DERIVATIVES OF QUINOLINE-7-CARBOXYLIC ACID

III*. 3-BENZYL-4-OXO-1,4-DIHYDROQUINOLINE-7-CARBOXYLIC ACIDS AND THEIR DERIVATIVES

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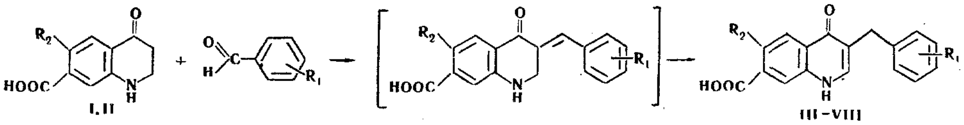
The condensation of 4-oxo-1,2,3,4-tetrahydroquinoline-7-carboxylic acid and its 6-chloro analog with aromatic aldehydes has given the corresponding 3-benzyl-4-oxo-1,4-dihydroquinoline-7-carboxylic acids and their 4-chloro derivatives.

We have previously effected the synthesis of 4-oxo- and 6-chloro-4-oxo-1,2,3,4-tetrahydroquinoline-7-carboxylic acids (I and II) from the corresponding aminoterephthalic acids [1-4].

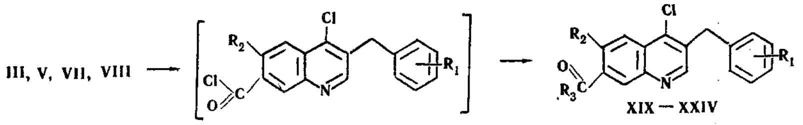
The present paper describes the aldol-crotonic condensation of the acids I and II with aromatic aldehydes in alkaline aqueous ethanol, leading to the 3-benzyl derivatives III-VIII (Table 1).



The acids III-VIII are high-melting substances readily forming the esters IX-XIV, from which the hydrazides XV-XVIII were obtained (Table 1).

The reaction of the acids III, V, VII, and VIII with thionyl chloride formed 3-benzyl-4-chloroquinoline-7-carbonyl chlorides. Without isolation, the latter were subjected to hydrolysis, alcoholysis, and ammonolysis, being converted into the acid XIX, the esters XX-XXIII, and the amide XXIV. The halogen in position 4 is not replaced under these conditions.

When the amide XXIV was heated with thionyl chloride, 3-benzyl-4-chloroquinoline-7-carbonitrile XXV was obtained in good yield.



The IR spectra of the acids and esters of the dihydroquinolin-4-one derivatives (III, VII, VIII, IX, XIII, and XV) have bands at 3240-3140 cm^{-1} relating to the ν_{NH} and ν_{OH} vibrations and two ν_{CO} bands in the 1726-1690 cm^{-1} region.

In the esters of the 4-chloro derivatives XX and XXII, the high-frequency bands mentioned disappear and there is one very strong ν_{CO} band in the 1728-1720 cm^{-1} region.

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*For Communication II, see [1].

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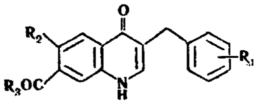
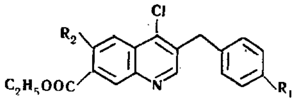
TABLE 1



Compound	R_1	R_2	R_3	mp, °C	Empirical formula	Element	Found, %	Calculated, %	Yield, %
III	H	H	OH	>360	$C_{17}H_{13}NO_3$	C H N	73,3 4,7 5,0	73,1 4,7 5,0	77
IV	*o*-OCH_3	H	OH	320—322	$C_{18}H_{15}NO_4$	C H N	69,7 4,8 4,6	69,9 4,9 4,5	68
V	p-Cl	H	OH	>360	$C_{17}H_{12}ClNO_3$	Cl N	11,4 4,4	11,3 4,5	67
VI	p-SO_2CH_3	H	OH	>360	$C_{18}H_{15}NO_5S$	N S	4,0 8,8	3,9 9,0	65
VII	H	Cl	OH	293—294	$C_{17}H_{12}ClNO_3$	C H Cl N	65,0 4,2 11,3 4,4	65,4 3,9 11,3 4,5	67
VIII	p-Cl	Cl	OH	297—298	$C_{17}H_{11}Cl_2NO_3$	Cl N	20,3 3,9	20,4 4,0	64
IX	H	H	OC_2H_5	239—240	$C_{19}H_{17}NO_3$	C H N	73,9 5,4 4,5	74,3 5,6 4,6	91
X	*o*-OCH_3	H	OC_2H_5	228—230	$C_{20}H_{19}NO_4$	C H N	71,3 5,6 4,3	71,2 5,7 4,2	89
XI	p-Cl	H	OC_2H_5	276—278	$C_{19}H_{16}ClNO_3$	Cl N	10,3 4,0	10,4 4,1	93
XII	p-SO_2CH_3	H	OC_2H_5	267—269	$C_{20}H_{19}NO_5S$	C H S	62,4 4,8 8,3	62,3 4,9 8,3	87
XIII	H	Cl	OC_2H_5	228—229	$C_{19}H_{16}ClNO_3$	C H Cl N	66,8 4,9 10,3 4,2	66,8 4,7 10,4 4,1	85
XIV	p-Cl	Cl	OC_2H_5	266—267	$C_{19}H_{15}Cl_2NO_3$	C H Cl N	60,7 4,0 18,7 3,7	60,9 4,1 18,9 3,7	89
XV	H	H	$NHNH_2$	>360	$C_{17}H_{15}N_3O_2$	N	14,3	14,4	87
XVI	*o*-OCH_3	H	$NHNH_2$	287—288	$C_{18}H_{17}N_3O_3$	N	13,0	13,0	91
XVII	p-Cl	H	$NHNH_2$	>360	$C_{17}H_{14}ClN_3O_2$	Cl N	10,8 12,5	10,9 12,5	89
XVIII	p-SO_2CH_3	H	$NHNH_2$	>360	$C_{18}H_{17}N_3O_4S$	N S	11,3 8,6	11,2 8,6	86

