HETEROCYCLIZATION OF N-ARYL-2-NAPHTHYLAMINES WITH FORMALDEHYDE AND DIMEDONE IN THE PRESENCE OF HCl AND HBr

M. Yu. Kornilov, A. V. Turov, M. V. Mel'nik, and B. M. Gutsulyak

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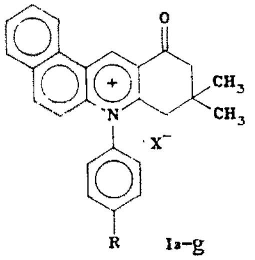
Reaction of N-aryl-2-naphthylamines with formaldehyde and dimedone in the presence of HCl or HBr gives, in addition to 7-aryl-9,9-dimethyl-11-oxo-8,9,10,11-tetrahydrobenzo[a]acridinium chlorides (or bromides), condensed chromeno[2,3-q]acridines, which show thermochromic properties.

N-Aryl-2-naphthylamines are known [1] to react with a mixture of formaldehyde and dimedone in the presence of perchloric acid to give 7-aryl-9,9-dimethyl-11-oxo-8,9,10,11-tetrahydrobenzo[*a*]acridinium perchlorates (Ia-c).



Ia-g

I a,d,e $R=H$, b,f $R=CH_3$, c,g $R=OCH_3$; a-c $X=ClO_4$; d $X=Cl$; e-g $X=Br$

When this reaction is carried out in the presence of other acids, particularly hydrochloric and hydrobromic, in addition to the salts (Id-g) there are obtained appreciable amounts of the nonsaline compounds (IIa-c), which display thermochromic properties.

The salts (Id-g) are bright yellow, crystalline compounds which are readily soluble in water and other polar solvents. Their UV spectra (Table 1), like those of the perchlorates (Ia-c) [1], show three absorption bands with maxima at 230-232, 282-289, and 350-354 nm.

The IR spectra of the salts (Id-g) show absorption bands for stretching vibrations of the aromatic and heteroaromatic rings at 1600-1500 cm^{-1}. In the region of out-of-plane deformational vibrations of the aromatic hydrogens, absorption is seen for isolated (925-950), two (814-832), four (782-758), and five [only in the case of (Id) and (Ie)] (772-750 and 700 cm^{-1}) hydrogen atoms. The spectra of all the salts (I) also show strong absorption for carbonyl group vibrations (1721-1712 cm^{-1}), and two bands for geminal methyl groups (1360-1350 and 1214-1218 cm^{-1}).

The PMR spectra of the salts (Id-g) (Table 1) show a singlet for the 12-H proton at low field (10.59-10.63 ppm). The doublet for the 1-H proton ($J = 8$ Hz) is located at 9.10-9.12 ppm. Assignment of this signal was made on the basis of the nuclear Oberhauser effect (NOE) on further irradiation of the signal for 12-H proton [for (If) the NOE was 26%]. The signals for the interacting protons 5-H and 6-H gave doublets ($J = 7$ Hz) located at 7.35-7.45 and 8.54-8.57 ppm, respectively. The remaining protons gave rise to a complex multiplet at 7.5-8.2 ppm. Signals for the methyl and methylene protons are seen at high field. The PMR spectral data for the salts (Id-g) leads to the 7-aryl-9,9-dimethyl-11-oxo-8,9,10,11-tetrahydrobenzo[*a*]acridine structure for these compounds. This conclusion was based on the NOE for the 1H {12H} proton, since only in this instance are the protons in close proximity.

As with perchloric acid, the cyclization is therefore directed toward the α-position of the β-naphthyl nucleus, to give the angular condensed benz[*a*]acridine system. The cyclization is strictly regioselective, no isomeric products with the linear benzo[b]acridine or N-(β)-naphthylacridine structure, such as would be formed from the β-position of the naphthalene nucleus, or the ortho-position of the benzene ring, being found.

Ivano-Frankovsk Institute of Oil and Gas, Ivano-Frankovsk 284018. T. G. Shevchenko Kiev State University, Kiev 252015. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1230-1234, September, 1990. Original article submitted June 23, 1987; revision submitted November 27, 1989.

