4-N-BENZAZOLYLAMINO DERIVATIVES OF 3-Y-3-BUTEN-2-ONE

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Dedicated to Professor L. Ebringer on the occasion of his 60th birthday.

Ethoxymethylene derivatives of 2,4-pentanedione (*Ia*), 3-oxobutanenitrile (*Ib*), methyl (*Ic*) or ethyl (*Id*) 3-oxobutanoate give with 4- or 5-aminobenzimidazole or benzotriazole, respectively, under mild conditions products of nucleophilic substitution *II* — *V*. Structure of these compounds was discussed on the basis of their spectral measurements — IR, UV, ^{1}H, ^{13}C NMR and mass spectra.

Benzazolylaminomethylene derivatives of ethyl malonate or methyl cyanoacetate were used in the synthesis of 3-substituted azoloquinolone derivatives[1]. Their synthesis is based on the reaction of aminobenzazole (4- or 5-aminobenzimidazole or benzotriazole) with the corresponding alkoxymethylene derivatives of ethyl malonate and methyl cyanoacetate[2], respectively. The ethoxymethylene derivatives of 2,4-pentanedione (*Ia*), 3-oxobutanenitrile (*Ib*), methyl (*Ic*) and ethyl (*Id*) 3-oxobutanoate give with 5-amino-1-arylbenzazoles[3], 5-amino-1-methylbenzazoles and 5-amino-2-methylbenzotriazole[4] products of nucleophilic substitution.

This work presents the synthesis and spectral properties of 4-N-benzazolylaminomethylene derivatives of 2,4-pentanedione, 3-oxobutanenitrile, methyl and ethyl 3-oxobutanoate, prepared by treatment of the latter with 4- or 5-aminobenzimidazole or benzotriazole (Scheme 1 and Table I). These aminomethylene derivatives contain always at least one acetyl group in the β-position of this substituent. The second electron-withdrawing group is either an acetyl, cyano or an ester group respectively. The amino group of the aminobenzazole occupies both posible position on the benzene nucleus, that means position 4(7)- or 5(6)-. No substitution products were observed from an attack of the imino hydrogen of the azole ring or formed by substitution through another possible centre of nucleophilic attack.

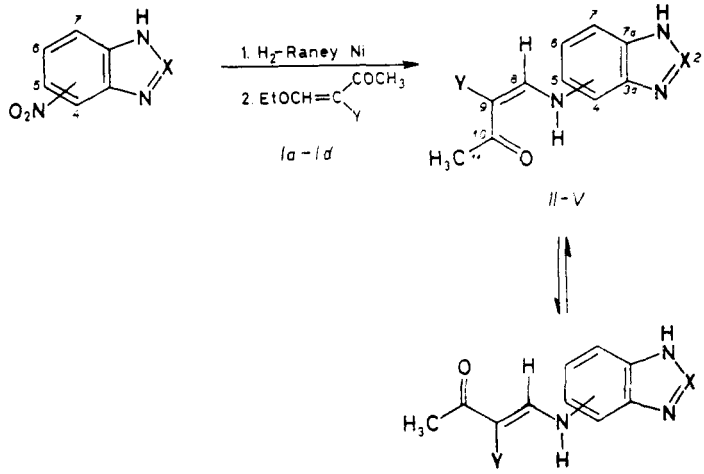
Spectral characteristics confirm the proposed structure of synthetized compounds: an intramolecular hydrogen bond between the imino hydrogen and the carbonyl

