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INVESTIGATIONS OF IMIDAZO[1,2-a]BENZIMIDAZOLES. 26.* 2-HALOMETHYLIMIDAZO[1,2-A]BENZIMIDAZOLES AND THEIR REACTIVE PROPERTIES

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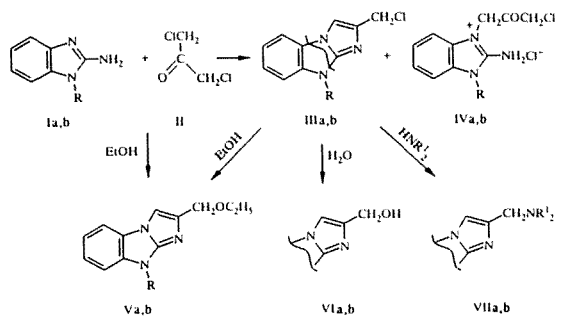
Treatment of 2-aminobenzimidazoles with 1,3-dichloroacetone or radical bromination of 3-alkoxycarbonyl- or 3-acetyl-2-methylimisazo[1,2-a]benzimidazoles leads to the 2-halomethyl derivatives of this heterocycle. The lability of the halogen atom in the synthesized compounds has been demonstrated.

Many imidazo[1,2-a]pyrimidines, including those substituted at position 3, show interesting pharmacological properties. The synthesis and properties of this heterocycle substituted at the 2 position have been little investigated [2-4]. In this study, we have synthesized 2-halomethylimidazol[1,2-a]benzimidazoles which serve as convenient synthons for functionalization at position 2 and so to physiologically active species.

It is known that nitrogen heterocyclic derivatives with an amino or mercapto group alpha to the heteroatom can cyclocondense with 1,3-dichloroacetone to form five membered imidazole or thiazole rings containing a halomethyl group [5-8].

However, 2-amino-1-methylbenzimidazole (Ia) reacts with 1,3-dichloroacetone (II) under the conditions in [5-7] (i.e., refluxing in ethanol) extremely ambiguously and much tarring occurs. Preparative TLC separation of the reaction mixture gave only one compound, in which the chlorine was absent. The PMR spectrum showed a multiplet for the aromatic protons at 7.3-7.12 ppm together with a triplet at 1.2 ppm (3H), a quartet at 3.58 ppm (2H) (ethoxy group), and singlets at 3.64 ppm (3H) and 4.5 ppm (2H) (NCH_3 and CH_2O groups, respectively). From this data, the elemental analysis, and from an independent synthesis described below, this product can be assigned as 9-methyl-2-ethoxymethylimidazo[1,2-a]benzimidazole (Va). This result suggested that the 2-chloromethyl derivative was highly unstable and prompted a change in the reaction conditions.

Reaction of amine Ia with ketone II in dry acetone at room temperature proceeds quite smoothly but leads to a mixture of 9-methyl-2-chloromethylimidazo[1,2-a]benzimidazole (IIIa) and 2-amino-1-methyl-3-(3-chloroacetonyl)benzimidazole chloride (IVa), which is confirmed by further reaction of this mixture. The PMR spectrum of the mixture (in CF_3COOH) shows singlets for two N-methyl groups at 3.34 and 3.57 ppm, methylene protons in the acetonyl radical of salt IVa at 4.05 and 4.3 ppm, the CH_2Cl group at 5.08 ppm, and a broad amino proton signal for IVa at 6.52 ppm. The IR spectrum showed absorption bands for the quaternary salt IVa "immonium" $=N^+=C$ group at 1680 cm^{-1}, a carbonyl group at 1770 cm^{-1}, and an NH_2 group at 3170 and 3345 cm^{-1}.



