ISSN 1068-1620, Russian Journal of Bioorganic Chemistry, 2010, Vol. 36, No. 7, pp. 877–883. © Pleiades Publishing, Ltd., 2010.
Original Russian Text © A.V. Kuchin, E.V. Ashikhmina, S.A. Rubtsova, I.A. Dvornikova, 2010, published in Khimiya Rastitel'nogo Syr'ya, 2009, No. 1, pp. 59–66.

PLANT BIOPOLYMERS

Terpene Ligands as the Basis of Catalytic Systems for the Asymmetric Oxidation of Phenylphenacyl Sulfide

A. V. Kuchin, E. V. Ashikhmina, S. A. Rubtsova, and I. A. Dvornikova

Institute of Chemistry, Komi Research Center, Ural Division, Russian Academy of Sciences, ul. Pervomaiskaya 48, Syktyvkar, 167982 Russia
e-mail: ashihmina-ev@chemi.comisc.ru

Received October 22, 2008

Abstract—Terpene ligands (*1S,2S,5S*)-3-[{2-[(2-hydroxybenzylidene)amino]ethyl}imino]-2,6,6-trimethylbicyclo[3.1.1.]heptane-2-ol and 3-({2-[(2-hydroxy-2,6,6-trimethylbicyclo[3.1.1.]hept-3-ilidene)amino]ethyl}imino)-2,6,6-trimethylbicyclo[3.1.1.]heptane-2-ol have been synthesized for the first time. The efficiency of complexes based on terpene and salen ligands in asymmetric sulfoxidation has been compared. Catalytic systems based on terpene ligands have been used for the first time in the asymmetric oxidation of phenylphenacyl sulfide with the formation of sulfoxide with an enantiomeric excess of 47%.

Keywords: terpenes, ligands, catalytic systems, chiral Schiff bases, asymmetric oxidation, sulfoxidation, phenylphenacyl sulfide, titanium isopropylate, vanadyl(IV) acetylacetonate, chlorine dioxide

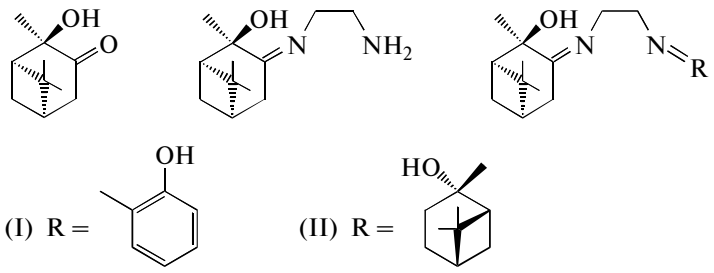
DOI: 10.1134/S1068162010070150

INTRODUCTION

In recent years considerable attention has been focused on chemical transformations of terpene compounds, which is due to their accessibility and chemical activity.[1] The use of these compounds in organic synthesis, especially in catalytic asymmetric synthesis of nitrogen-containing ligands, has attracted particular interest [1]. Chiral, nonracemic imines and their derivatives have been used for the synthesis of heterocyclic compounds and secondary amines; for protecting the aldehyde group, e.g., in the cyclization of terpenes; and in analytical chemistry. They find application as azomethine dyes for staining acetate and synthetic fibers and in color photography for reducing the light sensitivity of photographic emulsion [2].

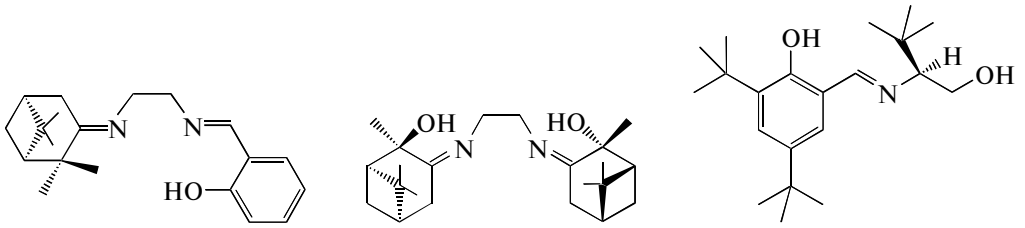
Symmetric 1,2-diimines are used to separate racemates [3, 4] and determine the enantiomeric purity of chiral compounds by NMR spectroscopy [4, 5]. The accessibility, a plausible optical purity, and the presence of both enantiomers make it possible to synthesize promising chiral ligands on their basis. These compounds can serve as the basis of catalytic systems that can be used for solving the problems of asymmetric oxidation, in particular sulfoxidation. Although there are many 1,2-diimines, the design of novel enantiomerically pure ligands is constantly in progress.

