ALKYLATED BENZIMIDAZOLE AND BENZOTRIAZOLE DERIVATIVES OF 3-AMINO-2-PROPENOIC ACID

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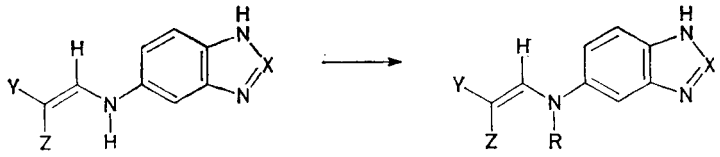
Received May 10, 1988
Accepted June 13, 1988

The alkylation of unsubstituted 3-(5-benzimidazolyl- and 5-benzotriazolyl)amino derivatives of 2-propenoic acid (*I*) results in the replacement of hydrogen atom at the nitrogen of YZC==CH—NH— substituent (*II—IV*). The model compounds with a methyl group in the azole nucleus (*V— VII*) have been prepared by an independent synthesis. The structure of all products has been confirmed and confronted with their IR, UV, ^{1}H and ^{13}C NMR spectra.

In previous papers we described the preparation and spectral properties of 3-(4- and 5-benzimidazolyl- and 4- and 5-benzotriazolyl)amino derivatives of 2-propenoic acid. These compounds occur in two tautomeric forms and have the antiperiplanar conformation of the YZC=CH—NH— grouping.



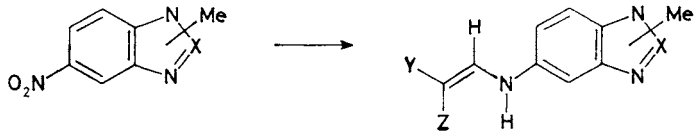
I *II-IV*

I: *a*, X = N; Y = COOEt; Z = COOEt *b*, X = N; Y = COOMe; Z = CN
c, X = N; Y = CN; Z = CN *d*, X = CH; Y = COOEt; Z = COOEt
e, X = CH; Y = COOMe; Z = CN *f*, X = CH; Y = CN; Z = CN
II: R = Me; X, Y, Z for *a-f* same as for *I*
III: R = Et; X = CH; Y = COOEt; Z = COOEt
IV: R = $C_6H_5CH_2$; X = CH; Y = COOEt; Z = COOEt

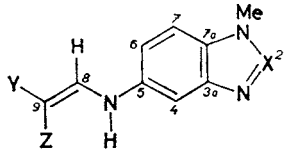
SCHEME 1

In this present work we have studied the effects of reaction conditions of the alkylation of tautomeric 3-(5-benzotriazolyl- or benzimidazolyl)amino derivatives of 2-propenoic acid (Scheme 1) on the position of the alkylation. The products of me-

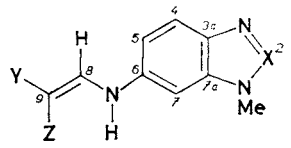
thylation were compared with the model compounds obtained by indepedent syntheses from 1-methyl-5- or -6-nitro- or 2-methyl-5-nitrobenzotriazole and 1--methyl-5- or -6-nitrobenzimidazole: the catalytic hydrogenation followed by the reaction with 3-alkoxy derivatives of 2-propenoic acid (Scheme 2).



V - VII

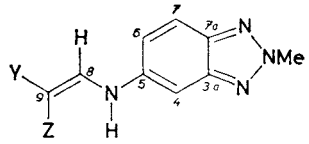


Va - Vf



VIa - VIf

X, Y, Z for *a - f* same as for *I*



VII a, Y = COOEt ; Z = COOEt
VII b, Y = COOMe ; Z = CN
VII c, Y = CN ; Z = CN

SCHEME 2

1-Methyl-5-nitrobenzotriazole and benzimidazole were prepared by ring closure of 4-nitro-1-N-methyl-1,2-phenylenediamine with sodium nitrite in 80% sulfuric acid[3] and with formic acid[4], respectively. 2-Methyl-5-nitro- and 1-methyl-6-nitrobenzotriazole were isolated from the reaction mixture after the methylation of 5(6)--nitrobenzotriazole with dimethyl sulfate in alkaline medium[5]. 6-Nitro-1-methylbenzimidazole was obtained by fraction crystallization from its mixture with the respective 5-isomer, both isomers formed by the methylation of 5(6)-nitrobenzimidazole with phase-transfer catalysis. The purity of all nitro derivatives was checked by means of gas chromatography.

