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STUDIES OF IMIDAZO[1,2-a]BENZIMIDAZOLE DERIVATIVES.

21.* SYNTHESIS OF HALOKETONES IN THE IMIDAZO[1,2-a] BENZIMIDAZOLE SERIES

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Methods for the synthesis of imidazo[1,2-a]benzimidazole haloketone derivatives have been investigated. It has been found that α-bromoketone derivatives of this heterocycle can be prepared either by bromination of 3-acylimidazo[1,2-a]benzimidazoles with bromine in glacial acetic acid or by acylation of 3-unsubstituted imidazo[1,2-a]benzimidazoles with haloanhydride derivatives of α-bromoalkanoic acids. Treatment of imidazo[1,2-a]benzimidazoles with 3-chloropropionyl chloride results in the formation of imidazo[1,2-a]benzimidazolyl-3-propionyl chloride and bis(imidazo[1,2-a]benzimidazolyl)propan-3-one derivatives as side products. Reaction of 2-phenylimidazo[1,2-a]benzimidazoles with 3-bromopropionic acid in polyphosphoric acid gives benzocyclohepten[5',6':4,5]imidazo[1,2-a]benzimidazole derivatives.

Haloketones are widely used as synthons for the preparation of aminoalcohols, aminoketones, and heterocyclic and other compounds. In order to expand the synthetic possibilities for the preparation of biologically active compounds in the imidazo[1,2-a]benzimidazole series, we have been studying various methods for the preparation of haloketone derivatives of this heterocyclic system.

One of the most common methods for the synthesis of α-haloketones involves the direct halogenation of ketones. All efforts to brominate ketones I directly failed, either with N-bromosuccinimide in CCl_4, in the absence of a catalyst or in the presence of benzoyl peroxide, or with copper bromide in chloroform or chloroform–ethyl acetate mixtures. When ketones I were treated with either dioxanedibromide in ether or with dioxane and bromine in chloroform or methanol, only perbromides of the starting ketones were obtained; these perbromides decomposed upon extended refluxing in either water or alcohol, but did not generate the bromoketones II as expected (cf. [2, 3], for example).

*For Communication 20, see [1].

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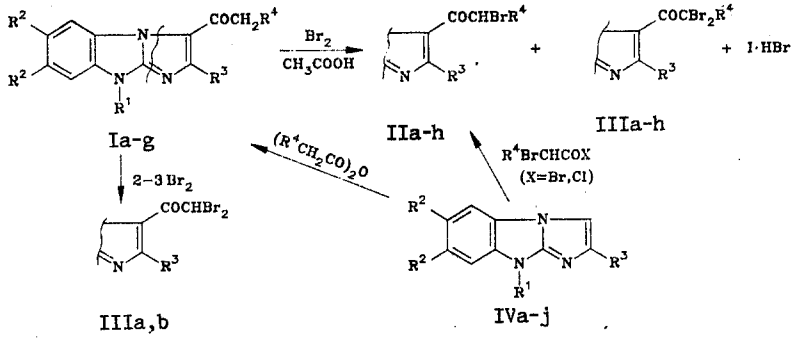
TABLE 1. Bromoketone Derivatives in the Imidazo[1,2-a]benzimidazole Series, IIa-h

Compound	mp, °C (dec.)	Found, %				Molecular formula	Calculated, %				Yield, %	
		C	H	Br	N		C	H	Br	N	A	B
IIa	187—188	58,6	3,7	21,3	11,6	$C_{18}H_{14}BrN_3O$	58,7	3,8	21,7	11,4	77	89—93*
IIb	164—165	50,9	4,1	26,6	13,6	$C_{13}H_{12}BrN_3O$	50,7	4,0	26,1	13,7	68	91—95*
IIc	167—168	59,5	4,3	20,9	11,2	$C_{19}H_{16}BrN_3O$	59,7	4,2	20,9	11,0	70	—
IId	179	64,6	4,1	18,4	9,8	$C_{24}H_{18}BrN_3O$	64,9	4,1	18,0	9,5	65	—
IIe	195—196	61,6	5,0	19,1	10,0	$C_{21}H_{20}BrN_3O$	61,5	4,9	19,5	10,2	82	90
IIf	197—198	52,6	4,4	24,7	13.0	$C_{14}H_{14}BrN_3O$	52,5	4,4	25,1	13,1	—	81*
IIg	205	60,0	4,1	21,4	10,7	$C_{19}H_{16}BrN_3O$	59,7	4,2	20,9	11,0	61,8	84*
IIh	137—138	61,4	5,0	19,3	10,4	$C_{21}H_{20}BrN_3O$	61,5	4,9	19,5	10,2	—	90

*When the acylation reactions were carried out in benzene, the yields of bromoketones IIa, b, f, and g were 39, 46, 48, and 37%, respectively.