Thus, on the basis on the enantiomerically pure 2-hydroxypinane-3-on [6], the ligands (*1S,2S,5S*)-3-[{2-[(2-hydroxybenzylidene)amino]ethyl}imino]-2,6,6-trimethylbicyclo[3.1.1.]heptane-2-ol (**I**) and the symmetric diimine 3-({2-[(2-hydroxy-2,6,6-trimethylbicyclo[3.1.1.]hept-3-ilidene) amino]ethyl}imino)-2,6,6-trimethylbicyclo[3.1.1.]heptane-2-ol (**II**) have been synthesized for the first time according to the following scheme:

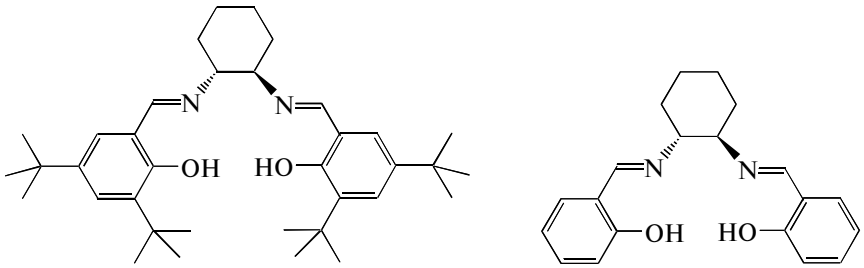


[1] Abbreviations: CHP, cumyl hydroperoxide.

Of the great variety of ligands synthesized for the first time in our institute, asymmetric diimine (**I**) and symmetric diimine (**II**) were chosen for the asymmetric oxidation of phenylphenacyl sulfide. The efficiency of complexes with terpene ligands in the asymmetric sulfoxidation of phenylphenacyl sulfide was compared using the complexes with salen compounds. These are the commercial compounds (S)-(-)-2-(3,5-di-*tert*-butylsalicilidenamine)-3,3-dimethyl-1-butanol (**III**), (S,S)-(+)-N,N'-*bis*(3,5-bi-*tert*-butylsalicilidene)-1,2-cyclohexanediamine (**IV**), and 2-{(E)-[((1S,2R)-2-{[(E)-(2-hydroxyphenyl)-methylidene]amino}cyclo-hexyl)imino]methyl}phenol (**V**), which was obtained by the method described [7]. Ligands (**I**) and (**II**) have not been used previously in reactions of this type.



I **II** **III**



IV **V**

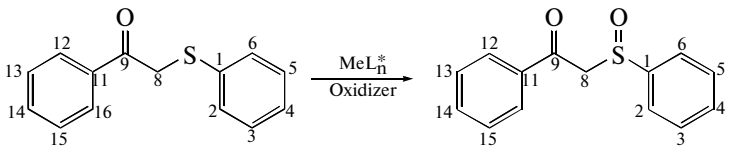
Optically pure and enantiomerically enriched sulfoxides with the chiral sulfur atom are convenient mediators in asymmetric synthesis, which make it possible to perform various chemical transformations [8, 9]. Interest in chiral sulfoxides is also promoted owing to the isolation of native compounds containing the asymmetric sulfoxide group [10, 11] and the discovery of biologically active sulfoxides of a particular configuration [12, 13]. Comparatively recently optically active sulfoxides with outstanding antiulcerous activity have been patented: the derivatives of 2-mercaptobenzimidazole and 2-mercapto-4,5-diphenylimisazole [14]. A number of chiral sulfoxides have found application as liquid ferroelectric crystals [15].

In the present work, we applied symmetric and asymmetric diimines containing a chiral terpene fragment in the asymmetric oxidation of phenylphenacyl sulfide and compared the catalytic activity of systems based on terpene diimines and salen ligands.

All known compounds were identified by comparing their physicochemical constants (melting temperature) and spectral data (mass spectrometry, ^{1}H- and ^{13}C NMR spectroscopy) with the literature data.

RESULTS AND DISCUSSION

Phenylphenacyl sulfide **1** was oxidized by hydrogen peroxide (H_2O_2), CHP, and chlorine dioxide (ClO_2) in the presence of catalytic systems based on vanadium(IV) and titanium(IV) according to the scheme:

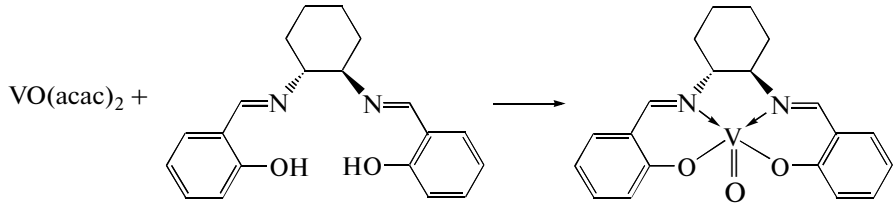


1 **2**

In the literature there is no information about the use of chlorine dioxide in asymmetric oxidation, although it is one of the accessible oxidizers manufactured on an industrial scale. We have previously shown that the use of ClO_2 in organic synthesis is convenient and promising [18]. Chlorine dioxide is used in indus-

try as an oxidizer in the treatment of drinking water and as a paper bleach in paper and pulp plants [19]. There are a few communications concerned with the oxidation by chlorine dioxide of amines [20–22], phenols [23, 24], olefins [25, 26], and carbonyl compounds [21]. In addition, we have shown that ClO_2 chemoselectively oxidizes sulfides to sulfoxides [18, 27, 28].