I, III–VI a R = CH_3, b R = $CH_2C_6H_5$, VII R = CH_3; a R_2^1 = $(C_2H_4)_2O$, b R_2^1 = $(CH_2)_5$

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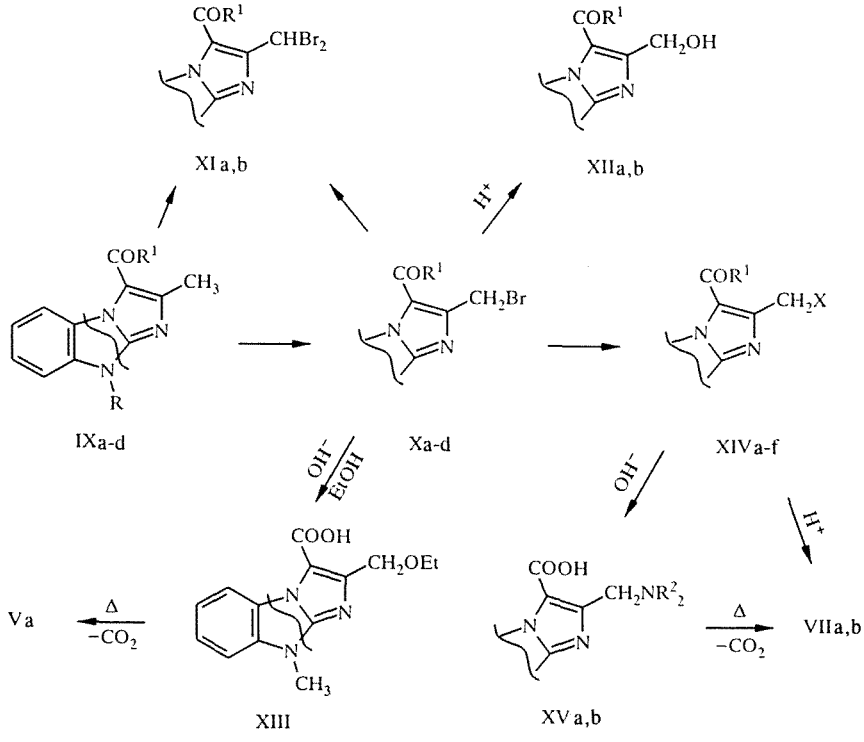
A similar mixture was obtained when ketone II was treated with 2-amino-1-benzylbenzimidazole (Ib). When the mixture was allowed to stand in CF_3COOH for a day, complete cyclization of IV occurred and the PMR spectrum showed in solution only the 2-chloromethyl derivative III.

Due to the high lability of III, the chlorine atom is very reactive, even towards weak nucleophiles and the individual components could not be separated. Thus attempts to crystallize the mixture of III and IV led to 2-hydroxymethylimidao[1,2-a]benzimidazole VI. Treatment of the mixture with ethanol gave the difficultly soluble salts IVa, b virtually pure since III was completely converted to ether V. Heating the mixture of III and IV with secondary amines in an inert solvent gave the 2-aminomethyl products VII.

Bearing in mind the ambiguity of the above reaction we studied the possible preparation of 2-halomethylimidazo[1,2-a]benzimidazoles by direct introduction of the halogen atom in 2-methylimidazol[1,2-a]benzimidazoles.

It was previously reported [9] that bromination of 2-methylimidazo[1,2-a]benzimidazole VIII with bromine in $CHCl_3$ or AcOH gives the 3-bromo derivatives of the heterocycle. The methyl group is not brominated under these conditions. The action of one equivalent of bromosuccinimide on VIII gives a hard to separate, complex mixture containing unreacted VIII together with its mono-, dir-, and tribromo derivatives. Hence we chose 2-methylimidazo[1,2-a]benzimidazoles IX as starting materials which had position 3 substituted by the labile alkoxycarbonyl or acetyl groups [10, 11]. Radical bromination of IX using bromosuccimide gave the 2-bromomethyl derivatives X in high yield. The reaction occurred smoothly without a catalyst upon refluxing the reagents in dry $CHCl_3$ or CCl_4. As previously reported [12], the acetyl group was not brominated under these conditions. Together with product X there were obtained traces of the dibromo product XI and 1,1′-dialkyl-2-2′-azobenzimidazoles, which had been obtained previously by treatment of imidazo[1,2-a]benzimidazoles with various oxidants [13] and by oxidation of 1- substituted 2-aminobenzimidazoles using sodium hypochlorite solution [14]. Compound XI was prepared in high yield by treating the ester or ketone IX with a twofold excess of bromosuccinimide. In the PMR spectra of X, the singlet for the 2-CH_3 group at 2.4-2.5 ppm was replaced by a proton signal for CH_2Br at 4.7-4.8 ppm. The signal for he $CHBr_2$ proton in XI was even further shifted downfield (7.3-7.5 ppm).



