SYNTHESES BASED ON BIS(β-DIKETONES). REACTION OF DI(4-ACETOACETYLPHENYL) OXIDE WITH AMINES

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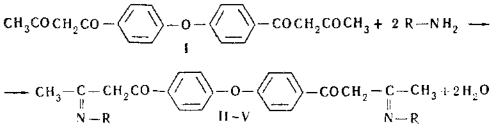
The reaction of di(4-acetoacetylphenyl) oxide (I) with β-napthylamine, aniline, 4-aminobiphenyl, and 4-aminodiphenylamine has given the corresponding dianils, and the conditions for their cyclization have been studied. It has been shown that the dianil of I and β-napthylamine cyclizes under the action of HF into the linear di(benzoquinoline) compound and in the presence of β-naphthylamine hydrochloride into the angular di(benzoquinoline) compound; the other dianils do not cyclize under these conditions.

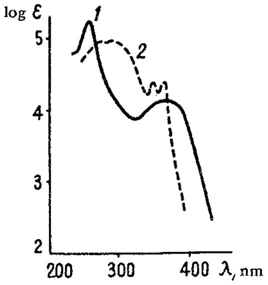
Syntheses of quinolines by the Doebner-Miller method from paraldehyde, acetone, and β-naphthylamine and by Combes' method from β-naphthylamine and acetylacetone have been studied in fairly great detail [1, 2]. The reactions take place readily and lead to the formation of benzoquinolines.

The reaction of the bis(β-diketone) I with aniline, 4-aminodiphenylamine, 4-aminobiphenyl, and β-naphthylamine also takes place readily and leads to the formation of dianils with high yields (see table). The reaction can be represented by the following scheme:



II $R = C_6H_5-$; III $R = C_6H_5NHC_6H_4-$; IV $R = C_6H_5-C_6H_4-$; V $R = C_{10}H_7-$

However, in attempts to achieve the subsequent cyclization of the anils so obtained by the usual methods employed for the synthesis of quinoline derivatives (treatment with concentrated H_2SO_4 with heating, concentrated H_2SO_4 in the cold, treatment with anhydrous HF, and thermal treatment of the anil), considerable difficulties were encountered. Attempts to convert the dianils II–IV into quinolines proved unsuccessful. The reactions gave only the unchanged dianils or products of their hydrolytic cleavage [the initial bis(β-diketone) and the corresponding amine]. Goldyrev [3] found a similar situation in an attempt to obtain a biquinoline from the anil of o-dianisidine and acetylacetone.



UV spectra of the di(benzoquinoline) compounds in dioxane: 1) the di(benzoquinoline) compound VI; 2) the di(benzoquinoline) compound VII.

Di(benzoquinoline) compounds could be obtained from compound I only by using β-naphthylamine as the amine, either with the isolation of the intermediate dianil and its subsequent cyclization or directly from the bis(β-diketone) in an excess of the free amine in the presence of its hydrochloride.

The treatment of the dianil V with concentrated H_2SO_4 with heating (50° C, 2–3 min), at 0° C, and at −2° C obviously leads to the formation of a very small amount of the quinoline base, as is shown by the bright blue fluorescence in UV light of an ethereal extract of the reaction product. However, we were unable to isolate the quinoline base in the pure state. The same result was obtained by the treatment of the dianil with anhydrous HF at room temperature and on heating in

Dianils from Di(4-acetoacetylphenyl) Oxide

Initial amine	Reaction temperature, °C	Reaction time, hr	Mp, °C	Empirical formula	Found, %			Calculated, %			Yield, %
					C	H	N	C	H	N	
β-Naphthylamine	160	9	194—195	$C_{40}H_{32}N_2O_3$	81.78 81.37	5.53 5.50	4.71 4.61	81.61	5.48	4.76	93
4-Aminobiphenyl	150	0.5	240—242	$C_{44}H_{36}N_2O_3$	82.70 82.68	5.61 5.58	4.43 4.43	82.47	5.66	4.37	98.6
4-Aminodiphenylamine	160—170	1	204—206	$C_{44}H_{38}N_4O_3$	78.85 78.90	5.78 5.76	8.39 8.41	78.78	5.71	8.35	93
Aniline	170	8	156.5—157.5*	$C_{32}H_{28}N_2O_3$	78.48 78.48	5.80 5.75	5.70 5.73	78.66	5.77	5.73	95

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*Crystallized from a mixture of ethanol and benzene (10 : 1).

a tube with a catalytic amount of HCl at 150° C for 16 hr.