In the literature there is a description of the formation of a VO/ligand complex (**V**) according to the following scheme [17]:



We proposed that the complexing of vanadium with ligands (**I**)–(**IV**) proceeds in a similar way. By the oxidation of phenylphenacyl sulfide **1**, we obtained phenylphenacyl sulfoxide **2** whose structure is consistent with the data reported by the authors of the paper. The course of the reaction was controlled by HPLC. The enantiomeric excess was determined by HPLC at the chiral phase (Table 1).

The greatest enantiomeric excess of the product on the oxidation by an aqueous chlorine dioxide solution was obtained using the complexes of $VO(acac)_2$ with terpene ligand (**I**) (Table 1). The use of complexes based on salen ligands gave unsatisfactory results. Presumably, this is related to the destruction of complexes by water and their low resistance to this oxidizer. Under these conditions, the complex of VO with the asymmetric diimine (**I**) appears to be more stable. This is confirmed by experiments with an anhydrous medium. If the reaction is carried out in chloroform, the catalyzer based on ligand (**I**) gives the same value of enantiomeric excess as in the aqueous medium (Table 1).

The application of hydrogen peroxide (an oxidizer most frequently used for oxidation in the presence of vanadium-based complexes) and terpene ligand (**II**) was inefficient; the reaction product was formed with a moderate yield and had a low optical purity. The use of the asymmetric diimine (**I**) as a ligand also gave poor results. Catalytic systems with salen ligands gave better results; the enantiomeric excess of the reaction product was maximum with the use of compound (**III**) and was somewhat higher compared with the published data (Table 1).

Phenylphenacyl sulfide was oxidized in the presence of binuclear bridge complexes of titanium (**IV**) and ligands (**I**)–(**V**) [29]. The greatest enantiomeric excess of the product with the use of complexes with terpene ligands was obtained on the oxidation of the substrate by chlorine dioxide. The use of the system chlorine dioxide–complex with asymmetric diimine (**I**) was particularly effective; the enantiomeric excess of the product was 47%.

The use of CHP as an oxidizer and the asymmetric terpene ligand was not very effective; the reaction product was formed with a moderate yield and had a low optical purity. The use of the symmetric diimine as a ligand with the same oxidizer also gave poor results (Table 2). The maximum enantiomeric excess of sulfoxide was obtained using the catalytic system with ligand (**V**).

The oxidation by systems chlorine dioxide–complexes with salen-type ligands leads to a decrease in the enantiomeric excess of sulfoxide as compared with the use of CHP in these systems with the same ratio of reagents. The decrease in the enantiomeric excess results from the destruction of the complex in the presence of chlorine dioxide. During the reaction, along with asymmetric oxidation, predominant oxidation with the formation of racemic ketosulfoxide takes place. The opposite result is obtained if chlorine dioxide is used with complexes with terpene ligands; the enantiomeric excess is greater than upon oxidation by CHP.

CONCLUSIONS

It is evident from the results obtained that compounds (**III**) and (**V**) are the most promising candidates as ligands for asymmetric sulfoxidation. Asymmetric oxidation can be carried out using chlorine dioxide in the presence of the complex $VO(acac)_2$ with the terpene asymmetric ligand (**I**).

Thus, we have shown here for the first time that catalytic systems based on terpene ligands can be used in the asymmetric oxidation of phenylphenacyl sulfide. The enantioselective oxidation of this ketosulfide by chlorine dioxide has been performed for the first time.

EXPERIMENTAL

IR spectra were recorded on a Schimadzu IR Prestige21 IR-Fourier spectrometer. Samples were examined using KBr pellets or in CCl_4. ^1H NMR (400.13 MHz) and ^{13}C NMR (100.62 MHz) spectra

Table 1. Asymmetric oxidation by complexes based on vanadium(IV)

