SYNTHESIS AND PROPERTIES OF AZOLES AND THEIR DERIVATIVES.

35.* SYNTHESIS OF CERTAIN AZOLES CONTAINING STERICALLY HINDERED PHENOL RESIDUES

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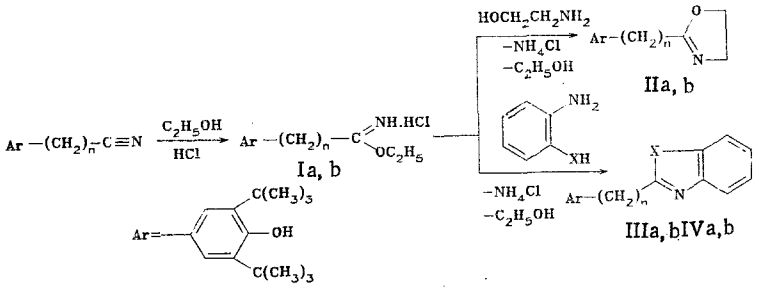
The condensation of hydrochlorides of ethyl iminoesters of 4-hydroxy-3,5-di-tert-butylbenzoic and β-(4-hydroxy-3,5-di-tert-butylphenyl)propionic acids with monoethanolamine, o-aminophenol, and o-phenylenediamine was studied. As a result, Δ^2-oxazolines, benzoxazoles, and benzimidazoles containing sterically hindered phenol residues in the 2-position were synthesized.

Derivatives of azoles have recently been finding use as corrosion inhibitors, bactericidal, antistatic, and antioxidant additives to fuels and oils, as well as stabilizers of polymer materials [2]. From this standpoint it may be of definite interest to introduce fragments of sterically hindered phenols, which, as is well known, are effective antioxidants [3], into the ring of the azoles as substituents. However, there is little information in the literature [4, 5] on azoles containing residues of shielded phenols.

To obtain 2-substituted Δ^2-oxazolines, benzoxazoles, and benzimidazoles containing sterically hindered phenol residues, we used hydrochlorides of ethyl iminoesters of 4-hydroxy-3,5-di-tert-butylbenzoic (Ia) and β-(4-hydroxy-3,5-di-tert-butylphenyl)propionic (Ib) acids as the initial compounds. These compounds were produced according to the Finner reaction — by passage of a stream of dry HCl into a mixture of ethanol and the corresponding nitrile in absolute ether [6].



I—IV a n=0, b n=2; IIIa, b X=O; IVa, b X=NH

The condensation of hydrochlorides of ethyl iminoesters Ia, b with monoethanolamine, o-aminophenol, and o-phenylenediamine results in the formation of Δ^2-oxazolines IIa, b, benzoxazoles IIIa, b, and benzimidazoles IVa, b, respectively, which contain a 4-hydroxy-3,5-di-tert-butylphenyl or β-(4-hydroxy-3,5-di-tert-butylphenyl)ethyl radical in the 2-position (Table 1). When these conversions are conducted, it is noteworthy that the hydrochloride of the iminoester Ib is more reactive than the hydrochloride of the iminoester Ia. While the formation of compounds IIb-IVb is completed after the reagents are boiled in alcohol for 1 h 30 min to 2 h, in the production of heterocyclic compounds from the hydrochloride of the

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iminoester Ia heating for 8-10 h is needed. The lower activity of the hydrochloride of the iminoester Ia with respect to the nucleophilic reagents studied can evidently be explained by the fact that the electron donor oxyphenyl radical bonded to the iminoester group decreases the partial positive charge on the carbon atom of this group, i.e., decreases its nucleophilicity, whereas in compound Ib this radical is distant from the iminoester group, and its action is significantly weaker.

We also attempted to synthesize the benzimidazole IVa by heating 4-hydroxy-3,5-di-tert-butylbenzonitrile and o-phenylenediamine in the presence of hydrochloric acid (Phillips method [7]). However, even after prolonged boiling (more than 40 h) of a mixture of the nitrile and o-phenylenediamine in the presence of 4 N HCl, the initial nitrile was recovered virtually entirely in an unchanged state.

