

BENZAZOLYLMETHYLHETEROARYLAMINES

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Recently, Katritzky and coworkers¹⁻³ in a series of papers described preparation of various 1-(1-aryl/alkylaminoalkyl)benzotriazoles by reaction of benzotriazole, an aliphatic aldehyde (or the product of their reaction – 1-(1-hydroxyalkyl)benzotriazole) and an amine in ethanol. In some cases the formation of 1-bis(1-benzotriazolyl-alkyl)aryl/alkylamines was also observed^{2,3}.

The aim of our study was to compare the reactivity of 2-, 3- and 4-aminopyridine in the reaction with 1-hydroxymethylbenzotriazole, and to find out whether and under which conditions also 1-hydroxymethylbenzimidazole enters an analogous reaction. We further studied the reaction of these two compounds with 5-amino-1-arylbenzazoles and the structure of the products.

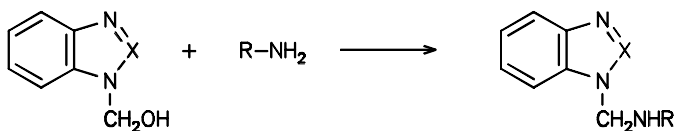
1-Hydroxymethylbenzimidazole⁴ and 1-hydroxymethylbenzotriazole⁵ were prepared by reaction of benzimidazole and benzotriazole, respectively, with formaldehyde in 50% methanol or dilute acetic acid. The preparation of 5-amino-1-arylbenzazoles was described elsewhere⁶.

The formation of the benzotriazole derivatives was generally faster and the product often crystallized upon warming the reaction components; on the other hand, the benzimidazole derivatives were less soluble and one cannot therefore compare the reactivity of the triazole and imidazole derivative on the basis of reaction yields. Similar situation was also in the case of variously substituted aminopyridines.

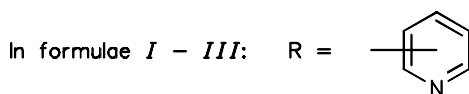
In all cases we observed the formation of only monosubstituted derivatives and no bis-product^{2,3} was detected. The lower yields of compounds *Ib* and *IIIb* than those reported¹ are apparently due to a different isolation procedure.

The UV spectra of compounds *I – III* exhibit absorption maximum at about 280 nm ascribable to the benzotriazole chromophore: this assignment is supported by the fact that intensity of this band increases upon attachment of arylbenzazolylaminomethyl chromophore. The introduction of the arylbenzazolylaminomethyl or pyridylaminomethyl substituent into the position 1 of the benzotriazole nucleus (and not into the position 2) is evident from ¹H NMR spectra¹. Whereas the CH₂ signals in the spectra of benzimidazoles appear at 5.2 – 5.9 ppm, in the spectra of benzotriazoles they are

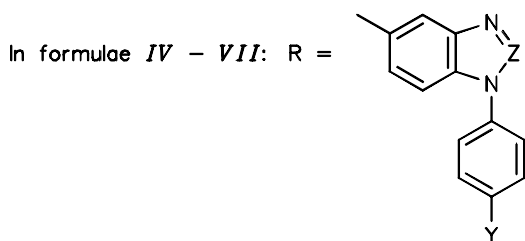
shifted downfield for 0.4 – 1.0 ppm. The infrared spectra exhibit bands due to NH vibrations at about $3\ 300\text{ cm}^{-1}$.



I - VII



	X	R
<i>Ia</i>	CH	2-pyridyl
<i>Ib</i>	N	2-pyridyl
<i>IIa</i>	CH	3-pyridyl
<i>IIb</i>	N	3-pyridyl
<i>IIIa</i>	CH	4-pyridyl
<i>IIIb</i>	N	4-pyridyl



	X	Z	Y
<i>IVa</i>	CH	N	Me
<i>IVb</i>	N	N	Me
<i>Va</i>	CH	CH	Me
<i>Vb</i>	N	CH	Me
<i>VIa</i>	CH	CH	Cl
<i>VIb</i>	N	CH	Cl
<i>VIIa</i>	CH	CH	Br
<i>VIIb</i>	N	CH	Br