Experiment	Catalyzer	Oxidizer	Yield (%)**	Enantiomeric purity (%)***	$[\alpha]_D$
a	$VO(acac)_2$/**I** 1 : 1.5	H_2O_2	67	3	+0.6
b	$VO(acac)_2$/**I** 1 : 1.5	ClO_2 ($CHCl_3$)	78	32	+6.0
c	$VO(acac)_2$/**I** 1 : 1.5	ClO_2 (H_2O)	69	32	+6.1
d	$VO(acac)_2$/**II** 1 : 1.5	H_2O_2	65	8	–1.4
e	$VO(acac)_2$/**II** 1 : 1.5	ClO_2 ($CHCl_3$)	76	9	–1.6
f	$VO(acac)_2$/**II** 1 : 1.5	ClO_2 (H_2O)	69	15	–2.8
g	$VO(acac)_2$/**III** 1 : 1.5	H_2O_2	67 (65)[17]	75.6 (57)[17]	–16.0
h	$VO(acac)_2$/**III** 1 : 1.5	ClO_2 ($CHCl_3$)	82	8	–1.4
i	$VO(acac)_2$/**III** 1 : 1.5	ClO_2 (H_2O)	76	9	–1.6
j	$VO(acac)_2$/**IV** 1 : 1.5	H_2O_2	73	59	+12.0
k	$VO(acac)_2$/**IV** 1 : 1.5	ClO_2 ($CHCl_3$)	84	27	+5.3
l	$VO(acac)_2$/**IV** 1 : 1.5	ClO_2 (H_2O)	78	20	+3.9
m	$VO(acac)_2$/**V** 1 : 1.5	H_2O_2	77	48	–10.0
n	$VO(acac)_2$/**V** 1 : 1.5	ClO_2 ($CHCl_3$)	87	11	–2.2
o	$VO(acac)_2$/**V** 1 : 1.5	ClO_2 (H_2O)	80	1.5	–0.3

Notes: * All experiments were carried out at 0°C with $VO(acac)_2$ in $CHCl_3$, the duration of the experiment was 16 h, the substrate–oxidizer–catalyzer ratio was 1 : 1 : 0.02.

** The yield of sulfoxide after column chromatography on SiO_2 is given.

*** The enantiomeric purity of sulfoxide was determined by HPLC on the chiral phase (see the Experimental section).

were recorded on a Bruker AM spectrometer. Signals of chloroform (δ_H 7.24 ppm, δ_C 77.00 ppm) were used as an internal standard. The melting temperatures were determined on a Gallenkamp device (Sanyo). Specific rotation was measured on a P3002 RS automatic digital polarimeter; the specific rotation is expressed in (degree × ml) × (g × dm)$^{-1}$, and the concentration of the solution is expressed in g × (100 ml)$^{-1}$. The elemental analysis was carried out using an EA 1110 CHNS-O automatic analyzer.

The purity of starting substances was controlled by GLC on a Chrom-5 chromatograph equipped with a flame ionization detector, on a 2500 × 0.25 mm column; the stationary phase was Carbowax on a Chromaton-N-AW-DMCS carrier; the carrier gas was helium. The enantiomeric composition of sulfoxide was determined by HPLC on a Surveyor LC device on a column with the chiral phase Chiralcel OB-H, λ = 254 nm, 0.5 ml/min (eluent hexane : *i*PrOH 50 : 50).

TLC was carried out on Sorbfil plates using a system of solvents C_7H_{16}–Et_2O 1 : 2. For the detection of substances, plates were treated with a $KMnO_4$ solution. Column chromatography was carried out on silica gel (70–230 μ; Alfa Aesar) using a system of solvents C_7H_{16}–Et_2O 5 : 1 ⟶ 1 : 2.

Table 2. Asymmetric oxidation by complexes based on titanium(IV)

Experiment	Catalyzer	Oxidizer	Yield (%)**	Enantiomeric purity (%)***	$[\alpha]_D$
a	$Ti(OPr^i)_4/H_2O$/**I** 1 : 10 : 2	CHP	69	10	+2.1
b	$Ti(OPr^i)_4/H_2O$/**I** 1 : 10 : 2	ClO_2 (Toluene)	80	47	–9.7
c	$Ti(OPr^i)_4/H_2O$/**II** 1 : 10 : 2	CHP	69	1	–0.2
d	$Ti(OPr^i)_4/H_2O$/**II** 1 : 10 : 2	ClO_2 (Toluene)	76	6	+1.2
e	$Ti(OPr^i)_4/H_2O$/**III** 1 : 10 : 2	CHP	76	59	–12.1
f	$Ti(OPr^i)_4/H_2O$/**III** 1 : 10 : 2	ClO_2 (Toluene)	79	8	+1.4
g	$Ti(OPr^i)_4/H_2O$/**IV** 1 : 10 : 2	CHP	80	42	–8.7
h	$Ti(OPr^i)_4/H_2O$/**IV** 1 : 10 : 2	ClO_2 (Toluene)	83	28	+5.6
i	$Ti(OPr^i)_4/H_2O$/**V** 1 : 10 : 2	CHP	78	84	+17.5
j	$Ti(OPr^i)_4/H_2O$/**V** 1 : 10 : 2	ClO_2 (Toluene)	84	27	–5.3

Notes: * All experiments were carried out at 0°C with $Ti(OPr^i)_4$ in CH_2Cl_2, the duration of the experiment was 16 h, and the substrate–oxidizer–catalyzer ratio was 1 : 1 : 0.65.

