SYNTHESIS OF CONDENSED PYRIMIDINE SYSTEMS BASED ON 2,4,6-TRIPHENYLPYRYLIUM PERCHLORATE

É. A. Zvezdina, M. P. Zhdanova, A. M. Simonov, and G. N. Dorofeenko

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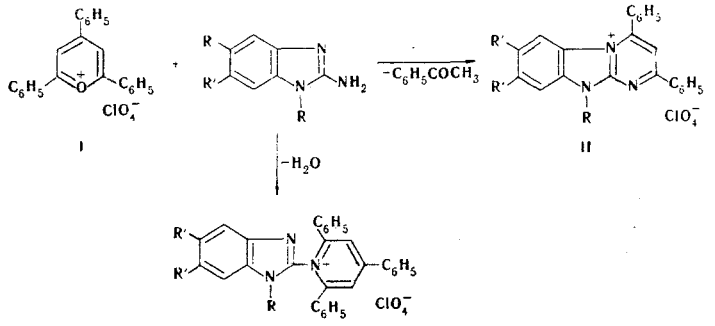
1,3-Diphenylpyrimido[1,2-a]benzimidazolium perchlorates were obtained by reaction of 2,4,6-triphenylpyrylium perchlorate with 2-aminobenzimidazoles.

The reaction of unsubstituted 2-aminobenzimidazole with β-diketones, which gives pyrimido[1,2]-benzimidazoles, has been studied by many investigators [1], but 2-aminobenzimidazole with a methyl or phenyl substituent attached to the nitrogen atom was subjected to reaction with acetylacetone only recently [2].

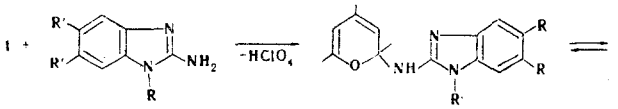
We have found that 1,3-diphenylpyrimido[1,2-a]benzimidazolium perchlorates (II) are formed in the reaction of 1-substituted 2-aminobenzomidazoles with 2,4-6-triphenylpyrylium perchlorate (I):



II a R=CH_3, R′=H; b R=C_2H_5, R′=H; c R=*n*-C_3H_7, R′=H; d R=$CH_2C_6H_5$, R′=H; e R=C_9H_{19}, R′=H; f R=R′=CH_3; V a R=CH_3, R′=H; b R=C_2H_5, R′=H; c R=R′=H

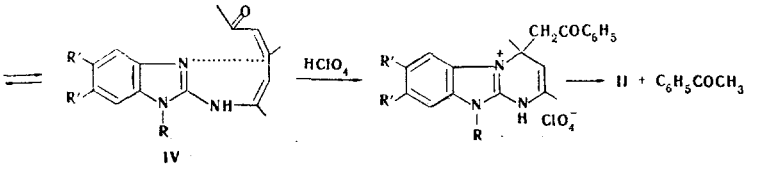
It is known [3, 4] that pyrylium salts are converted to pyrydinium salts under the influence of primary aliphatic, aromatic, and some heterocyclic amines. The conversion of pyrylium salt to pyrimidine systems by reaction with heterocyclic amines has remained unknown up until now.

The reaction probably commences with attack on the α position of the pyrylium ring by the amino group to give a substituted α-pyran (III), which is in equilibrium with its open form (IV). The pyridine nitrogen atom of the benzimidazole fragment in IV subsequently reacts with the carbon atom of the side chain to give a pyrimidinium ring:



III

Scientific-Research Institute of Physical and Organic Chemistry, Rostov State University. Scientific-Research Institute of Biology, Rostov State University, Rostov-on-Don. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1180-1183, September, 1975. Original article submitted July 15, 1974.



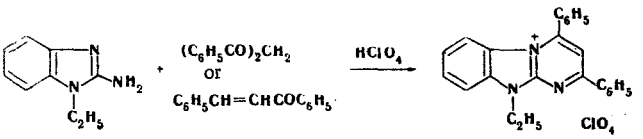
IV

A similar mechanism is known for the reactions of pyrylium salts with hydrazine, phenylhydrazine, and hydroxylamine, as a result of which pyrazoles and isoxazoles are formed [5, 6].

The formation of N-(2-benzimidazolyl)-2,4,6-triphenylpyridinium perchlorates (V) in 36 and 32% yields, respectively, is also observed for 1-methyl(or 1-ethyl)-2-aminobenzimidazoles, along with the formation of the above-examined perchlorates II [7]. The formation of pyrimidine derivatives in yields close to quantitative is preferable for aminobenzimidazoles with other substituents.

