CONDENSED IMIDAZO-1,2,4-AZINES.

21.* SYNTHESIS OF 2-ARYLFURO(PYRROLO-, THIENO-)[2,3-e]-1,2,4-TRIAZINO[2,3-a]BENZIMIDAZOLES BY CYCLIZATION OF 2-AROYL-1,2,4-TRIAZINO[2,3-a]BENZIMIDAZOL-4H-3-ONES

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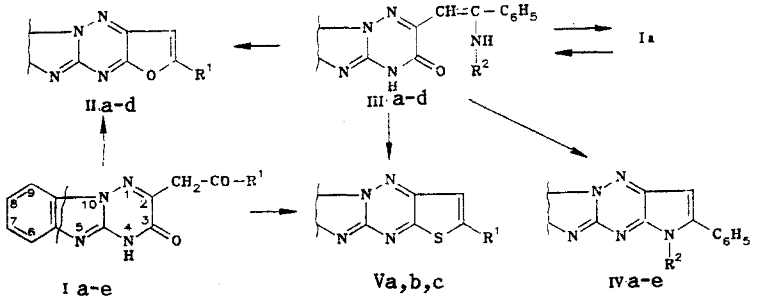
2-[(β-Ethyl-, arylimino)phenethyl]-1,2,4-triazino[2,3-a]benzimidazoles were obtained by reaction of 2-aroylmethyl-1,2,4-triazino[2,3-a]benzimidazol-4H-3-ones with ethyl(aryl)amines or urea. By the action of phosphorus oxychloride, these benzimidazoles cyclize into substituted pyrrolo[2,3-e]-1,2,4-triazino[2,3-a]benzimidazoles, heating of which in polyphosphoric acid leads to the formation of furo[2,3-e]-1,2,4-triazino[2,3-a]benzimidazoles, while by the action of P_4S_{10}, they are transformed into thieno[2,3-e]-1,2,4-triazino[2,3-a]benzimidazoles.

We have already reported [2] that 2-phenylfuro[2,3-e]-1,2,4-triazino[2,3-a]benzimidazole (IIa) is formed by boiling 2-benzoylmethyl-1,2,4-triazino[2,3-a]benzimidazol-4H-3-one (Ia) in phosphorus oxychloride with PCl_5. Extending the research in this direction, in order to synthesize new luminescing heterocyclic compounds, we studied the reaction of aroylmethyl derivatives Ia-d with ethyl(aryl)amines, urea, and phosphorus pentasulfide.

It was found that boiling of ketone Ia with ethylamine leads to the formation of 2-[(β-ethylimino)phenethyl]-1,2,4-triazino[2,3-a]benzimidazol-4H-3-one (IIIa). More rigorous conditions are required when aromatic amines are used in this reaction. Thus an attempt to obtain compound IIIb by boiling the starting compounds in alcohols, CH_3COOH, DMFA were unsuccessful, while on heating ketone Ia with 4-methylaniline in phenol, a compound was isolated in a poor yield, which differs in its physicochemical properties from IIIc and is identical with 1-(4-methylphenyl)-2-phenylpyrrolo[2,3-e]-1,2,4-triazino[2,3-a]benzimidazole (IVc). Compounds IIIb-d were obtained in good yield (Table 1) by boiling ketone Ia in an excess of the corresponding aromatic amines.



I, II, V a $R^1=C_6H_5$, b $R^1=p\text{-}CH_3C_6H_4$, c $R^1=p\text{-}BrC_6H_4$, d $R^1=p\text{-}ClC_6H_4$, e $R^1=p\text{-}CH_3OC_6H_4$;
III, IV a $R^2=C_2H_5$, b $R^2=C_6H_5$, c $R^2=p\text{-}CH_3C_6H_4$, d $R^2=m\text{-}CH_3C_6H_4$, e $R^2=H$

In the IR spectra of the tricyclic compounds IIIa-d, the stretching vibrations band of the C=O group of the benzoylmethyl substituent (1670-1690 cm^{-1}) disappears [3], and the band of the amide carbonyl in the triazine ring (1640-1655 cm^{-1}) is retained, while the

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*For Communication 20, see [1].