The methylation of the tautomeric substitution products *I* with methyl iodide and potassium carbonate in dimethylformamide (method *A*) gives, in all cases, the products *II* whose spectral characteristics as well as comparison with the isomeric compounds *V–VII* show that the methylation exclusively attacked the nitrogen atom of the YZC=CH—NH— residue.

The methylation of compound *Id* was performed also with methyl iodide and sodium hydride in dimethoxyethane (method *B*) or with dimethyl sulfate and sodium hydride in tetrahydrofurane (method *C*). In both these cases the compound *IId* was formed as the only reaction product, the yields of all three methods being approximately the same (see Experimental). The method *A* is the most convenient of all because of the necessity of inert medium in the case of application of sodium hydride as the base (methods *B* and *C*).

The alkylation of compound *Id* with ethyl iodide or benzyl chloride (potassium carbonate in dimethylformamide, method *A*) gives the respective 3-N-alkylamino-derivatives of 2-propenoic acid *III* and *IV* in the yields comparable with those of the methylation (Table I).

The comparison of spectral characteristics (^{1}H NMR, UV, and IR spectra) of the starting (*I*), alkylated (*II–IV*), and model compounds (*V–VII*) indicates univocally that the alkylation proceeds at the nitrogen atom of the YZC=CH—NH— residue. Instead of two doublets with the coupling constants about 14 Hz characteristic of the antiperiplanar conformation of the protons of the enamine grouping —NH— —CH= in compounds[1,2] *I*, *V–VII* in the ^{1}H NMR spectra a singlet of the methine proton is observed. The singlet of the methyl group at nitrogen atom of the enamine grouping is found in a region different from that of the model compounds *V–VII* (Table II). The IR spectra (Table I) of compounds *II–IV* document the absence of the intramolecular hydrogen bond between the imine hydrogen atom and carbonyl group in 3-amino-2-propenoyl grouping, this hydrogen bond being observed in compounds *I* and *V–VII* (*a*, *b*, *d*, *e*) (refs[1,2]); the absence of this hydrogen bond in compounds *II–IV* makes itself felt by an increase by 20–30 cm^{-1} in the vibration frequence of the carbonyl group. Formation of an absorption band at 225 nm in the UV spectra (Table III) indicates the alkylation of enamine nitrogen atom.

The conformation of enamine grouping can only be estimated in compounds *VIa*, *VIe*, and *VIIa*. With other derivatives, only broad signals of the protons bound to nitrogen or carbon atom are observed due probably to the chemical exchange[6]. The presence of the interaction ^3J(CH–NH) $\approx$ 14 Hz in compounds *VIa*, *VIe*, and *VIIa* indicates the antiperiplanar conformation of this grouping (ref.[7]: *Va* ($CDCl_3$) has ^3J(CH–NH) $\approx$ 14 Hz). The ethyl ester *Va* in methanol showed only a singlet of the proton H-8 (δ = 8·30 ppm), in acetonitrile a doublet overlapping with a singlet (δ = 8·43 ppm), the same as that of the proton at the nitrogen atom (δ = 10·86 ppm). In benzene, acetone, and trifluoroacetic acid, the