** The yield of sulfoxide after column chromatography on SiO_2 is given.

*** The enantiomeric purity of sulfoxide was determined by HPLC on the chiral phase OB-H (see the Experimental section).

The starting phenylphenacyl sulfide **1** was obtained by the reaction of thiophenol and 2-bromo-1-phenylethanone as described [16]. The yield of the product was 98%; mp 51–52°C.

*The Asymmetric Oxidation of Phenylphenacyl Sulfide **1** in the Presence of a VO/Ligand Complex was Carried out by the Method Described in [17]*

(a) Sulfide (**1**) (228 mg, 1.0 mmol) was oxidized by 33% H_2O_2 (120 μl, 1.0 mmol) in the presence of $VO(acac)_2$ (1 mg, 4.0 μmol) and ligand (**I**) (1.9 mg, 5.7 μmol) to yield 0.72 g (67%) of compound (**2**). $[\alpha]_D$ +0.6 (*c* 1.0, EtOH); the enantiomeric excess was 3.0%.

(b) Sulfide (**1**) (228 mg, 1.0 mmol) was oxidized by ClO_2 (11 ml, 0.5 mmol) in chloroform (0.20 mol/l) in the presence of $VO(acac)_2$ (1 mg, 4.0 μmol) and ligand (**I**) (1.9 mg, 5.7 μmol) to yield 0.83 g (78%) of compound (**2**). $[\alpha]_D$ +6.0 (*c* 1.0, EtOH); the enantiomeric excess was 32.0%.

(c) Sulfide (**1**) (228 mg, 1.0 mmol) was oxidized by 15 ml (0.5 mmol) of an aqueous solution of ClO_2 (0.148 mol/l) in the presence of $VO(acac)_2$ (1 mg, 4.0 μmol) and ligand (**I**) (1.9 mg, 5.7 μmol) to yield 0.74 g (69%) of compound (**2**). $[\alpha]_D$ +6.1 (*c* 1.0, EtOH); the enantiomeric excess was 32.0%.

(d) Sulfide (**1**) (228 mg, 1.0 mmol) was oxidized by 33% H_2O_2 (120 μl, 1.0 mmol) in the presence of $VO(acac)_2$ (1 mg, 4.0 μmol) and ligand (**II**) (2.2 mg, 6.5 μmol) to yield 0.70 g (65%) of compound (**2**). $[\alpha]_D$ –1.4 (*c* 1.0, EtOH); the enantiomeric excess was 8.0%.

(e) Sulfide (**1**) (228 mg, 1.0 mmol) was oxidized by ClO_2 (4.2 ml, 0.5 mmol) in chloroform (0.52 mol/l) in the presence of $VO(acac)_2$ (1 mg, 4.0 μmol) and ligand (**II**) (2.2 mg, 6.5 μmol) to yield 0.82 g (76%) of compound (**2**). $[\alpha]_D$ –1.6 (*c* 1.0, EtOH); the enantiomeric excess was 9.0%.

(f) Sulfide (**1**) (228 mg, 1.0 mmol) was oxidized by 17 ml (0.5 mmol) of an aqueous solution of ClO_2 (0.13 mol/l) in the presence of $VO(acac)_2$ (1 mg, 4.0 μmol) and ligand (**II**) (2.2 mg, 6.5 μmol) to yield 0.74 g (69%) of compound (**2**). $[\alpha]_D$ –2.8 (*c* 1.0, EtOH); the enantiomeric excess was 15.0%.

(g) Sulfide (**1**) (228 mg, 1.0 mmol) was oxidized by 33% H_2O_2 (120 μl, 1.0 mmol) in the presence of $VO(acac)_2$ (1 mg, 4.0 μmol) and ligand (**III**) (2 mg, 6.0 μmol) to yield 0.72 g (67%) of compound (**2**).

$[\alpha]_D$ −16.0 (*c* 1.0, EtOH); the enantiomeric excess was 75.6%.

(h) Sulfide (**1**) (228 mg, 1.0 mmol) was oxidized by ClO_2 (4.2 ml, 0.5 mmol) in chloroform (0.52 mol/l) in the presence of $VO(acac)_2$ (1 mg, 4.0 μmol) and ligand (**III**) (2 mg, 6.0 μmol) to yield 0.88 g (82%) of compound (**2**). $[\alpha]_D$ −1.4 (*c* 1.0, EtOH); the enantiomeric excess was 8.0%.

(i) Sulfide (**1**) (228 mg, 1.0 mmol) was oxidized by 22 ml (0.5 mmol) of an aqueous solution of ClO_2 (0.10 mol/l) in the presence of $VO(acac)_2$ (1 mg, 4.0 μmol) and ligand (**III**) (2 mg, 6.0 μmol) to yield 0.82 g (76%) of compound (**2**). $[\alpha]_D$ −1.6 (*c* 1.0, EtOH); the enantiomeric excess was 9.0%.

