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Studies on Benzimidazoles and Related Compounds. V.[1] Reaction of 2-Azido-1-methylbenzimidazole with Unsaturated Compounds[2]

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Cycloaddition reactions of 2-azido-1-methylbenzimidazole (I) with such reagents as diphenylketene, dimethyl acetylenedicarboxylate, methyl propiolate, and N,N-diethylphenylethynylamine were investigated. The diester exclusively reacted with the carbon-nitrogen double bond of imidazole ring to give the 1:1 molar adduct (IV). On the other hand, the ynamine added to azido group at C_2-position and only triazole derivative (XI) was obtained.

For thermal decomposition of the adduct (XI), the presence of 2-azirine compound (XIX), a four electron system, as intermediate was assumed from consideration of structures of the decomposition products (XII and XIII).

Reaction of I with the ester gave a mixture of the triazole derivative (VI) as major product and the 1:1 molar adduct (VII). Also, diphenylketene exothermically reacted with I and gave 2,3-dihydro-9-methyl-3-oxo-2,2-diphenyl-9H-imidazo[1,2-*a*]benzimidazole (II).

It is known that diphenylketene and dimethyl acetylenedicarboxylate add to the carbon-nitrogen double bond in benzimidazole ring.[4,5] For example, two molecules of diphenylketene reacted with 1-methylbenzimidazole at 25° to give the 1:2 molar adduct.[4] Also, reaction of dimethyl acetylenedicarboxylate with 2-benzyl-1-methylbenzimidazole gave a mixture consisted of the 1:2 molar adduct and another four products.[5b] On the other hand, N-[(2-azido-1-benzimidazolyl)carbonyl]glycine isopropyl ester did not react with benzyne because of interaction between the azido group and the endocyclic nitrogen atom.[6] In the preceding paper,[1] we reported on the reaction of 2-azido-1-methylbenzimidazole (I) with such reagents as aluminum chloride in toluene, thiobenzophenone, hydrogen bromide, and acetic anhydride. As a part of further studies on reactivity of the azide (I), cycloaddition reaction with diphenylketene, dimethyl acetylenedicarboxylate, methyl propiolate, and N,N-diethylphenylethynylamine was attempted under its decomposition temperature.

Reaction of I with diphenylketene in dioxane or tetrahydrofuran at room temperature exothermically occurred with elimination of nitrogen and almost quantitatively gave II (Chart 1). The structure of II was supported by infrared (IR) and nuclear magnetic resonance (NMR) spectra respectively showed absorptions of carbonyl (1740 cm^{-1}) and imino (1690 cm^{-1}) groups and signals at 6.51 τ (singlet, N-CH_3) and 2.30—3.16 τ (14H, multiplet, aromatic). However, spectroscopic data do not exclude the possibility of 2,3-dihydro-9-methyl-2-oxo-3,3-diphenyl-9H-imidazo[1,2-*a*]benzimidazole, isomeric to II, as the structure of the product. In order to confirm the structure, therefore, ethanolysis of II in the presence of 35% sulfuric acid was attempted. As expected, the ester (III) was obtained and its structure was deter-

1) Part IV: Y. Shiokawa and S. Ohki, *Chem. Pharm. Bull.* (Tokyo), **19**, 401 (1971).
2) This work was presented at the 92th Annual Meeting of Pharmaceutical Society of Japan, Osaka, April 1972.
3) Location: *Women's Division, Ueno Sakuragi 1-10-19, Daito-ku, Tokyo.*
4) R.D. Kimbrough, Jr., *J. Org. Chem.*, **29**, 1242 (1964).
5) *a*) R.M. Acheson, M.W. Foxton, P.J. Abbot, and K.R. Mills, *J. Chem. Soc.* (*C*), **1967**, 882; *b*) R.M. Acheson and W.R. Tully, *J. Chem. Soc.* (*C*), **1968**, 1623.
6) G.A. Reynold, *J. Org. Chem.*, **29**, 3733 (1964).