I—IV a,b,f,g $R^1=CH_3$, c,d $R^1=CH_2C_6H_5$, e,j $R^1=C_2H_5$, h $R^1=C_4H_9$, and $R^1=C_3H_7$; a—d f—i R^2=H, e, f $R^2=CH_3$; a,d,e,g-j $R^3=C_6H_5$, b, c $R^3=CH_3$; a-c R^4=H, f,g $R^4=CH_3$

Treatment of ketones I with bromine in glacial acetic acid at room temperature also led to the formation of perbromides; in refluxing acid, however, high yields of the bromoketones II were produced (65-80%). The reactions are accompanied by the formation of small amounts of the hydrobromides of I as well as of the dibromoketones III. The yields of dibromoketones are increased to 50-89% when the amount of bromine used is increased to 2-3 moles.

The α-bromoketones II can also be prepared directly by the alkylation of 3-unsubstituted imidazo[1,2-a]benzimidazoles IV with haloanhydride derivatives of α-bromoalkanoic acids. The yields of II do not exceed 40-48% when the reactions are carried out in refluxing benzene, since half of the starting material is consumed by reaction with the liberated HBr, and the resulting hydrobromides cannot be acylated under these conditions. It was not possible to increase the yield of bromoketones using anhydrous potassium hydroxide as an HBr scavenger, and introduction of either triethylamine or pyridine to the reaction mixtures resulted in considerable resinification. The yields of compounds II could be increased to 70-90% by employing high boiling solvents such as toluene or xylene as the reaction medium. In refluxing xylene it is possible to acylate not only the bases IV, but also their salts; this is especially convenient in cases where the precursor imidazo[1,2-a]benzimidazole is an oil (for instance, compound IVh). The IR spectra of the bromoketones II, taken in Vaseline mulls, exhibit C-Br stretches at 630-640, and C=O absorption bands at 1630-1645 cm^{-1}.

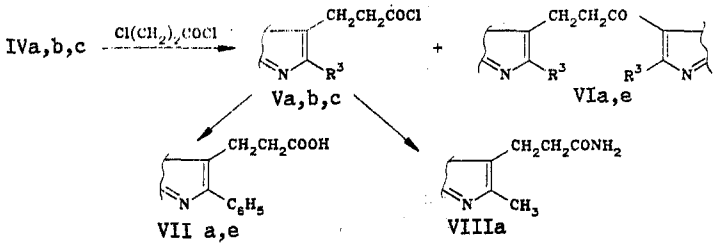
Haloacylation of compound IVa with 3-chloropropionyl chloride gave a mixture of two compounds, one of which proved to be the chloroanhydride of imidazo[1,2-a]benzimidazolyl-3-propionic acid (Va) (yield about 80%, based on the corresponding acid), whereas the second has been assigned the ketone structure VIa. The IR spectrum of compound VIa contains a carbonyl group absorption band at 1620 cm^{-1}. The PMR spectrum in CF_3COOH shows two partially overlapping three-proton singlets at 3.59 and 3.54 ppm, corresponding to the two N-CH_3 group protons. Two slightly broadened signals at 3.22 and 2.65 ppm, with intensities corresponding

TABLE 2. 13-Alkyl-6,7-dihydro-5-oxobenzocyclohepten[5',6':4,5]imidazo[1,2-a]benzimidazoles (IXa-e)