IX, Xa R = CH_3;b,d R = $CH_2C_6H_5$; a,b R^1 = OCH_3, c,d R^1 = CH_3; XI, XII R = CH_3; a R^1 = OCH_3, b R^1 = CH_3; XIV a-c R = CH_3, d-f R = $CH_2C_6H_5$;a,b,e,f R^1 = OCH_3, c,d R^1 = CH_3; a X = $N(C_2H_4)_2O$, b X = $NHC(CH_3)_3$, в X = $N(CH_2)_5$, d X = $N(C_2H_5)_2$, e X = $N^+(C_2H_5)_3Br^-$, f X = $SCNH_2(N^+H_2)Br^-$; XV R = CH_3; a R_2^2 = $(C_2H_4)_2O$, b R_2^2 = $(CH_2)_5$

As for III, the obtained bromo derivatives also have a highly labile halogen atom. It is readily substituted by primary, secondary, and tertiary amines by a short reflux of the reagents in benzene. For primary and secondary amines it is necessary

to use a twofold excess since it also acts to remove the hydrogen halide formed in the reaction. Compound X also reacts readily with triphenylphosphine and urea.

Refluxing Xa with NaOH in absolute ethanol gives both substitution of the bromine atom for ethyl and hydrolysis of the carbomethoxy group to give the acid XIII. Heating the latter at 190°C gives 2-ethoxymethylimidazo[1,2-a]benzimidazole Va, also obtained by treating amine Ia with ketone II in alcohol (see above).

Attempting to transfer the conditions for hydrolysis of the carbalkoxy and acetyl groups of X using HCl or HBr to the 2-bromomethylimidazo[1,2-a]pyrimidine unsubstituted at position 3 led to alcohol XII. By contrast, acid hydrolysis of amines XIVa-d gave compound VII. Base hydrolysis of esters XIVa, b to acid XV and subsequent thermal decarboxylation provided another route to these compounds.

Since the nucleophilic substitution reaction of the halogen in the 2-halomethyl imidazo[1,2-a]benzimidazoles occurs even with weak nucleophile (EtOH, H_2O) and its rate depends strongly on solvent polarity, an S_N1 mechanism is proposed. The occurrence of the reaction by this mechanism probably makes the imidazo[1,2-a]benzimidazole nucleus a powerful electron donor.

EXPERIMENTAL

IR spectra were taken on a Specord 71-IR in vaseline oil. PMR spectra were recorded on a Tesla Bs-487 (80 MHz) instrument in $CDCl_3$, CF_3COOH, or DMF-d_6 at a concentration of 0.3-0.4 M and with HMDS as internal standard. Monitoring of the reaction course and the product purity was carried out on Al_2O_3 TLC plates using $CHCl_3$ eluent and iodine visualization in a spray chamber.

Elemental analytical data for C, H, N, and halogen agreed with that calculated.

Reaction of 2-Amino-1-methylbenzimidazole (Ia) with 1,3-Dichloroacetone (II) in Acetone. Amine Ia (2.94 g, 20 mmole) was dissolved with heating in dry acetone (70 ml). The solution was cooled and ketone II (2.52 g, 20 mmole) added. The mixture was stirred until complete solution of the latter and left in a tightly sealed flask in the dark at 20-25°C. After 6 days, the precipitate from the dark solution was filtered and thoroughly washed with acetone and ether to give a mixture of IIIa and IVa (4.54 g) with mp 193-195°C (decomp).

A similar reaction of amine Ib (2.23 g, 10 mmole) with ketone II (1.26 g, 10 mmole) in dry acetone (80 ml) gave a beige precipitate (1.57 g) which was a mixture of IIIb and IVb.

2-Amino-1-methyl-3-(3-chloroacetonyl)benzimidazolium Chloride (IVa, $C_{11}H_{13}Cl_2N_3O$) and 9-Methyl-2-chloromethylimidao[1,2-a]benzimidazole (IIIa). A mixture of IIIa and IVa (3 g) was refluxed in ethanol (40 ml) for 2 h. The insoluble precipitate of chloride IVa (0.68 g) was filtered from the hot reaction mixture, washed with alcohol (2 × 5 ml), and crystallized twice from 90% acetic acid. The snow-white, microcrystalline product began to darken at ~225°C on heating and finally decomposed at 242-243°C. IR spectrum: 715 (CCl), 1490, 1620 (C=C), 1680 (C=N^+), 1770 (C=O), 3170, 3350 cm^{-1} (NH_2).