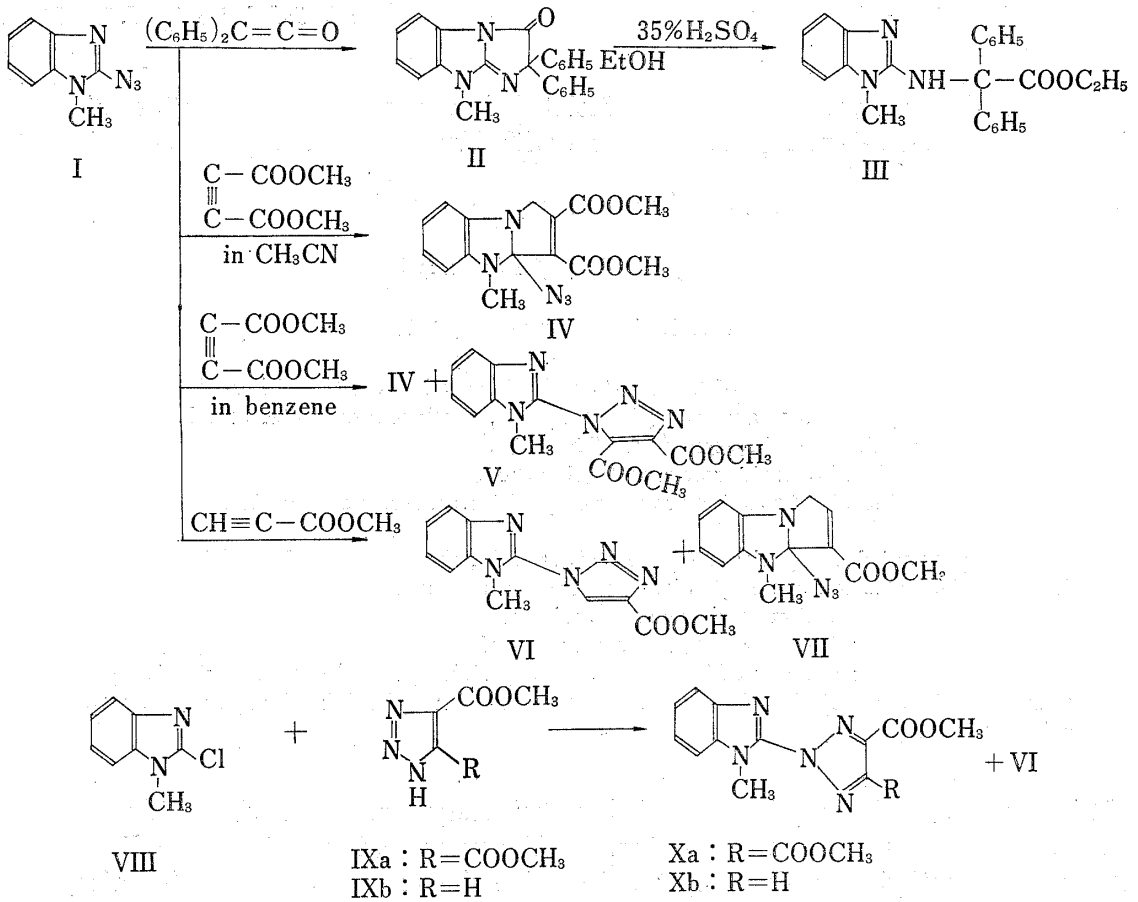

Chart 1

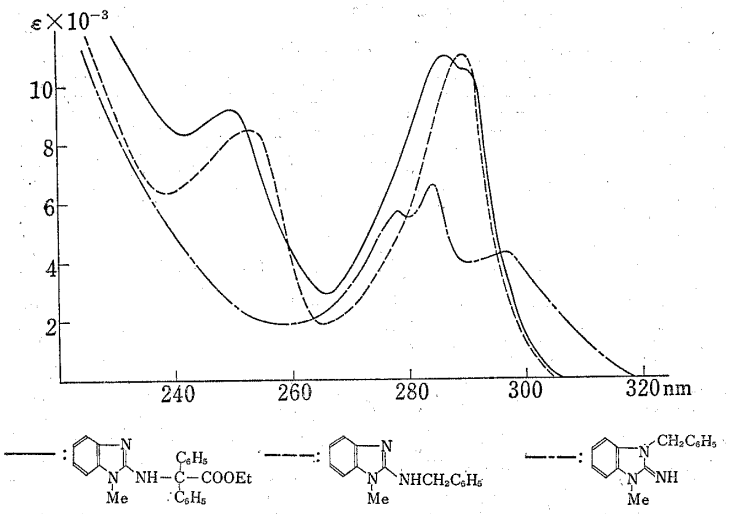

Fig. 1

mined to be ethyl α-(1-methyl-2-benzimidazolylamino)-α,α-diphenylacetate by spectroscopic data and elemental analysis. That is, IR spectrum of III exhibits absorptions of amino (3400 cm^{-1}) and ester carbonyl (1730 cm^{-1}) groups and its NMR spectrum indicates signals at 8.91 τ (triplet, J=7 Hz, $C\underline{H}_2$-CH_3), 6.42 τ (singlet, N-CH_3), 5.76 τ (quartet, J=7 Hz, $C\underline{H}_2$-CH_3), 4.16 τ (broad singlet, NH), and 2.30—3.01 τ (14H, multiplet, aromatic). Furthermore, its ultraviolet (UV) absorption spectrum is very similar to that of 2-benzylamino-1-methylbenzimidazole[7] regarded as a model compound of III, but is considerably different from that of isomeric 3-benzyl-2-imino-1-methylbenzimidazoline obtained by treatment of 2-amino-3-benzyl-1-methylbenzimidazolium iodide[8] with 5% ammonia (Fig.

7) E.A. Zvezdina, A.F. Pozharskii, and V.I. Sokolov, *Khim. Geterotsikl. Soedin.*, **1970**, 419 [*C.A.*, **73**, 25362q (1970)].
8) A.M. Simonov and Y.M. Yutilov, *Zh. Obshch. Khim.*, **32**, 2670 (1962) [*C.A.*, **58**, 9048b (1963)].

1). Therefore, it was decided that product (II) was 2,3-dihydro-9-methyl-3-oxo-2,2-diphenyl-9H-imidazo[1,2-*a*]benzimidazole.