(j) Sulfide (**1**) (228 mg, 1.0 mmol) was oxidized by 33% H_2O_2 (120 μl, 1.0 mmol) in the presence of $VO(acac)_2$ (1 mg, 4.0 μmol) and ligand (**IV**) (3.1 mg, 9.4 μmol) to yield 0.78 g (73%) of compound (**2**). $[\alpha]_D$ +12.0 (*c* 1.0, EtOH); the enantiomeric excess was 59.1%.

(k) Sulfide (**1**) (228 mg, 1.0 mmol) was oxidized by ClO_2 (4.2 ml, 0.5 mmol) in chloroform (0.52 mol/l) in the presence of $VO(acac)_2$ (1 mg, 4.0 μmol) and ligand (**IV**) (3.1 mg, 9.4 μmol) to yield 0.90 g (84%) of compound (**2**). $[\alpha]_D$ +12.0 (*c* 1.0, EtOH); the enantiomeric excess was 27.0%.

(l) Sulfide (**1**) (228 mg, 1.0 mmol) was oxidized by 22 ml (0.5 mmol) of an aqueous solution of ClO_2 (0.10 mol/l) in the presence of $VO(acac)_2$ (1 mg, 4.0 μmol) and ligand (**IV**) (3.1 mg, 9.4 μmol) to yield 0.84 g (78%) of compound (**2**). $[\alpha]_D$ +3.9 (*c* 1.0, EtOH); the enantiomeric excess was 20.0%.

(m) Sulfide (**1**) (228 mg, 1.0 mmol) was oxidized by 33% H_2O_2 (120 μl, 1.0 mmol) in the presence of $VO(acac)_2$ (1 mg, 4.0 μmol) and ligand (**V**) (1.9 mg, 5.8 μmol) to yield 0.82 g (77%) of sulfoxide (**2**). $[\alpha]_D$ −10.0 (*c* 1.0, EtOH); the enantiomeric excess was 48.0%.

(n) Sulfide (**1**) (228 mg, 1.0 mmol) was oxidized by ClO_2 (17.7 ml, 0.5 mmol) in chloroform (0.124 mol/l) in the presence of $VO(acac)_2$ (1 mg, 4 μmol) and ligand (**V**) (1.9 mg, 5.8 μmol) to yield 0.93 g (87%) of compound (**2**). $[\alpha]_D$ −2.2 (*c*, 1.0, EtOH); the enantiomeric excess was 11.0%.

(o) Sulfide (**1**) (228 mg, 1.0 mmol) was oxidized by 20 ml (0.5 mmol) of an aqueous solution of ClO_2 (0.108 mol/l) in the presence of $VO(acac)_2$ (1 mg, 4.0 μmol) and ligand (**V**) (1.9 mg, 5.8 μmol) to yield 0.86 g (80%) of compound (**2**). $[\alpha]_D$ −0.3 (*c*, 1.0, EtOH); the enantiomeric excess was 1.5%.

*The Asymmetric Oxidation of Phenylphenacyl Sulfide **1** in the Presence of a Ti/Ligand Complex*

(a) A mixture of titanium isopropylate (0.031 g, 0.11 mmol) and ligand (**I**) (0.070 g, 0.22 mmol) in dichloromethane (10 ml) was stirred for 1 h at room temperature after which distilled water (1.9 ml, 1.1 mmol) was added. The temperature was lowered to 0°C, and sulfide (**1**) (0.5 g, 2.2 mmol) was added; 5 min later, CHP (0.86 ml, 2.2 mmol) in toluene (2.55 mol/l) was added dropwise. The final mixture was stirred for 16 h at 0°C. The reaction mixture was poured into a solution of ferrous sulfate heptahydrate (3 g, 10.8 mmol) and citric acid (1 g, 4.8 mmol) in 30 ml of water, 15 ml of 1,4-dioxane, and 25 ml diethyl ether and stirred for 15 min. The organic layer was separated. The aqueous layer was extracted three times with dichloromethane. The combined organic layer was washed with a saturated aqueous NaCl solution (25 ml), dried over $MgSO_4$, filtered, and evaporated at low pressure. After separation by column chromatography, 0.74 g (69%) of compound (**2**) was obtained. $[\alpha]_D$ +2.1 (*c* 1.0, EtOH); the enantiomeric excess was 10%.

(b) Sulfide (**1**) (0.5 g, 2.2. mmol) was oxidized by ClO_2 (9.1 ml, 1.1 mmol) in toluene (0.12 mol/l) in the presence of $Ti(OPr^i)_4$ (0.031 g, 0.11 mmol), ligand (**I**) (0.070 g, 0.22 mmol), and H_2O (1.9 ml, 1.1 mmol) to yield 0.86 g (80%) of compound (**2**). $[\alpha]_D$ −9.7 (*c* 1.0, EtOH); the enantiomeric excess was 47%.

