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New Chiral Diamines of the Dioxolane Series: (+)-(4*S*,5*S*)-2,2-Dimethyl-4,5-bis(diphenylaminomethyl)-1,3-dioxolane and (+)-(4*S*,5*S*)-2,2-Dimethyl-4,5-bis(methyl-aminomethyl)-1,3-dioxolane

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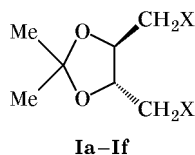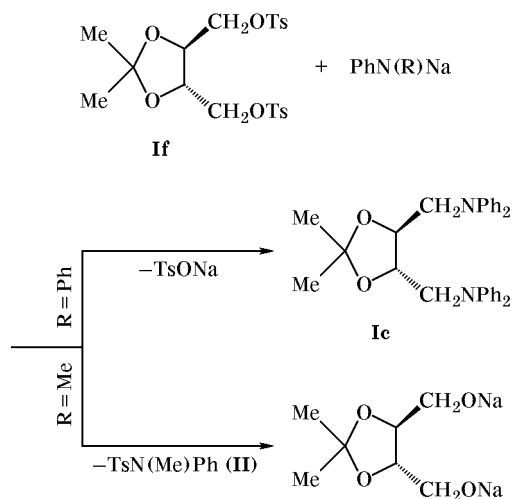
Abstract—The reaction of sodium diphenylamide with 2,2-dimethyl-4,5-bis(tosyloxymethyl)-1,3-dioxolane gave (+)-(4*S*,5*S*)-2,2-dimethyl-4,5-bis(diphenylaminomethyl)-1,3-dioxolane, which was brought into complex formation with cobalt chloride. Treatment of 2,2-dimethyl-4,5-bis(tosyloxymethyl)-1,3-dioxolane with sodium *N*-methylanilide resulted in cleavage of the S−O bond in the *p*-toluenesulfonate moiety with formation of *N*-methyl-*N*-phenyl-*p*-toluenesulfonamide and 4,5-bis(hydroxymethyl)-2,2-dimethyl-1,3-dioxolane disodium salt. Diethyl (4*R*,5*R*)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate reacted with methylamine to give the corresponding dicarboxamide which was reduced with lithium aluminum hydride to (4*S*,5*S*)-2,2-dimethyl-4,5-bis(methylaminomethyl)-1,3-dioxolane having chiral carbon and nitrogen atoms.

In continuation of our studies in the field of chiral ligands, specifically of diamines derived from (+)-(4*S*,5*S*)-4,5-bis(aminomethyl)-1,3-dioxolane (**Ia**), we planned to examine the behavior of compounds having bulky group on the nitrogen atoms, which should increase the rigidity of chelate ring in complexes with metals, as well as of those with chiral amino nitrogen atoms (i.e., containing three different substituents), with a view to compare them with previously studied compounds **Ia** and **Ib** [1–3]. For this purpose, we tried to synthesize diamines **Ic** and **Id** by reaction of *p*-toluenesulfonate **If** with sodium derivatives of diphenylamine, methylamine, and also diamine **Ie**.

Compounds **Ia** and **Ib** were synthesized by us previously [1, 2] by aminolysis of 2,2-dimethyl-1,3-

dioxolane-4,5-dicarboxylate and subsequent reduction of the diamides thus formed to diamines. However, both diethyl 2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate and its precursor, diethyl tartrate, failed to react with weakly basic aromatic amines. Therefore, diphenylamine and *N*-methylaniline were preliminarily

Scheme 1.