From the fact that the azide (I) is considerably thermally stable, its decomposition to the nitrene is almost negligible under the reaction conditions. Therefore, the route *via* 1,3-dipolar cycloaddition of the nitrene with the ketene was excluded. Considering reactivity of the azido group of I under the same conditions, the route *via* the triazoline derivative produced by 1,3-dipolar cycloaddition of the ketene with the azido group of I was ruled out. Therefore, formation of II would be explained nucleophilic attack of endocyclic nitrogen atom on a carbon-carbon double bond in the ketene, followed by nucleophilic displacement on the substituted nitrogen atom of azido group by carbanion.

Reaction of I with excess dimethyl acetylenedicarboxylate in acetonitrile gave the 1:1 molar adduct (IV) in a good yield and its structure was determined by the following spectral data and elemental analysis. IR spectrum of IV showed the presence of azido (2220 cm^{-1}) and two ester carbonyl (1748 and 1735 cm^{-1}) groups and its NMR spectrum indicated signals at 7.03 τ (singlet, N–CH_3), 6.08 τ (singlet, $COOCH_3$), 5.98 τ (singlet, $COOCH_3$), and 2.23—2.58 τ (4H, multiplet, aromatic). These spectral data were suggested that the diester selectively added to the carbon-nitrogen double bond in imidazole ring to produce benzimidazoline derivative. In the NMR spectrum, that is, N-methyl group appears at a substantially high magnetic field than that of I or 1,2-dimethylbenzimidazole because of loss of ring-current in imidazole ring. Furthermore, UV absorption spectrum of IV showed maximum at 233 nm, which excluded the possibility of ring-expansion to produce 1H-1,5-benzodiazepine derivative.[9] Although mass spectrum of IV does not show the molecular ion (M^+) peak at *m/e* 315 ($C_{14}H_{13}O_4N_5$), it shows a fragment peak (M^+-N_2) at *m/e* 287 ($C_{14}H_{13}O_4N_3$), giving another support for the structure.

It was noteworthy that the diester exclusively reacted with the carbon-nitrogen double bond rather than the azido group to give the 1:1 molar adduct (IV) without ring-expansion to seven-membered ring system as the reaction of 2-ethoxy-1-methylindole with the diester.[10]

When reaction of I with the diester was performed in benzene the isomeric adduct (V) was obtained in addition to the major product (IV). The structure of V was assumed on the basis of spectroscopic data and its independent synthesis from 2-chloro-1-methylbenzimidazole (VIII) and dimethyl 1(3)H-1,2,3-triazole-4,5-dicarboxylate (IXa) was attempted. However, the product was confirmed to be dimethyl 2-(1-methyl-2-benzimidazolyl)-2H-1,2,3-triazole-4,5-dicarboxylate (Xa), isomeric to V, by spectral data and elemental analysis. That is, NMR spectrum of Xa indicates that two ester methyl groups are equivalent, its UV spectrum shows absorption at the longer wavelength than V, and its mass spectrum shows the molecular ion peak as base peak at *m/e* 315. Therefore, it may be considered that substitution on N_1- or N_3-position in 1,2,3-triazole ring of IXa is very difficult because of steric hindrance due to two methoxycarbonyl groups.

Although the independent synthesis of V was unsuccessful, its structure was determined to be dimethyl 1-(1-methyl-2-benzimidazolyl)-1H-1,2,3-triazole-4,5-dicarboxylate by the comparison with the spectral data of VI obtained from reaction of I with methyl propiolate as described later.

When I was treated with excess methyl propiolate in acetonitrile at reflux temperature, a mixture of VI, VII, and unreacted I was obtained. The mixture was separated into each component by column chromatography over silica gel. The structure of minor product was assumed to be VII from the following spectral data and the polarized direction of the carbon-nitrogen double bond and methyl propiolate. That is, IR spectrum of VII shows the presence of azido (2220 cm^{-1}) and ester carbonyl (1740 cm^{-1}) groups and its NMR spectrum indicates

9) J.A. Barltrop, C.G. Richards, D.M. Russell, and G. Ryback, *J. Chem. Soc.*, **1959**, 1132.
10) H. Plieninger and D. Wild, *Chem. Ber.*, **99**, 3070 (1966).

signals at 6.96 τ (singlet, N–CH_3), 5.99 τ (singlet, $COOCH_3$), 2.28—2.60 τ (4H, aromatic), and 1.49 τ (singlet, CH). Furthermore, its UV absorption spectrum is similar to that of IV.

On the other hand, the structure of major product (VI) was supported by its spectral data corresponded with those of V and concluded to be methyl 1-(1-methyl-2-benzimidazolyl)-1H-1,2,3-triazole-4-carboxylate by identification with a sample obtained from the independent synthesis as described later. As expected from the result of the independent synthesis of V, it may be considered that substitution at nitrogen atom adjacent to methoxycarbonyl group does not occur in the reaction of VIII with methyl 1(3)H-1,2,3-triazole-4(5)-carboxylate (IXb). In fact, a mixture of Xb and VI was obtained in 89% yield and separated into each component by silica gel column chromatography. The minor product, isolated in 27% yield, was identified with VI by mixed melting point determination and by IR and NMR spectral comparison. Also, the structure of major product (Xb), isolated in 51% yield, was assumed on the basis of the spectroscopic data and elemental analysis.