(c) Sulfide (**1**) (0.5 g, 2.2. mmol) was oxidized by CHP (0.86 ml, 2.2 mmol) in toluene (2.55 mol/l) in the presence of $Ti(OPr^i)_4$ (0.031 g, 0.11 mmol), ligand (**II**) (0.073 g, 0.22 mmol), and H_2O (1.9 ml, 1.1 mmol) to yield 0.74 g (69%) of compound (**2**). $[\alpha]_D$ −0.2 (*c* 1.0, EtOH); the enantiomeric excess was 1%.

(d) Sulfide (**1**) (0.5 g, 2.2. mmol) was oxidized by ClO_2 (9.1 ml, 1.1 mmol) in toluene (0.12 mol/l) in the presence of $Ti(OPr^i)_4$ (0.031 g, 0.11 mmol), ligand (**II**) (0.073 g, 0.22 mmol), and H_2O (1.9 ml, 1.1 mmol) to yield 0.82 g (76%) of compound (**2**). $[\alpha]_D$ +1.2 (*c* 1.0, EtOH); the enantiomeric excess was 6%.

(e) Sulfide (**1**) (0.5 g, 2.2. mmol) was oxidized by CHP (0.86 ml, 2.2 mmol) in toluene (2.55 mol/l) in the presence of $Ti(OPr^i)_4$ (0.031 g, 0.11 mmol), ligand (**III**) (0.073 g, 0.22 mmol), and H_2O (1.9 ml, 1.1 mmol) to yield 0.82 g (76%) of compound (**2**). $[\alpha]_D$ −12.1 (*c* 1.0, EtOH); the enantiomeric excess was 59%.

(f) Sulfide (**1**) (0.5 g, 2.2. mmol) was oxidized by ClO_2 (9.1 ml, 1.1 mmol) in toluene (0.12 mol/l) in the presence of $Ti(OPr^i)_4$ (0.031 g, 0.11 mmol), ligand (**III**) (0.073 g, 0.22 mmol), and H_2O (1.9 ml, 1.1 mmol) to yield 0.85 g (79%) of compound (**2**). $[\alpha]_D$ +1.4 (*c* 1.0, EtOH); the enantiomeric excess was 8%.

(g) Sulfide (**1**) (0.5 g, 2.2. mmol) was oxidized by CHP (0.86 ml, 2.2 mmol) in toluene (2.55 mol/l) in the presence of $Ti(OPr^i)_4$ (0.031 g, 0.11 mmol), ligand (**IV**) (0.120 g, 0.22 mmol), and H_2O (1.9 ml, 1.1 mmol) to yield 0.87 g (80%) of compound (**2**). $[\alpha]_D$ −8.7 (*c* 1.0, EtOH); the enantiomeric excess was 42%.

(h) Sulfide (**1**) (0.5 g, 2.2. mmol) was oxidized by ClO_2 (9.1 ml, 1.1 mmol) in toluene (0.12 mol/l) in the

presence of $Ti(OPr^i)_4$ (0.031 g, 0.11 mmol), ligand (**IV**) (0.120 g, 0.22 mmol), and H_2O (1.9 ml, 1.1 mmol) to yield 0.90 g (83%) of compound (**2**). $[\alpha]_D$ +5.6 (*c* 1.0, EtOH); the enantiomeric excess was 28%.

(i) Sulfide (**1**) (0.5 g, 2.2. mmol) was oxidized by CHP (0.86 ml, 2.2 mmol) in toluene (2.55 mol/l) in the presence of $Ti(OPr^i)_4$ (0.031 g, 0.11 mmol), ligand (**V**) (0.071 g, 0.22 mmol), and H_2O (1.9 ml, 1.1 mmol) to yield 0.84 g (78%) of compound (**2**). $[\alpha]_D$ +17.5 (*c* 1.0, EtOH); the enantiomeric excess was 84%.

(j) Sulfide (**1**) (0.5 g, 2.2. mmol) was oxidized by ClO_2 (9.1 ml, 1.1 mmol) in toluene (0.12 mol/l) in the presence of $Ti(OPr^i)_4$ (0.031 g, 0.11 mmol), ligand (**V**) (0.071 g, 0.22 mmol), and H_2O (1.9 ml, 1.1 mmol) to yield 0.90 g (84%) of compound (**2**). $[\alpha]_D$ −5.3 (*c* 1.0, EtOH); the enantiomeric excess was 27%.