Compound	mp, °C (dec.)	IR spectrum, $\nu_{C=O}$, cm^{-1} (in chloroform)	PMR spectrum in $CDCl_3$, δ, ppm	M+	Found, %			Molecular formula	Calcd., %		
					C	H	N		C	H	N
IXa	227—228	1682	3,62 (3H, s., N—CH_3), 3,15 (4H, q, —CH_2CH_2—), 6,88—7,53 (8H, m., Arprotons)	301	75,8	4,6	14,2	$C_{19}H_{15}N_3O$	75,7	5,0	13,9
IXb	206—207	1680	1,18 (3H, t, CH_3), 3,15 (4H, q, —CH_2CH_2—), 4,12 (2H, q, N—CH_3), 7,25 (8H, m, Ar protons)	315	76,1	5,2	13,6	$C_{20}H_{17}N_3O$	76,2	5,4	13,3
IXc	153	1680	0,62 (3H, t, CH_3), 1,62 (2H, m, CH_2CH_3), 3,15 (4H, q, —CH_2CH_2—), 4,0 (2H, t, N—CH_2), 7,25 (8H, m, Ar protons)	329	76,7	6,0	12,8	$C_{21}H_{19}N_3O$	76,6	5,8	12,8
IXd	150	1680	0,52 (3H, t, CH_3), 1,0 (2H, m, CH_2CH_3), 1,5 (2H, broad signal N—CH_2CH_2), 3,15 (4H, q, —CH_2CH_2—), 4,0 (2H, t, N—CH_2), 7,25 (8H, m, Arprotons)	343	76,8	6,4	12,4	$C_{22}H_{21}N_3O$	76,9	6,2	12,2
IXe	221—222	1670	1,2 (3H, t, CH_2CH_3), 2,06 (6H, s, $2CH_3$), 3,12 (4H, q, —CH_2CH_2—), 4,12 (2H, q, N—CH_2), 7,06 (2H), 7,25—7,35 (4H, Arprotons)	343	76,9	6,3	12,5	$C_{22}H_{21}N_3O$	76,9	6,2	12,2

to 2 protons apiece, may be attributed to protons in the ethylene bridge. The aromatic protons (17H) appear as a complex multiplet at 6.92-7.23 ppm, while the signal due to the ortho-proton of the phenyl substituent appears as a doublet at 8.12 ppm. The reactions of other imidazo[1,2-a]benzimidazole derivatives IV proceed in an analogous manner.

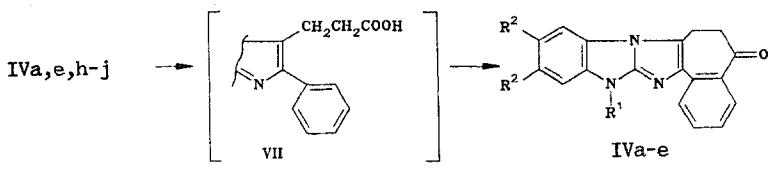
The acyl halides V can be readily converted to the acids VII or amides VIII by treatment with solutions of sodium bicarbonate and ammonia, respectively; these compounds are identical to the derivatives prepared by substitution and addition reactions of compounds IV with acrylic acid or acrylonitrile in polyphosphoric acid (PPA) [4, 5]. The IR spectra of the chloroanhydrides V, taken in Vaseline mulls, contain strong absorption bands at 1790-1800 cm^{-1}, corresponding to C=O stretching vibrations; these bands disappear upon conversion to derivatives VII and VIII.



The identities of the substituent groups in compounds Va, b, e are the same as those in the precursor compounds IV.

In the first 10-15 min of the reactions of compounds IV with chloropropionyl chloride, a large amount of precipitate, consisting of hydrochloride salts of IV, is deposited; this fact, coupled with the absence of other imidazo[1,2-a]benzimidazole derivatives, leads us to assume that the starting materials IV act as dehydrochlorinating agents (bases), resulting in the conversion of chloropropionyl chloride to acryloyl chloride. The ease of addition of the latter compound to imidazo[1,2-a]benzimidazole derivatives IV, or their salts, has been demonstrated by independent syntheses. Reaction of compound V with a molecule of imidazo[1,2-a]benzimidazole, which has not entered into an addition reaction (this is the basis of the independent synthesis), or attack of the latter reagent by the two reactive sites in acryloyl chloride ($C_{(1)}$ and $C_{(3)}$) can generate ketone VI. The yields of VI are low, which indicates that the rate of the acylation sequence is slow relative to the rate of the addition reaction.