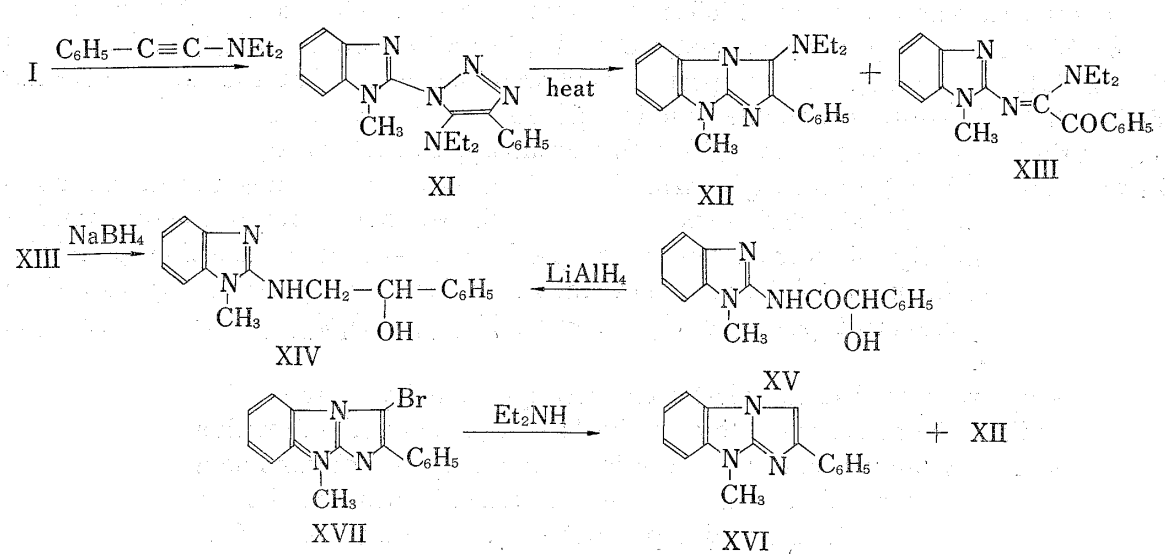

Chart 2

Reaction of I with N,N-diethylphenylethynylamine in dioxane or tetrahydrofuran at reflux temperature regioselectively gave the 1:1 molar adduct (XI) in a good yield (Chart 2). The structure of XI was assumed on the basis of the following spectroscopic data, elemental analysis, and polarized direction of azido group and ynamine. IR spectrum of XI exhibits the absence of azido group, its NMR spectrum indicates signals at 9.02 τ (6H, triplet, J=7 Hz, $2\times CH_2\underline{CH_3}$), 6.96 τ (4H, quartet, J=7 Hz, $2\times \underline{CH_2}CH_3$), 6.24 τ (singlet, N–CH_3), 2.40—2.70 τ (6H, aromatic), 2.12 τ (1H, multiplet, C_4–H), and 1.99 τ (2H, d,d, J=2, 8Hz, aromatic), and its UV absorption spectrum shows maxima at 255, 278, and 285 (shoulder) nm. Although its mass spectrum does not show the molecular ion peak at m/e 346, it shows a fragment peak (M^+-N_2) at m/e 318.

Decomposition of the adduct (XI) in p-cymene under nitrogen atmosphere afforded a mixture of XII, XIII, and minor products. The mixture was separated into each component by silica gel column chromatography. The structure of XII, obtained in 20.7% yield, was supported by spectral data and confirmed by independent synthesis as shown in Chart 2. Reaction of XVII with diethylamine in a sealed tube gave a mixture of XVI and XII which was entirely identical with the compound obtained from decomposition of the adduct (XI). In comparison with that reaction of XVII with piperidine and morpholine respectively gave the corresponding amino compound in a good yield,[11] the reaction with diethylamine was

11) A.M. Simonov and V.A. Anisimova, *Khim. Geterotsikl. Soedin.*, **1968**, 1102 [*C.A.*, **70**, 77868s (1969)].

necessary more drastic conditions because of steric hindrance. Therefore, formation of XVI, major product, may be considered as result of predominantly homolytic fission of the carbon-bromo bond in XVII rather than substitution of bromo-carbon bond by the amine.

The molecular formula of the major product (XIII), obtained in 46.7%, was established from elemental analysis and the molecular ion (M^+) in mass spectrum as $C_{20}H_{22}ON_4$. Furthermore, its structure was confirmed by the spectral data and the following chemical evidence shown in Chart 2.

Reduction of XIII with sodium borohydride afforded XIV in a good yield. The structure of XIV was supported by IR and NMR spectra respectively showed the presence of hydroxy (3385 cm^{-1}), amino (3270 cm^{-1}), and hydrogen bond (3500—3000 cm^{-1}) and signals at 6.70 τ (singlet, N–CH_3), 6.29 τ (complex, N–CH_2), 5.80 τ (broad singlet, NH and OH), and 5.02 τ (quartet, J=3 Hz, C_6H_5–CH) in addition to aromatic hydrogen signal and concluded to be 2-(β-hydroxy-β-phenethylamino)-1-methylbenzimidazole by identification with a sample obtained from reduction of XV, prepared from 2-amino-1-methylbenzimidazole and methyl mandelate, with lithium aluminum hydride.