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TABLE 1. Characteristics of Compounds II-V

Compound	Empirical formula	mp, °C*	UV spectrum, λ_{max}, nm (log ε)**	Yield, %
IIb	$C_{18}H_{12}N_4O$	345...346	291 (4,02), 392 (4,03)	83
IIc	$C_{17}H_9BrN_4O$	>350	295 (4,30), 390 (4,38)	74
IId	$C_{17}H_9ClN_4O$	>350	295 (4,32), 390 (4,36)	77
IIIa	$C_{19}H_{17}N_5O$	274...276	270 (4,08), 405 (4,24)	67
IIIb	$C_{23}H_{17}N_5O$	306...307	290 (4,07), 415 (4,11)	83
IIIc	$C_{24}H_{19}N_5O$	313...314	280 (4,07), 415 (4,13)	89
IIId	$C_{24}H_{19}N_5O$	308...309	265 (4,17), 420 (4,24)	83
IIIe	$C_{17}H_{13}N_5O$	>350	265 (3,98), 400 (4,12)	79
IVa	$C_{19}H_{15}N_5$	190...191	290 (4,73), 375 (4,75)	53
IVb	$C_{23}H_{15}N_5$	302...303	290 (4,42), 380 (4,11)	73
IVc	$C_{24}H_{17}N_5$	283...284	290 (4,22), 380 (3,88)	69
IVd	$C_{24}H_{17}N_5$	272...273	290 (4,45), 380 (4,11)	66
IVe	$C_{17}H_{11}N_5$	320...322	280 (4,51), 380 (4,31)	47
Va	$C_{17}H_{10}N_4S$	279...280	300 (4,48), 395 (4,13)	84
Vb	$C_{18}H_{12}N_4S$	298...299	305 (4,58), 405 (4,24)	89
Vc	$C_{18}H_{12}N_4OS$	283...284	315 (4,82), 410 (4,58)	85

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*Compounds IIb-d, IIIb-d, IVb-e, and Va, b, e were purified by recrystallization from DMFA; IIIa, e – from butanol, IV – from methanol.

**The spectra of compounds IIIa-e, IVa, IVe were run in dioxane, IIb-d, IVb-d, Va, b, e – in DMFA; c = (3-6)·10^{-5} mole/liter.

stretching vibration band of the NH bond lies in the 3080-3105 cm^{-1} region. The characteristic feature of the absorption spectra of compounds IIIa-d compared with the spectra of the aroylmethyl derivatives Ia-d (Table 1) is the bathochromic shift of the two absorption bands, which indicates elongation of the principal chromophore system due to inclusion of a substituent at the $C_{(2)}$ atom in the π-electronic system of triazinobenzimidazoles IIIa-d.

In the mass spectrum of compound IIIc (Table 2), a peak is recorded of the molecular ion M^+ with m/z 393. The maximally intense peak with m/z 194 (100) corresponds to to the structure $[C_6H_5{=}N{-}C_6H_4{-}CH_3]^+$ (a β-cleavage with respect to the heteroaryl ring) and together with ions having m/z 77 – $[C_6H_5]^+$, 91 – $[C_6H_4CH_3]^+$ – tropylium cation, confirms the structure of the substituent at the $C_{(2)}$ atom and proves the existence of compound IIIc in the imine form. The fragmentary ions with m/z 160, 233, 234, which are formed due to the cleavage of the "weak" $N_{(1)}{-}N_{(10)}$ and $C_{(2)}{-}C_{(3)}$ bonds [3] are important from the structural point of view. The occurrence of ions with m/z 160 and 233 is accompanied by migration of the hydrogen atom (probably from the methylene group) to the carbonyl group. Further dissociation of the ion with m/z 160 proceeds with subsequent elimination of the COH particles (m/z 131), HCN (m/z 104). The observed splitting of water from M^+ (m/z 375) presumes an enolization of the triazine fragment of the molecule of IIIc, followed by cyclization with the participation of the phenyl ring (a stable six-membered ring is formed). The realization of this process is determined by the ortho-effect phenomenon.

Examination of the cyclization of triazinobenzimidazoles IIIa-d showed that the direction of the reaction is dependent on the nature of the cyclizing agent and the structure of the substrate itself. Thus, boiling of compounds IIIa-d in acetic acid is accompanied by hydrolysis of the imine residue of the tricyclic compound IIIa-d with the formation of a benzoylmethyl derivative Ia, whereby the hydrolysis of the ethylimino-substituted derivative IIIa proceeds more rapidly (chromatographic control) than of its arylimine analogs IIIb-d. Heating of compounds IIIa, b at 110-120°C in polyphosphoric acid (PPA) is accompanied by the formation of benzimidazole IIa [2] and the corresponding arylamine in a high yield. When the tricyclic compounds IIIa-d were boiled in $POCl_3$ or thionyl chloride, representatives of a new heterocyclic system were isolated – substituted pyrrolo[2.3-e]-1,2,4-triazino[2,3-a]benzimidazoles IVa-d.

