SYNTHESIS AND STUDY OF SOME 4-SUBSTITUTED 2-(BENZIMIDAZOL-2'-YL) QUINOLINES

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The reaction of 4-chloro- and 4-chloro-6-methoxyquinoline-2-carbaldehydes with o-phenylenediamine has given the corresponding 4-chloro-2-(benzimidazol-2'-yl)quinolines. 4-Methoxy-, 4-diethylamino-, 4-cyclohexylamino-, and 11 different 4-anilino-substituted 2-(2'-benzimidazol-2'-yl)quinolines have been synthesized from these by replacement of the halogen. A study of their UV spectra has shown that absorption at 310 nm is characteristic for the 4-anilino-2'-(benzimidazol-2'-yl)quinolines but not for the other 4-substituted derivatives. The compounds obtained form colored complexes with cuprous ions.

Linked heterocyclic systems with two nitrogen-containing nuclei are of interest as potential organic complex-forming agents [1, 2]. The aim of the present work was the synthesis of various 2-(benzimidazol-2'-yl)quinolines containing substituents in position 4 of the quinoline ring, since it is known that it is in position 4 that substituents have the greatest influence on the heteroatom and, consequently, on interaction with metal ions.

For the synthesis of these substances, by oxidizing the corresponding quinaldines with selenium dioxide we obtained 4-chloro- and 4-chloro-6-methoxyquinoline-2-carbaldehydes, which have not been described previously. The reaction of these aldehydes with o-phenylenediamine led to 4-chloro-substituted 2-(benzimidazol-2'-yl)quinolines. The mobility of the halogen in position 4 of the quinoline ring enabled it to be replaced by various substituents fairly readily (see Table 1).

From a consideration of the UV spectra of 2-(benzimidazol-2'-yl)quinoline and its derivatives containing substituents in position 4 of the quinoline nucleus, it follows that the absorption bands characteristic for the unsubstituted 2-(benzimidazol-2'-yl)quinoline (290, 330, and 350 nm) are retained, in the main, in its 4-substituted (4-methoxy, 4-chloro, and 4-phenyl) derivatives. However the introduction of an anilino group into position 4 changes the nature of the absorption, and an absorption band at 310 nm is characteristic for various 4-anilino derivatives. The spectrum of the 4-diethylamino derivative is similar.

As we had assumed, the compounds obtained form red alcohol-soluble complexes with Cu^+ ions.

EXPERIMENTAL

4-Chloroquinoline-2-carbaldehyde. A flask with a stirrer, thermometer, dropping funnel, and reflux condenser was charged with 5.5 g (0.050 mole) of selenium dioxide, 50 ml of dioxane, and 3 ml of water. The mixture was heated to 40°C and, with stirring, 8 g (0.045 mole) of 4-chloroquinaldine was added over 4 min. Then the reaction mixture was boiled for 3 h, cooled, and filtered, and the filtrate was treated with 200 ml of water. The precipitate that had deposited was filtered off and crystallized from 100 ml of 50% methanol. Yield 5 g (58%). mp 134-135°C. Found, %: N 7.4; Cl 18.0. $C_{10}H_6ClO$. Calculated, %: N 7.35; Cl 18.5.

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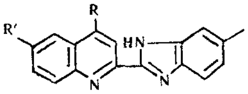
TABLE 1



Compound	R	R′	Mp, °C	Empirical formula	N, %		Yield, %
					found	calc.	
I	Cl	H	240—241	$C_{16}H_{10}ClN_3$[a]	14,9	15,0	76
II	OCH_3	H	258—259	$C_{17}H_{13}ON_3$	15,0	15,3	44
III	$N(C_2H_5)_2$	H	244—245	$C_{20}H_{20}N_4$	17,8	17,7	50
IV	NHC_6H_{11}	H	235—236	$C_{22}H_{21}N_4$	16,4	16,4	41
V	NHC_6H_5	H	243—244	$C_{22}H_{16}N_4$	16,6	16,7	58
VI	$NHC_6H_4C_6H_5$-*p*	H	245—246	$C_{28}H_{20}N_4$	13,4	13,6	51
VII	$N(CH_3)C_6H_5$	H	238	$C_{23}H_{18}N_4$	16,3	16,0	56
VIII	$NHC_6H_4N(C_2H_5)_2$-*p*	H	260	$C_{26}H_{25}N_5$	17,0	17,2	62
IX	NHC_6H_4COOH-*p*	H	314—315	$C_{23}H_{16}O_2N_4$	14,8	14,7	52
X	$NHC_6H_4COOC_2H_5$-*p*	H	147—148	$C_{25}H_{20}O_2N_4$	14,0	13,7	45
XI	NHC_6H_4Cl-*p*	H	252	$C_{22}H_{15}ClN_4$[b]	14,9	15,1	45
XII	$NHC_6H_4OCH_3$-*p*	H	226—227	$C_{23}H_{18}ON_4$	15,8	15,3	34
XIII	Cl	OCH_3	233—234	$C_{17}H_{12}ClN_3O$[c]	13,9	13,6	36
XIV	NHC_6H_5	OCH_3	217—218	$C_{23}H_{18}ON_4$	15,0	15,3	51
XV	$NHC_6H_4N(C_2H_5)_2$-*p*	OCH_3	172—173	$C_{27}H_{21}N_5O$	15,8	16,0	36
XVI	$NHC_6H_4COOC_2H_5$-*p*	OCH_3	149—150	$C_{26}H_{22}N_4O_3$	12,9	12,8	35

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[a] Found, %: Cl 12.0. Calculated, %: Cl 12.2. [b] Found, %: Cl 9.2. Calculated, %: Cl 9.3. [c] Found, %: Cl 10.7. Calculated, %: Cl 10.9.

