thermal factors. The weighting scheme was $W^1 = \sigma^2(F_o^2) + (0.0692P)^2 + 0.3273P$, where $P = (F_o^2 + 2F_c^2)/3$. The refinement converged to final $R = 0.0463$, $Rw = 0.1239$, $S = 1.009$, $(\Delta/\sigma)_{max} = 0.000$ and $(\Delta/\sigma)_{min} = 0.000$. The maximum and the minimum residual peaks are 0.196 and -0.138 e Å^{-3}. Molecular graphics were drawn with the program package XP.

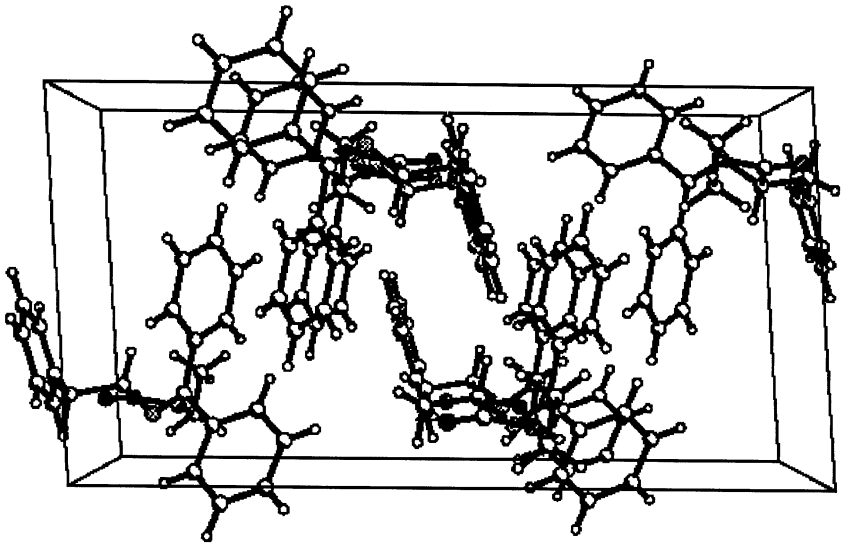

Fig. 2. Packing of molecules in unit cell.

3. Results and discussion

3.1. Synthesis and general characterization

The homogeneous phase catalytic reaction is shown in Scheme 1. The alkylation of glycine ester derivatives with catalysts supported by the chemical modification of polyethylene glycol was a practical asymmetric synthesis of α-amino acids using homogeneous phase catalysis.

3.2. Crystal and molecular structure

The molecular structure of the title compound is shown in Fig. 1. The packing of molecules in unit cell is shown in Fig. 2. The atomic coordinates and equivalent thermal parameters of non-hydrogen atoms are listed in Table 1. The selected bond lengths and bond angles are in Tables 2 and 3, respectively.

An interesting feature observed in the molecular structure is the monoclinic system belonging to the

Table 1
Atomic coordinates ($\times 10^4$) and thermal parameters ($Å^2 \times 10^3$) (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)
N(1)	1528(1)	5422(2)	868(1)	47(1)	C(12)	2103(2)	6069(2)	1352(1)	44(1)
O(1)	1626(2)	2754(2)	1076(1)	98(1)	C(13)	3518(2)	6013(2)	1538(1)	50(1)
O(2)	1772(2)	2348(2)	− 6(1)	98(1)	C(14)	4324(2)	7006(2)	1314(1)	67(1)
C(1)	2464(3)	524(3)	1314(2)	110(1)	C(15)	5625(2)	6967(3)	1492(2)	85(1)
C(2)	1313(3)	1323(3)	1207(2)	106(1)	C(16)	6120(3)	5960(4)	1897(1)	94(1)
C(3)	1849(2)	3110(2)	457(1)	60(1)	C(17)	5347(3)	4968(3)	2122(1)	93(1)
C(4)	2251(2)	4593(2)	415(1)	49(1)	C(18)	4036(2)	4987(3)	1943(1)	73(1)
C(5)	2019(2)	5123(2)	− 304(1)	55(1)	C(19)	1329(2)	6981(2)	1764(1)	46(1)
C(6)	2607(2)	6500(2)	− 399(1)	55(1)	C(20)	151(2)	7471(2)	1500(1)	60(1)
C(7)	3862(2)	6613(3)	− 558(1)	84(1)	C(21)	− 562(2)	8336(3)	1875(1)	78(1)
C(8)	4411(3)	7853(4)	− 647(2)	123(1)	C(22)	− 125(3)	8723(3)	2512(2)	84(1)
C(9)	3733(4)	9014(4)	− 581(2)	115(1)	C(23)	1028(3)	8244(3)	2779(1)	79(1)
C(10)	2476(4)	8939(3)	− 421(1)	96(1)	C(24)	1759(2)	7390(2)	2408(1)	61(1)
C(11)	1915(2)	7678(2)	− 327(1)	71(1)	H(4*A*)	3167	4667	549	59