X = NH₂ (**a**), NMe₂ (**b**), NPh₂ (**c**), NMePh (**d**), NHMe (**e**), OTs (**f**).

converted into sodium derivatives in order to enhance their basicity. The reaction of sodium diphenylamide with *p*-toluenesulfonate **If** smoothly afforded target diamine **Ic** (Scheme 1). Unexpectedly, our attempt to obtain diamine **Id** with chiral nitrogen atoms by reaction of sodium *N*-methylanilide with sulfonate **If** resulted in cleavage of the S−O rather than O−C bond (as in the reaction with sodium diphenylamide). In other words, nucleophilic substitution at the sulfur atom occurred instead of S_N2 reaction at the carbon atom, and the products were *N*-methyl-*N*-phenyl-*p*-toluenesulfonamide (**II**) and 4,5-bis(hydroxymethyl)-2,2-dimethyl-1,3-dioxolane disodium salt (Scheme 1). With the use of methylamine (which is more basic than *N*-methylaniline), we succeeded in obtaining N-chiral diamine **Ie** by the scheme reported previously for the synthesis of diamine **Ia** [3] (Scheme 2).

Scheme 2.
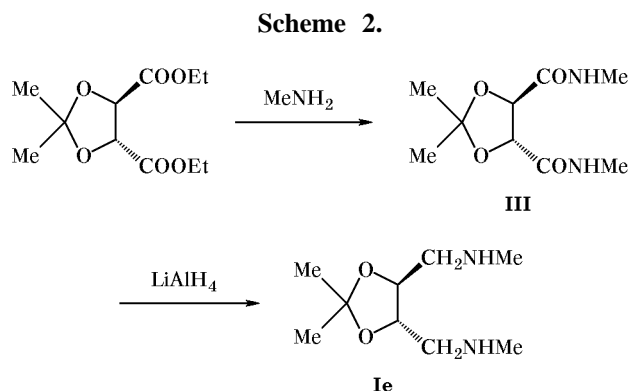
Diamine **Ic** was used as ligand for rhodium and cobalt catalysts of enantioselective hydrogenation. The hydrogenation with molecular hydrogen under pressure over cationic rhodium catalyst containing diamine **Ic** ensures quantitative yield of the products and moderate (~20%) optical yield. The reduction of ketones with sodium tetrahydridoborate over cobalt catalyst in the presence of diamine **Ic** is also characterized by quantitative chemical yields, but the optical yields are close to zero, in contrast to the reaction over rhodium complexes with diamines **Ia** and **Ib**.* These data led us to examine the complex formation of diamine **Ic** with cobalt(II) chloride in more detail using UV spectroscopy. It is known that the optical yield is directly related to the structure and rigidity of metal-complex catalyst. The reaction of cobalt(II) chloride with diamine **Ic** was studied in tetrahydrofuran (where the hydrogenation was carried out), propylene carbonate, dioxane, acetonitrile, and chloro-

form. At an equimolar ratio of diamine **Ic** and $CoCl_2$, no complex formation was observed in the four latter solvents which are less protophilic than THF. When cobalt(II) chloride and diamine **Ic** were dissolved in THF, an absorption band appeared in the visible region of the electron absorption spectrum of the solution (ν 19500 cm^{-1}, see figure), which indicated formation of a complex. This band is much stronger than that arising from *d–d* transitions in $CoCl_2$ [4]. The electron absorption spectrum of a solution of $CoCl_2$ in THF contains the following components, ν_{max}, cm^{-1}: 14600, 15700, 16000, and 17300.

At an equimolar diamine **Ic**-to-$CoCl_2$ ratio, the *d–d*-transition band appears as an inflection on the low-frequency flank of the band at 19500 cm^{-1}. High-frequency shift of absorption bands in the spectra of cobalt complexes with organic ligands relative to the *d–d*-transition band of cobalt halides is usually attributed to distortion of symmetry in the complex [4]. It should be emphasized that the complex formation of diamine **Ic** with cobalt(II) chloride occurs at a fairly low rate: the maximal concentration of the complex is attained in several hours at an initial $CoCl_2$ (and diamine) concentration of 1×10^{-3} M. Later on, absorption at higher frequencies increases, while the band at 19500 cm^{-1} disappears.