Compound IVa was difficultly soluble in organic solvents; solution in CF_3COOH being accompanied by cyclization to tricycle IIIa. The PMR spectrum of a freshly prepared solution of salt IVa in CF_3COOH showed IIIa and IVa, but after one day only IIIa was seen. PMR spectrum: 3.57 (3H, s, NCH_3), 5.08 (2H, s, CH_2Cl), 6.97-7.01 ppm (5H, m, aromatic H).

9-Methyl-2-ethoxymethylimidazo[1,2-a]benzimidazole (Va, $C_{13}H_{15}N_3O$). A. The alcohol filtrate after removal of IVa from the mixture of IIIa and IVa was evaporated and the residue purified by column chromatography (2 × 13 cm) on Al_2O_3 (eluent $CHCl_3$), collecting the fraction with R_f 0.55. Evaporation of $CHCl_3$ gave ether Va, identical to that produced by refluxing equimolar amounts of compounds Ia and II in EtOH; mp 73-74°C (from hexane). IR spectrum: 1500, 1600, 1630 (C=C, C=N), 1100 cm^{-1} (COC). PMR spectrum ($CDCl_3$): 1.2 (3, t, CH_3), 3.58 (2H, q, OCH_2), 3.64 (3H, s, NCH_3), 4.5 (2H, s, 2-CH_2), 7.3-7.12 ppm (5H, m, aromatic H).

B. Acid XIII (0.54 g, 2 mmole) was heated at 190°C (bath temperature) in an open tube for 5-7 min. The melt was cooled, dissolved in $CHCl_3$ (5 ml), and the solution passed through an Al_2O_3 layer (d = 3 cm, l = 2 cm), eluting ether Va with chloroform. After evaporation of chloroform, the oil crystallized on standing to give 0.38 g (82.6 %), identical to that obtained by method A.

2-Amino-1-benzyl-3-(3-chloroacetonyl)benzimidazole Chloride (IVb, $C_{17}H_{17}Cl_2N_3O$) and 9-Benzyl-2-chloromethylimidazo[1,2-a]benzimidazole (IIIb). A mixture of IIb and IVb (1.5 g) in ethanol (30 ml) was refluxed for 1.5 h. The soluble chloride precipitate of IVb (0.17 g) was filtered and crystallized from 95% acetic acid. With melting point

determination, the salt began to darken at ≈250°C and finally decomposed at 266-268°C. IR spectrum: 710 (CCl), 1490, 1610 (C=C), 1670 (C=N^+), 1740 (C=O), 3150, 3330 cm^{-1} (NH_2).

After the salt IVb solution had stood for 1 day, the PMR spectrum showed only IIIb in solution: 5.09 (2H, s, CH_2Cl), 5.59 (2H, s, NCH_2), 6.69-7.06 ppm (10H, m, aromatic H).

9-Benzyl-2-ethoxymethylimidazo[1,2-a]benzimidazole (Vb, $C_{19}H_{19}N_3O$). Separated similarly to ether Va after removal of chloride IVb (see previous details) to give 0.85 g with mp 117-118°C (from hexane or isooctane). IR spectrum: 1080 (COC), 1490, 1590, 1615 cm^{-1} (C=C, C=N). PMR spectrum ($CDCl_3$): 1.67 (3H, t, CH_3), 3.55 (2H, q, OCH_2), 4.46 (2H, s, 2-CH_2), 5.25 (2H, s, NCH_2), 6.99-7.21 ppm (10H, m, aromatic H).

2-Hydroxymethyl-9-methylimidazo[1,2-a]benzimidazole (VIa, $C_{11}H_{11}N_3O$). A mixture of IIIa and IVa (2 g) was dissolved in water (25 ml) and refluxed for 7-10 min. The acid solution formed (pH 1-2) was cooled, neutralized with NH_4OH (22%) to pH 7-8, and extracted with chloroform (3 × 10 ml). The extract was filtered through an Al_2O_3 layer (d = 4 cm, l = 1.5 cm), and the latter was washed with $CHCl_3$. The filtrate was evaporated to dryness and the residue (1.2 g) crystallized from dioxan and then acetonitrile to give snow-white, fine needles with mp 188-189°C (decomp). IR spectrum: 1500, 1600, 1610 (C=C, C=N), 3170 cm^{-1} (OH). PMR spectrum: 3.65 (3H, s, NCH_3), 4.55 (2H, s, CH_2), 7.05-7.67 ppm (5H, m, aromatic H).