TABLE I

3-Benzazolylaminoderivatives of 2-propenoic acid

Compound	M.p., °C Yield, %	Formula Mol. mass	Calculated/Found			ν(C≡N) ν(C=O)	ν(NH) ν(CH)
			% C	% H	% N		
IIa	182—185	$C_{15}H_{18}N_4O_4$	56·60	5·70	17·60	—	3 415
	91	318·3	56·82	5·52	17·24	1 705, 1 680	2 975
IIb	152—154	$C_{12}H_{11}N_5O_2$	56·03	4·31	27·22	2 205	3 460
	50	257·3	56·13	4·26	27·42	1 690	2 950
IIc	243—246	$C_{11}H_8N_6$	58·92	3·60	37·48	2 220, 2 210	3 430
	62	224·2	59·06	3·50	37·21	—	3 010
IId	225—229	$C_{16}H_{19}N_3O_4$	60·56	6·03	13·24	—	3 450
	61	317·4	60·35	5·95	13·08	1 690, 1 665	2 950
IIe	193—196	$C_{13}H_{12}N_4O_2$	60·93	4·72	21·86	2 210	3 430
	63	256·3	60·86	4·83	21·72	1 690, 1 655	2 950
IIf	236—238	$C_{12}H_9N_5$	64·56	4·06	31·37	2 220	3 425
	91	223·2	64·28	4·02	31·27	—	3 020
III	159—163	$C_{17}H_{21}N_3O_4$	61·62	6·39	12·68	—	3 435
	29	331·4	61·83	6·28	12·36	1 695, 1 650	2 985
IV	111—113	$C_{22}H_{33}N_3O_4$	67·16	5·89	10·68	—	3 475
	78	393·5	67·04	6·17	10·83	1 680, 1 650	2 975
Va	123—125	$C_{15}H_{18}N_4O_4$	56·60	5·70	17·60	—	3 450
	66	318·3	56·48	5·65	17·39	1 680, 1 630	2 975
Vb	221—223	$C_{12}H_{11}N_5O_2$	56·03	4·31	27·22	2 200, 2 205	3 430
	58	257·3	56·12	4·26	27·14	1 680, 1 630	2 940
Vc	306—310	$C_{11}H_8N_6$	58·92	3·60	37·48	2 205, 2 210	3 475
	72	224·2	58·81	3·52	37·12	—	3 160
Vd[a]	128—130	$C_{16}H_{19}N_3O_4$	10·56	6·03	13·24	—	3 460
	27	317·4	60·20	6·12	13·03	1 690, 1 645	2 970
Ve	252—253	$C_{13}H_{12}N_4O_2$	60·93	4·72	21·86	2 205	3 460
	73	256·3	60·92	4·51	21·56	1 690, 1 630	2 940
Vf	330—334	$C_{12}H_9N_5$	64·56	4·06	31·37	2 200, 2 215	3 475
	53	223·2	64·96	3·96	31·29	—	3 205
VIa	103—105	$C_{15}H_{18}N_4O_4$	56·60	5·70	17·60	—	3 460
	53	318·3	56·60	5·61	17·48	1 680, 1 655	2 980
VIb	210—214	$C_{12}H_{11}N_5O_2$	56·03	4·31	27·22	2 210	3 440
	80	257·3	55·87	4·17	27·08	1 685, 1 645	2 945
VIc	302—310	$C_{11}H_8N_6$	58·92	3·60	37·48	2 205, 2 210	3 490
	55	224·2	58·61	3·36	37·48	—	3 200

TABLE I
(*Continued*)

Compound	M.p., °C Yield, %	Formula Mol. mass	Calculated/Found			ν(C≡N) ν(C=O)	ν(NH) ν(CH)
			% C	% H	% N		
VId	113–117	$C_{16}H_{19}N_3O_4$	60·56	6·03	13·24	—	3 420
	43	317·4	60·52	5·79	13·08	1 685. 1 645	2 970
VIe	206–208	$C_{13}H_{12}N_4O_2$	60·93	4·72	21·86	2 210	3 410
	57	256·3	60·83	4·56	21·66	1 680, 1 635	2 960
VIf	266–272	$C_{12}H_9N_5$	64·56	4·06	31·37	2 205, 2 210	3 435
	89	223·2	64·48	4·03	31·31	—	3 200
VIIa	89–91	$C_{15}H_{18}N_4O_4$	56·60	5·70	17·60	—	3 475
	71	318·3	56·49	5·65	17·52	1 690, 1 630	2 960
VIIb	253–254	$C_{12}H_{11}N_5O_2$	56·03	4·31	27·22	2 206	3 475
	79	257·3	55·87	4·30	27·09	1 670, 1 630	2 945
VIIc	277–285	$C_{11}H_8N_6$	58·92	3·60	37·48	2 205, 2 210	3 475
	75	224·2	58·79	3·52	37·34	—	3 200

[a] Ref.[7] gives m.p. 129–130°C, yield 67%, ν(C=O) 1 650 and 1 700, ν(NH) and ν(CH) 2 950 and 3 000 cm^{-1}.

coupling constants ^3J(CH–NH) about 14 Hz were observed which correspond to the antiperiplanar conformation.

