

Dedicated to the 115th anniversary of B.A. Arbuzov's birth

## Chiral Salts of Phosphorus Dithioacids Based on Quinine

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**Abstract**—Reactions of quinine with dithioacids based on (1*R*)-endo-(+)-fenchol, (1*S*)-endo-(–)-borneol, and (1*S*)-(–)-menthol have afforded optically active quinine salts. Chiral diquinine salts have been obtained in the reactions of quinine with bithiophosphonic acids based on triethylene glycol and resorcinol.

**Keywords:** quinine, phosphorus dithioacids, optical activity, chirality

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Fundamental studies by academician B.A. Arbuzov in the field of terpenoids, starting from the method of conifer boxing and galipot collecting without loss of volatile components [1–5] have laid the foundation of terpenoids stereochemistry, scaffold rearrangements, and creation of utilitarian compounds and materials including drugs. Rearrangement of bicyclic terpene  $\alpha$ -pinene in aliphatic aldeocimene, discovered and investigated by B.A. Arbuzov, was named after him. B.A. Arbuzov discovered isomerization of  $\alpha$ -pinene oxide into campholene aldehyde. He paid much attention to the issues of the synthesis of biologically active organophosphorus compounds, including natural ones [6]. Natural compounds, many of which are chiral and can be easily isolated from raw materials, can be converted into new biologically active organophosphorus compounds.

Here we report on the study of new derivatives of phosphorus dithioacids based on alkaloids, natural organic nitrogen compounds containing chiral sites and pharmacophore moieties. Quinine and cinchonidine are widely applied as chiral ligands of metal complex catalysts in asymmetric synthesis, chiral agents for NMR spectroscopy, and chromatographic selectors. These chiral alkaloids are among most important bidentate *P,N*-ligands in the metal complexes which

have been used as chiral stationary phases in high-performance liquid chromatography, electrolytic additives, and chiral solvating agents [7–10]. Diastereomers of quinine alkaloids (R = MeO) include 8*R*,9*S*-quinidine **1** and 8*S*,9*R*-quinine **2**. Cinchone alkaloids (R = H) are also represented by diastereomeric 8*R*,9*S*-cinchonine **3** and 8*S*,9*R*-cinchonidine **4** (Scheme 1) [9].

Methods of synthesis of phosphorus-containing derivatives of cinchone and quinine alkaloids are based on the reactions with chlorophosphines, chlorophosphites, and chlorophosphates [10–14]; the data on the synthesis and properties of dithiophosphoryl derivatives of cinchone and quinine alkaloids have been scarce. For example, preparation of dithiophosphate derivatives of quinine and cinchonidine via stereoselective dithiophosphorylation of alkaloids *O*-mesylates with substitution of the mesylate group under the action of *O,O*-diethyldithiophosphoric acid in the presence of triethylamine has been described [7]. *O,O*-Di[(8*S*,9*S*)-quinin-9-yl]dithiophosphate as a zwitter-ion has been obtained in the reaction of quinine with tetraphosphorus decasulfide [15]. At the same time, the preparation of new compounds of such ionic structure based on dithiophosphoryl derivatives of quinine and cinchone alkaloids can be a promising