9-Benzyl-2-hydroxymethylimidazo[1,2-a]benzimidazole (VIb, $C_{17}H_{15}N_3O$). A suspension of mixed IIIb and IVb (1.5 g) in water (30 ml) was refluxed for 30 min. The hot reaction mixture was filtered, the filtrate neutralized with Na_2CO_3, and extracted with $CHCl_3$ (2 × 20 ml). The extract was evaporated and the residue washed with acetone and crystallized from ethanol to give VIb (1 g) as small, colorless needles with mp 175°C. IR spectrum: 1510, 1600, 1620 (C=C, C=N), 3200 cm^{-1} (OH). PMR spectrum ($CDCl_3$): 4.62 (2H, s, 2-CH_2), 5.25 (2H, s, NCH_2), 7.06-7.15 ppm (10H, m, aromatic H).

9-Methyl-2-morpholinomethylimidazo[1,2-a]benzimidazole (VIIa, $C_{15}H_{18}N_4O$). A. A mixture of IIIa and IVa (2 g) and morpholine (2 ml) in absolute benzene (50 ml) was refluxed for 4 h. After cooling, the precipitate (unreacted mixture and morpholine hydrochloride) was filtered, washed with benzene, and the filtrate evaporated. The residue was chromatographed on an Al_2O_3 column (3 × 10 cm) using $CHCl_3$ eluent. Evaporation of solvent from the eluate gave 1.4 g of colorless oil with R_f 0.45. IR spectrum: 1500, 1600, 1610 cm^{-1} (C=C, C=N).

Dihydrobromide of VIIa ($C_{15}H_{18}N_4O \cdot 2HBr$). A. The dibromide was obtained quantitatively by acidification of an acetone solution of base VIIa with concentrated HBr to pH 2-3. The colorless or slightly pink small needles ha.Id mp 234°C (decomp., from alcohol).

B. Ester XIVa (0.66 g, 2 mmole) in conc. HBr (10 ml) was refluxed until the hydrolysis and decarboxylation reactions were complete (6-8 h). The solution was neutralized with 22% NH_4OH to pH 6-7 and extracted with $CHCl_3$. The extract was passed through an Al_2O_3 layer (d = 3 cm, 1 = 1.5 cm) and evaporated to give VIIa (0.52 g, 96%) of VIIa as a colorless oil, the hydrobromide of which was identical to that in method A.

C. Acid XVa (0.31 g, 1 mmole) was slowly heated in a silicone bath to 220°C. At the end of the vigorous decomposition, the melt was cooled, dissolved in $CHCl_3$ (3 ml) and purified on an Al_2O_3 column (1.5 × 12 cm) eluting amine VIIa with chloroform and collecting the fraction with R_f 0.45. The dihydrobromide (0.34 g, 79.6%), obtained from the oil, remaining after evaporation of the eluate was identical to that reported in method A.

9-Methyl-2-piperidinomethylimidazo[1,2-a]benzimidazole (VIIb, $C_{16}H_{20}N_4$). A. Obtained similarly to VIIa from a mixture of IIIb and IVb (2 g) and piperidine. It was purified chromatographically, and dried in vacuum desiccator over P_2O_5 to give 1.2 g of slightly beige crystals with mp 110°C. IR spectrum: 1500, 1595, 1615 cm^{-1} (C=C, C=N).

B. A solution of amine XIVd (0.62 g, 1 mmole) in conc. HBr (10 ml) was refluxed until reaction completion (8-10 h), diluted twofold with water carefully neutralized with NH_4OH solution, and extracted with $CHCl_3$ (2 × 8 ml). The extract was passed through a silica layer, evaporated, and dried in a vacuum desiccator to give amine VIIb (0.47 g, 87%), identical to that reported in method A.