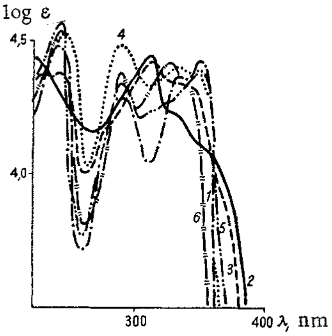

Fig. 1. UV spectra: 1) 2-(Benzimidazol-2′-yl)-quinoline; 2) 4-anilino-2-(benzimidazol-2′-yl)quinoline (V); 3) 2-(benzimidazol-2′-yl)-4-diethylaminoquinoline (III); 4) 2-(benzimidazol-2′-yl)-4-phenylquinoline; 5) 2-(benzimidazol-2′-yl)-4-chloroquinoline (I); 6) 2-(benzimidazol-2′-yl)-4-methoxyquinoline (II).

4-Chloro-6-methoxyquinoline-2-carbaldehyde was obtained similarly by the oxidation of 4-chloro-6-methoxyquinaldine. Yield 7 g (82%). mp 145-146°C. Found, %: N 6.7; Cl 15.6. $C_{11}H_8ClO$. Calculated, %: N 6.4; Cl 16.0.

2-(Benzimidazol-2′-yl)-4-chloroquinoline (I). A mixture of 2.15 g (0.02 mole) of o-phenylenediamine, 3.85 g (0.02 mole) of 4-chloroquinoline-2-carbaldehyde, 6 g of copper acetate, 50 ml of propanol, and 50 ml of water was heated in the water bath for 1 h. The precipitate that deposited after cooling was filtered off, mixed with 100 ml of hot 70% propanol, and treated with a current of hydrogen sulfide until all the copper had been precipitated. The precipitate was separated off and boiled with 100 ml of propanol and the mixture was filtered, and the combined alcoholic filtrates were mixed with 200 ml of water. The yellow precipitate that deposited was separated off, dried at room temperature, and recrystallized twice from ethanol. Compound XIII was obtained similarly, starting from 4-chloro-6-methoxyquinaldine.

The substances obtained are soluble in alcohols, pyridine, ether, and acetone and sparingly soluble in water.

2-(Benzimidazol-2′-yl)-4-methoxyquinoline (II). A mixture of 1.4 g (0.005 mole) of I and 8 ml of an alcoholic solution of sodium methoxide (0.1 g of sodium and 8 ml of methanol) was heated in a sealed tube at 190°C for 5 h. After cooling, the contents of the tube were mixed with 30 ml of water, and the precipitate was separated off, washed with water, dried, and twice recrystallized from 20 ml of dioxane.

2-(Benzimidazol-2′-yl)-4-diethylaminoquinoline (III). A mixture of 0.6 g (0.004 mole) of I and 2 ml of diethylamine was heated in a sealed tube at 190°C for 5 h. The contents of the tube were mixed with 80 ml of methanol (50%), and 8 ml of concentrated aqueous ammonia was added. The precipitate was filtered off, dried in the air, and twice recrystallized from 50% dioxane. Compound IV was obtained similarly, using cyclohexylamine.

4-Anilino-2-(benzimidazol-2'-yl)quinoline (V). A mixture of 2.24 g (0.008 mole) of I and 7.2 g (0.080 mole) of aniline was boiled for 30 min, cooled, and treated with 100 ml of ether, and the precipitate was filtered off and washed with ether and then with methanol. Then it was mixed with 40 ml of dioxane, the mixture was treated with 50 ml of 10% aqueous ammonia, and the precipitate was filtered off, dried, and twice recrystallized from 40 ml of a mixture of dioxane and water (1:1).

Compounds VII, VIII, XIV, and XV were obtained similarly by heating the 4-chloro-substituted derivatives with aniline, N-methylaniline, and p-diethylaminoquinoline. All the compounds obtained are soluble in organic solvents and sparingly soluble in water.

2-(Benzimidazol-2'-yl)-4-(p-phenylanilino)quinoline (VI). A mixture of 1 g (0.004 mole) of I and 0.35 g (0.020 mole) of 4-aminobiphenyl was carefully stirred and heated at 230°C for 30 min. Then it was cooled, triturated with 50 ml of ether, and filtered, and the residue was washed with ether and ethanol, after which it was mixed with 20 ml of 10% aqueous ammonia, filtered off again, dried, and twice recrystallized from 30 ml of 50% aqueous dioxane.

Compounds IX-XII, and XVI were obtained similarly. For this purpose, condensation was carried out with p-aminobenzoic acid, ethyl p-aminobenzoate, p-chloroaniline, and p-anisidine.

The UV spectra were measured on an SF-4A spectrophotometer in one-centimeter quartz cells. The solvent was specially purified ethanol. The concentration of the sample was $2 \cdot 10^{-5}$ M.

LITERATURE CITED

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