REFERENCES

1. Fache, F., Schulz, E., Tommasino, M.L., and Lemaire, M., *Chem. Rev.*, 2000, vol. 100, no. 6, pp. 2159–2232.
2. Dzhenis, V., *Kataliz v khimii i enzimologii* (Catalysis in Chemisstry and Enzymology), Moscow, 1972.
3. Cucciolito, M.E., Ruffo, F., and Vitagliano, A., *Tetrahedron Lett.*, 1994, vol. 35, pp. 169–178.
4. Cucciolito, M.E., Flores, G., and Vitagliano, A., *Organometallics,* 2004, vol. 23, no. 1, pp. 15–17.
5. Alexakis, A., Frutos, J.C., Mutti, S., and Mangeney, P., *J. Org. Chem.*, 1994, vol. 59, no. 12, pp. 3326–3334.
6. Dvornikova, I.A., Frolova, L.L., Churakov, A.V., and Kuchin, A.V., *Izv. Akad. Nauk, Ser. Khim.*, 2004, no. 6, pp. 1270–1276.
7. Jha, S.C. and Joshi, N.N., *Tetrahedron: Asymmetry*, 2001, vol. 12, pp. 2463–2466.
8. Prilezhaeva, E.N., *Poluchenie i svoistva organicheskikh soedinenii sery* (Obtaining and Properties of Organic Sulfur-Containing Compounds), Belen'kii, L.I., Ed., Moscow, 1998.
9. Carreno, M.C., *Chem. Rev.*, 1995, vol. 95, no. 6, pp. 1717–1760.
10. Yunusov, S.Yu., *Alkaloids*, Tashkent, 1981.
11. Takaishi, Y., Murakami, Y., Uda, M., Ohashi, T., Hamamura, N., Kido, M., and Kadota, S., *Phytochemistry*, 1997, vol. 45, no. 5, pp. 997–1001.
12. Hogan, P.J., Hopes, P.A., Moss, W.O., Robinson, G.E., and Patel, I., *Org. Proc. Res. Dev.*, 2002, vol. 6, no. 3, pp. 225–229.
13. Pitchen, P., France, C.J., McFarlane, I.M., Newton, C.G., and Thompson, D.M., *Tetrahedron Lett.*, 1994, vol. 35, no. 3, pp. 485–486.
14. Kubo, K., Oda, K., Kaneko, T., Satoh, H., and Nohara, A., *Chem. Pharm. Bull.*, 1990, vol. 38, pp. 2853–2858.
15. Nishide, K., Nakayama, A., and Kusumoto, T., *Chem. Lett.*, 1990, pp. 623–625.
16. *Sintez sul'fidov, tiofenolov i tiolov tipa soedinenii, vstrechayushchikhsya v neftyakh* (Synthesis of Sulfides, Thiophenols, and Thiols of the Type of Compounds Occurring in Oils), Karaulov, E.N., Ed., Moscow, 1988.
17. Lin, G., Cogan, D.A., and Ellman, J.A., *J. Am. Chem. Soc.,* 1997, vol. 119, no. 41, pp. 9913–9917.
18. Kuchin, A.V., Rubtsova, S.A., and Loginova, I.V., *Izv. Akad. Nauk, Ser. Khim.*, 2001, no. 3, pp. 413–416.
19. Gordon, B.G., Kieffer, R.G., and Rosenblatt, D.H., *J. Prog. Inorg. Chem.,* 1972, vol. 15, pp. 201–204.
20. Rosenblatt, D.H., Hayes, A.J., Harrison, B.L., Streaty, R.A., and Moore, K.A., *J. Org. Chem.,* 1963, vol. 28, no. 10, pp. 2790–2794.
21. Rosenblatt, D.H., Hull, L.A., De Luca, D.C., Davis, G.T., Weglein, R.C., and Williams, K.R., *J. Am. Chem. Soc.,* 1967, vol. 89, no. 5, pp. 1158–1163.
22. Hull, L.A., Davis, G.T., Rosenblatt, D.H., Williams, K.R., and Weglein, R.C., *J. Am. Chem. Soc.,* 1967, vol. 89, no. 5, pp. 1163–1170.
23. Grimley, E. and Gordon, G., *J. Inorg. Nucl. Chem.*, 1973, vol. 35, pp. 2383–2388.
24. Alfassi, Z.B., Huie, R.E., and Neta, P., *J. Phys. Chem.*, 1986, vol. 90, no. 17, pp. 4156–4158.
25. Lindgren, B.O. and Svahn, C.M., *Acta Chem. Scand.*, 1965, vol. 19, pp. 7–11.
26. Rav-Acha, C., Choshen, E., and Sarel, S., *Helv. Chim. Acta,* 1986, vol. 69, pp. 1728–1730.
27. Kuchin, A.V., Rubtsova, S.A., Loginova, I.V., and Subbotina, S.N., *Zh. Org. Khim.*, 2000, no. 12, pp. 1873–1874.
28. Kuchin, A.V., Rubtsova, S.A., Karmanova, L.P., Subbotina, S.N., and Loginova, I.V., *Izv. Akad. Nauk, Ser. Khim.*, 1998, no. 10, pp. 2110–2111.
29. Belokon, Y.N., *Lel. Chim. Acta*, 2002, vol. 85, pp. 3301–3312.