In the case of 2-phenylsubstituted derivatives of IV, attempts to synthesize α-haloketones via reaction with 3-bromopropionic acid in PPA led to yellow colored substances which did not contain bromine. The IR spectra of these materials, taken in chloroform, displayed characteristic bands at 1505, 1600, 1615, 1635 (C=C and C=N) and 1670-1685 cm^{-1} (C=O). The PMR spectra, taken in trifluoroacetic acid, exhibited in all cases a quartet at 3.15 ppm, with an integrated intensity corresponding to 4 protons; this signal may be ascribed to the $-CH_2-CH_2-$ group. Based on this spectroscopic data, as well as elemental analysis, molecular weight data (obtained by mass spectrometry), and comparison with compounds obtained upon heating 2-phenylimidazo[1,2-a]benzimidazolyl-3-propionic acids in PPA at 110-120°C [5], the compounds noted above have been assigned structures IX, i.e., benzocycloheptene[5',6':4,5] imidazo[1,2-a]benzimidazole oxo derivatives.



IX **a-d** $R^2=H$, **e** $R^2=CH_3$; **a** $R^1=CH_3$, **b,e** $R^1=C_2H_5$, **c** $R^1=C_3H_7$, **d** $R^1=C_4H_9$

Treatment of 2-phenylimidazo[1,2-a]benzimidazoles IV with 3-bromopropionic acid in PPA results, first of all, in alkylation of the heterocyclic ring at position 3, followed by intramolecular acylation of the ortho phenyl substituent in the 2-position. It was not possible to isolate the intermediate acids VII, apparently because the rate of formation of these acids under the reaction conditions is considerably slower than the rate of the subsequent intramolecular cyclization. When the analogous reaction was carried out with the 2-methyl substituted derivative IVb, 2,9-dimethylimidazo[1,2-a]benzimidazolyl-3-propionic acid was isolated in low yield; this compound was unchanged by heating in PPA even under much harsher reaction conditions (130-150°C).

EXPERIMENTAL

IR spectra were taken on a UR-20 spectrophotometer using either Vaseline mulls or solutions in chloroform; PMR spectra were recorded on Tesla BS-467 (60 MHz) or Tesla BS-487 C (80 MHz) spectrometers using solutions in either deuterochloroform or trifluoroacetic acid versus HMDS as internal standard. Molecular weights were determined by mass spectrometry on an MU-1305 spectrometer at an ionizing current of 60 eV. The course of the reactions, as well as purities of the products, were monitored by TLC on Al_2O_3 with chloroform or benzene as eluent and visualization with iodine vapor in a moist cell.

9-Butyl-2-phenylimidazo[1,2-a]benzimidazole (IVh). A hot solution of 9.45 g (50 mmoles) of 2-amino-1-butylbenzimidazole in 100 ml of acetone was treated with 10 g (50 mmoles) of phenacyl bromide; the mixture was carefully stirred and allowed to stand at room temperature. After 1 h the precipitate of 2-amino-1-butyl-3-phenacylbenzimidazole was removed by filtration and washed with acetone. Yield 18.1 g (93%). Snow-white crystals, mp 212-213°C (from alcohol). IR spectrum: 1490, 1600 (C=C), 1670 (C=N), 1690 (C=O), 3160, 3300 cm^{-1} (NH_2). Found: C 58.7; H 5.8; Br 20.3; N 10.6%. $C_{19}H_{21}N_3O \cdot HBr$. Calculated: C 58.8; H 5.7; Br 20.6; N 10.8%.

A mixture of 16.8 g (42 mmoles) of the above bromide, 8.9 g (84 mmoles) of sodium carbonate, 100 ml ethanol, and 50 ml water was refluxed for 4-5 h. The alcohol was evaporated, and compound IVh was extracted from the residue with chloroform (3 × 15 ml). The extract was dried over anhydrous sodium sulfate, solvent was evaporated, and 12.96 g (quantitative yield) of compound IVh was obtained as a viscous yellow oil, which was used without further purification. If necessary, it could be purified by column chromatography on Al_2O_3 (benzene eluent). IR spectrum: 1500, 1605, 1630 cm^{-1} (C=C, C=N). Found: C 78.7; H 6.5; N 14.7%. $C_{19}H_{19}N_3$. Calculated: C 78.9; H 6.6; N 14.5%. The hydrochlorides salt of IVh was prepared by acidification of an ethanolic or acetone solution of the free base with conc. HCl. Snow-white crystals, mp 207-208°C (from alcohol). Found: C 70.1; H 6.0; Cl 10.5; N 12.8%. $C_{19}H_{19}N_3 \cdot HCl$. Calculated: C 70.0; H 6.2; Cl 10.9; N 12.6%.