TABLE I

Yield, physico-chemical and analytical data of compounds *II*—*V*

Compound	Formula (M.w.)	M.p., °C Yield, %	Calculated/Found		
			% C	% H	% N
IIa	$C_{13}H_{13}N_3O_2$ (243·3)	199—200 78	64·19 64·20	5·39 5·18	17·27 17·14
IIb	$C_{12}H_{10}N_4O$ (226·2)	240—242 89	63·71 63·59	4·46 4·34	24·76 24·67
IIc	$C_{13}H_{13}N_3O_3$ (259·3)	171—173 69	60·23 60·11	5·05 5·00	16·21 16·13
IId	$C_{14}H_{15}N_3O_3$ (273·3)	172—174 62	61·53 61·37	5·53 5·39	15·38 15·19
IIIa	$C_{12}H_{12}N_4O_2$ (244·3)	223—226 82	59·01 59·00	4·95 4·91	22·94 22·89
IIIb	$C_{11}H_9N_5O$ (227·2)	260—263 89	58·15 58·01	3·99 3·86	30·82 30·68
IIIc	$C_{12}H_{12}N_4O_3$ (260·3)	209—213 72	55·38 55·29	4·65 4·56	21·53 21·34
IIId	$C_{13}H_{14}N_4O_3$ (274·3)	171—174 63	56·93 56·77	5·14 5·01	20·43 20·22
IVa	$C_{13}H_{13}N_3O_2$ (243·3)	198—201 86	64·19 64·10	5·39 5·28	17·27 17·17
IVb	$C_{12}H_{10}N_4O$ (226·2)	228—231 91	63·71 63·73	4·46 4·46	24·76 24·72
IVc	$C_{13}H_{13}N_3O_3$ (259·3)	151—154 68	60·23 60·09	5·05 4·99	16·21 16·01
IVd	$C_{14}H_{15}N_3O_3$ (273·3)	170—173 71	61·53 61·35	5·53 5·39	15·38 15·24
Va	$C_{12}H_{12}N_4O_2$ (244·3)	227—229 8	59·01 58·99	4·95 5·01	22·94 22·88
Vb	$C_{11}H_9N_5O$ (227·2)	236—240 93	58·15 58·09	3·99 4·00	30·82 30·59
Vc	$C_{12}H_{12}N_4O_3$ (260·3)	162—164 74	55·38 55·18	4·65 4·45	21·53 21·36
Vd	$C_{13}H_{14}N_4O_3$ (274·3)	205—209 68	56·93 56·76	5·14 5·00	20·43 20·26

of acetyl or ester group (IR spectra, Table II) stabilize the antiperiplanar conformation of the enamine moiety of compounds *II* – *V*.



		4-Substituted compounds			5-Substituted compounds		
I	Y		X	Y		X	Y
a	$COCH_3$	*IIa*	CH	$COCH_3$	*IVa*	CH	$COCH_3$
b	CN	*IIb*	CH	CN	*IVb*	CH	CN
c	$COOCH_3$	*IIc*	CH	$COOCH_3$	*IVc*	CH	$COOCH_3$
d	$COOC_2H_5$	*IId*	CH	$COOC_2H_5$	*IVd*	CH	$COOC_2H_5$
		IIIa	N	$COCH_3$	*Va*	N	$COCH_3$
		IIIb	N	CN	*Vb*	N	CN
		IIIc	N	$COOCH_3$	*Vc*	N	$COOCH_3$
		IIId	N	$COOC_2H_5$	*Vd*	N	$COOC_2H_5$

SCHEME 1

The absorption bands between 250 and 270 nm in UV spectra (Table II) correspond to benzotriazole and benzimidazole chromophore[5], respectively. The longest wavelength absorption band belongs to the interaction of benzazole with the aminoethylene substituent[6].

The doubling of signals of the aminoethylene substituent and the benzene ring of the benzazole in proton and carbon NMR spectra, respectively, of compound *IIIb* – *IIId* to *Vb* – *Vd* (Tables III, IV) confirm, unlike in *IIa* – *Va*, the existence of geometrical isomerism: derivatives of 3-oxobutanenitrile (*IIb* – *Vb*) are formed in the 1 : 1 ratio, while in 3-oxobutanoates *IIc*, *IId* – *Vc*, *Vd* predominate (over 85 per cent) the *E*-isomer[7].