TABLE 2



Compound	R_1	R_2	mp, °C	Empirical formula	Found, %		Calculated, %		Yield, %
					Cl	N	Cl	N	
XX	H	H	101—102	$C_{19}H_{16}ClNO_2$	10,9	4,3	10,9	4,3	85,7
XXI	Cl	H	124—125	$C_{19}H_{15}Cl_2NO_2$	19,7	3,9	19,7	3,9	86,6
XXII	H	Cl	103—104	$C_{19}H_{15}Cl_2NO_2$	19,6	3,9	19,7	3,9	82,9
XXIII	Cl	Cl	105—106	$C_{19}H_{14}Cl_3NO_2$	26,7	3,5	27,0	3,6	88,1

The UV spectra of the dihydroquinolin-4-ones studied have three absorption maxima close to the maxima of the unsubstituted dihydroquinolin-4-one and of 1-methyldihydroquinolin-4-one and differing from the spectrum of 4-methoxyquinoline [6].

Thus, the dihydroquinolin-4-ones that we have studied exist mainly in the oxo form [6,7].

EXPERIMENTAL

The IR spectra were taken on a UR-20 instrument in the form of mulls in paraffin oil. The UV spectra were taken in ethanol on an SF-4 spectrophotometer. The yields and constants of compounds III-XVIII and XX-XXIII are given in Tables 1 and 2, respectively.

3-Benzyl-4-oxo-1,4-dihydroquinoline-7-carboxylic Acids (III-VIII). An aqueous solution of 25 mmoles of the sodium salt of the acid I or II in 25 ml of water was treated with 30 mmoles of an aromatic aldehyde in 50 ml of ethanol and the mixture was boiled for 8 hr, treated with activated carbon and filtered, and the filtrate was evaporated to dryness. The solid residue was dissolved in 20 ml of water and the product was precipitated by acidification with hydrochloric acid, filtered off, and washed with water. The acids III-VIII were purified by reprecipitation and crystallization from dimethylformamide.

Ethyl 3-Benzyl-4-oxo-1,4-dihydroquinoline-7-carboxylates (IX-XIV). A suspension of 5 mmoles of an acid III-VIII in 25 ml of absolute ethanol was treated with 0.5 ml of H_2SO_4 (d 1.84), and the mixture was boiled until a clear solution had been obtained (~5 hr). After the volatile products had been distilled off in vacuum, the residue was treated with an aqueous solution of Na_2CO_3, and the solid that deposited was filtered off, washed with water, and purified by crystallization from ethanol or aqueous dimethylformamide.

3-Benzyl-4-oxo-1,4-dihydroquinoline-7-carbohydrazides (XV-XVIII). A mixture of 2 mmoles of one of the esters IX-XIV and 1.5 ml of hydrazine hydrate was boiled for 15 min, and, after cooling, the reaction mixture was diluted with water and the solid product was filtered off, washed with water, and crystallized from dimethylformamide. The hydrazides XV-XVIII formed colorless substances.

3-Benzyl-4-chloroquinoline-7-carboxylic Acid (XIX). A mixture of 2.8 g (10 mmoles) of III and 3 ml of thionyl chloride was boiled for 1 hr. After the excess of thionyl chloride had been driven off, the residue was treated with 15 ml of water and the mixture was boiled for 2 hr, after which the product was filtered off; yield 2.5 g (84%), colorless crystalline powder, mp ~275°C (decomp., from dimethylformamide). Found, %: C 68.6; H 4.3; Cl 11.8; N 4.6. Calculated for $C_{17}H_{12}ClNO_2$, %: C 68.6; H 4.1; Cl 11.9; N 4.7.

Esters of 3-Benzyl-4-Chloroquinoline-7-carboxylic Acids (XX-XXIII). A mixture of 10 mmoles of III, V, VII, or VIII and 3 ml of thionyl chloride was heated at the boil for 1 hr, the excess of thionyl chloride was driven off in vacuum, the solid residue was treated with 5 ml of absolute ethanol, and the mixture was boiled for 30 min. After the elimination of the ethanol, the residue was treated with sodium carbonate solution and the solid substance was filtered off, washed with water and crystallized from aqueous ethanol. The esters XX-XXIII obtained are pale yellow crystalline substances.

3-Benzyl-4-chloroquinoline-7-carbonamide (XXIV). A mixture of 2.8 g (10 mmoles) of III and 3 ml of thionyl chloride was boiled for 1 hr, the excess of thionyl chloride was driven off in vacuum, the residue was formed into a suspension with dry dichloroethane, and a current of warm air was passed through this suspension at 90-95°C for 15 min. The yield was 2.65 g (89%), colorless crystals, mp 231-232°C (decomp. from dimethylformamide). Found, %: Cl 11.7; N 9.7. Calculated for $C_{17}H_{13}CLN_2O$, %: Cl 11.9; N 9.4.

3-Benzyl-4-chloroquinoline-7-carbonitrile (XXV). A mixture of 1.48 g (5 mmoles) of XXIV, 10 ml of dry dichloroethane, and 10 ml of thionyl chloride was boiled until a clear solution had been obtained (1 hr 30 min). After the elimination of the volatile products, the solid residue was purified by crystallization from aqueous ethanol. Yield 1 g (72%), colorless needles, mp 87-89°C. IR spectrum: 2220 cm^{-1} ($C \equiv N$). Found, %: Cl 12.6; N 10.1. Calculated for $C_{17}H_{11}ClN_2$, %: Cl 12.8; N 10.1.

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