9-Methyl-3-propionyl-2-phenylimidazo[1,2-a]benzimidazole (Ig). A mixture of 1.24 g (5 mmoles) of compound IVg, 1 g fused sodium acetate, and 7 ml propionic anhydride was refluxed 1 h, cooled, and poured into 30 ml of water. After decomposition of excess anhydride, the mixture was neutralized with ammonia to pH 7-8 and extracted with chloroform (2 × 10 ml). The latter was evaporated, and the residue was treated with 10 ml of ether. The precipitate was filtered and washed with ether. Yield 1.4 g (92.1%). Snow-white crystals, mp 145-146°C (from alcohol). IR spectrum: 1490, 1585, 1624 (C=C, C=N), 1646 cm^{-1} (C=O). PMR spectrum (80 MHz, CF_3COOH): 0.67 (3H, t, C–CH_3), 2.25 (2H, q, CH_2), 3.62 (3H, s, N–CH_3), 8.32 (1H, d and 7.25 ppm (8H, s, aromatic protons). Found: C 75.0; H 5.7; N 13.8%. $C_{19}H_{17}N_3O$. Calculated: C 75.2; H 5.7; N 13.9%. Ketone Ig could also be prepared in 13% yield by reaction of propionic acid (10 mmole) with compound IVg (1.24 g, 5 mmole) in PPA (12 h, 110°C).

3-α-Bromoacylimidazo[1,2-a]benzimidazoles (IIa-h, Table 1). A. A solution of 10 mmole of the appropriate ketone Ia-h in 30 ml glacial acetic acid was heated to 110-115°C, stirred vigorously, and a solution of 1.6 g (0.5 ml, 10 mmole) of bromine in 3 ml of glacial acetic acid was added slowly, at such a rate that the solution decolorized immediately and bromine did not accumulate in the reaction mixture. After addition was complete the mixture was stirred an additional 5-10 min and then poured onto 150 ml of cold water. The resulting precipitate was filtered, washed with water, and dried, then subjected to preliminary purification through a small layer of Al_2O_3 ($CHCl_3$ eluent); the light yellow fraction was collected ($R_f \sim 0.85$-0.9) and crystallized from the solvent of choice: bromoketones IIa, b from benzene, IIa,c,f-h from alcohol, IId,e from DMF. Recrystallization of compounds IIa and b permitted separation by crystallization from the corresponding dibromoketones.

B. An energetically stirred solution of 10 mmole of compound IVa, b, e-h or a suspension of the corresponding hydrochloride in 60 ml of absolute xylene was heated at 120-130°C and treated with 20 mmole of bromoacetyl halide or 2-bromopropionic acid, and the reaction mixtures were stirred until the reactions were complete (TLC control). The reaction time depends primarily on the structure of the haloanhydride used. After being cooled, the mixture was filtered to remove precipitate, which was washed with xylene and petroleum ether, dried in air, and suspended in water for reaction with either sodium hydroxide solution or ammonia to neutrality. The precipitate was separated, dried in air, and treated several times with diethyl ether to remove traces of IV, then finally recrystallized from the appropriate solvent.

3-Dibromoacetyl-9-methyl-2-phenylimidazo[1,2-a]benzimidazole (IIIa). A refluxing solution of 2.89 g (10 mmoles) of ketone Ia in 30 ml CH_3COOH was treated dropwise with stirring with 4.8 g (1.5 ml, 30 mmole) of bromine in 5 ml CH_3COOH; the mixture was refluxed an additional h, cooled, and poured onto 100 ml of water. The resulting precipitate was filtered and washed with water. Yield 4 g (89%). Pale yellow crystals, mp 245.5°C (dec., from butanol). IR spectrum ($CHCl_3$): 645 (CBr_2), 1500, 1590, 1625 (C=C, C=N), 1645 cm^{-1}(C=O). PMR spectrum (80 MHz, CF_3COOH): 3.69 (3H, s, N–CH_3), 5.7 (1H, s, CH), 8.25 (1H, d and 7.33 ppm (8H, s, aromatic protons). Found: C 48.5; H 2.8; Br 35.9; N 9.3%. $C_{18}H_{13}Br_2N_3O$. Calculated: C 48.4; H 2.9; Br 35.7; N 9.4%.

