Synthesis of 4,7-Phenanthroline Methyl Derivatives

K.N. Gusak, A.B. Tereshko, and N.G. Kozlov

Institute of Physical Organic Chemistry, National Academy of Sciences of Belarus, Minsk, 220072 Belarus
e-mail: loc@ifcho.bas-net.by

Received January 8, 2004

Abstract—6-Aminoquinidine condensation with aromatic aldehydes and cyclic β-diketones (1,3-cyclohexanediione or dimedone) in butanol afforded new 12-aryl-3-methyl-8,9,10,12-tetrahydro-7H-benzo[b][4,7]phenanthroline-11-ones and their 9,9-dimethyl derivatives.

Methyl derivatives of 4,7-phenanthroline are not yet sufficiently understood despite the published information on their possible application as respiration stimulators [1], bactericides [2], diagnostics for leucocytes and erythrocytes [3, 4], and initial compounds for synthesis of aldehydes, styryl, and dyes [5–8].

The known Debner–Miller procedure for preparation of methyl-substituted nitrogen-containing heterocycles involving reaction between an aromatic amine and α,β-unsaturated carbonyl compounds (methyl vinyl ketone, crotonaldehyde, or with their precursors (acetone, formaldehyde, paraaldehyde) did not find appreciable application to the synthesis of 4,7-phenanthrolines proceeding from p-phenylenediamine or 6-quinolylamine due to the low yield of target product because the initial amines showed limited reactivity in this reaction, and thus prevailed condensation and polymerization of carbonyl compounds.

In this connection we developed a new approach to building up the methylphenanthroline structure based on introduction in the phenanthroline molecule of a methylquinoline fragment applying 6-aminoquinidine as an initial compound. We formerly developed efficient synthetic methods for 4,7-phenanthroline derivatives by reacting 6-aminoquinoline with aromatic aldehydes and CH-acids of the aliphatic-aromatic and alicyclic series [9, 10]. In this study aiming at preparation methyl substituted 4,7-phenanthrolines we for the first time investigated a three-component condensation of 6-aminoquinidine (I) with ary lacrolefines II and cyclic β-diketones, 1,3-cyclohexanediione (IIIa) and dimedone (IIIb).

6-Aminoquinidine (I) was prepared by reducing 6-nitro-quinidine [11] with tin(II) chloride in a mixture of acetic and hydrochloric acids.

The condensation of amine I with aldehydes II and diones IIIa, b was carried out by boiling in butanol equimolar amounts of reagents. Due to the high reactivity of the β-dicarbonyl compound its reaction with amine and aldehyde in the alcohol environment did not require a catalyst, for the role of the latter played the proton of the dissociated enol form of the β-diketone. As a result the reaction afforded selectively in 43–92% yield previously unknown 12-aryl-3-methyl-8,9,10,12-tetrahydro-7H-benzo[b][4,7]phenanthroline-11-ones IVa–z and their 9-dimethyl derivatives Va–d.

We believe that the formation of benzo[b]-phenanthrolines IV and V occurs either through reaction of 6-aminoquinidine (I) with diones IIIa, b giving enamine A that subsequently undergoes the condensation with aldehydes II, or by interaction of aminoquinidine (I) with 2-aryl-methylene-1,3-cyclohexanedione B arising from condensation of diketones IIIa, b with aldehyde II. Both processes involve formation of the same intermediate C that undergoes dehydrocyclization into the system of 3-methyl-substituted benzo[b][4,7]-phenanthroline.

The R substituent in aldehyde molecule exerts some influence on the yield of target reaction products IVa–x. Benzaldehydes IIc, d, f, j–l, n, o, r containing in the ortho- and para-positions of the phenyl ring halogen atoms, alkoxy and alkoxy carbonyl groups that activate the aldehyde molecule due to –I or –I' and –M-effect afforded high yield of reaction products IVc, d, f, j–l, n, o, r and Vb, c). A fairly high yield of phenanthrolines IVw–y was obtained with pyridine- and thiophene-carbaldehydes IIw–y. Here the increase in polarization and reactivity of the C=O bond of the aldehyde molecule occurs due to the –I-effect of the nitrogen or sulfur in the heterocyclic ring. The replacement of a cyclohexene
The synthesized methyl derivatives of 4,7-phenanthroline IVa–z and Va–d are high-melting crystalline colorless or light-yellow substances. Their IR spectra contain characteristic absorption bands of stretching vibrations of NH and CO groups at 3290–3195 and 1625–1580 cm\(^{-1}\) respectively. The stretching vibrations of alkylic groups and alicyclic C–H bonds give rise to absorption in the region of 2960–2870 cm\(^{-1}\), those of the C–H bonds in the aromatic rings appear at 3060–3030 cm\(^{-1}\). In the IR spectra of compounds IVq–p, r–t, v, Ve, d the bands of the fragment C–O–C are observed in the region 1240–1230 Cm\(^{-1}\), in the spectrum of compound IVq the strong band of the stretching vibrations of C–S bond is seen at 1125 cm\(^{-1}\), in the spectra of phenanthrolines IVr, s the band of C=O in the ester group appears at 1725–1720 cm\(^{-1}\).

The electron absorption bands in the spectra of compounds IVa–z and Va–d are located in the UV region and possess a pronounced vibronic structure. The molecules of benzo[b]phenanthroline IVa–z and Va–d contain three independent chromophore fragments: an aryl substituent, a carbonyl group, and a quinoline ring. The latter provides the main contribution into the system of \(\pi–\pi^*\)-electron transitions. In this connection the bands of \(\lambda_{\text{max}}\) 212–220, 240–255, 292–296 nm may be assigned to the system of 6-quinolylamine [UV spectrum, \(\lambda_{\text{max}}\) nm (log \(\varepsilon\)): 206(4.08), 247 (4.35), 279 (3.59)]. The notable red shift and the increased intensity of the first and third bands in the spectra of phenanthrolines IVa–z and Va–d are likely to originate from superposition of absorption bands of the phenyl, heteroaromatic, or cyclohexenyl substituent R. The appearance of absorb-tion bands in the long-wave spectral region (331–340, 370–388 nm) is due according to [12] to the presence of a carbonyl group. The substituents in the phenyl ring of compounds IVa–v...