TABLE I
Physicochemical data of compounds I – VII

Compound	Formula (M.w.)	M.p., °C (Yield, %)	Calculated/Found			
			% C	% H	% N	% Hal
<i>Ia</i>	C ₁₃ H ₁₂ N ₄ (224.3)	194 – 195 (72)	69.62 69.48	5.39 5.26	24.98 25.11	–
<i>Ib^a</i>	C ₁₂ H ₁₁ N ₅ (225.3)	137 – 138 (76)	63.99 –	4.92 –	31.09 –	–
<i>IIa</i>	C ₁₃ H ₁₂ N ₄ (224.3)	163 – 164 (70)	69.62 69.68	5.39 5.45	24.98 25.06	–
<i>IIb</i>	C ₁₂ H ₁₁ N ₅ (225.3)	150 – 151 (65)	63.99 63.70	4.92 4.84	31.09 30.88	–
<i>IIIa</i>	C ₁₃ H ₁₂ N ₄ (224.3)	129 – 130 (81)	69.62 69.52	5.39 5.41	24.98 24.82	–
<i>IIIb^b</i>	C ₁₂ H ₁₁ N ₅ (225.3)	202 – 204 (60)	63.99 –	4.92 –	31.09 –	–
<i>IVa</i>	C ₂₁ H ₁₈ N ₆ (354.0)	218 – 220 (76)	71.19 70.96	5.08 5.30	23.73 23.58	–
<i>IVb</i>	C ₂₀ H ₁₇ N ₇ (355.0)	174 – 176 (82)	67.61 67.90	4.79 4.62	27.60 27.58	–
<i>Va</i>	C ₂₂ H ₁₉ N ₅ (353.0)	173 (78)	74.79 74.65	5.38 5.26	19.83 19.91	–
<i>Vb</i>	C ₂₁ H ₁₈ N ₆ (354.0)	198 – 200 (89)	71.19 70.98	5.08 5.02	23.73 23.62	–
<i>VIa</i>	C ₂₁ H ₁₆ ClN ₅ (373.5)	205 (76)	67.47 67.62	4.28 4.21	18.74 18.54	9.50 9.28
<i>VIIb</i>	C ₂₀ H ₁₅ ClN ₆ (374.5)	212 – 214 (88)	64.09 63.89	4.00 3.88	22.43 22.21	9.47 9.42
<i>VIIIa</i>	C ₂₁ H ₁₆ BrN ₅ (418.0)	208 – 210 (80)	60.29 60.27	3.83 3.62	16.75 16.82	19.14 19.02
<i>VIIIb</i>	C ₂₀ H ₁₅ BrN ₆ (419.0)	202 (91)	57.28 57.21	3.58 3.43	20.05 19.82	19.09 18.79

Ref. ¹: ^a Yield 98%, m.p. 137 – 138 °C; ^b yield 85%, m.p. 200 – 201 °C.

TABLE II
UV (methanol, $c \cdot 10^{-4} \text{ mol l}^{-1}$) and IR (KBr) spectra of compounds I–VII

Compound	λ_{max} , nm (log ϵ)	ν_{max} , cm^{-1}
<i>Ia</i>	238 (3.28), 274 (2.83), 281 (2.84), 294 (2.59)	3 255, 1 610, 1 530, 1 485, 1 420, 1 320, 1 290, 1 280, 735, 730
<i>Ib</i>	235 (3.19), 262 (2.86), 284 (2.93)	3 360, 1 610, 1 515, 1 485, 1 330, 1 290, 1 235, 1 165, 760, 730
<i>IIa</i>	245 (3.27), 247 (2.70), 281 (2.70), 301 (2.54)	3 270, 3 070, 1 590, 1 565, 1 485, 1 505, 1 280, 1 220, 1 100, 745
<i>IIb</i>	243 (3.25), 259 ^a (2.93), 284 (2.81)	3 340, 1 585, 1 560, 1 300, 1 285, 1 245, 1 150, 800, 735, 710
<i>IIIa</i>	248 (3.40), 273 ^a (2.95), 279 (2.74)	3 360, 2 975, 1 600, 1 540, 1 315, 1 220, 1 200, 900, 815, 760
<i>IIIb</i>	246 (3.34), 263 ^a (3.10), 283 (2.74)	3 280, 1 610, 1 565, 1 530, 1 310, 1 305, 1 220, 1 160, 815, 735
<i>IVa</i>	236 (3.53), 265 ^a (3.33), 272 (3.35), 278 (3.28), 344 (2.66)	3 280, 1 620, 1 520, 1 500, 1 300, 1 195, 1 180, 1 080, 810, 735
<i>IVb</i>	220 (3.35), 236 (3.43), 261 (3.24), 272 (3.27), 344 (2.55)	3 320, 1 515, 1 295, 1 240, 1 195, 1 160, 1 075, 810, 760, 730
<i>Va</i>	221 (3.53), 232 ^a (3.51), 249 ^a (3.35), 264 (3.32), 271 ^a (3.28), 278 (3.13)	3 290, 1 520, 1 490, 1 270, 1 230, 1 215, 1 180, 820, 785, 735
<i>Vb</i>	221 (3.49), 234 ^a (3.45), 260 (3.33), 317 (2.65)	3 320, 1 520, 1 490, 1 265, 1 230, 1 185, 1 150, 830, 795, 780
<i>VIa</i>	222 (3.51), 238 (3.39), 265 (3.26), 272 (3.27), 278 (3.18), 319 (2.60)	3 300, 1 505, 1 270, 1 220, 1 190, 1 175, 1 095, 840, 790, 740
<i>VIb</i>	222 (3.45), 240 ^a (3.40), 261 (3.32), 320 (2.65)	3 360, 1 625, 1 505, 1 260, 1 180, 1 150, 1 090, 820, 780, 760
<i>VIIa</i>	221 (3.54), 240 ^a (3.42), 265 (3.28), 272 (3.30), 278 (3.23), 317 (2.65)	3 290, 1 500, 1 450, 1 260, 1 215, 1 180, 1 170, 835, 785, 735
<i>VIIb</i>	222 (3.51), 241 (3.37), 261 (3.30), 270 (3.27), 283 (3.10), 318 (2.60)	3 290, 1 625, 1 590, 1 500, 1 265, 1 225, 1 140, 830, 800, 735