The cyclization of the dianil V (see Scheme) was effected by treatment with anhydrous HF with strong cooling [4, 5] and by the thermal treatment of a mixture of the dianil, the initial amine, and its hydrochloride in a current of inert gas [6]. The yields of di(benzoquinoline) compounds were 35–32% in both cases. In a study of the di(benzoquinoline) compounds obtained by the two different methods of cyclization (with HF and by thermal treatment), it was found that these products were not identical. They differed in their melting points, solubilities, UV spectra, the colors of the hydrochlorides obtained from them, the picrates, and the intensities and colors of the fluorescence of their solutions (in ether and toluene) in UV light.

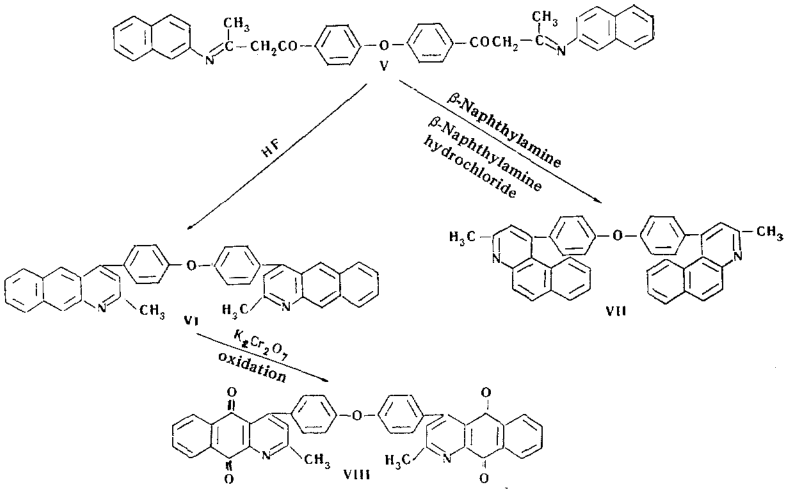
The di(benzoquinoline) compound VI obtained by the cyclization of the dianil V with HF melted at 232–234° C and was soluble in ether, chloroform, toluene, and dimethylformamide; its hydrochloride and picrate were bright orange, and its ethereal solution fluoresced a very intense bright blue in UV light.

The di(benzoquinoline) compound VII obtained by the thermal treatment of the dianil V had a melting point of 256–258° C, was insoluble in ether, and considerably less soluble in the other solvents. It formed a bright yellow hydrochloride and picrate, and exhibited a moderate blue-violet fluorescence in UV light.

The figure gives the UV spectra of the two compounds, which also differ considerably from one another. The spectrum of VI is similar to that of anthracene while that of VII is similar to that of phenanthrene.

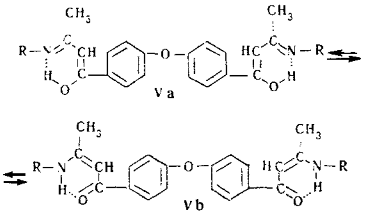
To prove the structure of the linear adduct VI, it was oxidized with $K_2Cr_2O_7$ in acetic acid to the corresponding quinone VIII.

The experimental results obtained can be interpreted in the following way: Obviously, under different conditions cyclization takes place differently leading to the formation of different cyclic products which can be represented in a general manner by the following scheme.



Similar ring closures in two directions with the formation of linear and angular benzoquinolines have been reported previously [4, 5, 7]. The decisive factor for the direction of cyclization is generally assumed to be the structure of the side chain of the adducts, but contradictory opinions exist on this question [7–9].

It appears to be necessary to take into consideration the fact that amino derivatives of β-dicarbonyl compounds are characterized by ketimide-enamine tautomerism, with the consequent possibility of the formation of chelate structures with intramolecular hydrogen bonds. For the dianils II–V, out of a number of possible tautomeric forms we consider the following to be the most likely.



In the case of the transition of Va to Vb we have, in essence, a peculiar case of the simultaneous appearance of ketimide-enamine and keto-enol tautomerism. Conversion takes place within a six-membered quasi-aromatic ring and reduces to a shift in the electron density and some rearrangement of the hydrogen attached to oxygen and nitrogen, without a change in the geometrical form (conformation) of the molecules. It is not surprising that such a type of transition has no substantial influence on the spectral characteristics of the two forms. Consequently we have been unable to assign one structure or the other to the dianils on the basis of their IR spectra. However, according to a number of authors [10, 11], raising the reaction temperature in the preparation of the anils leads to a shift in the equilibrium in the direction of the ketimide form. The synthesis of dianils from I takes place only at high temperatures (150–170° C) which undoubtedly favors the formation of the ketimide form Va. Also in favor of this is the fact that the initial bis(β-diketone) exists predominantly in the cis-enolic form [12].

