CONDENSATION OF SCHIFF BASES WITH COMPOUNDS CONTAINING LABILE HYDROGEN ATOMS

V.* REACTION OF BENZYLIDENE-β-NAPHTHYLAMINE DERIVATIVES WITH CYCLOHEPTANONE

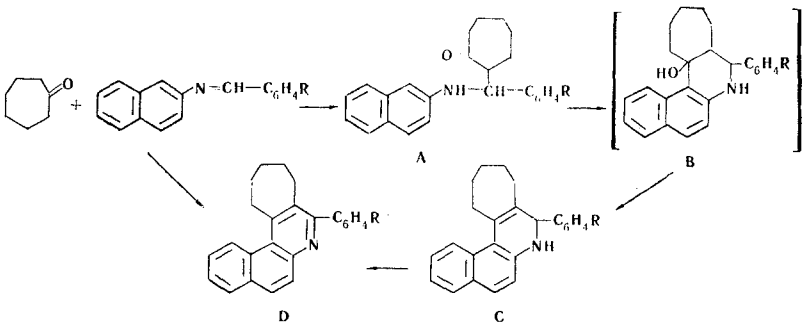
N. S. Kozlov and G. V. Vorob'eva

UDC 547.837:542.953.4:543.422.4.6

5,6-Benzoquinoline derivatives are formed by the reaction of cycloheptanone with arylidene-β-naphthylamines. The order of activity of cyclic ketones in this reaction ($C_5 > C_6 > C_7$) is discussed, and the UV spectra are presented.

5,6-Benzoquinoline derivatives condensed with the alicyclic hydrocarbon at the 3- and 4-positions [1] are formed by the reaction of cyclopentanone or cyclohexanone with Schiff bases obtained from β-naphthylamine and aromatic aldehydes.

In this investigation we have introduced cycloheptanone into the reaction.



R = H, *p*-Cl, *p*-Br, *p*-NO_2, *m*-NO_2, *p*-OCH_3

It turned out that amino ketone A is formed by the reaction of cycloheptanone with benzylidene-β-naphthylamine (R = H) under mild conditions (acid catalyst, 10 min at 100°). A mixture of aminoketone A and 5,6-benzoquinoline derivative D was obtained when the heating time was increased to 1 h. Intermediates B and C, previously obtained in the reaction with cyclohexanone [1], could not be detected.

A mixture of the dihydrobenzoquinoline (C) and the 5,6-benzoquinoline (D) could be obtained by the reaction with nitrobenzylidene-β-naphthylamine (R = NO_2) under mild conditions.

Compounds with electron-donating substituents (R = Cl, Br, OCH_3) do not react with cycloheptanone under mild conditions. Cyclization to form the 5,6-benzoquinoline derivative occurs under more severe conditions (30-60 min, 100°, in the presence of an acid catalyst). An amino ketone could be obtained only for p-chlorobenzylidene-β-naphthylamine from an equimolecular mixture of an alcohol solution of the azomethine and ketone after standing for 1 week at room temperature in the presence of a catalyst. Intermediates B and C could not be isolated.

*See [11] for communication IV.

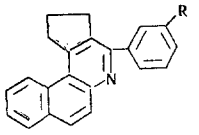
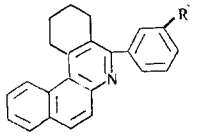
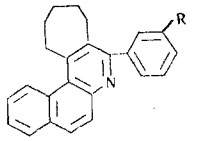
Institute of Physical Organic Chemistry, Academy of Sciences of the BelorussianSSR, Minsk. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 519-523, April, 1971. Original article submitted March 16, 1970.

TABLE 1. Characteristics of the Products of the Reaction of Arylidene-β-naphthylamines with Cycloheptanone