2-Bromomethyl-9-methyl-3-carbomethoxyimidaz0o[1,2-]benzimidazole (Xa, $C_{13}H_{12}BrN_3O_2$). N-Bromosuccinimde (1.78 g, 10 mmole) was added in small portions with vigorous stirring and heating over 30-40 min to ester IXa (2.43 g, 10 mmole) in dry chloroform (50 ml). The product was refluxed for 1 h, evaporated to 15 ml volume, and passed through an Al_2O_3 layer (4 × 6 cm) eluting the bromo substituted ester Xa with chloroform. After evaporation of eluate the residue was treated with acetone (10 ml) to remove traces of 1,1′-dimethyl-2,2′-azobenzimidazole, filtered, washed with acetone and crystallized from alcohol to give 2.44 g (76%) with mp 188-189°C (decomp.). IR spectrum ($CHCl_3$): 1095, 1152 (COC), 1492, 1600, 1625 (C=C, C=N), 1702 cm^{-1} (C=O). PMR spectrum ($CDCl_3$): 3.67 (3H, s, NCH_3), 3.94 (3H, s, OCH_3), 4.8 (2H, s, 2-CH_2), 7.16 (3H, m, 6,7,8-H), 8.25 ppm (1H, m, 5-H).

2-Dibromomethyl-9-methyl-3-carbomethoxyimidazo[1,2-a]benzimidazole (XIa, $C_{13}H_{11}Br_2N_3O_2$). Obtained by bromination of ester IXa (5 mmole) with bromosuccinimide (10 mmole) or bromo substituted Xa (5 mmole) with an equivalent of the same reagent in $CHCl_3$ or CCl_4 (65% and 74% yields respectively). The strongly electrostatic, fibrous crystals had mp 213°C (decomp., capillary containing sample introduced into hot apparatus). IR spectrum: 1090, 1130, 1310 (COC), 1495, 1600, 1620 (C=C, C=N), 1700 cm^{-1} (C=O). PMR spectrum ($CDCl_3$): 3.75 (3H, s, NCH_3), 3.94 (3H, s, OCH_3), 7.2 (3H, m, 6,7,8-H), 7.5 (1H, s, CH), 8.25 ppm (1H, m, 5-H).

9-Benzyl-2-bromomethyl-3-carbomethoxyimiazo[1,2-a]benzimidazole(Xb,$C_{19}H_{16}BrN_3O_2$). Bromsuccinimide(1.78 g, 10 mmole) was added in small portions over 40 min with stirring to a reflexing solution of ester IXb (3.2 g, 10 mmole) in dry CCl_4 (70 ml). The mixture was refluxed for a further 1.5 h, filtered hot to removed succinimide, and evaporated. The residue was purified initially using column chromatography (Al_2O_3, eluent $CHCl_3$) and then recrystallization from alcohol and acetonitrile to give 2.7 g (67.8%) with mp 152°C. IR spectrum: 1100, 1150, 1350 (COC), 1490, 1600, 1620 (C=C, C=N), 1710 cm^{-1} (C=O). PMR spectrum ($CDCl_3$): 3.92 (3H, s, CH_3), 4.82 (2H, s, 2-CH_2), 5.3 (2H, s, NCH_2), 7.17 (8H, m, aromatic H), 8.25 ppm (1H, d, 5-H).

3-Acetyl-2-bromomethyl-9-methylimidazo[1,2-a]benzimidazole (Xc, $C_{13}H_{12}BrN_3O$). Obtained similarly to ester Xb by bromination of ketone IXc with one equivalent of bromosuccinimde in CCl_4. Reaction time 4 h. Yield 78%, mp 202°C (decomp., from acetonitrile). IR spectrum: 1500, 1600, 1615 (C=C, C=N), 1635 cm^1 (C=O). PMR spectrum ($CDCl_3$): 2.63 (3H, s, $COCH_3$), 3.65 (3H, s, NCH_3), 4.7 (2H, s, 2-CH_2), 7.12 (3H, m, 6,7,8-H), 8.5 ppm (1H, d, 5-H).