The geometric isomerism of methyl 2-cyano-2-propenoates *V–VII*(*b*, *e*) was studied by means of ^{1}H and ^{13}C NMR. The ^{1}H NMR spectra of these compounds reveal the geometric isomerism only by the presence of two singlets of methyl group in methoxycarbonyl grouping (except for *VIb*). In the ^{13}C NMR spectra (Table IV), the geometric isomerism of YZC=CH—NH— substituent doubles the number of carbon signals not only of this substituent but also that of the nearest neighbouring carbon atoms of the benzene nucleus[1]. From the coupling constants ^3J(H-8–CN) and ^3J(H-8–CO) in ^{13}C NMR spectra we estimated the position of carbonyl and cyano group, respectively, with regard to the proton at the C-8 carbon atom: *cis* below 6 Hz, *trans* above 8 Hz. On this basis, the signals with lower shift values were assigned univocally to the *E* isomer, i.e. the isomer with cyano group and carbonyl group at the *trans* and *cis* position, respectively, with regard to the H-8 proton. The *E* : *Z* isomer ratio is 50 : 50 (±10%) from both the proton and the carbon spectra.

Polarization of the multiple bond is also reflected in the shifts of carbon atoms of the substituted vinyl group: introduction of a cyano group causes a down-field shift of the signal of C-8 by approximately 2 ppm and an upfield shift of C-9 by

TABLE II

The ^{1}H NMR spectra of the compounds *II*— *VII*

Compound	H-2	H-4	H-5(6)	H-7	H-8	NH	N—R	COOR		$^4J_{4,6}$ $^4J_{5,7}$	$^3J_{6,7}$ $^3J_{4,5}$
IIa	—	7·76d	7·39dd	7·86d	8·02s	10·69b 10·87b	4·40s	4·09q 4·16q	1·20t	2	9
IIb	—	7·81d	7·41dd	7·95d	8·04s	—	4·46s	3·63s	—	2	9
IIc	—	8·08d	7·39dd	8·07d	8·03s	—	4·25s	—	—	2	9
IId	8·46s	8·05d	7·59dd	7·83d	9·59s	10·80b	4·04s	4·08q 4·15q	1·23t	2	9
IIe	8·45s	8·06d	7·73dd	8·13d	9·73s	—	4·06s	3·63s 3·73s	—	2	9
IIf	8·10s	8·25d	7·76dd	8·10d	8·02s	—	4·06s	—	—	2	9
III	8·48s	8·12d	7·64dd	8·03d	9·75s	—	4·46q 1·50t	4·11q	1·21t	2	9·25
IV	8·39s	7·63d 7·63d	7·05dd 7·17dd	7·61d 7·48d	8·36s 8·41s	—	5·45s 7·27m	4·08q 4·15q	1·18t	1·5 1·5	8 9
Va	—	8·42d	7·55dd	7·95d	8·42b	10·78b	4·20s	4·10q 4·18q	1·18t	2	8·5
Vb	—	7·93d	7·58dd	7·81d	8·36b	10·80b	4·21s	3·65s 3·70s	—	2	9
Vc	—	8·00d	7·60dd	7·81d	8·54b	11·18b	4·24s	—	—	2	8·75

TABLE II
(*Continued*)

Compound	H-2	H-4	H-5(6)	H-7	H-8	NH	N—R	COOR		$^4J_{4,6}$ $^4J_{5,7}$	$^3J_{4,5}$ $^3J_{6,7}$
Vd[a]	8·18s	7·61d	7·24dd	7·54d	8·43b	10·61b	3·80s	4·10q 4·20q	1·21t 1·24t	2	10
Ve	8·30s	7·64d	7·32dd	7·70d	8·36b	—	3·83s	3·78s 3·72s	—	2	9
Vf	8·12s	8·09d	7·30dd	7·50d	8·40b	10·91b	3·73s	—	—	2	8·5
VIa	—	7·93d	7·31dd	7·75d	8·29d[b]	10·86d[b]	4·23s	4·11q 4·15q	1·23t	1·5	9
VIb	—	7·79d 7·79d	7·56dd 7·61dd	7·91d 8·07d	8·34b 8·44b	— —	4·21s	3·66s 3·71s	—	2 2	9 9
VIc	—	7·76d	7·51dd	7·93d	8·39b	—	4·19s	—		2	9
VId	7·64s	7·58d	7·11dd	8·51d	8·10b	10·78b	3·78s	4·04q 4·13q	1·13t 1·21t	2	9
VIe	7·55s	7·65d	7·20dd	8·11d	8·44d[b]	10·74d[b]	3·76s	3·70s 3·64s	—	2	9
VIf	8·13s	7·57d	7·23dd	8·09d	8·48b	—	3·75s	—	—	2	9
VIIa	—	7·77d	7·42dd	7·88d	7·88d[b]	10·71d[b]	4·39s	4·06q 4·15q	1·19t	2	9
VIIb	—	7·78d	7·44dd	7·83d	8·34b	—	4·39s	— 3·70s	—	2	9
VIIc	—	7·86d	7·50dd	7·88d	8·55b	—	4·39s	—	—	2	9