Comp.	Name	Reaction time, min; temp; amt of conc. HCl, ml	Mp °C	R_f	Empirical formula	Found, %			Calculated, %			Yield, %
						C	H	N	C	H	N	
I	2-[(Phenyl)(β-naphthylamino)methyl]cycloheptanone	25; 100; 0,1	145—146	0,57	$C_{24}H_{25}NO$	84,05 83,91	7,30 7,03	4,07 4,12	84,00	7,00	4,09	66
II	2-Phenyl-3,4-(1',2'-cycloheptylene)-5,6-benzoquinoline	60; 140; 0,3	126—127	0,37	$C_{24}H_{21}N$	89,00 88,87	6,51 6,73	4,39 4,37	89,13	6,52	4,35	61
III	2-(p-Nitrophenyl)-2,4-(1',2'-cycloheptylene)-1,2-dihydro-5,6-benzoquinoline	3; 70; 0,2	210—212	0,55	$C_{24}H_{22}N_2O_2$	77,98 78,08	6,02 5,84	7,48 7,79	77,90	5,95	7,57	38
IV	2-(p-Nitrophenyl)-3,4-(1',2'-cycloheptylene)-5,6-benzoquinoline	60; 140; 0,3	165—166	0,27	$C_{24}H_{20}N_2O_2$	78,31 78,50	5,73 5,71	7,70 7,54	78,30	5,44	7,61	55
V	2-(m-Nitrophenyl)-3,4-(1',2'-cycloheptylene)-1,2-dihydro-5,6-benzoquinoline	3; 70; 0,2	197—199	0,60	$C_{24}H_{22}N_2O_2$	77,72 78,10	5,79 6,05	7,62 7,59	77,90	5,95	7,57	22
VI	2-(m-Nitrophenyl)-3,4-(1',2'-cycloheptylene)-5,6-benzoquinoline	60; 140; 0,3	172—173	0,26	$C_{24}H_{20}N_2O_2$	78,37 77,92	5,59 5,80	7,60 7,57	78,30	5,44	7,61	38
VII	2-[(p-Chlorophenyl)(β-naphthylamino)methyl]-cycloheptanone	*; 20; 0,1	170—171	0,37	$C_{24}H_{24}NOCl$	76,69 76,50	6,42 6,78	3,59 3,94	76,40	6,35	3,70	62
VIII	2-(p-Chlorophenyl)-3,4-(1',2'-cycloheptylene)-5,6-benzoquinoline	60; 100; 0,3	145—146	0,63	$C_{24}H_{20}NCl$	80,81 80,63	5,57 5,68	3,90 3,84	80,54	5,63	3,91	54
IX	2-(p-Bromophenyl)-3,4-(1',2'-cycloheptylene)-5,6-benzoquinoline	60; 100; 0,3	152—153	0,62	$C_{24}H_{20}NBr$	71,95 71,87	5,06 5,08	3,50 3,46	71,64	5,02	3,48	62
X	2-(p Methoxyphenyl)-3,4-(1',2'-cycloheptylene)-5,6-benzoquinoline	60; 100; 0,3	170—171	0,29	$C_{25}H_{23}NO$	85,08 85,21	6,18 6,58	3,45 3,60	85,00	6,52	3,97	40

* The reaction mixture was held at this temperature for 1 week.

TABLE 2. Position of the UV Absorption Maxima in the Long-Wave Region for 5,6-Benzoquinoline Derivatives

Compound	λmax, nm ($\varepsilon \cdot 10^{-3}$)					
	R=H	R=*p*-NO_2	R=*m*-NO_2	R=*p*-Cl	R=*p*-Br	R=*p*-OCH_3
	360 (7,1)	Smoothed out maximum	362 (5,40)	362 (5,50)	362 (5,57)	360 (6,61)
	354 (3,82)	354 (5,55)	354 (4,03)	354 (4,60)	354 (4,08)	355—358 (5,38)
	360 (5,35)	358—360 (7,05)	360 (4,98)	358 (5,90)	358 (5,80)	358 (6,60)

In contrast to the similar compounds from cyclopentanone and cyclohexanone, the dihydro derivatives of 5,6-benzoquinolines condensed with cycloheptanone are apparently unstable compounds.

The cyclanones form the following activity series in an evaluation of the comparative reactivity of ketones in the nucleophilic addition to the azomethine double bond:

$$C_5 > C_6 > C_7.$$

In fact, cyclopentanone reacts with benzylidene-β-naphthylamine without a catalyst and heating to form the dihydroquinoline derivative; under the same conditions, cyclohexanone forms an amino ketone, while cycloheptanone does not react. Cyclopentanone reacts to form dihydroquinoline C in the presence of catalyst at 45-50°, cyclohexanone gives a mixture of amino ketone A and a hydroxy derivative of tetrahydroquinoline D, while cycloheptanone forms amino ketone A. Similar results are also observed in the reaction of cyclanones with benzylidene-β-naphthylamine derivatives (R = Cl, Br, OCH_3). The dependence of the reactivities of the cyclic compounds on the ring size is currently explained from the point of view of the concept of J strain, which takes into account the change in the inner steric stress during the formation and breaking of bonds [2, 3]. However, J strain is not always the determining factor. There are simultaneously data regarding the effect of the steric factor on the rate of addition of cyclic compounds to multiple bonds [4, 5]. For cyclic compounds, the overall steric effect increases with increasing ring size from four- to seven-membered rings. Our investigations apparently confirm the effect of the steric factor in the addition reactions of cyclic ketones at the azomethine double bond. The steric factor probably affects the stability of intermediate B, which could not be isolated in the case of cycloheptanone.