A solution of diamine **Ic** in THF is characterized by absorption bands at 33900 ($\varepsilon = 34700$), 40200 ($\varepsilon = 27400$), and ~48000 cm^{-1}, which belong to π–π^* transitions. The pattern in this region of the spectrum also changes with time. At a concentration of **Ic** and $CoCl_2$ equal to 8×10^{-5} M we observed two sets of narrow bands in the range from 40000 to 36500 cm^{-1}, which correspond to vibrational transitions typical of substituted aromatic compounds [5] (see figure). The long-wave absorption band of the ligand (arising from *n*–π^* transition in the diphenylamine fragment, $\nu_{max} = 33900$ cm^{-1}) becomes more symmetric, while its intensity does not change. The position and intensity of this band remain unchanged in the presence of excess cobalt(II) chloride ([**Ic**]:[$CoCl_2$] = 1:100). These data indicate that no chelation occurs via coordination of two nitrogen atoms in **Ic** at the metal ion. Under analogous conditions, diphenylamine as model compound with $CoCl_2$ forms a usual *n*–σ-like complex with participation of lone electron pair on the nitrogen. The UV spectrum of the complex lacks long-wave absorption band typical of the free ligand ($\nu_{max} = 34900$ cm^{-1}, $\varepsilon = 31100$) because of rupture of conjugation between the phenyl group and lone electron pair on the nitrogen [5]. The strong charge-transfer band at ν_{max} 41900 cm^{-1} has a weak shoulder

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* The results of hydrogenation over metal complexes with chiral diamines **Ic** and **Ie** will be reported elsewhere.
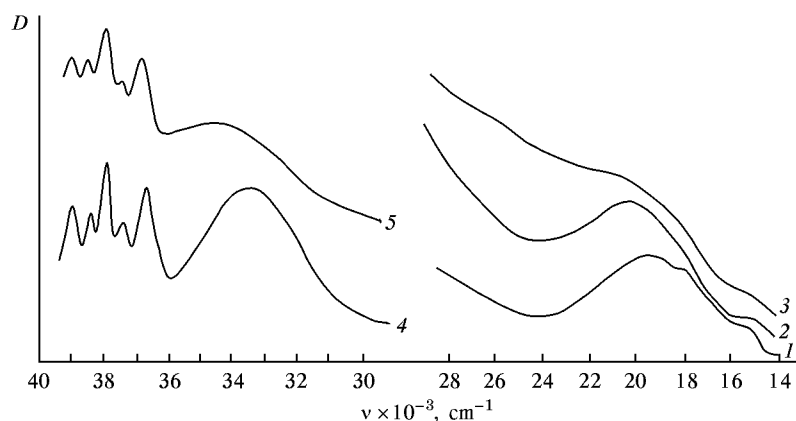
UV spectra of solutions of diamine **Ic** and cobalt(II) chloride (1:1) in THF (in parentheses is given the time elapsed from the moment of mixing of the reactants): (*1*) $c = 5 \times 10^{-3}$ M, $d = 1$ cm; (*2*) $c = 1 \times 10^{-3}$ M, $d = 1$ cm (1 h); (*3*) $c = 1 \times 10^{-3}$ M, $d = 0.5$ cm (20 h); (*4*) $c = 8 \times 10^{-5}$ M, $d = 0.5$ cm (24 h); (*5*) $c = 8 \times 10^{-5}$ M, $d = 0.2$ cm (72 h).

on the long-wave flank (ν 36 000 cm^{-1}), which corresponds to the transition forbidden in benzene.

