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Abstract

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N. S. Kozlov and O. K. Kozminykh

CATALYTIC SYNTHESIS OF PARA-, NITRO-, AMINO-, AND SULFAMIDE DERIVATIVES OF 2-PHENYLQUINOLINE AND 2-PHENYL-5,6-BENZOQUINOLINE

(Presented by Academician A. A. Balandin, 1 III 1957)

Nitro and amino derivatives of 2-phenylquinoline and 2-phenyl-5,6-benzoquinoline have been described in the literature ([1–3]) as individual representatives, while sulfamide derivatives of this series have not been considered in the literature. Nevertheless, a considerable antibacterial action is known for certain amines ([4]) and sulfamides ([4,5]) of the quinoline series.

To obtain nitro derivatives of 2-phenylquinoline we used the known method ([6–9]) of joint catalytic condensation of acetylene with aromatic amines and aromatic aldehydes, by means of which substances I—III were synthesized (Table 1). Into the condensation reaction

Table 1

Compound No.	Substance, its empirical formula	m.p., °C	Calculated (%) C	Calculated (%) H	Calculated (%) N	Found (%) C	Found (%) H	Found (%) N	Picrate m.p., °C	Pt platinates, % calc.	Pt platinates, % found
I	6-methoxy-2-(4′-nitrophenyl)quinoline $C_{16}H_{12}O_3N_2$	156—157	68.56	4.31	9.99	68.54 68.67	4.57 4.41	9.93 10.12	222—224 (decomp.)	20.11	19.91 19.96

Compound No.	Substance, its empirical formula	m.p., °C	Calculated (%) C	Calculated (%) H	Calculated (%) N	Found (%) C	Found (%) H	Found (%) N	Picrate m.p., °C	Pt platinates, % calc.	Pt platinates, % found
II	6-ethoxy-2-(4′-nitrophenyl)quinoline $C_{17}H_{14}O_3N_2$	140—141	69.37	4.79	9.51	69.43 69.11	4.66 4.91	9.64 9.33	187—188	19.65	19.57 19.50
III	2-(4′-nitrophenyl)-5,6-benzoquinoline $C_{19}H_{12}O_2N_2$	196.5—197	75.98	4.02	9.32	76.18 76.21	4.02 4.22	9.52 9.41	142—143	19.31	19.30 19.13
IV	6-methoxy-2-(4′-aminophenyl)quinoline $C_{16}H_{14}ON_2$	220—221	76.77	5.63	11.19	76.70 76.59	5.96 5.81	11.12 11.11	189—190 (decomp.)	21.44	21.42 21.23
V	6-ethoxy-2-(4′-aminophenyl)quinoline $C_{17}H_{16}ON_2$	188—189	77.24	6.10	10.59	77.47 77.40	6.48 6.31	10.57 10.38	203—205 (decomp.)	20.79	20.56 20.69
VI	2-(4′-aminophenyl)-5,6-benzoquinoline $C_{19}H_{14}N_2$	218—219	84.41	5.22	10.36	84.51 84.52	5.29 5.49	10.37 10.26	181—182	20.53	20.38 20.24

Note. Melting points of the acetyl derivatives: IV —234—235°, V —229°, VI —250—251°.

we introduced *p*-nitrobenzaldehyde and aromatic amines: *p*-anisidine, *p*-phenetidine, and 2-naphthylamine. The nitro compounds obtained were converted by us into amines by the usual reduction methods, and substances IV—VI were isolated (Table 1). From the amines obtained, a series of sulfamide derivatives of 2-phenylquinoline and 2-phenyl-5,6-benzoquinoline (compounds VII—XXX, Table 2) was synthesized by condensation in a pyridine medium of the amines obtained by us with acid chlorides of various sulfonic acids: benzenesulfonyl chloride, *β*-pyridinesulfonyl chloride, *p*-methoxybenzenesulfonyl chlori-

with *m*-nitrobenzenesulfochloride, and with *m*- and *p*-acetylaminobenzenesulfochlorides.

All the compounds listed (I–XXX, Tables 1 and 2) have not been described in the literature.

Table 2

R	A: Compound No.	A: m.p., °C	A: N found, %	A: N calc., %	B: Compound No.	B: m.p., °C	B: N found, %	B: N calc., %	C: Compound No.	C: m.p., °C	C: N found, %	C: N calc., %
phenyl	VII	222–223	7.17	7.33; 7.44	VIII	206–207	6.92	7.05; 6.91	IX	229–230	6.82	6.87; 6.69
pyridyl (N shown)	X	224–225	10.73	10.63; 10.67	XI	215–215.5	10.36	10.28; 10.41	XII	241 (decomp.)	10.21	10.14; 10.03
methoxyphenyl (OCH_3)	XIII	182–183	6.66	6.45; 6.37	XIV	232–233	6.44	6.38; 6.23	XV	229–230	6.36	6.47; 6.54
nitrophenyl (NO_2)	XVI	179–180	9.65	9.50; 9.76	XVII	206–207	9.34	9.37; 9.53	XVIII	228–229	9.22	9.11; 9.27
acetylaminophenyl ($NHCOCH_3$)	XIX	213–214	9.39	9.43; 9.48	XX	209–211	9.10	8.79; 8.92	XXI	250 (decomp.)	8.98	9.20; 9.15
acetylaminophenyl ($NHCOCH_3$)	XXII	243–244	9.39	9.28; 9.10	XXIII	227–228	9.10	9.33; 9.37	XXIV	215–216	8.98	8.79; 8.90
aminophenyl (NH_2)	XXV	225–226	10.36	10.51; 10.31	XXVI	211–212	10.17	9.91; 10.00	*XXVII	254–255	9.87	10.08; 10.06
aminophenyl (NH_2)	XXVIII	255–257 (decomp.)	10.36	10.28; 10.10	XXIX	226–227	10.17	10.37; 10.39	XXX	225–227	9.87	9.60; 9.85

Note. For VIII, XI, XV, and XVI, $S_{\text{calc.}}$, respectively: 7.92; 7.90; 7.27 and 7.36%; S_{found} 7.78; 7.98; 7.54 and 7.57%.

