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Synthesis and Optical Properties of (*S*)-Nobin

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Abstract—A preparative method of synthesis of optically pure *S*-2-amino-2'-hydroxy-1,1'-binaphthyl (*S*-Nobin), the precoursor in the synthesis of other asymmetric 1,1-binaphthyls applied as the ligands at the creation of the catalysts of asymmetric synthesis, is modified. The UV and CD spectra of this compound were studied in detail and essential dependence of spectral information on the solvent nature was shown.

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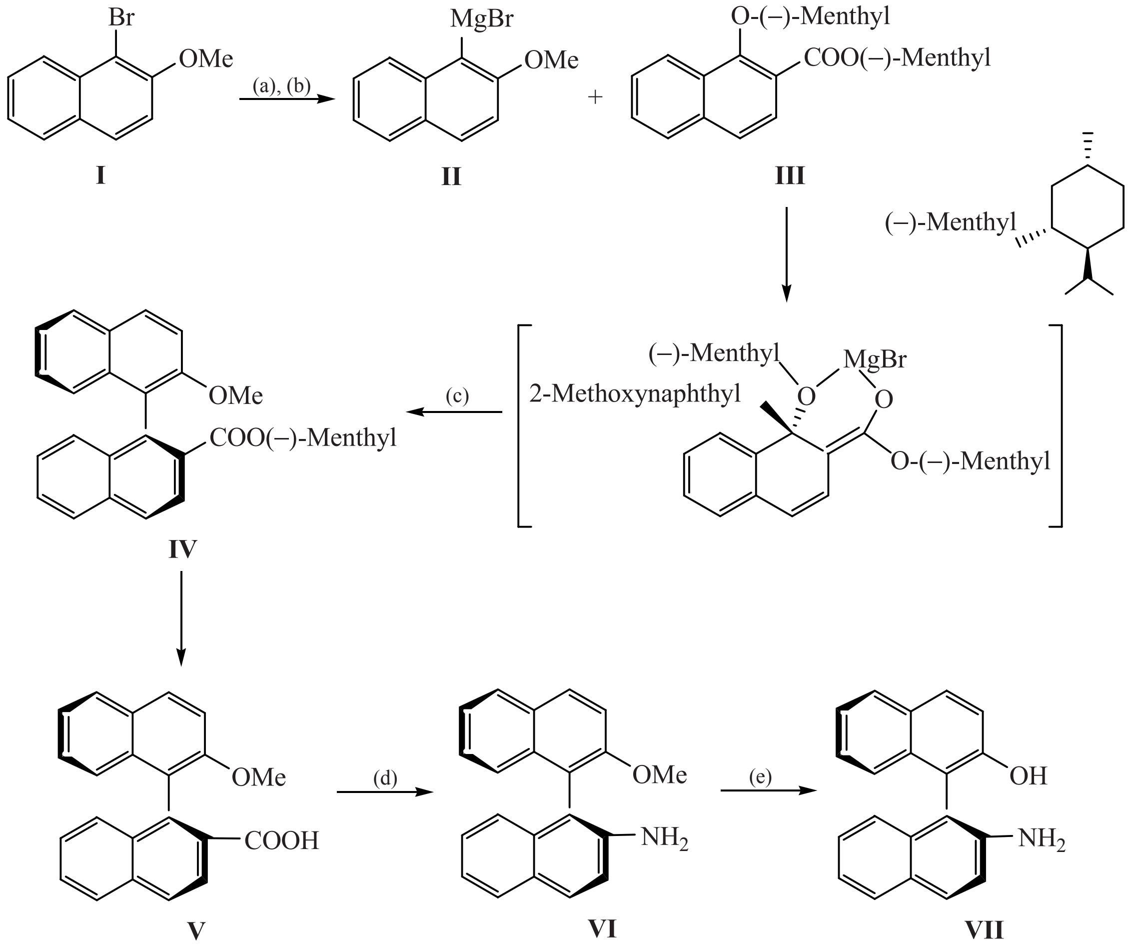
The class of chiral compounds (*R*,*S*)-binaphthyls, whose optical activity is based on the restricted rotation of the connected naphthalene rings around C_1–C'_1 asymmetric axis is of great interest for the creation of the catalysts of asymmetric reactions. The *R*/*S* binaphthyls as the ligands in the metal complexes are abile to transfer the chiral information at the enantioselective catalysis of different chemical transformations [1]. In particular, at the asymmetric synthesis of natural α-amino acids and their derivatives (*S*)-Nobin (*S*-2-amino-2'-hydroxy-1,1'-binaphthyl) is used, which is in turn the parent compound of others asymmetric 1,1'-binaphthyls (Binol, Binam and Binap) [2, 3], applied to the catalytic reactions of hydrogenation, hydrosilylation etc.