3-Acetyl-9-benzyl-2-bromomethylimidazo[1,2-a]benzimidazole (Xd, $C_{19}H_{16}BrN_3O$). Obtained in 91% yield by bromination of ketone IXd in CCl_4. Reaction time 3 h, mp 158-159°C (decomp., from acetonitrile). IR spectrum: 1500, 1600, 1615 (C=C, C-N), 1635 cm^{-1} (C=O). PMR spectrum ($CDCl_3$): 2.62 (3H, s, CH_3), 4.72 (2H, s, 2-CH_2), 5.27 (2H, s, NCH_2), 7.07-7.15 (8H, m, aromatic H), 8.5 ppm (1H, d, 5-H)

9-Methyl-3-carbomethoxy-2-hydroxymethylimidazo[1,2-a]benzimidazole (XIIa, $C_{13}H_{13}N_3O_3$). Ester Xa (0.96 g, 3 mmole) in dilute HBr (1:1, 9 ml) was refluxed for 1 h, cooled, and the precipitated hydrobromide of XIIa filtered and washed with water to give 0.64 g (62.7%) with mp 200-201°C (decomp., from alcohol). The salt was treated with 10% NH_4OH and the alcohol produced (XIIa) as snow-white crystals with mp 190-191 (from ethanol). IR spectrum: 1100 (COC), 1500, 1600, 1620 (C=C, C=N), 1690 (C=O), 3250 cm^{-1} (OH). PMR spectrum ($CDCl_3$), 3.65 s, NCH_3), 3.92 (3H, s, OCH_3), 4.98 (2-CH_2), 7.3 (3H, m, 6,7,8-H), 8.3 ppm (1H, d, 5-H).

3-Acetyl-9-benzyl-2-hydroxymethylimidazo[1,2-a]benzimidazole (XIIb, $C_{19}H_{17}N_3O_2$). Bromoketone Xd (0.76 g, 2 mmole) in aqueous dioxan (1:1, 10 ml) was refluxed for 1 h. The dioxan was evaporated and the residue treated with NH_4OH solution. The alcohol XIIb was separated and crystallized from ethanol to give shining white plates (0.47 g, 73%), mp 167°C. IR spectrum: 1510, 1600, 1615 (C=C, C=N), 1635 (C=O), 3220 cm^{-1} (OH). PMR spectrum (DMF-d_6): 2.63 (3H, s, CH_3), 4.83 (2H, s, 2-CH_2), 5.45 (2H, s, NCH_2), 7.02-7.5 (8H, m, aromatic H), 8.56 ppm (1H, d, 5-H).

9-Methyl-2-ethoxymethylimidazo[1,2-a]benzimidazolyl-3-carboxylic Acid (XIII, $C_{14}H_{15}N_3O_3$). Bromoester Xa (0.96, , 3 mmole) and NaOH (0.6 g, 15 mmole) were refluxed in absolute ethanol (10 ml) for 40 min. Cooling the solution gave a snow-white precipitate of the sodium salt of acid XIII which was filtered and washed with ether. After drying, the salt was dissolved in water (10 ml) and acidified with acetic acid to pH 5. The precipitated acid was filtered and washed with water to give 0.6 g (74.1%) with mp 177°C (decomp., from alcohol). IR spectrum: 1100 (COC), 1300 (CO), 1400 (COH), 1695 (C=O), 2500-3250 cm^{-1} (broad OH band). PMR spectrum (CF_3COOH): 0.95 (3H, t, CH_3), 3.55 (2H, q, OCH_2), 3.62 (3H, s, NCH_3), 4.85 (2H, s, CH_2O), 7.22 (3H, m, 6,7,8-H), 8.13 ppm (1H, d, 5-H).

2-Morpholinomethyl-3-carbomethoxy-9-methylimidazo[1,2-a]benzimidazole (XIVa, $C_{17}H_{20}N_4O_3$). Morpholine (0.35 g, 4 mmole) was added to a hot solution of bromoester Xa (0.64 g, 2 mmole) in dry benzene (10 ml) and refluxed for 10 min. The precipitated morpholine hydrobromide was filtered from the cooled solution and washed with benzene. The benzene solution was passed through Al_2O_3 to remove traces of morpholine hydrobromide and evaporated to give 0.65 g (100%) of chromatographically pure free amine (XIVa) with mp 143-144 °C (from isooctane). IR spectrum: 1500, 1600, 1625 (C=C, C=N), 1700^{-1} (C=O).