TABLE 1. Properties of Compounds (I) and (II)

Compound	Empirical formula	mp, °C	λ_{max}, nm (log ε) (in ethanol)	Chemical shifts, δ, ppm						Yield, %
				12-H, d	1-H, d	5-H, d	6-H, d	8,10-CH_2	9-CH_3	
Id	$C_{25}H_{22}ClNO$	278...280	231 (4,55); 289 (4,23); 350 (3,75)	10,63	9,12	8,56	7,40	3,18 s; 3,06 s	1,27 s	41
Ie	$C_{25}H_{22}BrNO$	289...290	232 (4,56); 291 (3,34); 348 (3,85)	10,62	9,12	8,54	7,38	3,21 s; 3,07 s	1,26 s	39
If	$C_{26}H_{24}BrNO$	278...280	230 (4,83); 285 (4,65); 354 (4,20)	10,59	9,10	8,54	7,44	3,23 s; 3,06 s	1,25 s	22
Ig	$C_{26}H_{24}BrNO_2$	252...254	230 (4,37); 282 (4,25); 352 (3,88)	10,58	9,10	8,57	7,45	3,25 s; 3,07 s	1,27 s	20
IIa	$C_{34}H_{31}NO_3$	257...259	234 (3,62); 346 (3,94); 387 (4,52); 602*	10,60	9,12	8,54	6,42	1,8...2,3 m	0,8...1,0 m	36
IIb	$C_{35}H_{33}NO_3$	241...242	242 (4,21); 350 (4,12); 385 (4,60); 605*	10,60	9,10	8,55	6,42	1,8...2,4 m	0,8...1,1 m	18
IIc	$C_{35}H_{33}NO_4$	237...239	245 (4,33); 355 (4,35); 385 (4,57); 608*	10,60	9,10	8,56	6,47	1,8...2,5 m	0,82...0,96 m	16

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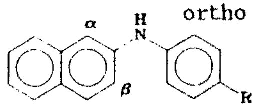
*The absorption appears on heating the solution, and disappears on cooling. (IIa) 548 (o-xylene), 571 (MEK), 573 (acetone), 584 (chloroform), and 590 (butanol).

TABLE 2. Reactivity Indices of Phenyl-2-naphthylamines



R	q_r			$2C^2_{HOMO}$			π_{rr}			E_{loc}		
	ortho	α	β	ortho	α	β	ortho	α	β	ortho	α	β
H	1,0445	1,0647	1,0277	0,0689	0,4339	0,0009	0,4115	0,4597	0,4170	2,3347	2,0882	2,3696
CH_3	1,0392	1,0664	1,0282	0,1006	0,3562	0,0014	0,4128	0,4600	0,4172	2,3248	2,0804	2,3654
OCH_3	1,0456	1,0659	1,0281	0,1017	0,3091	0,0029	0,4112	0,4601	0,4172	2,3311	2,0816	2,3659

These findings are in accordance with calculations of the reactivity indices (RI) by the MOC method [2] for phenyl-2-naphthylamine and its p-methyl- and p-methoxy-derivatives, taking into account conjugation between the amino-group and the aromatic nuclei [3]. Since the closure of the pyridine ring is an electrophilic reaction, the most likely site for attack will be the α-position of the naphthalene nucleus, since this has the greatest overall π-electron density (q_r), limiting π-electron density at the HOMO ($2C_{HOMO}^2$), self-polarizability ($\pi_{r,r}$), and the least value of the localization energy (E_{loc}) (Table 2).

The thermochromic compounds (IIa-c) are similar in appearance to the salts (Id-g), but they are soluble in both polar and nonpolar organic solvents, and insoluble in water. The UV absorption bands in the spectra of compounds (IIa-c) (Table 1) are shifted bathochromically with respect to the bands for (Id-g).