We modified the preparative method of synthesis of the optically pure (*S*)-Nobin by an improvement of the procedures of the synthesis of some known intermediates **I–VII**, shown in the scheme below [4, 5].

The central stage is Meyers reaction of the synthesis of 1,1'-binaphthyls [6–8]. In this case the nucleophilic substitution was carried out in the menthyl 1-(–)-menthyloxy-2-naphthylcarboxylate **III** by 1-naphthylmagnesium bromide **II**, that leads to the synthesis of (*S*)-2-menthyloxycarbonyl-2'-methoxy-1,1'-binaphthyl **IV**. High stereospecificity (98%) of the formation of product **IV** is reached due to the presence of two chiral menthyl substituents in compound **III** and the appearance of intermediate with the six-membered ring where magnesium atom is coordinated with two oxygen atoms of *O*-menthyl groups [9, 10]. As a result of the alkaline hydrolysis of menthyl ester **IV** to (*S*)-2-carboxy-2'-methoxy-1,1'-binaphthyl **V** and its subsequent transformation according to Curtius reaction (*S*)-2-amino-2'-methoxy-1,1'-binaphthyl **VI** was obtained in high yield. Demethylation of compound **VI** with phosphorus tribromide affords (*S*)-Nobin **VII** with the content of the title compound 99% and with total yield 25% on the initial product **I**, therewith, the preparation can be obtained in amount of tens of grams taking into account the synthetic accessibility of the intermediates. The physicochemical characteristics of compound **VII** correspond to the published data [11, 12]: mp. 169–171°C; $[\alpha]_D^{20}$ (–) 118° (C1, THF); mass-spectrum: 285.25 (100%, M^+, $C_{20}H_{15}NO$) ^1H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm: 7.94 d (1H, CH-binaphthyl), 7.90–7.77 m (CH-binaphthyl), 7.40 d (1H, CH-binaphthyl), 7.38–7.33 m (1H, CH-binaphthyl), 7.29–7.20 m (3H, CH-binaphthyl), 7.18–7.74 m (1H, CH-binaphthyl), 7.12 d (1H, CH-binaphthyl), 7.08–7.05 m (1H, CH-binaphthyl), 4.88 br (1H, OH), 3.48 br (2H, NH_2).

This method of synthesis of (*S*)-Nobin is definitely more advantageous than the method of the oxidative coupling (cross-coupling) of 2-naphtol and 2-naphthylamine in the presence of the Cu(II) or Fe(III) salts and chiral amines (for example, α-methylbenzylamine) followed by the separation of *R* enantiomers by the crystallization of complexes with (1*S*)-(+)-10-camphorsulfonic acid or by affine chromatography, that is suitable for synthesis of (*R*)- or (*S*)-Nobin only in a small amount [10–12].



(a) **I**, Mg, C_6H_6, 1.5 h; (b) **II** + **III**, THF, 80°C, 12 h, recryst. from C_2H_5OH, 79%**IV**; (c) **IV**, KOH/C_2H_5OH, 80°C, 24 h; HCl, 96%**V**; (d) $ClCO_2Me$, $(C_2H_5)_3N$, acetone, –15°C, 0.5 h; $NaN_3/H_2O–CH_3COCH_3$, 1.5 h, –15°C; 92%**VI**; (e) **VI**, BBr_3/CH_2Cl_2, –20–0°C; recryst. From benzene; 95%**VII**.

In the ultraviolet range the *S*-Nobin solutions display the absorption spectra and circular dichroism (CD), typical for 2,2'-substituted 1,1'-binaphthyls [13–15]. A system of three absorption bands is observed (Fig. 1), which corresponds to three basic absorption bands of β-mono-substituted naphthalene, and they can be conventionally assigned to three electron transitions of naphthalene: ^1B_b, ^1L_a and ^1L_b . Significant circular dichroism occurs in all three regions. Change in the solvent leads to changes in the band shapes, therewith in the series dioxane–ethanol–water–trifluoroethanol (TFE) the changes are rather similar for all three bands. (the order of solvents corresponds to the increase in dipole moments of their molecules).