^a Inflex.

EXPERIMENTAL

Infrared spectra were taken on a Specord M 80 spectrometer, UV spectra on a Specord M 40 instrument (both Zeiss, Jena). ^1H NMR spectra were obtained with an 80 MHz BS 487 C Tesla spectrometer in hexadeuteriodimethyl sulfoxide with tetramethylsilane as internal standard.

Benzazolymethylheteroarylaminines *I* – *VII*

The appropriate 1-*N*-hydroxymethylbenzazole (2.96 g of 1-hydroxymethylbenzimidazole or 2.98 g of 1-hydroxymethylbenzotriazole; 20 mmol) was dissolved in hot ethanol (50 ml). The corresponding heterocyclic amine (20 mmol) was then added and the mixture was heated at reflux, the reaction being monitored by thin-layer chromatography (Silufol 254 UV sheets, eluent chloroform–methanol 20 : 1, UV-detection). After the reaction had ended (usually 2 h), the reaction mixture was set aside at 5 °C overnight. If no crystals deposited, a part of the ethanol (30 ml) was distilled off and the residue was again allowed to stand at 5 °C overnight. The crystalline product was collected, washed with cold ether and crystallized from ethanol (if necessary, with addition of water). The physico-chemical properties of the products and yields are given in Table I, IR and UV spectral data in Table II and ^1H NMR spectral data in Table III.

TABLE III
 ^1H NMR spectra of compounds *I* – *VII*

Compound	N–CH ₂ –NHR	=CH–	H _{arom}	Other signals
<i>Ia</i>	5.80 s, 5.86 s	8.39 s	6.56 – 8.34 m, 8 H	–
<i>Ib</i>	6.18 s, 6.25 s	–	6.80 – 8.14 m, 8 H	–
<i>IIa</i>	5.75 s, 5.82 s	8.54 s	7.11 – 8.31 m, 8 H	–
<i>IIb</i>	6.18 s, 6.25 s	–	7.02 – 8.23 m, 8 H	–
<i>IIIa</i>	5.65 s	8.32 s	7.17 – 7.75 m, 8 H	–
<i>IIIb</i>	6.18 s, 6.25 s	–	6.80 – 8.14 m, 8 H	–
<i>IVa</i>	5.71 s, 5.80 s	8.48 s	7.03 – 7.91 m, 11 H	2.34 s, (Me)
<i>IVb</i>	6.18 s, 6.21 s	–	6.72 – 8.34 m, 11 H	2.32 s, (Me)
<i>Va</i>	5.23 s, 5.26 s	8.45 s, 8.68 s	6.60 – 8.60 m, 11 H	2.78 s, (Me)
<i>Vb</i>	6.17 s, 6.20 s	8.28 s	7.15 – 8.15 m, 11 H	2.72 s, (Me)
<i>VIa</i>	5.66 s, 5.69 s	8.24 s, 8.36 s	7.06 d, 1 H; 7.29 d, 1 H; 6.77 dd, 1 H; 7.07 – 7.83 m, 8 H	6.85 t, (NH)
<i>VIIb</i>	6.20 s, 6.26 s	–	7.20 – 8.40 m, 12 H	–
<i>VIIIa</i>	5.66 s, 5.69 s	8.52 s	6.85 – 8.42 m, 12 H	–
<i>VIIIb</i>	6.23 s, 6.27 s	–	7.27 – 8.70 m, 12 H	–

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