Solutions of (IIa-c) in neutral polar and nonpolar compounds, which are nearly colorless at ambient temperatures, turn blue on heating, with absorption maxima in ethanol of 602 (IIa), 605 (IIb), and 608 nm (IIc). The intensity of this absorption increases as the temperature is raised, the intensity of the absorption at 385-387 nm simultaneously decreasing. This effect is fully reversible, and can be repeated many times. The presence of an isobestic point (at 350 nm) indicates that here is an equilibrium between the two forms (colorless and colored). The colored form shows positive solvatochromism, as shown by the bathochromic shift of the absorption maximum as the polarity of the solvent is increased (Table 1). In terms of hydrogen bonding, this is equivalent to an increase in the contribution of the nonpolar structure to the ground state, and of polar structures to the excited state.

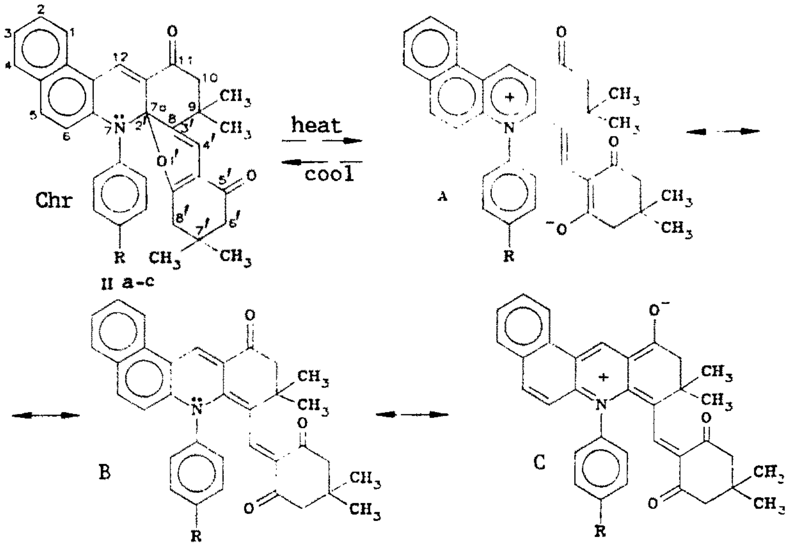
Treatment of ethanolic solutions of (IIa-c) with perchloric acid results in their decomposition to give the perchlorates of (Ia-c). This explains why, when the heterocyclization of diarylamines is carried out in the presence of $HClO_4$, the thermochromic compounds (IIa-c) were not found among the reaction products.

Characteristic differences between the IR spectra of (IIa-c) and (Id-g) are the presence in the first of bands of medium intensity at 1130 cm^{-1}, attributed to C–O–C vibrations, and the displacement of the CO absorption by 50 cm^{-1} toward the lower-frequency region (1665-1658 cm^{-1}) as compared with the CO band for the quaternary salts (Id-g) (1721-1712 cm^{-1}). This shift is in accordance with the previously observed shift of the CO band when 1-phenyl-3-acetyllepidinium perchlorate is converted into its free base [4].

A feature of the PMR spectra of the thermochromic compounds (IIa-c) is the presence of a singlet at 5.70-5.72 ppm (1H). This singlet is assumed to correspond to the 4-H proton of the pyran ring.

A doublet for the 6-H proton is seen in the spectra of (IIa-c) at somewhat lower field (6.40-6.42 ppm). The diamagnetic shift of the signal for this proton as compared with the corresponding salts (Id-g) is due to the effects of the ring current in the adjacent N-phenyl ring. In the region of absorption of aliphatic protons, compounds (IIa-c) show a doubled number of signals for the methyl groups.

These findings support the structure (II) for these compounds, which are chromeno[2,3-q]acridines. While they exist at ambient temperatures in the colorless chromene (Chr) form, compounds (IIa-c) are converted on heating into the colored merocyanine form, represented by structures A-C.



II a R=H; b R=CH_3; c R=OCH_3

It was not possible to obtain the PMR spectra of the colored forms of these compounds, since at the temperatures attainable in practice (180°C) the amounts of the colored form in solution were small although the color of the compounds became quite intense.