The most clearly expressed element of the spectrum is the system of absorption bands in the region 220–260 nm, which corresponds to the allowed transitions ^1B_b of the naphthyl chromophores [14, 16], ε_{max} ~80000 M^{-1} cm^{-1}. In the absorption spectrum of the solution in dioxane there are two distinct absorption bands with the maxima at 230 and 250 nm. In the more polar solvents the band at 250 nm weakens and is converted into the small shoulder completely disappearing in the spectrum of solution in TFE. In the CD spectrum in this region appears a strong doublet of two bands with the opposite signs and the approximately equal rotatory forces. The position of the doublet changes with the change of solvent, but its general form remains conservative. By the optical properties in the range of 220–260 nm this compound can be easily detected spectroscopically at micromolar concentrations, including the aqueous solutions (solubility of *S*-Nobin in water at 25°C is of the order of magnitude 10 μg ml^{-1}).

Nature of the optical activity of chiral binaphthyls on the band 230–250 nm is well studied [13–15], the

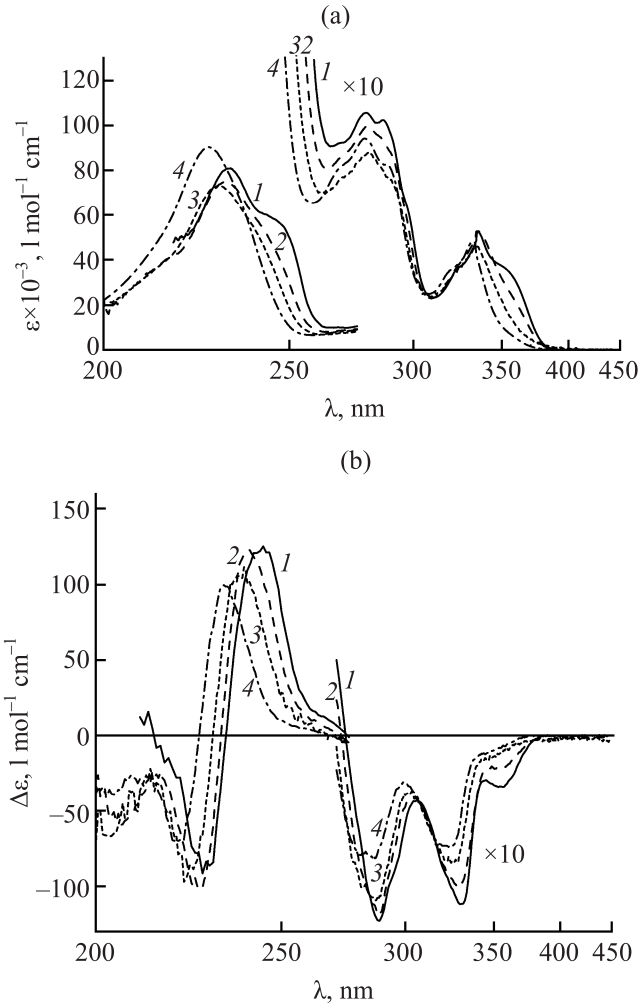


Fig. 1. Absorption (a) and circular dichroism (b) spectra of (–)-*S*-Nobin in various solvents: (*1*) 1,4-dioxane, (*2*) 96% ethanol, (*3*) water, and (*4*) 2,2,2-trifluoroetanol.

decisive role in its appearance plays interaction of two naphthyl chromophores, whose rotation relative to each other is restricted. The rotatory force of the chromophore in a small molecule which interacts with another chromophore is composed of its own rotatory force, a magneto-electric correction, and a dipole-dipole correction [17]. Flat naphthyl chromophore does not possess its own rotatory force. In the spectra the ratio $\Delta\varepsilon/\varepsilon \sim \mu/d \sim 0.001$ is observed, where μ and *d* are respectively magnetic and electric dipole moments of transition, μ is relatively small, and magneto-electric component of rotatory force is extremely small. Therefore it is possible to consider that the rotatory force of the binaphthyl transitions is caused only by dipole-dipole component. Contribution to the rotatory force caused by dipole–dipole interaction in the first most significant approximation is proportional to the value of dipole-dipole interaction *V* multiplied by the value $r_{DD} = R_{12}[d_1 \times d_2]$, where R_{12} is a vector connecting the centers of chromophores, d_1 and d_2 are electric dipole moments of the chromophores transitions [17]. The sign of the r_{DD} value is related uniquely to the absolute configuration of the molecule. At the positive r_{DD} and *V* values the long-wave transition obtains positive correction to the rotatory force, and short-wave transition obtains equal by the absolute value negative correction. In the case of two isolated transitions this leads to the appearance in the CD spectrum of the identical bands of opposite sign.