3-Dibromoacetyl-2,9-dimethylimidazo[1,2-a]benzimidazole (IIIb). This was prepared in 52% yield by bromination of ketone Ib (10 mmole) with bromine (20 mmole) in refluxing acetic acid. Pale yellow crystals mp 216-218°C (from butanol). IR spectrum ($CHCl_3$): 645 (CBr_2), 1510, 1595, 1620 (C=C, C=N), 1640 cm^{-1} (C=O). Found: C 40.1; H 2.9; Br 41.0; N 10.8%. $C_{13}H_{11}Br_2N_3O$. Calculated: C 40.5; H 2.9; Br 41.5; N 10.9%.

Reaction of 9-Methyl-2-phenylimidazo[1,2-a]benzimidazole (IVa) with 3-Chloropropionyl Chloride. A solution of 1.24 g (5 mmoles) of compound IVa in 25 ml of absolute xylene was treated with stirring with 1 ml (about 10 mmoles) of chloropropionyl chloride and the mixtures was refluxed for 2-3 h. The mixture was cooled and the precipitate of chloroanhydride hydrochloride Va was filtered and washed with petroleum ether until all traces of chloropropionyl chloride had been removed. After drying the precipitate was suspended in 20 ml of water, neutralized with sodium hydroxide solution to pH 7, and filtered again. The dry solid was treated with 10 ml of $CHCl_3$. The acid VIIa remained undissolved and was separated and washed with $CHCl_3$. Yield 1.28 g (80%) of VIIa, mp 271°C (dec., from DMF). IR spectrum (Vaseline mull): 1500, 1608, 1630 (C=C, C=N), 1690 (C=O), 920, 2400-2800 cm^{-1} (OH). PMR spectrum (60 MHz, CF_3COOH): 3.62 (3H, s, N–CH_3), 2.55 (2H, t, CH_2), 3.25 (2H, t, CH_2) 7.15 ppm (9H, m, aromatic protons). Found: C 71.4; H 5.7; N 13.1%, $C_{19}H_{17}N_3O_2$. Calculated: C 71.4; H 5.4; N 13.2%. The compound was identical in all respects to a sample prepared earlier [5].

The residue which remained after evaporation of the chloroform solution after separation of acid VIIa was purified by chromatography on a 1.5 cm (diameter) by 10 cm (length) column (Al_2O_3, $CHCl_3$ eluent) to remove traces of the acid and then recrystallized from ethyl acetate to give 0.19 g (13.9%) of ketone VIa as snow-white crystals, mp 212-213°C (dec.). Found: C 76.6; H 5.0; N 15.5%. $C_{35}H_{28}N_6O$. Calculated: C 76.6; H 5.1; N 15.3%.

1,3-Bis(9-Methyl-2-phenylimidazo[1,2-a]benzimidazolyl-3)propan-3-one (VIa) (Independent Synthesis). A solution of 0.75 g (3 mmoles) of compound IVa in 15 ml of absolute xylene was stirred vigorously at room temperature and 0.3 ml (3 mmoles) of freshly prepared acryloyl chloride was added; the mixture was stirred until TLC indicated all of the starting material IVa had been consumed (about 2 h). Another 1.5 g (6 mmoles) of IVa was added to the reaction mixture, and the mixture was refluxed for 4 h. The mixture was cooled and the precipitate was filtered and washed with 5 ml of benzene followed by petroleum ether (2 × 5 ml). The precipitate was then treated at room temperature with 10 ml of $CHCl_3$ and the undissolved hydrochloride of IVa was separated by filtration. The chloroform solution was passed through a layer of Al_2O_3 with $CHCl_3$ eluent, and the eluate was evaporated and the residue crystallized from ethyl acetate. Yield 1.28 g (78%) of ketone VIa, mp 212-213°C (dec.), identical to the sample prepared as described above.