The characteristics of the compounds obtained are presented in Table 1. The structure of the synthesized products were confirmed by the IR and UV spectra. The IR spectra of A contain an intense absorption band at 3400 cm^{-1}, which corresponds to the valence vibrations of the N−H group, and at 1695 cm^{-1}, which is characteristic for the C=O group of cycloheptanone [6]. The absorption band of the carbonyl group vanishes in the IR spectra of C, while the absorption band of the secondary amino group is retained. The complete cyclization of D was judged from the IR spectrum, in which bands characteristic for the C=O and N−H groups are absent.

The UV spectra of the amino ketones of cycloheptanone, like the amino ketones of cyclohexanone, are similar to the spectrum of β-naphthylamine [7]. The UV spectra of the amino ketones of cyclohexanone and cycloheptanone are very close with respect to the positions and intensities of the absorption maxima. The UV spectra of 5,6-benzoquinoline derivatives are characteristic for such structures (see Fig. 1).

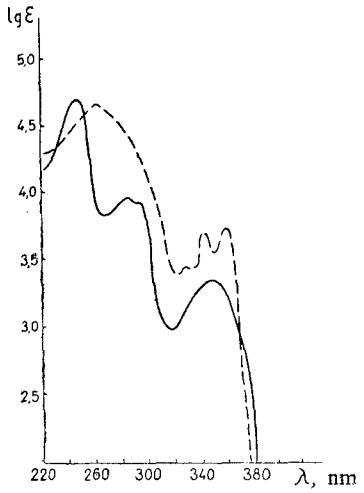


Fig. 1. UV spectra (in dioxane): 1) 2-[(phenyl)(β-naphthylamino)-methyl]cycloheptanone; 2) 2-phenyl-3,4-(1',2'-cycloheptylene)-5,6-benzoquinoline.

The presence of an alicycle condensed with the 5,6-benzoquinoline ring induces a bathochromic shift of the absorption maxima with a simultaneous increase in their intensities as compared with unsubstituted 5,6-benzoquinoline (λ_{max} 348 nm, $\varepsilon \cdot 10^{-3}$ 2.97) and 4-phenyl-5,6-benzoquinoline (λ_{max} 352 nm, $\varepsilon \cdot 10^{-3}$ 2.80). This is explained by the positive inductive effect of the alicycle. The long-wave maximum for the benzoquinoline derivative in compounds with cyclohexene is shifted hypsochromically in comparison with the analogous compounds condensed with cyclopentene and cycloheptene. The band intensities change in the same fashion (Table 2). This is apparently associated with the hyperconjugation of the CH_2 groups adjacent to the aromatic system [8]. The size of the ring condensed with the aromatic system and the position of the remaining CH_2 groups of the ring affect the intensity and position of the long-wave maximum [9, 10].

EXPERIMENTAL

The purity of the synthesized compounds was monitored by ascending thin-layer chromatography on a loose layer of activity II (Brockmann) aluminum oxide. The eluant was benzene, and the chromatographs were developed with iodine vapors. The R_f values for all of the synthesized compounds were obtained as a result of repeated measurements under standard conditions. The UV spectra in dioxane (10^{-4} mole/liter) were obtained with an SF-4 spectrophotometer. The IR spectra of KBr pellets were recorded with a UR-20 spectrophotometer at 400-3600 cm^{-1}.

Synthesis of I-X. This was accomplished via the following general method: several drops of concentrated HCl and an equimolecular amount of cycloheptanone were added to a solution of 0.01 mole of the appropriate Schiff base in alcohol, and the mixture was heated. Compounds II, IV, and VI were synthesized in an ampule with the addition of 0.01 mole of nitrobenzene. Cooling precipitated a crystalline product which was filtered, treated with ammonium hydroxide, and recrystallized from alcohol or toluene.

Compound II. This compound was also synthesized from I: a mixture of 1 g of I, 1 ml of nitrobenzene, and 5 drops of concentrated HCl was heated for 1 h at 140° in an ampule. The subsequent workup was similar to that described above.

A benzoyl derivative was obtained for III by the Schotten-Baumann method and had mp 217-218°. Found %: C 78.30, 78.46; H 5.50, 5.63. $C_{31}H_{26}N_2O_3$. Calculated %: C 78.50; H 5.49.

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