Table 2
Selected bond lengths (Å)

Bond	Distance	Bond	Distance	Bond	Distance	Bond	Distance
N(1)–C(12)	1.272(2)	C(5)–C(6)	1.504(3)	C(12)–C(13)	1.503(3)	C(19)–C(20)	1.393(3)
N(1)–C(4)	1.461(2)	C(6)–C(7)	1.374(3)	C(13)–C(18)	1.380(3)	C(20)–C(21)	1.380(3)
O(1)–C(3)	1.314(3)	C(6)–C(11)	1.377(3)	C(13)–C(14)	1.382(3)	C(21)–C(22)	1.373(4)
O(2)–C(3)	1.471(3)	C(7)–C(8)	1.364(4)	C(14)–C(15)	1.384(3)	C(22)–C(23)	1.370(4)
O(2)–C(3)	1.186(2)	C(8)–C(9)	1.355(5)	C(15)–C(16)	1.359(4)	C(23)–C(24)	1.380(3)
C(1)–C(2)	1.442(4)	C(9)–C(10)	1.373(4)	C(16)–C(17)	1.361(4)	C(4)–H(4A)	0.980
C(3)–C(4)	1.521(3)	C(10)–C(11)	1.390(4)	C(17)–C(18)	1.394(3)		
C(4)–C(5)	1.526(3)	C(12)–C(19)	1.498(2)	C(19)–C(24)	1.388(3)		

Table 3
Selected bond angles (°)

Angle	(°)	Angle	(°)	Angle	(°)
C(12)–N(1)–C(4)	120.49(16)	C(8)–C(7)–C(6)	121.2(3)	C(15)–C(16)–C(17)	120.4(2)
C(3)–O(1)–C(2)	118.3(2)	C(9)–C(8)–C(7)	120.9(3)	C(16)–C(17)–C(18)	120.1(3)
C(1)–C(2)–O(1)	110.8(2)	C(8)–C(9)–C(10)	119.5(3)	C(13)–C(18)–C(17)	120.1(2)
O(2)–C(3)–O(1)	123.5(2)	C(9)–C(10)–C(11)	119.8(3)	C(24)–C(19)–C(20)	118.27(18)
O(2)–C(3)–C(4)	124.6(2)	C(6)–C(11)–C(10)	120.5(3)	C(24)–C(19)–C(12)	121.80(18)
O(1)–C(3)–C(4)	111.94(18)	N(1)–C(12)–C(19)	118.07(16)	C(20)–C(19)–C(12)	119.91(17)
N(1)–C(4)–C(3)	110.15(16)	N(1)–C(12)–C(13)	125.32(16)	C(21)–C(20)–C(19)	120.3(2)
N(1)–C(4)–C(5)	109.24(15)	C(19)–C(12)–C(13)	116.60(16)	C(22)–C(21)–C(20)	120.7(2)
C(3)–C(4)–C(5)	110.59(16)	C(18)–C(13)–C(14)	118.71(19)	C(23)–C(22)–C(21)	119.7(2)
C(6)–C(5)–C(4)	112.51(16)	C(18)–C(13)–C(12)	120.94(19)	C(22)–C(23)–C(24)	120.3(2)
C(7)–C(6)–C(11)	118.2(2)	C(14)–C(13)–C(12)	120.34(18)	C(23)–C(24)–C(19)	120.8(2)
C(7)–C(6)–C(5)	120.4(2)	C(13–C(14)–C(15)	120.5(2)	C(5)–C(4)–H(4A)	108.94
C(11)–C(6)–C(5)	121.48(19)	C(16)–C(15)–C(14)	120.2(3)	N(1)–C(4)–H(4A)	108.94
				C(3)–C(4)–H(4A)	108.94

symmetric space group, but the specific rotation of the dichloromethane solution showed that it has a low optical yield. Perhaps the racemic compound crystals are generally more stable than the enantiomeric crystals [10].

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