3-(6,7-Dimethyl-2-phenyl-9-ethylimidazo[1,2-a]benzimidazolyl-3)propanoic Acid (VIIe). This was prepared in a manner analogous to acid VIIa by refluxing 1.45 g (5 mmoles) of compound IVe with 10 mmole of chloropropionyl chloride in xylene for 4 h. Yield 1.37 g

(76.1%), mp 283°C (dec., from propanol). IR spectrum (Vaseline mull): 1500, 1610, 1630 (C=C, C=N), 1705 (C=O), 920, 2400-2800 cm^{-1}(OH). PMR spectrum (80 MHz, CF_3COOH): 1.16 (3H, t, CH_2CH_3), 4.0 (2H, q, N-CH_2), 2.08 (6H, s, 2 CH_3), 2.55 (2H, t, CH_2), 3.2 (2H, t, CH_2), 7.13 ppm (7H, m, aromatic protons). Found: C 73.3; H 6.5; N 11.8%. $C_{22}H_{23}N_3O_2$. Calculated: C 73.1; H 6.4; N 11.6%.

When 1.45 g (5 mmole) of IVe was heated with 0.7 ml (10 mmoles) of acrylic acid in 25 ml of PPA (80°C, 2 h), acid VIIe was obtained in 95% yield and was identical with respect to mp and IR and PMR spectra to the sample prepared according to part A.

1,3-Bis(6,7-dimethyl-2-phenyl-9-ethylimidazo[1,2-a]benzimidazolyl-3)propan-3-one (VIe). A. The chloroform solution which remained after separation of acid VIIe from the reaction mixture of IVe and chloropropionyl chloride was evaporated until 3-4 ml volume remained and then passed through a layer of Al_2O_3 ($CHCl_3$ eluent). The eluate was evaporated and the residue was recrystallized from acetonitrile to give 0.24 g (15.2%) of ketone VIe as snow-white fibrous crystals, mp 219-220°C (dec.). IR spectrum (Vaseline mull): 1620 cm^{-1} (C=O). Found: C 77.5; H 6.4; N 13.4%. $C_{41}H_{40}N_6O$. Calculated: C 77.8; H 6.4; N 13.3%.

In analogy with the method used for ketone VIa, refluxing chloroanhydride Ve, prepared from 0.72 g (2.5 mmoles) of IVe and 0.25 ml (2.5 mmoles) acryloyl chloride in 25 ml xylene, with 1.44 g (5 mmoles) of compound IVe over 5 h gave 1.3 g (82.3%) of ketone VIe, mp 219-220°C (dec.). A mixed melting point probe with a sample prepared from part A did not exhibit a mp depression.

3-(2,9-Dimethylimidazo[1,2-a]benzimidazolyl-3)propanamide (VIIIb). The chloroanhydride Vb precipitate, isolated by treatment of compound IVb with chloropropionyl chloride in refluxing xylene, was treated with a 22% solution of NH_4OH; the amide was separated, washed with water, and crystallized from aqueous acetone. Yield 78% mp 234°C (dec.). IR spectrum (Vaseline mull): 1675 (C=O), 3160, 3370 cm^{-1} (NH_2). Found: C 65.4; H 6.5; N 21.9%. $C_{14}H_{16}N_4O$. Calculated: C 65.6; H 6.3; N 21.9%.

A solution of 1.85 g (10 mmoles) of compound IVb in 30 g PPA was heated to 125-130°C and 0.7 ml (10 mmoles) of acrylonitrile was added with stirring; the mixture was heated at this temperature for 3 h, an additional 0.7 ml of acrylonitrile was added, and the mixture was heated for 4 h. The mixture was cooled to 50-60°C and poured with vigorous agitation into 60 ml of cold water. The resulting solution was carefully neutralized with 22% aqueous ammonia to pH 7. After 30-40 min the precipitate was filtered and washed with water. Yield 2.4 g (93.8%), mp 234° C (dec.).