A: structural formula with CH_3O and $NH{-}SO_2{-}R$.

B: structural formula with C_2H_5O and $NH{-}SO_2{-}R$.

C: structural formula with $NH{-}SO_2R{-}R$.

In the present work we succeeded in substantially improving the method, proposed earlier by N. S. Kozlov[10,11], for the synthesis of 2-phenyl derivatives of quinoline from acetylene, aromatic amines, and aldehydes. The essence of the method is that a mixture of the primary aromatic amine

(2 gram-moles) with an aromatic aldehyde (1 gram-mole), in the presence of a catalyst, is saturated with acetylene. According to our ideas about the reaction mechanism, half the amount of the aromatic amine (1 gram-mole), reacting with the aromatic aldehyde, forms a Schiff base; the other half of the same aromatic amine, reacting with acetylene, forms the corresponding monoethylidene base. The bases then obtained react with one another, forming an intermediate product which, in one case, was isolated and its structure established [12]. The mass in which the intermediate product has formed is then subjected to cyclization by the thermal method or by heating with 10% hydrochloric acid, and the intermediate product is converted into 2-phenyl derivatives of the quinoline series.

In the practical performance of such syntheses we found that not all aromatic amines react equally actively with acetylene—aniline proved to be the most active. The monoethylideneaniline base formed by aniline and acetylene reacts most vigorously with one or another Schiff base, and the intermediate product formed has a great capacity for cyclization into a quinoline base. Proceeding from this, we developed a new method for the synthesis of phenylquinoline bases, namely: after obtaining a Schiff base from any aromatic aldehyde and aromatic amine, we added to it an equimolecular amount of aniline, and the resulting reaction mass, in the presence of a catalyst, was saturated with acetylene. Replacement of half the amount of aromatic amine by aniline makes the syntheses of phenylquinoline bases still more accessible, increases the yield of the product, and confirms the earlier views of N. S. Kozlov [13,14] on the mechanism of these syntheses. Hence the reactions for the synthesis of nitro derivatives of 2-phenylquinoline and 5,6-benzoquinoline have the following mechanism:

$$R\text{-substituted aromatic amine} + NO_2\text{-substituted aromatic aldehyde} \longrightarrow \text{Schiff base } I + H_2O,$$

$$\text{where } I: \quad R\text{-Ar-}N{=}CH\text{-Ar-}NO_2,$$

$$\text{aniline} + \mathrm{CH{\equiv}CH} \xrightarrow{\mathrm{HgCl_2}} \text{monoethylideneaniline } II,$$

$$II: \quad \mathrm{C_6H_5N{=}CH{-}CH_2}.$$

$$I + II \longrightarrow \text{intermediate product}$$

$$\xrightarrow{\mathrm{HCl}} R\text{-substituted nitrophenylquinoline} + \text{aniline} + \mathrm{H_2}.$$

Description of the procedure

Nitro derivatives of 2-phenylquinoline were obtained by the following procedure. First, from an aromatic amine and *p*-nitrobenzaldehyde, taken in equimolecular ratios, in alcoholic solutions with heating, the Schiff base was obtained in the form of a crystalline product. To the Schiff base, dissolved in toluene, there were added an equimolecular amount of aniline and a catalyst—sulema (in an amount of 10% of the total mass), and the mixture was saturated with acetylene for 15-20 hr with heating on a water bath to 80-90°. At the end of the saturation, a mixture of concentrated hydrochloric acid and alcohol (in a ratio of 1 : 2) was added to the mass, and the mass was heated for 30 min on a water bath at

in a water bath. The toluene layer was decanted, and the alcoholic solution, after cooling, gave a crystalline precipitate of the hydrochloride salt of the product, which was separated, purified by crystallization from alcohol, and dissolved in pyridine. The pyridine converted the product from the salt into the base, which was then crystallized from acetone or pyridine. The yield of the pure nitro base was not less than 50-60%. Reduction of the nitro derivatives to the amino derivatives of 2-phenylquinoline was carried out with tin in concentrated hydrochloric acid, with addition of a small amount of alcohol as the mixture thickened. The reduction proceeded for 10-15 hr with heating on a water bath. The mass was then neutralized with a concentrated solution of sodium hydroxide, the precipitate was separated and dried, and the product was extracted with acetone in a Soxhlet apparatus. The product was purified by crystallization from acetone or pyridine.

The sulfonamides were obtained by the procedure described in the literature (15, 16). The sulfonic acid chlorides were synthesized by the methods described in the literature (16-20).

The nitrosulfonamides (XVI-XVIII) obtained by us were converted into amino derivatives by reduction with iron in glacial acetic acid; in this process, substances were obtained that were completely identical with compounds XXV-XXVII, which in turn had been obtained by hydrolysis of acetylaminosulfonamides (XIX-XXI). This fact testifies to the correctness of the proposed structure of the sulfonamides.

Molotov State University
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