The structure Va is obviously stabilized by the conjugation of the quasi-aromatic ring with the benzene ring, and this also explains the difficulty of cyclizing the anils obtained in comparison with, for example, the corresponding anils of acetylacetone.

EXPERIMENTAL

Starting materials. The bis(β-ketone) I was obtained by the direct acetoacetylation of diphenyl oxide with acetic anhydride in the presence of BF_3 [13]. β-Naphthylamine was isolated from its hydrochloride by treatment with aqueous alkali. Mp was 110° C; 4-aminobiphenyl was obtained as described by Hach et al. [14] and purified, like the 4-aminodiphenylamine, by vacuum distillation.

Synthesis of the dianils. A mixture of 1 mole of I and 3 moles of the appropriate amine was heated in a current of inert gas at 150–170° C for 30 min–9 hr. The resulting crystalline product was washed with ether and recrystallized from toluene (see table).

Preparation of the di(benzoquinoline) compound VI. A polyethylene vessel cooled with dry ice was charged with 2.5 g (~0.0043 mole) of the dianil V, 50 ml of anhydrous HF was added, and the mixture was left to stand at room temperature. The orange residue left after the evaporation of the HF was neutralized with cold NaOH solution. The precipitate was filtered off, carefully washed with water, and dried in vacuum at 60° C. Then it was dissolved in ether (~3 *l*), and the yellow precipitate that separated out when the ether was distilled off was again filtered off and recrystallized from toluene. Yield was 0.78 g (35%); mp 232–234° C. Found, %: C 87.09, 87.11; H 5.10, 5.10, N 5.12, 4.92. Calculated for $C_{40}H_{28}N_2O$, %: C 86.93; H 5.11; N 5.07.

Preparation of the di(benzoquinoline) compound VII. a) A mixture of 1 g (0.0030 mole) of I, 1.7 g (0.0120 mole) of β-naphthylamine, and 0.26 g (0.0015 mole) of β-naphthylamine hydrochloride was heated at 180° C in a current of inert gas for 15 hr. The reaction product was washed with boiling ethanol and then with ether. The residue was crystallized from toluene or dimethylformamide. Yield was 0.5 g (31%); mp 256–258° C. Found, %: C 87.15, 87.06; H 5.14; 5.10; N 5.09, 5.11. Calculated for $C_{40}H_{28}N_2O$, %: C 86.93; H 5.11; N 5.07%.

b) A mixture of 1 g (0.0017 mole) of the dianil V, 0.49 g (0.0034 mole) of β-naphthylamine, and 0.3 g (0.0017 mole) of β-naphthylamine hydrochloride was heated at 180° C in a current of inert gas for 10 hr. The reaction product was carefully washed with ether. The residue was crystallized from dimethylformamide Yield was 0.3 g (32%); mp 256–258° C. A mixture with the di(benzoquinoline) compound VII obtained by the method described above gave no depression of the melting point.

Preparation of the picrates. The picrates were obtained by mixing benzene solutions of the di(benzoquinoline) compounds and picric acid. The precipitates were recrystallized from nitrobenzene.

Picrate of the di(benzoquinoline) compound VII—bright yellow substance with mp 246–248° C. Found, %: C 62.02, 62.10; H 3.40, 3.33; N 10.96, 10.96. Calculated for $C_{40}H_{28}N_2O \cdot 2C_6H_3N_3O_7$, %: C 61.78; H 3.39; N 11.09.

Picrate of the di(benzoquinoline) compound VI—bright orange substance with decomp. p. 276–280° C (introduced into the block at a temperature of 270° C). Found, %: C 61.50; 61.55; H 3.51; 3.48; N 11.06, 11.11. Calculated for $C_{40}H_{28}N_2O \cdot 2C_6H_3N_3O_7$, %: C 61.78; H 3.39; N 11.09.

Oxidation of the di(benzoquinoline) compound VI with potassium dichromate. A flask with a reflux condenser was charged with 0.6 g (~0.0011 mole) of **VI**, 13.5 ml of glacial acetic acid, 0.9 ml of water, and 0.67 g (~0.0023 mole) of potassium dichromate, and the mixture was boiled for 3 hr. The resulting green solution was poured into 50 ml of distilled water. Then, with stirring the mixture was made weakly alkaline. The precipitate that deposited was filtered off, carefully washed with water, dried in a vacuum at 50° C, and extracted with benzene. After the benzene had been distilled off, the residue was crystallized from bromobenzene and then from dimethylformamide. Yield 0.3 g (45%) of the quinone **VIII**, mp 275–276° C, Found, %: N 4.48, 4.48. Calculated for $C_{40}H_{24}N_2O_5$, %: N 4.57.

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