13-Alkyl-6,7-dihydro-5-oxobenzocyclohepten[5',6':4,5]imidazo[1,2-a]benzimidazoles (IXa-e, Table 2). A. A stirred mixture of 5 mmoles 9-alkyl-2-phenylimidazo[1,2-a]benzimidazole (IVa, e, h-i), 1.53 g (10 mmoles) bromopropionic acid, and 25 g PPA was heated for 3-4 at 100-105°C and then at 110-120°C until the reaction was complete (3-4 h, TLC control). The mixture was cooled to 40-50°C and poured with vigorous agitation into 75-100 ml water; the mixture was then basified to pH 8-9 with 22% NH_4OH solution, and the resulting precipitate was filtered, carefully washed with water, dried in air, and finally purified by recrystallization from alcohol. Yield 90-95% of ketones IXa-e. Compounds IXa and IXc were identical to those described in an earlier work [5].

A mixture of 0.72 g (2 mmoles) of acid VIIe in 10 g PPA was maintained at 120-125°C for 1 h. The hot reaction mixture was poured into 40 ml of cold water, and ketone IX e was separated and isolated in amanner analogous to that described in part A. Quantitative yield.

A mixture consisting of 1.65 g (5 mmoles) of the hydrochloride of IVh, 0.7 ml (10 mmoles) of acrylic acid, and 25 g PPA was stirred at 120-125°C for 3 h, and ketone IXd was isolated from the reaction mixture as described in part A. It was purified by passage through a layer of Al_2O_3 in chloroform solution, and then recrystallized from alcohol. Yield 90%. The sample was identical with a sample prepared in part A.

3-(2,9-Dimethylimidazo[1,2-a]benzimidazolyl-3)propanoic Acid (VIIb). A mixture of 0.92 g (5 mmoles) compound IVb, 1.53 g (10 mmoles) 3-bromopropionic acid, and 15 g PPA was stirred at 115-120°C for 28 h. The mixture was cooled and poured into 50 ml of water, then neutralized with NH_4OH to pH 7. The resulting oily material was separated and treated with 7 ml chloroform. The undissolved sample of acid VIIb was separated and crystallized from

DMF. Yield 0.18 g (15%), mp 250-251°C (dec.). Found: C 65.1; H 6.2; N 16.4%. $C_{14}H_{13}N_3O_2$. Calculated: C. 65.4; H 5.9; N 16.3%. The compound was identical to that described in [5].

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REACTION OF N-AMINOBENZIMIDAZOLIUM CATIONS WITH AROMATIC ALDEHYDES. SYNTHESIS OF 2,4-DIARYL-as-TRIAZINO[1,6-a] BENZIMIDAZOLES

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On heating with aromatic or heteroaromatic aldehydes in polar aprotic solvents, 1-amino-3-alkylbenzimidazolium salts form 2,4-diaryl derivatives of a new heterocyclic system of as-triazino[1,6-a]benzimidazole.

The reaction of 1-amino-3-alkylbenzimidazolium salts (I) with aromatic aldehydes in an alcoholic medium leads to the usual Schiff base analogs II in high yields [1]. We found that in boiling DMFA, DMSO, or HMPTA, at 150°C, this process is more complex in character and is accompanied by the formation of 2,4-diaryl derivatives of a new heterocyclic system — as-triazino[1,6-a]benzimidazole (III). With ketones and 2-methyl derivatives of salts I, the reaction does not proceed. According to our data, examples of this type of transformations are not known for N-amino derivatives of heterocycles. The present work was undertaken to establish the structure of compounds III and the factors influencing their formation (the structural features of cations II, temperature conditions, basicity of medium).

Examination of the PMR spectra of the non-salt-like bright-yellow compounds, which we isolated, showed clearly that at one of the reaction stages, salts I undergo dealkylation (absence of signals in the absorption region of the aliphatic protons in the spectrum of IIIa). Moreover, the more simple in character spectra of the model compounds IIIb,c, obtained from salts Ia,c with anisaldehyde, unequivocally indicated that compounds III include two aldehydic residues in their composition. This was confirmed by the data of the elemental analysis and mass spectrometric determination of the molecular weight. In the PMR spectrum of compound IIIb two singlets of the methyl group are observed in the region of 3.70 and 3.75 ppm, four doublets of the aromatic protons at 6.82, 6.90, 8.23, and 9.0 ppm, with SSCC (spin–spin coupling constant) of 9.0 Hz, which are assigned to ortho- and meta-protons of two benzene rings, and also two multiplets of the benzimidazole ring protons in the region of 7.35 and 7.90 ppm

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