Absorption bands due to the sterically hindered phenol residue are observed in the IR spectra of all the synthesized azoles II-IV: a rather narrow band at 3640-3630 cm^{-1} (OH) [8], intense bands 2990-2980 cm^{-1} (stretching vibrations of C–H in the methyl groups), bands of medium intensity at 1380-1370 cm^{-1} (C–H deformational vibrations in tert-C_4H_9), and an intense band at 880 cm^{-1} (deformational vibrations of the single C–H in the benzene ring) [9]. In the IR spectra of compounds IIa, b, the absorption bands of the C=N group appear at 1665-1650 cm^{-1}, which is characteristic of the C=N double bond in Δ^2-oxazolines [10]. The presence of this ring is also confirmed by the absorption maxima at 1275-1260 and 1015-1005 cm^{-1}, belonging to the stretching vibrations of the fragment =C–O–C– in Δ^2-oxazolines [11]. In the spectra of compounds III and IV the absorption of the C=N group appears at 1640-1610 cm^{-1}, which is characteristic of 2-substituted azoles [10]. The intense absorption maxima in the region 745-735 cm^{-1} belong to the out-of-plane deformational vibrations of C–H of the benzene ring in benzazoles. The structure of benzoxazoles IIIa, b is confirmed by the presence of intense absorption bands in the IR spectra at 1605-1590 and around 940 cm^{-1}, which is characteristic of the benzoxazole ring, as well as absorption maxima at 1250 and 1020-1010 cm^{-1}, belonging to the asymmetrical and symmetrical stretching vibrations of =C–O–C= of benzoxazole, respectively [12]. In the IR spectra of benzimidazoles IVa, b, there are absorption bands at 1555-1550 and 1320-1315 cm^{-1}, belonging to the vibrations of the benzimidazole ring, and in the high-frequency region at 3480-3430 cm^{-1} (broad band) characteristic of the stretching vibration of NH of benzimidazole [10]. In the PMR spectra of compounds IIa, b the signals of the protons of the methylene group of the Δ^2-oxazoline ring appear in the form of a multiplet, consisting of 10 lines in the interval 3.72-4.42 ppm (system A_2B_2).

EXPERIMENTAL

The IR spectra were recorded on a UR-20 instrument in $CHCl_3$ solution (for compounds IIa, b) or in tablets with KBr (for compounds III-IV), the PMR spectra on a Tesla BS-487C instrument (80 MHz) in CD_3OD, internal standard HMDS, δ scale. The course of the reactions and the purity of the compounds obtained were monitored by thin-layer chromatography on Silufol UV-254 plates in the solvent systems benzene–ethanol, 30:1 (A) or 20:1 (B); development with iodine vapors.

Hydrochlorides of ethyl iminoesters Ia, b were obtained earlier [6].

2-(4-Hydroxy-3,5-di-tert-butylphenyl)-Δ^2-oxazoline (IIa). The hydrochloride Ia (2.55 g, 7 mmoles) was added in portions at 0°C to a solution of 0.44 g (7 mmoles) monoethanolamine in 20 ml absolute ethanol with mixing. The reaction mixture was boiled with mixing for 8 h, cooled to 0°C, and a solution of sodium ethylate, obtained from 0.17 g (7 mg-atoms) sodium and 8 ml of absolute ethanol was added dropwise. The mixture was exposed for 2 h at 0°C, the precipitate formed was filtered off, the filtrate concentrated to a volume of 4-5 ml, and it was chromatographed on a column with Al_2O_3, degree of activity II according to Brockman (2.5 × 40 cm), then eluted with mixture B. After removal of the solvents under vacuum we obtained 1.04 g (46%) of the Δ^2-oxazoline IIa (Table 1).

PMR spectrum of Δ^2-oxazoline IIa: 1.84 (18H, br.s, tert-C_4H_9), 3.94-4.42 (4H, m, CH_2–CH_2 of oxazoline); 7.08-7.12 ppm (2H, m, aromatic protons).

2-[2-(4-Hydroxy-3,5-di-tert-butylphenyl)ethyl]-Δ^2-oxazoline (IIb) was produced analogously to IIa by heating the hydrochloride Ib with monoethanolamine in alcohol for 1 h 30 min. After chromatography on a column with Al_2O_3, the Δ^2-oxazoline IIb was obtained in the form of a slightly yellowish oil, which crystallized when exposed to cold (Table 1).