[a] Ref.[7] ($CDCl_3$): 1·2 (2t), 6 H (CH_3CH_2); 4·15 q and 4·20 q, 4 H (CH_3CH_2); 3·80 s, 3 H (NCH_3); 7·2—7·6, m, 3 H (H-4 through H-7); 8·15 s, 1 H (H-2); 8·4 d, 1 H (H-8); 11·0 d, 1 H (NH, exchangeable); ^3J(HNCH) = 12 Hz; [b] ^3J(HNCH) = 14 Hz.

about 20 ppm. The intramolecular hydrogen bond causes a differentiation of carbonyl vibrations in the IR spectra of the 2-propenoate esters *V–VII* (*a*, *b*, *c*, *d*). The wavenumber of vibration of the carbonyl group involved in the interaction with the imine group of the enamine residue is lower. The vibrations of the NH group involved in the intramolecular hydrogen bond are found at about 3 460 cm^{-1} and have the half-width of 200–300 cm^{-1}.

The UV spectra of the benzimidazole derivatives contain a band below 270 nm which is characteristic of the $\pi \rightarrow \pi^*$ transition of the amidine chromophore[4], whereas the benzotriazole derivatives have the respective band below 310 nm.

The ^1H NMR spectra exhibit the proton signals of the benzazole skeleton in the expected regions and with the anticipated multiplicities[1,7]. The assignment of the carbon signals of the benzene ring of benzazole skeleton in the ^{13}C NMR spectra

TABLE III
UV Spectra of compounds *II–VII*

Compound	λ_{max}, nm(log ε^a, m^2 mol^{-1})				
IIa	220 (3·36)	—	—	294 (3·25)	359 (3·26)
IIb	221 (3·42)	—	—	283 (3·36)	312 (3·16)
IIc	222 (3·30)	—	—	275 (2·76)	303 (2·81)
IId	222 (3·29)	262 (2·75)	—	298 (2·94)	332 (3·27)
IIe	223 (3·42)	267 (2·40)	—	294 (2·96)	340 (2·40)
IIf	222 (3·27)	265 (2·90)	—	285 (2·97)	310 (2·86)
III	221 (3·22)	263 (2·81)	—	298 (2·92)	332 (3·20)
IV	—	257 (3·16)	266 (3·12)	—	333 (3·52)
Va	223 (3·33)	—	270 (3·13)	308 (3·41)	332 (3·47)
Vb	—	—	270 (3·07)	310 (3·35)	330 (3·41)
Vc	—	—	269	307	326
Vd	227 (3·23)	258 (3·06)	—	—	329 (3·42)
Ve	—	260	—	—	330
Vf	—	257	—	—	320
VIa	223 (3·22)	—	270 (3·03)	308 (3·26)	333 (3·39)
VIb	—	—	271	308	330
VIc	—	—	270	307	328
VId	228 (3·37)	256 (3·18)	265 (3·15)	—	330 (3·58)
VIe	—	257 (3·44)	266 (3·44)	—	332 (3·78)
VIf	—	257 (3·15)	265 (3·13)	—	328 (3·48)
VIIa	225 (3·21)	—	276 (3·38)	—	334 (3·37)
VIIb	—	—	281	—	331
VIIc	—	—	280	—	328

[a] The saturated solutions were measured in the cases where no log ε value is given.