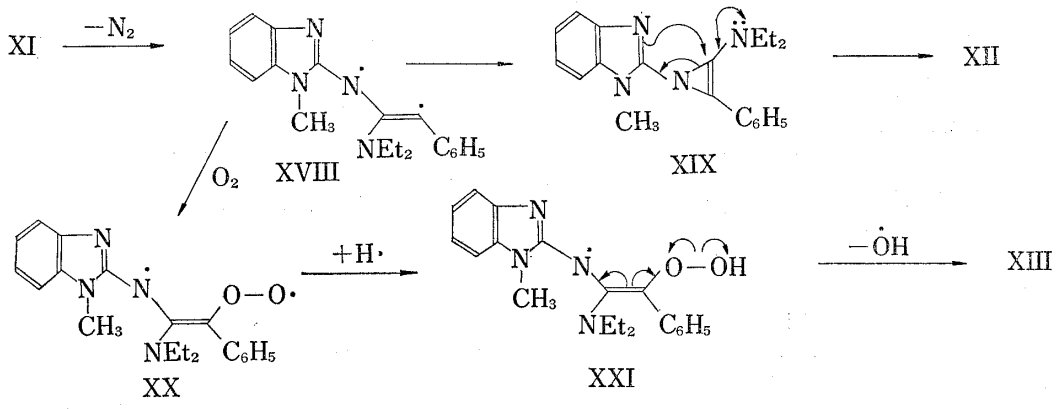

Chart 3

For the themal decomposition of the adduct (XI), it was noteworthy that formation of XII and XIII could not be explained elimination of nitrogen molecule, followed by a simple recyclization or reaction with oxygen molecule. Therefore, the presence of 2-azirine compound, a four electron system, as intermediate was assumed and the following mechanism was suggested (Chart 3). That is, it may be considered that the conversion of XI to XIII involves initially elimination of nitrogen molecule from XI to the biradical (XVIII), which then changes into XIII through XX and XXI produced by reaction of XVIII with oxygen molecule. On the other hand, formation of XII may be explained by radical coupling of XVIII to 2-azirine compound (XIX), which then rearranges to XII. Rearrangement is thought to proceed through predominant fission of carbon-nitrogen bond combined with diethylamino group because of its electron-donating effect.

Assuming that the structure of the azide-ynamine adduct is 4-diethylamino-1-(1-methyl-2-benzimidazolyl)-5-phenyl-1H-1,2,3-triazole, isomeric to XI, it may be difficult to explain formation of the amidine (XIII), major product of the thermal decomposition of XI. That is, recyclization of the biradical (XVIII) to the 2-azirine (XIX) and cleavage of carbon-nitrogen bond combined with phenyl group in XIX are necessary to occur predominantly. Therefore, it seemed reasonable to assume that the structure of the azide-ynamine adduct corresponded to XI rather than its isomer.

It was concluded from the experiment described above that the azide (I) predominantly reacted either at azido group or at carbon-nitrogen double bond depended on properties of the reagents.

Experimental[12]

Reaction of 2-Azido-1-methylbenzimidazole (I) with Diphenylketene——The calculated amount (0.112 g) of the ketene in anhyd. dioxane (2 ml) was added dropwise to a solution of I (0.1 g) in the same solvent (2 ml) at room temperature. The reaction exothermically occurred with elimination of nitrogen gas. The mixture was kept overnight at room temperature, then the precipitate was collected by filtration, and recrystallized from benzene–acetone to give 0.183 g (94%) of 2,3-dihydro-9-methyl-3-oxo-2,2-diphenyl-9H-imidazo-[1,2-*a*]benzimidazole (II), mp 237—238°. *Anal.* Calcd. for $C_{22}H_{17}ON_3$: C, 77.85; H, 5.05; N, 12.38. Found: C, 78.13; H, 4.99; N, 12.22. IR cm^{-1}(KBr): $\nu_{C=O}$ 1740; $\nu_{C=N}$ 1690. UV λ_{max}^{EtOH} nm: 235, 276 (shoulder), 286. NMR τ: 6.51 (s, N–CH_3), 2.30—3.16 (14H, aromatic). Mass Spectrum *m/e*: 339 (M^+).

Ethyl α-(1-Methyl-2-benzimidazolylamino)-α,α-diphenylacetate (III)——A mixture of II (0.325 g) and 35% H_2SO_4 (6.5 ml) in EtOH (13 ml) was heated under reflux for 4 hr and the solvent was evaporated *in vacuo*. The residue was made alkaline with 10% NH_4OH under ice cooling, extracted with $CHCl_3$, the extract was washed with H_2O, dried over anhyd. Na_2SO_4, and evaporated *in vacuo*. The residue was purified by column chromatography on silica gel (2 g) using benzene as eluent to give 0.059 g (16%) of III as colorless crystals (benzene–*n*-hexane), mp 143—144°. *Anal.* Calcd. for $C_{24}H_{23}O_2N_3$: C, 74.78; H, 6.01; N, 10.90. Found: C, 74.98; H, 6.17; N, 10.86. IR cm^{-1} (KBr): ν_{NH} 3400; $\nu_{C=O}$ 1730. UV λ_{max}^{EtOH} nm (ε): 250 (9200), 286 (11000), 290 (10600) (shoulder). NMR τ: 8.91 (t, J=7 Hz, $COOCH_2\underline{CH_3}$), 6.42 (s, N–CH_3), 5.76 (q, J=7 Hz, $COO\underline{CH_2}CH_3$), 4.16 (b.s., NH), 2.30—3.01 (14H, aromatic).