TABLE II

IR and UV spectra of compounds *II*– *V*

Compound	IR spectrum, cm^{-1}			UV spectrum				
	$\tilde{\nu}$(C=O)	ν(C≡N)	$\tilde{\nu}$(CH) $\tilde{\nu}$(NH)	λ_{max}, nm/log ε m^2 mol^{-1}				
IIa	1 615	–	2 915	–	–	254	–	349
			3 375			3·03		3·41
IIb	1 655	2 215	3 200	227	–	253	261	352
			3 520	2·98		2·85	2·72	3·32
IIc	1 630, 1 710	–	3 170	–	235	253	261	348
	1 640		3 400		3·07	3·00	2·88	3·37
IId	1 610, 1 710	–	3 220	224	236	252	260	348
	1 640		3 430	3·07	3·11	3·08	2·97	3·43
IIIa	1 620	–	3 105	230	–	259	269	354
	1 635		3 470	3·00		3·04	2·93	3·45
IIIb	1 645	2 205	3 170	226	–	262	–	355
			3 400	3·26		2·83		3·42
IIIc	1 640	–	3 220	229	–	260	269	354
	1 680		3 460	3·19		2·78	2·70	3·49
IIId	1 635	–	3 100	228	241	260	268	352
	1 710		3 440	3·16	3·03	2·75	2·68	3·43
IVa	1 620	–	2 000	–	–	255	263	342
			3 360			3·30	3·27	3·47
IVb	1 640, 1 675	2 210	2 820	225	–	254	261	345
	1 645		3 440	3·32		2·97	2·90	3·43
IVc	1 625, 1 670	–	3 230	–	238	252	259	341
	1 640		3 440		3·32	3·19	3·02	3·45
IVd	1 620, 1 670	–	3 220	–	238	253	260	342
	1 635		3 430		3·29	3·16	2·99	3·42
Va	1 640	–	3 040	–	–	–	258	342
			3 440				3·08	3·34
Vb	1 610	2 230	3 170	224	–	–	266	342
	1 655		3 450	3·25			2·79	3·37
Vc	1 630, 1 715	–	3 000	–	234	–	269	340
	1 645		3 435		3·31		2·88	3·49
Vd	1 630	–	2 980	–	234	–	266	341
	1 710		3 425		3·28		2·86	3·45

TABLE III

1H NMR spectra of compounds *II*– *V*

Compound	H-2	H-4(5)	H-6	H-7	H-8	NH	$COCH_3$	Y	^3J 8, NH	^3J 4, 6(5)	^3J 6, 7
IIa	8·33 s	7·30 m (3 H)			9·32 d	12·97 d	2·43 s	2·39 s	12·9	–	–
IIb	8·32 s	7·30 m (3 H)			9·01 d	12·65 d	2·33 s	–	13·2	–	–
	8·35 s				9·00 d	10·80 d	2·29 s				
IIc	8·33 s	7·35 d	7·19 dd	7·24 d	9·34 d	13·09 d	2·45 s	3·71 s	13·2	–	8·4
	8·31 s	7·37 d			9·32 d	11·26 d	2·38	3·81 s			7·2
IId	8·32 s	7·35 d	7·16 dd	7·24 d	9·32 d	13·05 d	2·44 s	4·17 q 1·28 t	13·5	1·8	7·5
	8·31 s	7·37 d		7·23 d	9·27 d	11·35 s	2·38 s	4·27 q 1·33 t			
IIIa	–	7·50 m (3 H)			9·34 d	12·98 d	2·43 s	2·41 s	12·0	–	–
IIIb	–	7·43 m (3 H)			8·97 d	12·65 d	2·32 s	–	12·6	–	–
						9·92 s	2·34 s				
IIIc	–	7·54 d	7·34 dd	7·46 d	9·42 d	13·09 d	2·46 s	3·73 s	13·2	–	8·4
		7·56 d		7·52 d		11·23 d	2·39 s	3·83 s			7·2
IIId	–	7·33 d	7·57 m (2 H)		9·43 d	13·06 d	2·45 s	4·19 q 1·29 t	13·2	–	–
					9·42 d	11·30 d	2·40 s	4·29 q 1·34 t			
IVa	8·26 s	7·70 d	7·29 dd	7·62 d	8·46 d	12·77 d	2·40 s	2·38 s	12·9	–	–
IVb	8·25 s	7·68 d	7·30 dd	7·59 d	8·48 d	12·30 d	2·32 s	–	13·5	2·1	8·7
	8·24 s	7·76 d	7·32 dd	7·59 d	8·38 d	10·81 d	2·30 s		14·1	–	–
IVc	8·26 s	7·61 d	7·18 dd	7·60 d	8·47 d	12·77 d	2·39 s	3·67 s	13·2	2·4	8·7
					8·46 d	10·76 d	2·34 s	3·76 s			
IVd	8·27 s	7·63 d	7·23 dd	7·62 d	8·49 d	12·72 d	2·42 s	4·16 q 1·27 t	13·5	2·1	9·0
					8·47 d	10·86 d	2·37 s	4·28 q 1·30 t	13·5	–	–
Va	–	8·06 d	7·57 d	7·97 d	8·52 d	12·65 d	2·43 s	2·41 s	12·9	2·1	9·0
Vb	–	8·00 d	7·58 dd	7·97 d	8·57 d	12·22 d	2·36 s	–	13·2	2·1	9·0
					8·48 d	10·90 s	2·32 s				
Vc	–	7·83 d	7·39 dd	7·91 d	8·47 d	12·62 d	2·39 s	3·67 s	13·2	–	9·0
		7·80	7·41 dd		8·45 d	10·70 d	2·33 s	3·76 s	13·2	–	–
Vd	–	7·88 d	7·46 dd	7·95 d	8·51 d	12·63 d	2·41 s	4·16 q 1·27 t	13·2	1·8	9·0
		7·83 d			8·47 d	10·82 d	2·36 s	4·26 q 1·30 t	13·2	–	–