The intensity of the narrow bands increases with time. After 72 h (from the moment of preparation of the solution), these bands become considerably stronger than the long-wave absorption band which shifts to 34 800 cm^{-1} and broadens (see figure). By raising the ligand and CoCl$_2$ concentration to 5×10^{-3} M, we succeeded in revealing only one band having a fine structure. Its components are located at ν 37 500, 38 500, and 39 500 cm^{-1}; the corresponding components of the most intense absorption band at lower concentration ($c = 8 \times 10^{-5}$) are observed at lower frequencies (by 700 cm^{-1}): ν_{max} 36 800, 37 800, and 38 800 cm^{-1}. In both cases, the vibrational range between the fine-structure components is 1000 cm^{-1}, as in the spectra of substituted benzenes [6]. Thus variations in both visible and UV regions of the electron absorption spectra suggest a slow and fairly sophisticated interaction between diamine **Ic** and cobalt(II) chloride. Presumably, the interaction involves metal coordination at the aromatic π-system of the ligand. To verify this assumption we compared the above data with the spectra of the system CoCl$_2$–toluene in THF, where only such a mode of coordination is possible. The reaction of CoCl$_2$ with both toluene and diphenylamine or diamine **Ic** at an amine-to-CoCl$_2$ ratio of 1:100 gives rise to a strong absorption band in the region 41 000–42 000 cm^{-1}. Therefore, there is the possibility for coordination of the above ligands in a common way, via η^6-binding to the metal atom.

Our results explain almost complete absence of enantioselectivity in the reduction of ketones with sodium tetrahydridoborate over the CoCl$_2$–**Ic** catalyst.

As shown above, the complex formation is a slow process; therefore, under standard hydrogenation conditions, the diamine **Ic**–cobalt(II) chloride complex has no time to be formed. Moreover, the coordination does not involve lone electron pairs on the nitrogen atoms, i.e., no seven-membered chelate ring, which is responsible for stereodifferentiation, is formed. As a result, the hydrogenation occurs mainly over an achiral catalyst, so that no appreciable excess of one of the enantiomers could be obtained.

EXPERIMENTAL

The electron absorption spectra were recorded on a Specord UV-Vis spectrophotometer. The NMR spectra were obtained on a Bruker DPX-400 instrument at 400 MHz for ^{1}H and 100 MHz for ^{13}C; HMDS was used as internal reference. The chemical shifts are given relative to TMS.

(+)-(4*S*,5*S*)-2,2-Dimethyl-4,5-bis(methylaminomethyl)-1,3-dioxolane (Ic). A solution of 3.9 g (0.03 mol) of naphthalene in 30 ml of anhydrous THF was added to 0.7 g (0.03 mol) of metallic sodium, the mixture was stirred for 2 h, and a solution of 5.1 g (0.03 mol) of diphenylamine in 20 ml of anhydrous dioxane was added in small portions while shaking. The mixture was kept for 30 min and was evaporated under reduced pressure almost to dryness, and the thick residue was washed with benzene (3 × 40 ml) to remove naphthalene. All operations were carried out in a closed evacuated system. The precipitate of sodium diphenylamide was dried and dissolved in 30 ml of THF, and a solution of 4.5 g (0.096 mol) of *p*-toluenesulfonate **If** in 20 ml of THF was added. The mixture was placed in an ampule, evacuated, and

shaken for 24 h. The ampule was opened, sodium *p*-toluenesulfonate was filtered off, and the filtrate was evaporated to dryness on a rotary evaporator. The product was purified by column chromatography on silica gel (160–200 μm) using (in succession) hexane, hexane–chloroform (2.5 : 1), and chloroform as eluent, followed by triple recrystallization from methanol. Yield 2.3 g (50%), mp 70–71°C. IR spectrum, cm^{-1}: 2983, 1590, 1496, 1361, 1249, 1170, 1076, 877, 754, 696. ^{1}H NMR spectrum (CDCl$_3$), δ, ppm: 1.38 s (6H, Me$_2$C), 3.84 m (4H, CH$_2$), 4.17 m (2H, CH), 6.95 m (6H, *o*-H, *p*-H), 7.19 m (4H, *m*-H). ^{13}C NMR spectrum (CDCl$_3$), δ$_C$, ppm: 27.51 (C**C**H$_3$), 55.72 (CH$_2$), 77.79 (CH), 109.68 (**C**CH$_3$), 121.49 (C^o), 121.82 (C^p), 129.38 (C^m), 148.26 (C^i). Found, %: C 79.57; H 6.91; N 6.20. C$_{31}$H$_{32}$N$_2$O$_2$. Calculated, %: C 80.14; H 6.94; N 6.03.