Reaction of I with Dimethyl Acetylenedicarboxylate——a) In CH_3CN: A solution of I (0.2 g) and the diester (0.33 g) in acetonitrile (4 ml) was heated under reflux for 2 hr and the solvent was removed reduced pressure to give oily residue, which was purified by silica gel (3 g) column chromatography. From benzene–*n*-hexane eluent the excess diester was recovered.

The fraction eluated with benzene was condensed and the residue was recrystallized from benzene–*n*-hexane to give 0.314 g (87%) of the adduct (IV) as colorless crystals, mp 79—80.5°. *Anal.* Calcd. for $C_{14}H_{13}O_4N_5$: C, 53.33; H, 4.16; N, 22.22. Found: C, 53.49; H, 4.23; N, 22.20. IR cm^{-1} (KBr): ν_{N_3} 2220; $\nu_{C=O}$ 1748 and 1735. UV λ_{max}^{EtOH}: 233. NMR τ: 7.03 (s, N–CH_3), 6.08 (s, $COOCH_3$), 5.98 (s, $COOCH_3$), 2.23—2.58 (4H, aromatic). Mass Spectrum *m/e*: 287.089 (M^+–N_2). Calcd. for $C_{14}H_{13}O_4N_3$: 287.090.

b) In Benzene: The reaction was repeated using benzene as solvent ,but reflux for 12 hr was necessary for disappearance of I on a TLC. The first fraction eluated with benzene was evaporated *in vacuo* and the residue was recrystallized from MeOH to give 0.015 g (4.1%) of V, mp 167.5—168.5° (decomp.). *Anal.* Calcd. for $C_{14}H_{13}O_4N_5$: C, 53.33; H, 4.16; N, 22.22. Found: C, 53.06; H, 4.04; N, 22.50. IR cm^{-1} (KBr): $\nu_{C=O}$ 1745. UV λ_{max}^{EtOH} nm: 237 (shoulder), 280 (shoulder), 287. NMR τ: 6.06 (s, CH_3), 6.03 (s, CH_3), 5.97 (s, CH_3), 2.44—2.70 (3H, aromatic), 2.19 (1H, m, C_4–H). Mass Spectrum *m/e*: 315 (M^+).

Subsequent elution with the same solvent gave 0.294 g (81%) of IV, mp 79—80.5°. This compound was identified with the product obtained from reaction a) by IR and NMR spectral comparison.

Reaction of I with Methyl Propiolate——A solution of I (0.173 g) and the ester (0.252 g) in acetonitrile (4 ml) was heated under reflux for 24 hr. Further, 0.252 g of the ester was added to the solution and reaction was continued for 24 hr under the same conditions. The solvent and the excess ester were removed under reduced pressure, the residue was dissolved in a small amount of benzene, and the solution was chromatographed on a silica gel (2 g) column. Unreacted I (0.039 g) was recovered from the fraction eluated with benzene.

The fractions eluated with benzene and benzene–$CHCl_3$ (4: 1) were evaporated *in vacuo* and the residue was recrystallized from MeOH to give 0.095 g (37%) of VI, mp 153—154° (decomp.). *Anal.* Calcd. for $C_{12}H_{11}O_2N_5$: C, 56.02; H, 4.31; N, 27.23. Found: C, 56.20; H, 4.28; N, 27.28. IR cm^{-1} (KBr): $\nu_{C=O}$ 1745. UV λ_{max}^{EtOH} nm: 238, 290. NMR τ: 5.96 (s, N–CH_3), 5.84 (s, $COOCH_3$), 2.44—2.67 (3H, aromatic), 2.17 (1H, m, C_4–H), 1.04 (s, triazole ring proton). Mass Spectrum *m/e*: 257 (M^+).

This product was identified with a sample prepared from 2-chloro-1-methylbenzimidazole and methyl 1(3)H-1,2,3-triazole-4(5)-carboxylate by mixed melting point determination and by IR and NMR spectral comparison.

Subsequent fraction eluated with benzene–$CHCl_3$ (1: 1) was evaporated *in vacuo* to give 0.014 g (5.5%) of oily VII. IR cm^{-1} (NaCl): ν_{N_3} 2220; $\nu_{C=O}$ 1740. NMR τ: 6.96 (s, N–CH_3), 5.99 (s, $COOCH_3$), 2.28—2.60 (4H, aromatic), 1.49 (s, CH).