It was shown in [4] that ω-(2-quinoxalon-3-yl)acetophenones, when reacted with urea, cyclize into pyrrolo[2,3-b]quinoxalines. We were unable to obtain pyrrolo[2,3-e]-1,2,4-triazino[2,3-e]benzimidazole IVe by heating compound Ia with urea in phenol. Instead, derivative IIIe was isolated from the reaction mixture. In its IR spectrum, the absorption

TABLE 2. Mass Spectra of Synthesized Compounds IIIc, e, IVb, c, Va

Compound	m/z (peak intensity in % of maximal)*
IIIc	394 (31), 393 (99), 392 (12), 376 (16), 375 (56), 374 (12), 234 (23), 233 (56), 208 (12), 207 (16), 195 (26), 194 (100), 160 (27), 133 (35), 131 (19), 105 (14), 104 (50), 91 (68), 90 (16), 77 (35), 65 (33)
IIIe	304 (23), 303 (100), 285 (10), 275 (16), 171 (10), 160 (10), 159 (16), 145 (12), 144 (13), 131 (10), 117 (11), 105 (12), 104 (33), 90 (12), 77 (29), 51 (11)
IVb	362 (26), 361 (100), 360 (52), 180 (18), 143 (10), 102 (10), 90 (12), 77 (50), 51 (17)
IVc	376 (29), 375 (100), 374 (14), 284 (15), 194 (21), 187,5 (11), 116 (12), 103 (26), 102 (32), 91 (60), 90 (15), 77 (42), 63 (10)
Va	303 (23), 302 (100), 301 (16), 151 (15), 143 (10), 102 (10), 91 (13), 90 (10), 77 (32), 51 (23)

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*Ion peaks with intensity of ≥ 10% are given.

of the carbonyl group of the benzoylmethyl substituent is absent, but as in the initial tricyclic compound Ia, a stretching vibrations band of the amide carbonyl at 1630 cm^{-1} is observed. The UV spectrum of compound IIIe is identical with the spectra of its analogs IIIa-d (Table 1).

In the mass spectrum of compound IIIe a peak of M^+ with m/z 303 (100) is recorded (Table 2). In the mass spectrum of compound IIIe, as for compound IIIc, ion peaks are observed due to a β-cleavage relative to the heteroaryl part of the molecule (an ion with m/z 104 – $[HN{-}CPh]^+$) and also of ions with m/z 144 and 160, due to the cleavage of the $N_{(1)}{-}N_{(10)}$ and $C_{(2)}{-}C_{(3)}$ bonds in the triazine ring. In analogy with IIIc, the elimination of the water molecule is observed (m/z 285). The new path of the fragmentation is caused by the contraction of the triazine ring to a triazole ring due to the elimination of CO from the M^+ (m/z 275) with subsequent splitting of the $[NH{=}C{-}Ph]^+$ particle (m/z 171).

On boiling in $POCl_3$, compound IIIe is dehydrated and 1-H-2-phenylfuro[2,3-e]-1,2,4-triazino[2.3-a]benzimidazole (IVe) is formed, the absorption spectrum of which differs from the spectrum of compound IIIe by a bathochromic shift of the short-wave (15 nm) and hypsochromic shift (20 nm) of the long-wave absorption bands. The same effect is observed when the spectra of imines IIIa-d are compared with the spectra of their cyclization products IVa-d. This shows that the same type of chromophoric system corresponds to the acyclic compounds (IIIa-e) and the cyclization products (IVa-e).

To synthesize the new derivatives of 1,2,4-triazinobenzimidazoles we have also carried out the reaction of 2-aroylmethyl derivatives Ia, b, e and ketimine IIIb with P_4S_{10}. It was found that when the starting components are boiled in pyridine or dioxane with P_4S_{10}, a single reaction path is obtained leading to the previously unknown 2-arylthieno[2,3-e]-1,2,4-triazinobenzimidazoles Va, b, e.

In the mass spectra of compounds IIa, IVa, c, Va (the mass spectrum of compound IIa is given in [2]) the course of the dissociation of M^+ confirms their structure. In all the spectra indications are observed of mass-spectrometric fragmentation of compounds with a diphenyl type of structure [5]. In the mass spectra of compounds IVb, ions are seen which characterize the R^2 substituent ($[C_6H_5]^+$ and $[CH_3C_6H_4]^+$) and also ions with m/z 102 – $[C_6H_5C{\equiv}CH]^+$ and 180.194 – $[R^2N{=}CC_6H_5]^+$, respectively for heterocycles IVb and IVc. The appearance of these ions indicates the position of the substituents in the pyrrole fragment of the molecule.