TABLE 1. Characteristics of the Compounds Synthesized

Compound	mp, °C[a]	R_f[b]	Found, %			Gross formula	Calculated, %			Yield, %
			C	H	N		C	H	N	
IIa	183—184	0,51 (A)	74,1	9,2	5,2	$C_{17}H_{25}NO_2$	74,2	9,1	5,1	46
IIb	93—94,5	0,87 (A)	75,2	9,4	4,8	$C_{19}H_{29}NO_2$	75,2	9,6	4,6	50
IIIa	162—163[c]	0,93 (B)	78,0	7,8	4,2	$C_{21}H_{25}NO_2$	78,0	7,7	4,3	73
IIIb	42—43,5	0,78 (B)	78,7	8,2	4,2	$C_{23}H_{29}NO_2$	78,6	8,3	4,0	66
IVa	340—341[d]	0,82 (B)	78,2	8,0	8,8	$C_{21}H_{26}N_2O$	78,0	8,0	8,7	88
IVb	230—231	0,88 (B)	81,3	8,3	3,9	$C_{23}H_{30}N_2O$	80,9	8,5	4,1	71

[a]Compounds were crystallized: IIa from aqueous alcohol, IIIa from acetonitrile, IVa, b from aqueous DMFA. [b]The solvent system is indicated in parentheses. [c]According to the data of [4], mp 165°C. [d]According to the data of [4] mp 347°C.

PMR spectrum of Δ^2-oxazoline IIb: 1.58 (18H, br.s, tert-C_4H_9); 3.72-4.16 (4h, m, CH_2—CH_2 oxazoline); 4.61 (2H, t, CH_2); 4.78 (2H, t, CH_2); 6.88 ppm (2H, m, aromatic protons).

2-(4-Hydroxy-3,5-di-tert-butylphenyl)- and 2-[2-(4-hydroxy-3,5-di-tert-butylphenyl)-ethyl]benzazoles (III-IV). A mixture of 0.01 mole o-aminophenol or o-phenylenediamine with 0.01 mole of the hydrochloride Ia or Ib was boiled with mixing in 25 ml of absolute alcohol for 10 h in the production of compounds IIIa and IVa or for 2 h for compounds IIIb and IVb. The reaction mixture was cooled to 0°C, and poured out dropwise into 100 ml of cold water containing 0.1 mole $NaHCO_3$. The benzimidazoles IVa and IVb precipitated, and the precipitate was collected and dried. The benzoxazoles IIa, b were isolated in the form of an oil, which was extracted with ether. The extract was dried over $CuSO_4$, the solvent removed at reduced pressure, the residue chromatographed on a column with Al_2O_3 and eluted with a benzene-ethanol mixture (20:1). After removal of the solvents the benzoxazoles IIIa, b were obtained in the form of colored viscous oils, which were recrystallized with exposure in the cold.

PMR spectrum of benzoxazole IIIa: 1.60-1.71 (18H, br.s, tert-C_4H_9); 7.10-7.17 (2H, m, aromatic protons); 7.21-7.54 ppm (4H, m, benzoxale). PMR spectrum of benzoxazole IIIb: 1.88-1.92 (18H, br.s, tert-C_4H_9); 4.48-4.84 (4H, m, CH_2—CH_2); 7.04-7.10 (2H, m, aromatic protons); 7.14-7.70 ppm (4H, m, benzoxazole). PMR spectrum of benzimidazole IVb: 1.64-1.70 (18H, br.s, tert-C_4H_9); 4.40 (2H, t, CH_2); 4.64 (2H, t, CH_2); 6.78-7.50 (6H, m, aromatic protons); 8.12 ppm (1H, s, 11H).

All the compounds II-IV obtained were readily soluble in alcohols, acetone, ether, DMFA, and methylene chloride; compounds IIb, IIIa, b, and IVb were also readily soluble in benzene, and compounds IIb and IVb in heptane. All the compounds II-IV were insoluble in water and CCl_4, compounds IIa and IVa in benzene, compounds IIa, IIIa, and IVa, b in alkanes.

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