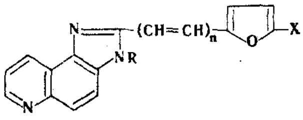
SYNTHESIS AND TRANSFORMATIONS OF 2-(2-FURYL)- AND 2-[β-(2-FURYL)VINYL]IMIDAZO[4,5-*f*]QUINOLINES

F. T. Pozharskii and L. Ya. Oleinikova

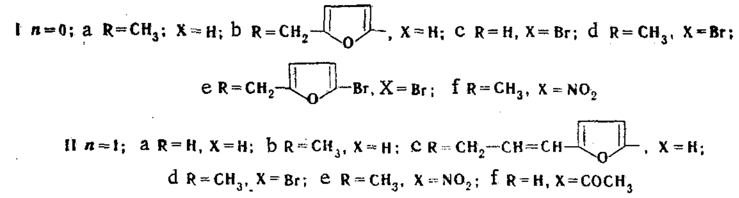
UDC 547.831'781'722.07

The corresponding 2-(2-furyl)- and 2-[β-(2-furyl)vinyl]imidazo[4,5-*f*]quinolines were obtained by condensation of 5,6-diaminoquinoline and 5-amino-6-methylaminoquinoline with furfural, furylacrolein, and their 5-bromo and 5-nitro derivatives and also with the hydrochlorides of imino esters of furancarboxylic and furylacrylic acids. Alkylation, acetylation, nitration, and substitution of the halogen in the furan ring by a nitro group were studied.

With the aim of making a further study of the effect of various aromatic systems on the reactivity of the imidazole and furan rings in a number of condensed 2-furyl- and 2-furylvinylimidazoles, we have investigated methods for the synthesis of and several transformations of 2-(2-furyl)imidazo[4,5-*f*]quinolines (Ia-f) and 2-[β-(2-furyl)vinyl]imidazo[4,5-*f*]quinolines (IIa-f).



I, II a-f



Compounds Ic and IIa were obtained by condensation of 5,6-diaminoquinoline with 5-bromofurfural and with furylacrolein under the conditions of the synthesis of other condensed furylimidazoles [1-3]. In this case, Ie and IIc, respectively, were isolated as side products. Each of the latter compounds is a mixture of two isomers that differ with respect to the position of the groups attached to the nitrogen atoms of the imidazole ring. Their indistinct melting points are evidence for this. We were unable to separate these mixtures chromatographically because of the close R_f values of the constituent isomers.

The low yields of furylimidazoquinolines in these syntheses [1-3] are apparently a consequence of the side transformations of the quinoline component under the relatively severe conditions used to carry out the reaction. In fact, Ic and IIa were obtained in 56% and 40% yields, respectively, when the condensation of 5,6-diaminoquinoline with hydrochlorides of imino esters of 5-bromofurancarboxylic and furylacrylic acids was carried out under mild conditions [4]. The yields of nitro compounds If and IIe were 75% and 62%, respectively, in the condensation of 5-amino-6-methylaminoquinoline with hydrochlorides of imino esters of 5-nitrofurancarboxylic and 5-nitrofurylacrylic acids via this method.

In contrast to other condensed furylimidazoles [1, 3, 5, 6], the characteristic reactions of I and II in the imidazole and furan rings proceed with complications and lead to low yields of the corresponding prod-

---

Rostov State University, Rostov-on-Don. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 440-442, April, 1973. Original article submitted February 3, 1972.

TABLE 1. Imidazo[4,5-*f*]quinolines (I, II)

Compound	mp, °C (from alcohol)	λ_{max}, nm	lg ε	Empirical formula	Found, %			Calc., %			Yield, % (method)
					C	H	N	C	H	N	
Ia	Oil	—	—	$C_{15}H_{11}N_3O$	—	—	16,5	—	—	16,8	25 (A)
Ib	139—142	242 285 331	4,37 4,50 4,18	$C_{19}H_{13}N_3O_2$	72,7	4,5	13,8	72,4	4,2	13,3	10 (B)
Ic	230—231	242 294 335	4,05 4,31 4,05	$C_{14}H_8BrN_3O$	53,3	3,1	13,5	53,5	2,6	13,4	13 (B) 56 (C)
Id	175—176	244 291 340	4,05 4,22 4,05	$C_{15}H_{10}BrN_3O$	54,0	3,6	12,4	54,4	3,4	12,7	27 (A)
Ie	170—174	241 291 333	4,61 4,63 4,42	$C_{19}H_{11}Br_2N_3O_2$	48,4	2,8	8,7	48,2	2,4	8,8	14*(B)
If	234—235	235 273 377	4,26 4,23 4,10	$C_{15}H_{10}N_4O_3$	61,0	3,9	18,7	61,1	3,8	18,9	25 (A) 75 (C) 17
IIa	204—205	251 311 357	4,28 4,38 4,72	$C_{16}H_{11}N_3O$	72,9	4,6	16,2	73,1	4,2	16,0	40 (C) 23 67 (B)
IIb	Oil	—	—	$C_{17}H_{13}N_3O$	—	—	15,0	—	—	15,2	23 (A)
IIc	192—198	259 310 365	4,44 4,21 4,33	$C_{23}H_{17}N_3O_2$	75,3	4,6	12,2	75,2	4,7	11,7	12 (A)
IId	143—145	247 294 350	4,35 4,39 4,32	$C_{17}H_{12}N_3O$	57,2	3,6	12,1	57,4	3,7	11,8	18 (A)
IIe	248—250	246 294 404	4,26 4,10 4,16	$C_{17}H_{12}N_4O_3$	63,3	4,3	17,6	63,5	4,1	17,4	24 (A) 62 (C) 15
IIf*	218—220	251 280 385	4,02 3,81 4,23	$C_{18}H_{13}N_3O_2$	71,0	4,6	13,8	17,2	4,3	13,9	13