Dimethyl 2-(1-Methyl-2-benzimidazolyl)-2H-1,2,3-triazole-4,5-dicarboxylate (Xa)——A solution of 2-chloro-1-methylbenzimidazole (VIII) (0.083 g), the diester (IXa) (0.092 g), and triethylamine (0.051 g) in xylene (3 ml) was heated under reflux for 0.5 hr. The solvent was removed under reduced pressure, the residue was extracted with $CHCl_3$, the extract was washed with H_2O, dried over anhyd. K_2CO_3, and evapo-

12) Melting points was measured on a Yanagimoto Micro Melting Point Apparatus and uncorrected. NMR spectra were taken on a JNM-4H-100 spectrometer in $CDCl_3$ with tetramethylsliane as internal standard. Mass Spectra were measured on a Hitachi Double Focusing Mass Spectrometer RMU-7L.

rated *in vacuo*. The residue was recrystallized from MeOH to give 0.106 g (67%) of colorless crystals, mp 137.5—138.5°. *Anal.* Calcd. for $C_{14}H_{13}O_4N_5$: C, 53.33; H, 4.16; N, 22.22. Found: C, 53.62; H, 4.13; N, 22.08. IR cm^{-1} (KBr): $\nu_{C=O}$ 1730. UV λ_{max}^{EtOH} nm: 247, 250 (shoulder), 301. NMR τ: 5.98 (s, 2×$COOCH_3$), 5.95 (s, N–CH_3), 2.50—2.70 (3H, aromatic), 2.15 (m, C_4–H). Mass Spectrum *m/e*: 315 (M^+).

Methyl 1-(1-Methyl-2-benzimidazolyl)-1H-1,2,3-triazole-4-carboxylate (VI) and Methyl 2-(1-Methyl-2-benzimidazolyl)-2H-1,2,3-triazole-4-carboxylate (Xb)——A solution of VIII (0.166 g), methyl 1(3)H-1,2,3-triazole-4(5)-carboxylate (IXb) (0.152 g), and triethylamine (0.121 g) in xylene (3 ml) was heated under reflux for 1 hr. The solvent was evaporated *in vacuo*, the residue was extracted with $CHCl_3$, the extract was washed with H_2O, dried over anhyd. K_2CO_3, and evaporated *in vacuo*. The residue was dissolved in a small amount of $CHCl_3$ and the solution was chromatographed on a silica gel (7 g) column. Elution with $CHCl_3$ gave 0.131 g (51%) of Xb as colorless crystals (MeOH), mp 156.5—157.5°. *Anal.* Calcd. for $C_{12}H_{11}O_2N_5$: C, 56.02; H, 4.31. Found: C, 56.32; H, 4.28. IR cm^{-1} (KBr): $\nu_{C=O}$ 1738. UV λ_{max}^{EtOH} nm: 247, 253 (shoulder), 299. NMR τ: 5.97 (s, N–CH_3 or $COOCH_3$), 5.93 (s, $COOCH_3$ or N–CH_3), 2.44—2.62 (3H, aromatic), 2.08 (m, C_4–H), 1.53 (s, triazole ring proton). Mass Spectrum *m/e*: 257 (M^+).

Subsequent elution with the same solvent gave 0.07 g (27%) of VI as colorless crystals (MeOH), mp 153—154° (decomp.). This compound was identified with the product obtained from reaction of I with methyl propiolate by mixed melting point determination and by IR and NMR spectral comparison.

Reaction of I with Diethyl Phenylethynylamine——A solution of I (0.105 g) and the ynamine (0.155 g) in anhyd. dioxane (6 ml) was heated under reflux for 1.5 hr and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel (2 g) using benzene and benzene–$CHCl_3$ to give 0.18 g (86%) of XI as colorless crystals (ether–*n*-hexane), mp 92—93°. *Anal.* Calcd. for $C_{20}H_{22}N_6$: C, 69.34; H, 6.40; N, 24.26. Found: C, 69.62; H, 6.60; N, 24.40. UV λ_{max}^{EtOH} nm: 255, 278, 285 (shoulder). NMR τ: 9.02 (6H, t, J=7 Hz, 2×$NCH_2C\underline{H}_3$), 6.96 (4H, q, J=7 Hz, 2×$NC\underline{H}_2CH_3$), 6.24 (s, N–CH_3), 2.40—2.70 (6H, aromatic), 2.12 (m, C_4–H), 1.99 (2H, d,d, J=2, 8 Hz; aromatic). Mass Spectrum *m/e*: 318 (M^+–N_2).

Essentially the same results were obtained using anhyd. tetrahydrofuran as solvent, although reflux for 3.5 hr was necessary for completion of the reaction.

Thermal Decomposition of 5-Diethylamino-1-(1-methyl-2-benzimidazolyl)-4-phenyl-1H-1,2,3-triazole (XI)——A solution of XI (0.173 g) in anhyd. *p*-cymene (2 ml) was heated under reflux for 0.5 hr in a stream of nitrogen and chromatographed on a silica gel (2 g) column. Elution with benzene gave 0.033 g (20.7%) of oily product (XII). IR cm^{-1} (NaCl): $\nu_{C=O}$ 1625. UV λ_{max}^{EtOH} nm: 245, 282. NMR τ: 8.94 (6H, t, J=7 Hz, 2×N–$CH_2C\underline{H}_3$), 6.75 (4H, q, J=7 Hz, 2×N–$C\underline{H}_2CH_3$), 6.21 (s, N–CH_3), 2.47—2.90 (6H, aromatic), 2.37 (d,d, J=2, 7 Hz, C_4–H), 1.71 (2H, d,d, J=2, 8 Hz; aromatic). Mass Spectrum *m/e*: 318.185 (M^+). Calcd. for $C_{20}H_{22}N_4$: 318.184.