The naphthyl chromophore possesses in the region of 230–250 nm a strong allowed ^1B_b transition whose large dipole moment is directed along the long axis of the molecule (*x* axis, Fig. 2a). In binaphthyls it is practically perpendicular to the axis connecting the centers of chromophores, which creates optimum conditions for the appearance of rotatory force. It is presumable that for these transitions $d_{1,2} \perp R_{12}$, and the angle θ between the vectors d_1 and d_2 is the angle between the planes of naphthyl rings (Fig. 2b). The second potential transition of naphthyl chromophore in this region, which is forbidden for naphthalene but permitted for its substituted analogs, has a transition dipole polarized along the *y* axis. For this transition *d* and R_{12} are almost parallel; therefore the corresponding values of r_{DD} are equal to zero, and the influence of this transition on the rotatory force is negligible. The mechanism of the appearance of CD spectrum of Nobin differs somewhat from that of the spectra of symmetrical binaphthyls. In symmetrical binaphthyls [13–14] both the naphthyl chromophores are identical, and two transitions in the CD spectrum are formed due to the exciton splitting of ^1B_b transition, the value of this splitting is equal to 2*V* and depends on θ. The exciton splitting is small; therefore in the absorption spectrum of symmetrical binaphthyls one unresolved peak is observed, and the CD spectrum reflects true exciton doublet. For Nobin the chromophores and energies of their ^1B_b transitions are initially different: the transition energy of naphthylamine chromophore is noticeably smaller, than that of naphthol [3]. For this reason the doublet in the CD spectrum of Nobin reflects dipole–dipole interaction of two different transitions rather than exciton splitting of one transition.

As shown in Fig. 2b in the Nobin *S*-enantiomer the vectors R_{12}, d_1 and d_2 form the right-handed triad (or, in other words, the ends of the vectors d_1 and d_2 form in

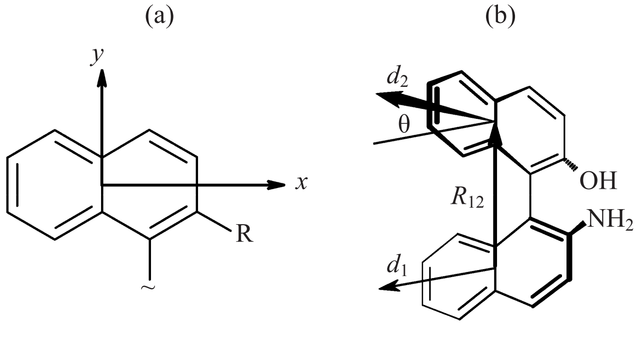


Fig. 2. (a) Coordinate system of naphthyl chromophore. (b) The relative alignment of the dipole moments of allowed transitions (220–260 nm) of (–)-*S*-Nobin naphthyl chromophores.

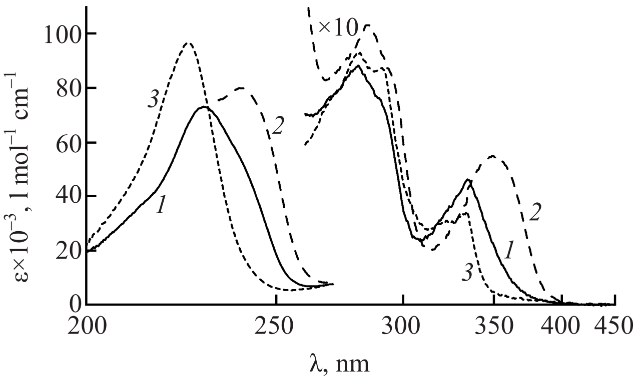


Fig. 3. Changes in the absorption spectrum of (–)-*S*-Nnobin in aqueous solution depending on pH: (*1*) distilled water, (*2*) 1.5 M NaOH, and (*3*) 0.01 M HCl.