* The 2,4-dinitrophenylhydrazone had mp 350° (dec.).

ucts. Thus, for example, methylation of IIa with methyl iodide gives a mixture of 1- and 3-isomers; the 3-isomer (IIb), which was isolated by chromatography, is formed in greater amounts.

In contrast to Ia, IIa is acetylated in the α position of the furan ring [6] to give methyl ketone IIf.

Direct nitration [6] of IIb gives IIe in a yield of only 14%. Under these conditions, Ia is not nitrated.

Replacement of the bromine atom by a nitro group, which proceeds smoothly in a number of other halofurylimidazoles [5-7], proceeds with difficulty in Id and IId to give nitro derivatives If and IIe in yields of only 17 and 15%, respectively.

EXPERIMENTAL

3-Methyl-2-(2-furyl)imidazo[4,5-*f*]quinoline (Ia). A. A mixture of 1.79 g (0.01 mole) of 5-amino-6-methylaminoquinoline, 0.96 g (0.01 mole) of furfural, 20 ml of dimethylformamide, and two to three drops of piperidine was refluxed for 1 h. It was then cooled and treated with 50 ml of water, and the precipitate was separated from it by flow chromatography with aluminum oxide as the adsorbent and chloroform as the solvent to give Ia.

Compounds Id, If, IIb, IId, and IIe (see Table 1) were similarly obtained.

2-(5-Bromo-2-furyl)imidazo[4,5-*f*]quinoline (Ic). B. A solution of 3.5 g (0.02 mole) of 5-bromofurfural in 10 ml of ethanol was added to a solution of 4.64 g (0.02 mole) of 5,6-diaminoquinoline dihydrochloride in 30 ml of ethanol, and 8 g (0.04 mole) of copper acetate in 200 ml of water was then added to the mixture, after which it was refluxed for 2 h. It was then cooled, and the precipitated copper salt of Ic was removed by filtration and suspended in 200 ml of ethanol. A strong stream of hydrogen sulfide was passed through the suspension. The hydrogen sulfide was then removed by boiling, and the copper sulfide was removed by filtration. The filtrate was diluted to twice its volume with water and neutralized to pH 7 with 10% sodium carbonate solution. The precipitate was separated and dissolved in chloroform, and Ic was isolated by passage of the solution through a column filled with aluminum oxide.

Compounds Ib,e and IIa (see Table 1) were similarly obtained.

3-Methyl-2-(5-nitro-2-furyl)imidazo[4,5-*f*]quinoline (If). C. A mixture of 2.45 g (0.01 mole) of 5-amino-6-methylaminoquinoline dihydrochloride, 2.2 g (0.01 mole) of the hydrochloride of the ethyl imino ester of 5-nitrofuran-2-carboxylic acid, and 50 ml of absolute methanol was refluxed for 1 h, after which it was cooled and treated with an equal volume of water. The precipitate was removed by filtration, and If was isolated by chromatography.

Compounds Ic, IIa, and IIe (see Table 1) were similarly obtained.

The UV spectra of methanol solutions of the compounds were recorded with an SF-4A spectrophotometer.

LITERATURE CITED

1. F. T. Pozharskii, V. Ts. Bukhaeva, A. M. Simonov, L. Ya. Bakhmet, and O. M. Aleksan'yan, Khim. Geterotskikl. Soedin., 325 (1969).
2. D. Jerchel, H. Fischer, and M. Kracht, Ann., 575, 162 (1952).
3. F. T. Pozharskii and L. Ya. Oleinikova, Khim. Geterotsikl. Soedin., 1425 (1971).
4. P. M. G. Bavin, J. Med. Chem., 9, 788 (1966).
5. F. T. Pozharskii, L. Ya. Oleinikova, and L. G. Pupkova, Khim. Geterotsikl. Soedin., 1014 (1971).
6. L. Ya. Bakhmet and F. T. Pozharskii, Khim. Geterotsikl. Soedin., 832 (1970).
7. F. T. Pozharskii, V. Ts. Bukhaeva, A. M. Simonov, and R. A. Savel'eva, Khim. Geterotsikl. Soedin., 183 (1969).