TABLE IV

^{13}C NMR spectra of compounds *II* — *V*

Compound	C-2	C-4	C-5	C-6	C-7	C-3a	C-7a	C-8	C-9	C-10	C-11	Y(COCN)	Y(CH_3)	Y(CH_2)
IIa	142·3	129·4	108·6[a]	123·2	108·6[a]	133·7	134·6	153·4	112·5	199·6	31·7	195·1	27·5	
IIb	142·6	128·7	109·3	123·3	108·2	133·7	134·8	152·9	84·1	196·4	28·5	120·4		
	142·3	130·0	111·8	123·1	108·8	133·0	135·8	155·5	86·0	191·4	26·7	117·4		
IIc	142·3	129·1	108·7	123·2	108·4	133·6	114·7	152·6	101·8	198·7	30·8	166·8	51·0	
	142·1	129·4	108·2		108·0			152·4	102·0	196·3	30·4	166·4	51·1	
IId	142·3	129·2	108·6	123·2	108·2	133·7	134·7	152·6	102·1	198·7	30·9	166·4	59·5	14·
	142·1							152·2	103·2	194·0	30·6	166·7	59·9	14·3
IIIa	—	129·6	110·5[a]	127·9	110·5[a]	135·2	136·0	153·4	113·3	200·0	31·7	195·2	27·4	
IIIb	—	128·5	110·0	127·2	108·0	135·4[a]	135·6[a]	154·7	85·1	196·4	28·3	119·7		
		130·2	112·6	127·8	107·2	135·5[a]	135·5[a]	153·0	87·0	191·3	26·6	116·7		
IIIc	—	129·4	110·7	128·0	107·9	135·3	125·8	152·8	102·8	199·2	30·7	166·5	51·2	
								152·4	104·1	194·0	30·3	168·0	51·3	
IIId	—	129·4	110·5	128·0	107·7	135·4	135·8	152·8	103·2	199·1	30·9	166·1	59·7	14·3
			110·0		107·5			152·2	102·5	194·0	30·5	166·2	60·1	14·2
IVa	143·3	104·9	134·1	114·1	116·1	136·2	138·6	153·6	112·0	199·2	31·6	195·1	27·5	
IVb	143·3	105·3	133·6	114·0	116·6	133·4	135·1	153·5	83·3	195·9	28·4	120·7		
	143·6	105·5		114·2	116·9			153·5	85·8	191·7	26·8	117·5		
IVc	143·3	101·4[a]	134·0	113·6[a]	113·6[a]	134·8[a]	134·8[a]	152·5	101·2[a]	198·1	30·6	166·8	50·9	
								152·4		194·0	30·5	166·4	51·0	
IVd	143·3	104·6	134·1	113·8	116·5	136·5	138·4	152·5	101·5	198·1	30·7	166·4	59·4	14·3
								152·2			30·5			
Va	—	102·0	133·5	116·9	118·4	137·4[a]	137·5[a]	153·4	112·9	199·6	31·6	195·5	27·6	
Vb	—	[b]	133·5	115·2	118·6	128·8	130·1	153·5	87·2	195·9	28·3	120·2		
			133·2			129·1		153·1	85·7	19·19	26·4	116·8		
Vc	—	102·2	137·2	117·2	117·5	137·9	138·3	152·2	102·2	198·4	30·8	166·6	51·0	
		103·3	137·8	117·3	117·7	138·0		152·1	102·5	193·9	30·1	166·2	51·1	
Vd	—	101·9	137·4	117·3	117·8	138·0	138·3	152·3	102·5	198·5	30·8	166·3	59·6	14·3
		101·8						151·6	103·6	194·2	30·4	167·8	59·9	14·2