EXPERIMENTAL

The UV-VIS spectra of the compounds obtained were recorded on a Specord M-40 spectrophotometer with a thermostated cell. Infra-red spectra were obtained on a UR-20 apparatus in KBr disks. Proton magnetic resonance spectra were measured on a Bruker WP-10 SY spectrometer (100.13 MHz), solvent DMSO-D_6, internal standard TMS. The purity of the compounds was checked by TLC on Silufol UV-254 plates, eluent a mixture of butanol–acetone–water, 5:4:1. The molecular mass was measured cryoscopically in benzene.

The elemental analyses for C, H, Hal, and N were in agreement with the calculated values.

9,9-Dimethyl-11-oxo-7-phenyl-7,7^a,8,9,10,11-hexahydrobenzo[*a*](7,7-dimethyl-5-oxo-5,6,7,8(2H)-tetrahydrochromeno)[2,3-q]acridine (IIa). A mixture of 21.9 g (0.1 mole) of N-phenyl-2-naphthylamine, 28 g (0.2 mole) of dimedone, 17 ml (0.2 mole) of concentrated HCl, and 80 ml (0.9 mole) of nitrobenzene was heated to 100°C, and a solution of 3.0 g (0.1 mole) of formaldehyde in 50 ml of butanol, obtained by heating 3.0 g of paraformaldehyde in butanol in the presence of 0.5 ml of HCl, was added dropwise over 3 h. Heating of the reaction mixture was continued for 9 h, then the nitrobenzene and butanol were removed by steam distillation. The distillation flask then contained an aqueous solution and a resinous mass. The solution was filtered and evaporated until crystallization commenced. On cooling the solution a solid separated, which on boiling with water gave the thermochromic compound (IIa). This was crystallized from acetone (found M 498, calculated M 502).

Compound (IIa) was obtained similarly by reacting N-phenyl-2-naphthylamine with formaldehyde and dimedone in the presence of 25.2 ml (0.22 mole) of 47% HBr.

Obtained similarly were **9,9-dimethyl-11-oxo-7-(p-tolyl-7,7^a,8,9,10,11-hexahydrobenzo[*a*](7,7-dimethyl-5-oxo-5,6,7,8(2H)-tetrahydrochromeno)[2,3-q]acridine (IIb)** [from 23.3 g (0.1 mole) of N-(p-tolyl)-2-naphthylamine (found M 508, calculated M 516)], and **9,9-dimethyl-11-oxo-7-(p-methoxyphenyl)-7,7^a,8,9,10,-11-hexahydrobenzo[*a*](7,7-dimethyl-5-oxo-5,6,7,8(2H)-tetrahydrochromeno)[2,3-q]acridine (IIc)** [found M 525, calculated M 532].

To an ether solution of the acridine (IIa-c) was added dropwise 42% $HClO_4$, until no more solid separated. The solid was filtered off and crystallized from ethanol to give (Ia-c) [1].

9,9-Dimethyl-11-oxo-7-phenyl-8,9,10,11-tetrahydrobenzo[*a*]acridinium Chloride (Id). The resinous mass obtained on steam distillation was treated with 50-ml portions of boiling water until a sample of the extract no longer gave a blue coloration with alkali. The aqueous extracts were combined and evaporated, and the resulting resinous solid treated portionwise (3 × 10 ml) with acetone and precipitated with ether to give (Id).

Obtained similarly were **9,9-dimethyl-11-oxo-7-phenyl-8,9,10,11-tetrahydrobenzo[*a*]acridinium bromide (Ie), 9,9-dimethyl-11-oxo-7-(p-tolyl)-8,9,10,11-tetrahydrobenzo[*a*]acridinium bromide (If)**, and **9,9-dimethyl-7-(p-methoxyphenyl)-11-oxo-8,9,10,11-tetrahydrobenzo[*a*]acridinium bromide (Ig).** Treatment of aqueous solutions of the acridinium salts (Id-g) with perchloric acid gave (Ia-c) [1].

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