Thus, through the examination of the cyclization of 2-aroylmethyl-1,2,4-triazino[2,3-a]benzimidazol-4H-3-ones, for the first time the possibility was shown of the annelation of the furan, thiophene, and pyrrole rings to the 1,2,4-triazino[2,3-a]benzimidazole fragment.

EXPERIMENTAL

The IR spectra were measured on a UR-20 spectrophotometer in KBr tablets and the electronic spectra in solutions (Table 1) on an SF-46 spectrophotometer. The mass spectra were recorded on a "Varian MAT-311A" spectrometer under standard conditions [2] (ionizing voltage

70 eV). The individual state of the compounds and the composition of the reaction mixtures was monitored by the TLC method on Silufol-254 plates, using an isopropanol—toluene (1:2) mixture as eluent.

The characteristics of the synthesized compounds are given in Tables 1 and 2. The data of the elemental analysis for C, H, and N correspond to the calculated data.

2-Arylfuro[2,3-e]-1,2,4-triazino[2,3-a]benzimidazoles (IIb-d). A. A 2 mmole portion of the corresponding 2-aroylmethyl-1,2,4-triazino[2,3-a]benzimidazol-4H-3-one [Ib-d] [3] in 10 ml of PPA is heated for 2 h at 110-120°C. The cooled reaction mixture is poured with stirring into 100 ml of ice water, the precipitate is filtered off and washed successively with water, 5% $NaHCO_3$ solution, and water again, and dried.

B. A 0.76 g portion (2 mmoles) of compound IIIb in 10 ml of PPA is heated for 2 h at 110-120°C. The reaction mixture is treated in a similar way as under A. Compound IIb is obtained in a yield of 0.45 g (78%).

2-[(β-Ethylimino)phenethyl]-1,2,4-triazino[2,3-a]benzimidazol-4H-3-one (IIIa). A mixture of 0.61 g (2 mmoles) of compound Ia, 0.33 g (4 mmoles) of ethylamine hydrochloride and 0.16 g (1.5 mmole) of Na_2CO_3 in 40 ml of butanol is boiled for 5 h. After cooling, the precipitate consisting of inorganic compounds is filtered off, and the filtrate is concentrated in vacuo to a volume of 7 ml. The precipitate is filtered off, washed with alcohol, water and dried.

2-[(β-Arylimino)phenethyl]1,2,4-triazino[2,3-a]benzimidazol-4H-3-ones (IIIb-d). A 0.61 g portion (2 mmoles) of compound Ia in 5.4-7.5 g (50-70 mmoles) of the corresponding arylamine is heated in the presence of a catalytic amount of hydrochloric acid for 4 h at 130-140°C. The cooled solution is diluted with a 4-5 volume of ether, the precipitate is filtered off, washed with ethanol, and dried.

Substituted 2-phenylpyrrolo[2,3-e]-1,2,4-triazino[2,3-a]benzimidazoles (IVa-e). A solution of 3 mmoles of the corresponding compound IIIa-e in 15 ml of phosphorus oxychloride is boiled for 3 h. Three fourths of the $POCl_3$ volume is distilled in vacuo, and the residue is poured with stirring onto 75 g of ice, the precipitate is filtered off, washed with water, 5% $NaHCO_3$ solution, water, and dried.

2-[(β-Imino)phenethyl]-1,2,4-triazino[2,3-a]benzimidazol-4H-3-one (IIIe). A solution of 0.61 g (2 mmoles) of compound Ia and 0.33 g (4 mmoles) of urea in 5-6 ml of phenol is heated in the presence of a catalytic amount of hydrochloric acid for 4 h. The solution is cooled to 20°C and is then diluted with a 5-fold volume of ether, the precipitate is filtered off, washed with alcohol, 5% KOH solution, water, and dried.

2-Arylthieno[2,3-e]-1,2,4-triazino[2,3-a]benzimidazoles (Va, b, e). A. A 0.67 g portion (3 mmoles) of P_4S_{10} is added to a solution of the corresponding compound Ia, b, e in 12 ml of anhydrous pyridine, and the mixture is boiled for 4 h. The reaction mixture is cooled, poured with stirring into 100 ml of water, the precipitate is filtered off, washed with water, alcohol, and dried.

B. A 0.76 g portion (2 mmoles) of P_4S_{10} is added to a solution of 0.76 g (2 mmoles) of compound IIIb in 20 ml of dioxane, and the mixture is boiled for 5 h. The reaction mixture is treated in a similar way as under A. Yield of compound Va, 0.47 g (79%).

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