The effect of substituent R in the 2-aminobenzimidazoles may be due to two reasons. 1. These substituents may create steric hindrance to reaction of the NH group with the carbonyl group in ketone IV. In fact, the reaction with unsubstituted 2-aminobenzimidazole proceeds primarily with the formation of perchlorate Vc, and 1,3-diphenylpyrimido[1,2-a]benzimidazole is formed in only 16% yield. The analogous pyrimidinium system is not formed at all in the case of the reaction of 2-aminopyridine, which does not contain substituents adjacent to the amino group, with perchlorate I. 2. Owing to the +I effect of substituent R, the basicity of the pyridine nitrogen atom may increase to a certain degree, and alkylation of this atom will be facilitated. This is evidently the reason that 1,5,6-trimethyl-2-aminobenzimidazole (pK_a 16.88) forms exclusively a pyrimidine derivative, in contrast to 1-methyl-2-aminobenzimidazole (pK_a 16.20).*

The structures of the compounds obtained were confirmed by alternative syntheses. 1,3-Diphenyl-5-ethylpyrimido[1,2-a]benzimidazolium perchlorate, identical to IIb, was obtained in 6.2% yield by reaction of 1-ethyl-2-aminobenzimidazole with dibenzoylmethane in the presence of 70% perchloric acid, and the same compound was obtained in 13.3% yield by reaction with benzalacetophenone:



IIb

1,5,6-Trimethyl-2-aminobenzimidazole reacts with dibenzoylmethane to give perchlorate IIf in 13% yield.

In order to confirm the II structure, we compared the PMR spectra of IIf and N-(1,5,6-trimethyl-2-benzimidazolyl)-2,4,6-triphenylpyridinium perchlorate (Vd), the structure of which was proved in [8]. Because of the possibility of free rotation about the $C-\overset{+}{N}\leqslant$ bond, the two C-methyl groups give one signal at 1.98 ppm in the spectrum of Vd, and the integral area of the peak is twice the area of the peak at 3.33 ppm (the signal of the $N-CH_3$ group). The spectrum of IIf contains three signals of equal intensity, disregarding those due to the presence of aromatic protons – 3.84 ppm (CH_3 group bonded to the N atom) and 2.06 ppm and 1.79 ppm (two CH_3 groups of the benzene ring). Thus, as expected, the $N-CH_3$ group in structure IIf has a large chemical shift, and this is associated with the high degree of anisotropy of the molecule. The $C-CH_3$ groups in IIf are chemically nonequivalent for the same reason.

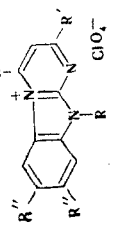
2,4,6-Trimethylpyrylium perchlorate does not form pyrimidine structures with 2-aminobenzimidazoles but is converted via splitting out of perchloric acid to a methylenepyran hexamer [7]. Pyrimido-[1,2-a]benzimidazolium perchlorates with methyl substituents in the 1 and 3 positions (VIa-d) are obtained only in the reaction of 1-substituted 2-aminobenzimidazoles with acetylacetone in the presence of 70% perchloric acid.

EXPERIMENTAL

The pK_a values were measured by potentiometric titration in absolute acetonitrile at 25 ± 0.1°C. The PMR spectra of trifluoroacetic acid solutions of the compounds were obtained with a BS-487c spectrome-

*The basicity constants were measured by our senior scientific co-worker V. A. Bren'.

TABLE 1. Pyrimido[1,2-a]benzimidazolium Perchlorates



Compound	R	R′,R″	mp, °C (from glacial acetic acid)	Empirical formula	Found, %				Calc., %				Yield, %	
					C	H	Cl	N	C	H	Cl	N	with I	with diketone
VIa	CH_3	CH_3	228—229[a]	$C_{13}H_{14}ClN_3O_4$	50,1	4,8	10,9	13,7	50,1	4,5	11,4	13,5	—	88,2
VIb	C_2H_5	CH_3	222	$C_{14}H_{16}ClN_3O_4$	52,0	5,4	10,9	13,1	51,6	5,0	10,9	12,9	—	63,0
VIc	$CH_2C_6H_5$	CH_3	245 [b]	$C_{19}H_{18}ClN_3O_4$	59,2	4,9	8,8	10,6	58,8	4,7	9,1	10,8	—	48,0
VId	C_9H_{19}	CH_3	138—139	$C_{23}H_{30}ClN_3O_4$	59,1	7,2	8,5	9,9	59,5	7,1	8,4	9,9	—	17,0
IIa	CH_3	C_6H_5	279—281	$C_{23}H_{18}ClN_3O_4$	63,7	4,6	7,9	10,1	63,4	4,2	8,1	9,6	46,0	—
IIb	C_2H_5	C_6H_5	282[c]	$C_{24}H_{20}ClN_3O_4$	63,7	4,9	7,7	9,4	64,1	4,5	7,9	9,3	46,7	6,2
IIc	n-C_3H_7	C_6H_5	268—270	$C_{25}H_{22}ClN_3O_4$	64,3	5,1	7,2	8,6	64,7	4,8	7,6	9,1	86,2	—
IId	$CH_2C_6H_5$	C_6H_5	294—295	$C_{29}H_{22}ClN_3O_4$	67,8	4,3	6,9	8,0	68,0	4,3	6,9	8,2	96,0	—
IIe	C_9H_{19}	C_6H_5	187	$C_{31}H_{34}ClN_3O_4$	67,9	6,2	6,6	7,7	67,9	6,3	6,5	7,7	84,0	—
IIf	CH_3	C_6H_5	270	$C_{25}H_{22}ClN_3O_4$	64,8	4,9	8,0	9,2	64,7	4,8	7,6	9,1	92,5	13,0