the space the element of the right-hand spiral), thus the value of r_{DD} for *S*-Nnobin and other *S*-binaphthols is positive. Unfortunately, the sign of CD band in this case is determined also by the sign of V, which is changed upon going of θ angle through 90° (in binaphthyl $V \approx d_1d_2\cos\theta/R^3_{12}$). For the binaphthyls with rigid connection of 2 and 2' positions the condition $\theta < 90°$ is assuredly fulfilled, therewith $V > 0$ and the positive sign of long-wave band unambiguously indicates *S*-configuration. For "nonrigid" binaphthyls the angle θ theoretically can change over a wide range, and the sign of V can change; therefore the connection between the sign of the CD spectrum bands and the absolute configuration is, generally speaking, not defined. Nevertheless, the analysis of the spectra of circular dichroism of 2,2'-disubstituted chiral binaphthyls with small substituents [13] shows that in these compounds the long-wave transition of doublet in the region of 220–240 nm in the CD spectrum of *S*-enantiomers also has a plus sign, and respectively the average value of angle θ is less than 90° (this corresponds to the configuration given in Fig. 2b, and to the traditional image of the formulas of binaphthyls. Thus, the positive CD sign of the long-wave B-transition of naphthylamine chromophore (~250 nm) we observed sufficiently reliably testifies to the *S*-configuration of the compound investigated.

The change in the CD spectrum in the region of B-transitions with an increase in the polarity of solvent (Fig. 1) indicates, taking into account the above stated, the strong displacement of the long-wave transition 250 nm into the region of short wavelengths rather than the weakening of its intensity.

In the region of ^1L_a and ^1L_b transitions (280–360 nm) in the spectra of *S*-Nobin there are several bands, which are conventionally decomposed into two systems: 240–310 nm and 310–400 nm. A change in the polarity of solvent also leads to spectral changes in this region, moreover in the region of 240–310 nm the solvent affects predominantly the absorption intensity, and in the region of 310–400 nm, mainly the spectrum shape. The CD spectrum in this region also is sufficiently conservative, but its interpretation is complex. In this region transitions appear with the electric dipoles both parallel and perpendicular to the axis connecting the chromophores. However, the symmetrical doublets of opposite sign are not observed here, since the influence of these transitions on each other is not of decisive importance, but the main role plays the dipole–dipole interaction with the strong short-wave ^1B_b transition [14]. The common negative sign of these bands coincides with the sign of analogous exciton bands of symmetrical *S*-binaphthyls and on the whole corresponds to the opposite direction of dipole moments for the B-transition and for the L-transitions polarized along the chromophore x axis [16]. The vibronic structure in the observed absorption spectra typical of the L-transitions is expressed weakly, and in the CD spectra it is almost imperceptible. This is partly caused by the selection of polar solvents, partly by the fact that all L-transitions of Nobin are permitted owing to the complete absence of symmetry, which decreases the significance of vibronic sublevels for the formation of the optical spectrum.

In accordance with its chemical structure, *S*-Nobin should possess weak amphoteric properties in aqueous solution. This is completely confirmed by the changes in the absorption spectra of Nobin at the change in pH (Fig. 3). In distilled water (pH ~6) the spectrum of

Nobin is well consistent with the spectra in the aprotic solvents and corresponds to the neutral form of the molecule. In 0.01M HCl (pH 2.0) due to the protonation occurs sharp decrease in the electron-donor properties of the amino group, and the band of naphthylamine chromophore it displaces strongly into the short-wave region, completely merging with the band of naphthol chromophore. The band at 350 nm considerably weakens and is displaced into the short-wave region. Under the alkaline conditions (1.5 M NaOH) a strong shift of bands occurs to the long-wave region and an increase in their intensity, in correspondence with the deprotonation of naphtholic chromophore. Unfortunately, the observation of the entire B-band under these conditions is impossible because of the strong absorption of solvent. Let us note that in 0.01M NaOH (pH ~11) Nobin has a spectrum identical with the spectrum in the neutral medium, hence p*K* of hydroxy group of Nobin is above 11.

EXPERIMENTAL

The absorption spectra were taken on a double-beam scanning spectrophotometer Specord-M40. The spectra of circular dichroism were obtained on a dichrograph Mark-V. The dichrograph was calibrated with the standard aqueous solution of (+)-10-D-camphorsulfonic acid (1 mg ml^{-1}) in the regions of 190 and 290 nm [18]. For the measurements were used rectangular quartz cuvettes with the length of optical path 0.5 cm. The measurements of absorption were carried out under temperature control at 25°C. In the spectral region of 200–275 nm the *S*-Nobin concentrations were 4 and 8 g ml^{-1}, in the region of 250–450 nm 40 g ml^{-1}. Aqueous solutions of *S*-Nobin with the concentration 4 g ml^{-1} were prepared by the dilution of the solution in ethanol (final content of ethanol in the aqueous solutions not higher than 2.5 vol %).

In the work were used the commercial reagents from Aldrich.

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