TABLE IV

The ^{13}C NMR spectra of the compounds *II*—*VII*

Compound	C-2	C-4	C-5	C-6	C-7	C-3a	C-7a	NMe	C-8	C-9	C=O *trans*	C≡N *cis*	—OR	
Va	—	105·84	136·44	120·00	111·75	145·74	131·23	34·35	151·94	93·50	167·50	165·05	59·68	14·29
Vb	—	106·72	136·44	119·88	111·52	145·45	131·17	34·29	153·29	74·43	115·84	164·99	51·73	—
									153·99	73·49	166·51	118·07	—	—
Vc	—	106·72	135·85	119·77	111·58	145·39	131·29	34·35	156·29	52·02	114·15	116·43	—	—
Vd	145·80	107·99	134·37	113·83	110·98	143·85	132·29	30·67	152·17	92·13	167·50	164·90	59·13	14·03
Ve	[a]	109·10	133·46	113·86	111·28	141·36	132·81	31·13	152·65	72·83	115·38	164·25	50·91	—
		112·77		114·44	111·93			31·78	153·23	71·88	166·08	117·66		
Vf	145·93	108·77	134·11	110·72[b]	110·72[b]	143·59	132·55	30·80	156·07	50·55	114·22	116·69	—	—
VIa	—	120·12	116·61	138·78	97·01	142·52	134·14	34·12	150·89	94·55	167·21	164·99	59·62	14·23
													59·80	15·11
VIb	—	119·82	116·84	139·01	97·65	142·52	133·92	34·00	152·59	75·65	115·44	164·70	51·73	—
				138·08					153·35	74·54	166·22	117·50		
VIc	—	120·17	116·86	138·79	98·06	142·17	134·10	34·22	156·16	53·37	114·03	116·42	—	—
VId	145·57	120·41	113·33	135·21	99·41	140·83	134·83	31·13	152·59	92·80	168·03	165·64	60·09	14·52
									152·24				59·92	
VIe	145·30	119·89	113·68	134·27	99·70	140·80	135·27	30·84	153·58	73·68	116·14	165·40	51·79	—
			113·45		99·35				153·06	72·73	166·80	118·42		
VIf	145·50	119·86	113·68	134·86[b]	99·76	141·01	134·86[b]	30·90	155·92	51·14	114·44	116·90	—	—
VIIa	—	103·27	137·90	120·00	119·01	144·28	141·65	43·19	151·36	93·91	167·27	164·93	59·56	14·23
VIIb	—	104·50	138·10	120·00	118·83	144·10	141·90	43·01	152·82	75·25	115·31	164·82	51·67	—
		104·15	137·10						153·52	74·10	166·39	117·69		
VIIc	—	104·38	137·67	118·55	116·55	144·11	141·88	43·61	156·28	52·55	114·27	115·55	—	—

[a] Not observed; [b] not resolved.

was carried out by comparison of the shift values measured for the compound investigated with the values calculated. The calculated values were estimated from the contributions of the chemical shifts of the YZC=CH—NH— substituents on the benzene ring[1] and superposed on 1-methylbenzimidazole, 1- and 2-methylbenzotriazole[8]. The correctness of assignment by this method was also confirmed in the spectra with the proton–carbon interactions. Due to the prototropic tautomerism, the ^{13}C NMR spectra of benzimidazole[9,10] and benzotriazole[9,10] show a coalescence of signals of chemically non-equivalent carbon atoms of the benzene ring of benzazole skeleton, three broader signals only being observed instead of six signals[9,10]. The elimination of prototropy by the measuring technique CP MAS in solid state[9] or by the substitution of hydrogen atom of the imino group of azole ring[11] make it possible (as it is the case in unsymmetrical substitution in bezene ring[1,11]) to differentiate between the carbon signals of the benzene ring[9–11], the carbon shift values being not much affected by the methylation of the azole ring[9,11]. The signals of the methyl group bound to the nitrogen atom are found at about 31 ppm, 34 ppm, and as far as about 43 ppm in the cases of the 1-methylbenzimidazole, 1-methylbenzotriazole, and 2-methylbenzotriazole derivatives, respectively.

The alkylations of tautomeric benzotriazole and benzimidazole systems *I* with the substituent YZC=CH—NH— at the 5 position give the respective benzazoles *II* with the substituent YZC=CH—NR— at the 5 position, which was confirmed by comparing the products with the starting compounds and with the model compounds having a methyl group at nitrogen atoms of the azole ring. The akylations proceed preferably at the nitrogen atom of the substituent YZC=CH—NH—, as confirmed by the fact, that no products of methylation at the azole ring were observed in the reaction mixture.

EXPERIMENTAL

The melting points were determined with a Kofler apparatus and were not corrected. The IR spectra were measured with a Specord IR 75 apparatus (Zeiss Jena) in KBr discs; the UV spectra were measured with a Specord UV VIS apparatus (Zeiss Jena) in methanol. The ^{1}H NMR spectra were measured with a Tesla BS 487 C apparatus at the operation frequence 80 MHz, ^{13}C NMR spectra were measured with a JEOL FX-100 apparatus at the operation frequence 25·04 MHz, both in hexadeuteriodimethyl sulfoxide at 25°C with hexamethyldisiloxane standard — the central signal of hexadeuteriodimethyl sulfoxide (δ 39·5 ppm). The purity of all the nitro derivatives was checked by means of gas chromatography (Hewlett–Packard 7620 A).