[a] Unresolved signal; [b] unobserved signal.

TABLE V

Mass spectra of compounds *II*— *V*; 10 most intensive peaks of each compound

Compound	*m/z* (H)
IIa	243 (M^+, 22), 210 (27), 200 (100), 158 (46), 144 (43), 132 (19), 118 (61), 117 (33), 90 (25), 43 (71), 39 (26)
IIb	226 (M^+, 38), 184 (16), 183 (100), 144 (34), 118 (85), 117 (22), 91 (19), 90 (25), 63 (19), 43 (51), 39 (33)
IIc	273 (M^+, 60), 230 (100), 202 (21), 199 (44), 184 (76), 157 (24), 144 (31), 118 (38), 117 (21), 43 (31)
IId	259 (M^+, 44), 216 (100), 212 (18), 184 (69), 157 (23), 156 (22), 144 (29), 118 (38), 117 (19), 43 (35)
IIIa	244 (M^+, 53), 201 (100), 183 (28), 159 (73), 145 (29), 131 (27), 119 (31), 112 (62), 104 (33), 103 (37)
IIIb	227 (M^+, 60), 184 (88), 159 (19), 157 (27), 156 (30), 130 (18), 129 (43), 105 (33), 103 (17), 43 (100)
IIIc	260 (M^+, 64), 217 (57), 200 (64), 185 (57), 172 (26), 159 (29), 158 (65), 130 (40), 129 (29), 43 (100)
IIId	274 (M^+, 60), 231 (45), 200 (57), 185 (45), 159 (28), 158 (55), 142 (19), 130 (21), 104 (19), 43 (100)
IVa	243 (M^+, 78), 228 (29), 210 (82), 200 (36), 186 (59), 158 (43), 132 (100), 118 (27), 117 (29), 43 (77)
IVb	226 (M^+, 76), 211 (48), 183 (100), 156 (33), 144 (21), 129 (25), 118 (41), 117 (27), 90 (27), 63 (31), 43 (81)
IVc	259 (M^+, 63), 227 (27), 199 (100), 184 (70), 157 (30), 156 (21), 133 (74), 132 (37), 117 (21), 43 (47)
IVd	273 (M^+, 43), 227 (19), 199 (100), 184 (84), 157 (36), 156 (27), 132 (25), 117 (20), 90 (18), 43 (88)
Va	244 (M^+, 32), 216 (21), 183 (19), 174 (18), 156 (19), 132 (20), 112 (62), 104 (31), 70 (22), 43 (100)
Vb	227 (M^+, 79), 199 (25), 184 (52), 157 (55), 156 (30), 130 (26), 129 (74), 63 (31), 52 (36), 43 (100)
Vc	260 (M^+, 39), 200 (91), 185 (78), 172 (35), 158 (33), 157 (47), 130 (46), 129 (37), 103 (37), 43 (100)
Vd	274 (M^+, 39), 246 (24), 200 (100), 185 (69), 172 (29), 158 (32), 157 (36), 129 (24), 130 (31), 43 (66)