2-(Tert-Butylaminomethyl)-9-methyl-3-carbomethoxyimidazo[1,2-a]benzimidazole (XIVb, $C_{14}H_{22}N_4O_2$). Obtained similarly to XIVa by refluxing ester Xa (0.64 g, 2 mmole) and tert-butylamine (0.44 ml, 4 mmoles) for 1 h. Yield 0.58 g (92%) with mp 237°C (from butanol). IR spectrum: 1500, 1605, 1625 (C=C, C=N), 1700 (C=O), 3200-3500 cm^{-1} (broad NH band).

3-Acetyl-9-methyl-2-piperidinomethylimidazo[12,2-a]benzimidazole (XIVc, $C_{18}H_{22}N_4O$). A mixture of bromoletone Xc (0.92 g, 3 mmole) and piperidine (0.6 ml, 6 mmole) in dry benzene (12 ml) was refluxed for 15 min, cooled, and the

precipitated piperidine hydrobromide filtered off. The filtrate was evaporated to give XIVc (0.93 g, 100%) as needles with mp 144-145°C (from acetonitrile). IR spectrum: 1500, 1590, 1600 (C=C, C=N), 1625 cm^{-1} (C=O).

3-Acetyl-9-benzyl-2-diethylaminoemthylimidazo[1,2-a]benzimidazole (XIVd, $C_{23}H_{26}N_4O$). Obtained by refluxing bromoketone Xd (0.76 g, 2 mmole) and diethylamine (0.42 ml, 4 mmole) in dry benzene (10 ml) for 30 min. Yield 0.66 g (88.6%) with mp 160°C (from alcohol). IR spectrum: 1500, 1595, 1605 (C=C, C=N), 1630 cm^{-1} (C=O).

9-Benzyl-3-carbomethoxy-2-triethylammoniummethylimidazo[1,2-a]-benzimidazole Bromide (XIVe, $C_{23}H_{31}BrN_4O_2$). A mixture of ester Xb (0.4 g, 1 mmole), triethylamine (0.2 ml, 1.4 mmole), and absolute benzene (5 ml) was refluxed for 15 min. With cooling, the bromide XIVe precipitated and was filtered and washed with benzene to give 0.48 g (96%) with mp 207°C (decomp., from ethanol). IR spectrum: 1490, 1600, 1620 (C=C, C=N), 1700 cm^{-1} (C=O).

9-Benzyl-2-(2-isothiouronylmethyl)-3-carbomethoxyimidazo[1,2-a]benzimidazole Bromide (XIVf, $C_{20}H_{20}BrN_5O_2S$). A mixture of Xb (0.4 g, 1 mmole) and thiourea (0.08 g, 1 mmole) in acetone (8 ml) was refluxed for 20 min and cooled. The precipitate was filter and washed with acetone to give 0.44 g (92.4%) with mp 206°C (from ethanol). IR Spectrum: 1490, 1600, 1620, 1630, 1650 (C=C, C=N, NH_2), 1700 (C=O), 3050-3350 cm^{-1} (broad NH_2 band).

9-Methyl-2-morpholinomethylimidazo[1,2-a]benzimidazolyl-3-carboxylic Acid (XVa, $C_{16}H_{18}N_4O_3$). A mixture of ester XIVa (0.66 g, 2 mmole) and NaOH (0.1 g, 2.5 mmole) in aquoues alcohol (1:1, 12 ml) was refluxed for 3 h. The alcohol was evaporated and the aqueous solution acidified with dilute AcOH to pH 4. The precipitated acid was separated and washed with acetone to give 0.54 g (85.7%) with mp 202-203°C (decomp., from ethanol). IR spectrum: 1500, 1605, 1620, (C=C, C=N), 1660 (C=O), 3300-3500 cm^{-1} (broad OH band). PMR spectrum (CF_3COOH): 3.42 (4H, t, $N(CH_2)_2$), 3.7 (3H, s, NCH_3), 3.92 (4H, t, $O(CH_2)_2$), 4.82 (2H, s, 2-CH_2), 7.32 (3H, m, 6,7,8-H), 8.25 ppm (1H, m, 5-H).

9-Methyl-2-piperidinomethylimidazo[1,2-a]benzimidazole-3-carboxylic Acid (XVb, $C_{17}N_{20}N_4O_2$). Obtained similarly to acid XVA in 81% yield with mp 200-201°C (decomp., from ethanol). IR spectrum: 1500, 1600, 1620 (C=C, C=N), 1650, (C=O), 3340 cm^{-1} (broad OH band).

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