(4*S*,5*S*)-2,2-Dimethyl-4,5-bis(methylamino-methyl)-1,3-dioxolane (Ie). A suspension of 3 g (0.08 mol) of lithium aluminum hydride in 100 ml of of a 1 : 1 mixture of diethyl ether and tetrahydrofuran was refluxed for 20 min, 7.3 g (0.034 mol) of amide **III** was added, and the mixture was refluxed for 4 h, cooled to 0°C, and decomposed by carefully adding in succession 4 ml of water, 4 ml of a 4 M solution of NaOH, and 10 ml of water. The solution was separated from the precipitate by decanting, and the precipitate was treated with three portions of boiling dioxane. The solution was combined with the dioxane extracts and evaporated, and the residue was distilled under reduced pressure to obtain 2.1 g (~30%) of product **Ie** as a colorless oily liquid. bp 74–75°C (0.5 mm), d_4^{20} = 0.971, [α]$_D$ = –4.77° (neat). ^{1}H NMR spectrum (CDCl$_3$), δ, ppm: 1.38 s (6H, Me$_2$C), 1.48 br.s (2H, NH), 2.44 s (6H, NMe), 2.73 m (4H, CH$_2$), 3.89 m (2H, CH). ^{13}C NMR spectrum (CDCl$_3$), δ, ppm: 26.75 (C**C**H$_3$), 36.27 (NCH$_3$), 53.66 (CH$_2$), 78.08 (CH), 108.21 (C^2). Found, %: C 57.18; H 10.44; N 14.33. C$_9$H$_{20}$N$_2$O$_2$. Calculated, %: C 57.42; H 10.71; N 14.88.

N-Methyl-N-phenyl-p-toluenesulfonamide (II). mp 93°C; published data [7]: mp 94–95. IR spectrum, ν, cm^{-1}: 1600, 1495, 1455, 1350, 1170, 1070, 875, 815, 780, 720, 700, 660. ^{1}H NMR spectrum (CDCl$_3$), δ, ppm: 2.40 s (3H, CMe), 3.15 s (3H, NMe), 7.08 m (2H, *o*-H in NPh), 7.24 m (5H, *m*-H, *p'*-H, *p*-H), 7.41 m (2H, *o*-H). ^{13}C NMR spectrum (CDCl$_3$), δ$_C$, ppm: 21.59 (C**C**H$_3$), 38.14 (NCH$_3$), 126.69 (C^o in NPh), 127.30 (C^p), 127.96 (C^m in NPh), 128.89 (C^o in Tol), 129.39 (C^m in Tol), 133.65 (NC), 141.71 (SC), 143.59 (C^p in Tol).

(4*R*,5*R*)-2,2-Dimethyl-1,3-dioxolane-4,5-dicar-boxamide (III). Diethyl 2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate, 10 g (0.046 mol), was placed in an ampule, and the latter was connected to an ampule containing 3 g (0.097 mol) of cooled methylamine. The system was frozen and evacuated, and the ampule containing methylamine was allowed to slowly warm up to room temperature in order to recondense it into the first ampule. The resulting colorless crystalline material was dried under reduced pressure and recrystallized from ethanol. Yield 8.6 g (90%). mp 132–134°C, [α]$_D$ = –7.81° (*c* = 1.9, EtOH). ^{1}H (CDCl$_3$), δ, ppm: 1.48 s (6H, Me$_2$C), 2.86 s (3H, NMe), 2.88 s (3H, NMe), 4.51 s (2H, CH), 7.10 br.s (2H, NH). ^{13}C NMR spectrum (CDCl$_3$), δ$_C$, ppm: 25.81 (C**C**H$_3$), 25.93 (NCH$_3$), 77.23 (CH), 112.00 (C^2), 170.05 (C=O). Found, %: C 49.67; H 7.80; N 12.95. C$_9$H$_{16}$N$_2$O$_4$. Calculated, %: C 49.99; H 7.46; N 12.95.

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