This product was identified with a sample obtained from reaction of 3-bromo-9-methyl-2-phenyl-9H-imidazo[1,2-*a*]benzimidazole (XVII)[11] with diethylamine by IR and NMR spectral comparison.

Further elution with benzene–$CHCl_3$ (5: 1—2: 1) gave a yellow fraction, from which was isolated XIII as yellow crystals (0.078 g, 46.7%) (from benzene–*n*-hexane), mp 152—153°. *Anal.* Calcd. for $C_{20}H_{22}ON_4$: C, 71.83; H, 6.63; N, 16.76. Found: C, 71.90; H, 6.62; N, 16.87. IR cm^{-1} (KBr): $\nu_{C=O}$ 1680. UV λ_{max}^{EtOH} nm: 255, 307, 370 (shoulder). NMR τ: 8.86 (t, J=7 Hz, N–$CH_2C\underline{H}_3$), 8.58 (t, J=7 Hz, N–$CH_2C\underline{H}_3$), 6.76 (q, J=7 Hz, N–$C\underline{H}_2CH_3$), 6.35 (s, N–CH_3), 6.24 (q, J=7 Hz, N–$C\underline{H}_2CH_3$), 2.40—3.10 (7H, aromatic), 2.08 (2H, d,d; J=2, 8 Hz; aromatic). Mass Spectrum *m/e*: 334 (M^+).

The last fraction eluated $CHCl_3$–MeOH gave a mixture of minor products. Separation of the mixture into each component and establishment of their structures were unsuccessful.

2-(β-Hydroxyphenethylamino)-1-methylbenzimidazole (XIV)——a) To a solution of XIII (0.05 g) in MeOH (6 ml)–H_2O (0.5 ml) $NaBH_4$ (0.021 g) was added gradually with stirring under ice cooling. After addition was completed, the solution was further stirred for 1 hr at room temperature and evaporated *in vacuo*. The residue was extracted with $CHCl_3$, the extract was washed with H_2O, dried over anhyd. K_2CO_3, and removed under reduced pressure. The residue was recrystallized from benzene to give 0.033 g (83%) of colorless crystals, mp 161.5—162.5°. *Anal.* Calcd. for $C_{16}H_{17}ON_3$: C, 71.88; H, 6.41; N, 15.72. Found: C, 71.50; H, 6.71; N, 15.77. IR cm^{-1} (KBr): $\nu_{associated OH,NH}$ 3500—3000. UV λ_{max}^{EtOH} nm: 251, 289. NMR τ: 6.70 (s, N–CH_3), 6.29 (2H, complex, CH_2), 5.80 (2H, b.s., NH, OH), 5.02 (q, J=3 Hz, CH), 2.50—3.05 (9H, aromatic).

b) To a solution of XV (0.2 g) in anhyd. THF (7 ml) $LiAlH_4$ (0.06 g) was added and the mixture was heated under reflux for 2 hr with stirring. After cooling, the excess reagent was decomposed by addition of aqueous MeOH under ice cooling and the solvent was evaporated *in vacuo*. The residue was extracted with $CHCl_3$, the extract was washed with H_2O, dried over anhyd. K_2CO_3, and removed under reduced pressure. The residue was purified by column chromatography on silica gel (2 g) using $CHCl_3$ as solvent to give 0.128 g (67%) of colorless crystals (benzene), mp 161.5—162.5°.

This compound was identified with the product drived from the route a) by mixed melting point determination and by IR and NMR spectral comparison.

2-Mandelamido-1-methylbenzimidazole (XV)——A mixture of 2-amino-1-methylbenzimidazole (0.441 g) and methyl mandelate (0.498 g) in xylene (6 ml) was heated under reflux for 20 hr and then the precipitate was filtered. The filtrate was evaporated *in vacuo* and the residue was purified by silica gel (4 g) column chromatography using benzene and benzene–$CHCl_3$ as eluent. The product was recrystallized from MeOH to give 0.474 g (56%) of colorless crystals, mp 170.5—172.5°. *Anal.* Calcd. for $C_{16}H_{15}O_2N_3$: C, 68.31; H, 5.38; N, 14.94. Found: C, 68.47; H, 5.14; N, 15.14. IR cm^{-1} (KBr): ν_{OH} 3375; ν_{NH} 3275. NMR τ: 6.41 (s, N–CH_3), 4.78 (s, CH), 2.30—2.85 (9H, aromatic).

3-Diethylamino-9-methyl-2-phenyl-9H-imidazo[1,2-*a*]benzimidazole (XII)——A mixture of XVII[11] (0.3 g), diethylamine (0.5 ml), and DMF (1 ml) was heated in a sealed tube at 210—220° for 4 hr and the solvent was removed under reduced pressure. The residue was extracted with $CHCl_3$, the extract was washed with H_2O, dried over anhyd. K_2CO_3, and evaporated *in vacuo*. The residue was dissolved in a small amount of benzene and the solution was chromatographed on a silica gel (2.5 g) column. Elution with benzene gave 0.013 g (4.4%) of XII as oil. This compound was identified with the product obtained from thermal decomposition of the adduct (XI) by IR and NMR spectral comparison.

Elution with benzene–$CHCl_3$ (2: 1) gave 0.121 g (53%) of XVI which was identified with an authentic sample[11] by IR and NMR spectral comparison.

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