6-Nitro-1-methylbenzimidazole

A mixture of 24·5 g (0·15 mol) 5(6)-nitrobenzimidazole, 210 ml 4% aqueous potassium hydroxide, 2 ml Ajatin, and 100 ml tetrachloromethane was stirred at room temperature and treated with a solution of 21 g (0·15 mol) methyl iodide in 50 ml tetrachloromethane added drop by drop. The reaction mixture was stirred overnight, the precipitated product was collected by suction

and dried in vacuum at 80°C. Yield 25·0 g (94%) of an isomeric mixture containing 56·3% 5-nitro- and 43·7% 6-nitro-1-methylbenzimidazoles.

Separation of the isomeric mixture: The dried isomeric mixture was dissolved in hot chloroform and filtered with charcoal. The filtrate was left to slowly evaporate. The plates of the 6-nitro isomer were separated mechanically from the needles of the 5-nitro isomer. The same procedure was repeated to give practically pure 6-nitro-1-methylbenzimidazole. Yield 4·5 g (17%), m.p. 181—182°C (ref.[4] gives m.p. 182°C).

3-Benzazolylamino Derivatives of 2-Propenoic Acid

The above nitro derivative (10 mmol) was dissolved in 100 ml of methanol, mixed with 200 mg 10% Pd–C catalyst, and hydrogenated (with magnetic stirring) under the pressure of 20 kPa hydrogen until the hydrogen consumption stopped (about 660 ml). The catalyst was filtered off, and the filtrate was treated with 10 mmol of the derivative of 3-alkoxy-2-propenoic acid. The reaction was monitored by means of TLC (Silufol 254 UV, chloroform–methanol 10 : 1 to 1 : 1, detection by means of UV lamp). The products *Vc*— *VIIc*, *Vf*, *VIf* were precipitated from the cool solutions, the compounds *Vb*— *VIIb*, *Ve*, *VIe* after heating and concentrating the solution. The other products which did not precipitate from the reaction mixture were obtained from the concentrated reaction mixtures by column chromatography (silica gel 100—150 μm, chloroform–methanol 100 : 1 to 1 : 1 as eluent). The yields of the syntheses and melting points of products are given in Table I.

Alkylation of 3-(5-Benzazolylamino)derivatives of 2-Propenoic Acid

A) A stirred solution of 5 mmol *I* in 20 ml dimethylformamide was treated with 0·9 g of anhydrous potassium carbonate. After 30 min, the alkyl halogenide was added drop by drop (1 ml methyl iodide, 1·1 ml ethyl iodide, or 0·8 ml benzyl chloride). The mixture was stirred 16 h at 20°C, whereupon it was evaporated, and the residue purified by column chromatography (silica gel 100—150 μm, eluent: chloroform for *III*, *IV*, *V*— *VII*(*a*, *d*), chloroform–methanol 100 : 1 for *V*— *VII*(*b*, *e*), and chloroform–methanol 10 : 1 for *V*— *VII*(*c*, *f*)).

B) A solution of 3·03 g (10 mmol) *Id* in 30 ml dimethoxyethane was stirred under argon and treated with 0·26 (11 mmol) sodium hydride until complete dissolution of *Ia*. Then 1·7 g (12 mmol) methyl iodide was added dropwise within 30 min, and the mixture was stirred 24 h. The product formed was collected by suction, washed with 20 ml dimethoxyethane, 20 ml diethyl ether, and dried. Yield 1·8 g (56·8%) *IId*, m.p. 129°C.

C) A solution of 0·75 g (2·5 mmol) *Id* in 30 ml tetrahydrofurane was stirred under argon and treated with 0·12 g (3 mmol) 60% sodium hydride. Then 0·5 g (4 mmol) dimethyl sulfate was added dropwise within 30 min, and the mixture was refluxed 6 h. The product was isolated as sub *A*. Yield 0·38 g (47·9%) *IId*, m.p. 128—130°C.

The authors are indebted to Mrs L. Livařová for measuring the ^{1}H NMR *spectra, to Mrs S. Markusová for measuring the* IR *spectra, to Mrs K. Kováčová for measuring the* UV *spectra, and to Mrs M. Ondrejkovičová for carrying out the elemental analyses.*

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Translated by J. Panchartek.