Acceptor influence of the group in position 3 rise in order CN > COOR > $COCH_3$ what is reflected by chemical shifts of carbon atoms C-9. Antiperiplanar conformation of enamine substituent is confirmed in proton spectra by the presence of interaction constant ^3J(H-8, NH) over 12 Hz, while signals under 11 ppm belong the imino-group bonding in the intramolecular hydrogen bond with carbonyl of ester and over 12 ppm with carbonyl of acetyl group. The chemical shifts of protons and carbons of the benzene ring of benzazole skeleton (with exception C-4) show that the electronaccepting effect of the triazole is greater that of the imidazole ring. Unusually high value of the chemical shift of proton H-8 (over 9 ppm with exception *IIIb*) can be accounted for by the existence of the non bonding interaction between nitrogen atom of the azole ring of benzazole skeleton with prototropy and the ethylene hydrogen of aminoethylene substituent in position 4 (structures *II* and *III*).

In the electron impact mass spectra (Table V) all of the studied compounds are observed the corresponding molecular ions with relative intensities 20 to 80 per cent (Table V). Compounds *II* favours the α-rupture next to nucleus (with hydrogen transfer) leading to the ionized benzimidazole nucleus with m/z 118. In the case of isomeric compounds *III* β-rupture over the α-rupture is favoured.

The origination of the most intensive fragment ions in spectra of compounds *IV* and *V* goes similarly as in the benzimidazole group unlike β-rupture with hydrogen transfer, that gives rise to the fragments with the charge in side chain, behaving like those described in the literature[6]. The β-rupture is not observed in cyano compounds (*IIb*–*Vb*).

EXPERIMENTAL

The melting points were measured on a Kofler micro hot-stage and are uncorrected. The IR spectra (KBr discs) and the UV spectra ($1 . 10^{-4}$ mol dm^{-3} in methanol) were recorded with Specord M 80 (Zeiss, Jena) and Specord M 40 (Zeiss, Jena) spectrometers, respectively. The ^1H and ^{13}C NMR spectra of hexadeuterodimethylsulfoxide solutions were measured on Varian VXR-300 instrument at 298 K and are relative to hexamethyldisiloxane (internal reference for ^1H NMR) and hexadeuterodimethylsulfoxide ($\delta = 39{\cdot}5$) or carbonyl of trifluoroacetic acid ($\delta = 164{\cdot}2$) for ^{13}C NMR spectra. Saturated solutions were measured in a 5 mm multinuclear probe. The ^{13}C NMR spectra were measured at 75 kHz operating frequency. The electron impact mass spectra were taken with an MS 902S (AEI-Kratos) instrument at 70 eV electron energy and 100 μA trap current.

2-Ethoxymethylene-3-oxobutanenitrile (*Ib*) was synthetized by condensation of ethyl orthoformate with 3-oxobutanenitrile, itself prepared by an acid hydrolysis of 3-amino-2-butenenitrile[6]. 3-Ethoxymethylene-2,4-pentanedione (*Ia*), methyl (*Ic*), and ethyl (*Id*) 2-ethoxymethylene-3-oxobutanoates were synthetized likewise by condensation of ethyl orthoformate with the corresponding methylene compound: 2,4-pentanedione, methyl or ethyl 3-oxobutanoates[8], respectively. 4- or 5-Nitrobenzazoles were synthetized according to literature[2].

3-Benzazolylamino Derivatives of 3-Y-3-Buten-2-one (*II*— *V*)

The corresponding nitrobenzazole (10 mmol) in methanol (100 ml) was hydrogenated at 120 kPa on Raney nickel (200 mg) till 660 ml of hydrogen consumed. The catalyst was filtered off, the respective alkoxymethylene derivative *I* (10 mmol) was added in 20 ml methanol and the mixture was refluxed for 30 min. The mixture was shortly boiled with charcoal, filtered, the most part of the solvent was evaporated, the separated product was filtered off and washed with cold methanol. Crystallization from methanol afforded analytically pure products. Yields and other data are presented in Table I.

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