[a] R″ = H; for IIf, R″ = CH_3.
[b] From methanol.
[c] From nitromethane.

eter (80 MHz) with hexamethyldisiloxane as the internal standard.

1,3-Diphenyl-5-ethylpyrimido[1,2-a]benzimidazolium perchlorate (IIb). A) A 0.82-g (2.0 mmole) sample of perchlorate I was refluxed with 0.38 g (2.4 mmole) of 1-ethyl-2-aminobenzimidazole in 4 ml of absolute dimethylformamide (DMF) for 1 h, after which the mixture was cooled, water was added, and the yellow precipitate was separated, washed with water and ether, dried, and treated with 5 ml of hot ethanol. The insoluble material was removed by filtration and washed with a small amount of hot alcohol to give 0.42 g (46.7%) of bright-yellow perchlorate IIb with mp 282° (from nitromethane). Cooling of the ethanol solution precipitated 0.36 g (32.4%) perchlorate Vb [7].

B) A mixture of 1-ethyl-2-aminobenzimidazole, dibenzoylmethane, and 70% $HClO_4$ in a ratio of 1:2:1 was refluxed for 2 h in absolute DMF. It was then cooled, and water was added to give an oil that gradually crystallized. The precipitate was removed by filtration, washed with ethanol and ether, and dried. The yield of perchlorate IIb was 6.2%.

C) An equimolar mixture of 1-ethyl-2-aminobenzimidazole and benzalacetophenone was refluxed for 3 h in absolute DMF, after which it was cooled, an equimolar amount of 70% $HClO_4$ was added, and the mixture was refluxed for another 15 min. It was then cooled and treated with water to give an oil that solidified on trituration with water and ether. The yield of perchlorate IIb was 13.3%.

1,3-Diphenyl-5,7,8-trimethylpyrimido[1,2-a]-benzimidazolium Perchlorate (IIf). A 0.82-g (2.0 mmole) sample of perchlorate I was refluxed with 0.42 g (2.4 mmole) of 1,5,6-trimethyl-2-aminobenzimidazole in 4 ml of absolute DMF for 1 h, after which the mixture was cooled and treated with ether to give an oil that crystallized on washing with ether. The solid was purified by recrystallization from glacial acetic acid to give 0.86 g (92.2%) of a product with mp 270°.

1,3-Dimethyl-5-ethylpyrimido[1,2-a]benzimidazolium Perchlorate. A mixture of 1-ethyl-2-aminobenzimidazole, acetylacetone, and 70% $HClO_4$ in a molar ratio of 1:2:1 was refluxed for 1 h in glacial acetic acid, after which it was cooled, and the resulting precipitate was removed by filtration. An additional amount of a substance with mp 222° (from glacial acetic acid) was precipitated from the filtrate by the addition of ether to give an overall yield of 63%.

Reaction of Perchlorate I with 2-Aminobenzimidazole. A 0.82-g (2.0 mmole) sample of perchlorate I was refluxed with 0.34 g (2.4 mmole) of 2-aminobenzimidazole in 4 ml of absolute DMF for 1 h, after which it was cooled to precipitate 0.1 g (16%) of 1,3-

diphenylpyrimido[1,2-a]benzimidazole with mp 311° (mp 312-315° [1]). The addition of ether to the filtrate liberated an oil that solidified on trituration with water to give 0.77 g (73.3%) of N-(2-benzimidazolyl)-2,4,6-triphenylpyridinium perchlorate with mp 255° (from nitromethane) (mp 255° [8]).

Data on the synthesized pyrimido[1,2-a]benzimidazolium perchlorates are presented in Table 1.

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