

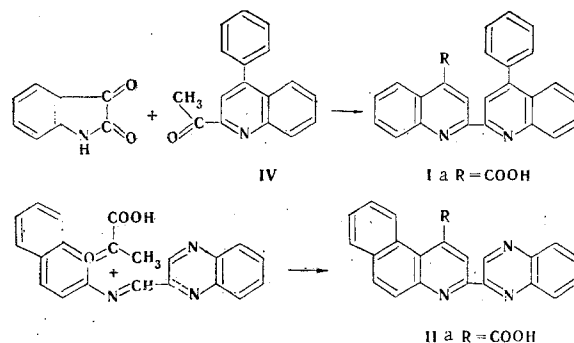
SYNTHESIS AND STUDY OF SOME DERIVATIVES OF CINCHONINIC ACID

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2-(4-Phenylquinolin-2-yl)cinchoninic and 2-(quinoxalin-2-yl)-5,6-benzocinchoninic acids have been synthesized. They have been subjected to decarboxylation and their chlorides and esters, amides, and anilides have been prepared. The spectral characteristics of the Cu(I) complexes of the derivatives synthesized have been obtained.

With the aim of their possible use as analytical reagents, we have obtained 2-(4-phenylquinolin-2-yl)-cinchoninic acid (Ia) (by the Pfitzinger reaction) and 2-(quinoxalin-2-yl)-5,6-benzocinchoninic acid (IIa) (by one of the variants of the Doebner synthesis [1, 2]). The required 2-acetyl-4-phenylquinoline (IV) has been obtained for the first time and its structure has been confirmed by elementary analysis and by conversion into the corresponding oxime (V).



The acids (Ia) and (IIa) were then decarboxylated or were converted into their chlorides, and then into amides, anilides, and esters. The characteristics of the substances obtained are given in Table 1.

Compounds (Ia-f) each have two absorption bands, in the 264 and 329 nm regions, due to $\pi \rightarrow \pi^*$ transitions. A small bathochromic shift is observed for the isoamyl ester (Ic). The bound systems of quinoline and quinoxaline nuclei (IIa-f) are characterized by three absorption bands, in the 255, 280, and 340 nm regions, the middle band having the greatest intensity.

Compounds (I-II) form colored cupra complexes soluble in alcohols. A comparison of the properties of the Cu(I) complexes (Ia, c-f) (Table 1) with the results obtained previously shows that the introduction of a phenyl radical into one of the nuclei increases the intensity of coloration. The replacement of the quinoline ring by a quinoxaline ring leads to the appearance of an additional stronger absorption band in the 390-405 nm region.

EXPERIMENTAL

Ethyl 4-Phenylquinaldinate (III). A mixture of 2.7 g (0.01 mole) of 4-phenylquinaldinic acid chloride [3] and 27 ml of absolute ethanol was boiled for 1 h 30 min. The excess of ethanol was distilled off and the crystals that deposited were separated off. Yield 2.55 g (92%), mp 130°C (from aqueous ethanol). Found: C 77.8, H 5.1; N 5.0%. $C_{18}H_{15}NO_2$. Calculated: C 77.9; H 5.4; N 5.1%.

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TABLE 1. Compounds (I-II) and Their Cu(I) Complexes

Compound	R	mp, °C	Empirical formula	N, %		IR* spec-trum, $\frac{1}{\text{cm}}$	Cu(I) complex		Yield, %
				found	calc.		λ_{max} , nm	log ϵ	
Ia	COOH	295—296	C ₂₅ H ₁₆ O ₂ N ₂	7.5; 7.6	7.4	1735	556	4.00	36
Ib	COCl	275—277	C ₂₅ H ₁₆ ON ₂ Cl	7.0; 7.2	7.1	1762	—	—	95
Ic	COOC ₂ H ₅	136—138	C ₃₀ H ₂₆ O ₂ N ₂	6.1; 6.2	6.3	1754	570	4.01	65
Id	CON(C ₂ H ₅) ₂	232—233	C ₂₉ H ₂₅ ON ₃	9.6; 9.6	9.7	1640	550	3.98	68
Ie	CONHC ₆ H ₅	328—330	C ₃₁ H ₂₁ ON ₃	9.2; 9.5	9.3	1660	560	4.08	72
If	H	196—198	C ₂₄ H ₁₆ N ₂	8.5; 8.7	8.5	—	550	3.96	60
IIa	COOH	266—267	C ₂₂ H ₁₃ N ₃ O ₂	12.0; 12.1	12.0	1735	400	4.61	23
							552	3.95	
IIb	COCl	257—258	C ₂₂ H ₁₂ ON ₃ Cl	11.5; 11.4	11.4	1780	—	—	95
IIc	COOC ₂ H ₅	334—335	C ₂₇ H ₃₃ O ₂ N ₃	10.1; 10.2	10.0	1716	405	4.56	55
							552	3.89	
IId	CON(C ₂ H ₅) ₂	200	C ₂₆ H ₂₂ N ₄ O	13.6; 13.7	13.8	1660	390	4.56	60
							552	3.92	
IIe	CONHC ₆ H ₅	345—346	C ₂₈ H ₂₆ N ₄ O	13.3; 13.3	13.1	1640	405	4.53	52
							552	3.84	
IIf	H	240	C ₂₁ H ₁₃ N ₃	13.6; 13.7	13.7	—	400	4.66	80
							552	3.89	

* In KBr tablets.

2-Acetyl-4-phenylquinoline (IV). A mixture of 1.1 g of metallic sodium, 2.3 g of absolute ethanol, and 40 ml of dry toluene was heated until the reaction ceased. Then 4.53 g (0.012 mole) of (III) and 3.1 g (0.018 mole) of ethyl acetate were added and the mixture was stirred at 110°C for 5 h. The yield of the sodium salt of the ester of 4-phenylquinaldinoylacetic acid was 5.2 g. This salt (10.5 g; 0.03 mole) was boiled with 400 ml of water and 14 ml of concentrated sulfuric acid for 12 h, then the mixture was cooled and filtered, the filtrate was made alkaline, and the precipitate was separated off. Yield 3.7 g (50%); mp 340–342°C (decomp., from water). Found: C 77.1; H 5.3; N 5.4%. C₁₇H₁₃NO. Calculated: C 79.3; H 5.1; N 5.3%.

2-Acetyl-4-phenylquinoline Oxime (V). A mixture of 2.47 g (0.01 mole) of (IV), 0.7 g (0.1 mole) of hydroxylamine hydrochloride, and 8 ml of a 5 M solution of sodium acetate was heated for 3 h. The precipitate that deposited (2.1 g, yield 80%) had mp 199–200°C (from ethanol). Found: C 77.6; H 5.1; N 10.9%. C₁₇H₁₄N₂O. Calculated: C 77.7; H 5.3; N 10.7%.

2-(Quinoxalin-2-yl)-5,6-benzocinchonic Acid (IIa). A mixture of 1.4 g (0.01 mole) of β -naphthylamine, 1.6 g (0.01 mole) of quinoxaline-2-carbaldehyde, and 50 ml of propanol was boiled for 10 min. Then 10 ml of a solution of 3.5 g (0.04 mole) of pyruvic acid and 0.5 g of hydrochloric acid in propanol was gradually added. The mixture was boiled for 3 h and cooled, and the precipitate was separated off and crystallized from dimethylformamide. The method of synthesizing compounds (I) and (II) and of obtaining their Cu(I) complexes has been given in a previous paper [4].

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