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Studies on Seven-membered Ring Compounds. XXV.[1] Chlorination of Cycloheptimidazol-2(1*H*)-one Derivatives[2]

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Chlorination of cycloheptimidazol-2(1*H*)-one (I) and 6-hydroxy derivative (XII) with phosphoryl chloride in the presence of various bases was examined. Reëxamination of the pubilshed procedure for the chlorination of I in the presence of pyridine mainly gave a hitherto unreported product, 2-(1,4-dihydropyridino)cycloheptimidazole (V), and the reported 2-chlorocycloheptimidazole (II) was obtained only in a poor yield. By the modified procedure, 1-(2-cycloheptimidazolyl)pyridinium chloride (VIII) and the pyridinium salt (XV) were obtained from I and XII, respectively, and the treatment of VIII with alkali solution gave V. When the chlorination was carried out in the presence of dimethylaniline, the attack of dimethylaniline in the *para*-position or nitrogen occurred, and consequently, 2-(N-methylanilino)cycloheptimidazole (XVI), 2-chloro-4(and 6-)-(*p*-dimethylaminophenyl)cycloheptimidazole (XVIII and XIX) were obtained from I, and 2-chloro-6-(N-methylanilino)cycloheptimidazole (XXVI) and 2,6-dichloro-4-(*p*-dimethylaminophenyl)cycloheptimidazole (XXVII) from XII, respectively. The use of diethylaniline in the chlorination of I prevented the side reaction and II was obtained in a good yield.

Recently, it was found that some cycloheptimidazole derivatives showed a strong analgesic and antiphlogistic activities.[4] During the course of an investigation on the syntheses of such cycloheptimidazole derivatives, it became desirable to prepare 2-chlorocycloheptimidazole derivatives. Previous workers[5,6] have reported that the chlorination of cycloheptimidazol-2(1*H*)-one (I) with phosphoryl chloride in the presence of pyridine gave 2-chlorocycloheptimidazole (II). This reaction was reëxamined and the some new results obtained are now reported in this paper.

When the chlorination was repeated according to the published procedures, the reported product II was obtained only in a poor yield and a hitherto unreported product was obtained sa red cryastls, $C_{13}H_{11}N_3$, mp 165—166° (decomp.). Hydrolysis of this product with hydrochloric acid gave 2-aminocycloheptimidazole (III) and glutaraldehyde (IV). This result of the hydrolysis corresponds to the formation of ammonia and dioxime of IV by the reaction of 1,4-dihydropyridine with hydroxylamine hydrochloride[7] and indicates the above red crystals to be 2-(1,4-dihydropyridino)cycloheptimidazole (V). A more definite chemical proof for the structure of V was obtained from the hydrogenation experiment. The hydrogenation product of V was confirmed to be 2-piperidino-1,4,5,6,7,8-hexahydrocycloheptimidazole (VII) by its identification with the authentic speciment prepared by the hydrogenation of 2-piperidinocycloheptimidazole (VI) obtained from II and piperidine. The structure of V was also supported by its nuclear magnetic resonance (NMR) spectrum shown in Fig. 1, which indicates three multiplets at around 2.7, 4.8 and 7.0 τ corresponding to the α, β, and γ protons of the

1) Part XXIV: Y. Sato and G. Sunagawa, *Chem. Pharm. Bull.* (Tokyo), **15**, 634 (1967).
2) Presented at the 18th Annual Meeting of the Pharmaceutical Society of Japan, Tokyo, November 2, 1963.
3) Location: *Hiro-machi, Shinagawa-ku, Tokyo.*
4) H. Minakami, H. Takagi, and S. Kobayashi, *Life Sci.*, 3, 305 (1964).
5) T. Nozoe, T. Mukai, and I. Murata, *Proc. Japan Acad.*, **30**, 482 (1954).
6) I. Murata, *Sci. Rept. Res. Inst., Tohoku Univ.*, Ser. A, **12**, 271 (1960).
7) B.D. Shaw, *J. Chem. Soc.*, **127**, 215 (1925); *ibid.*, **1937**, 300.

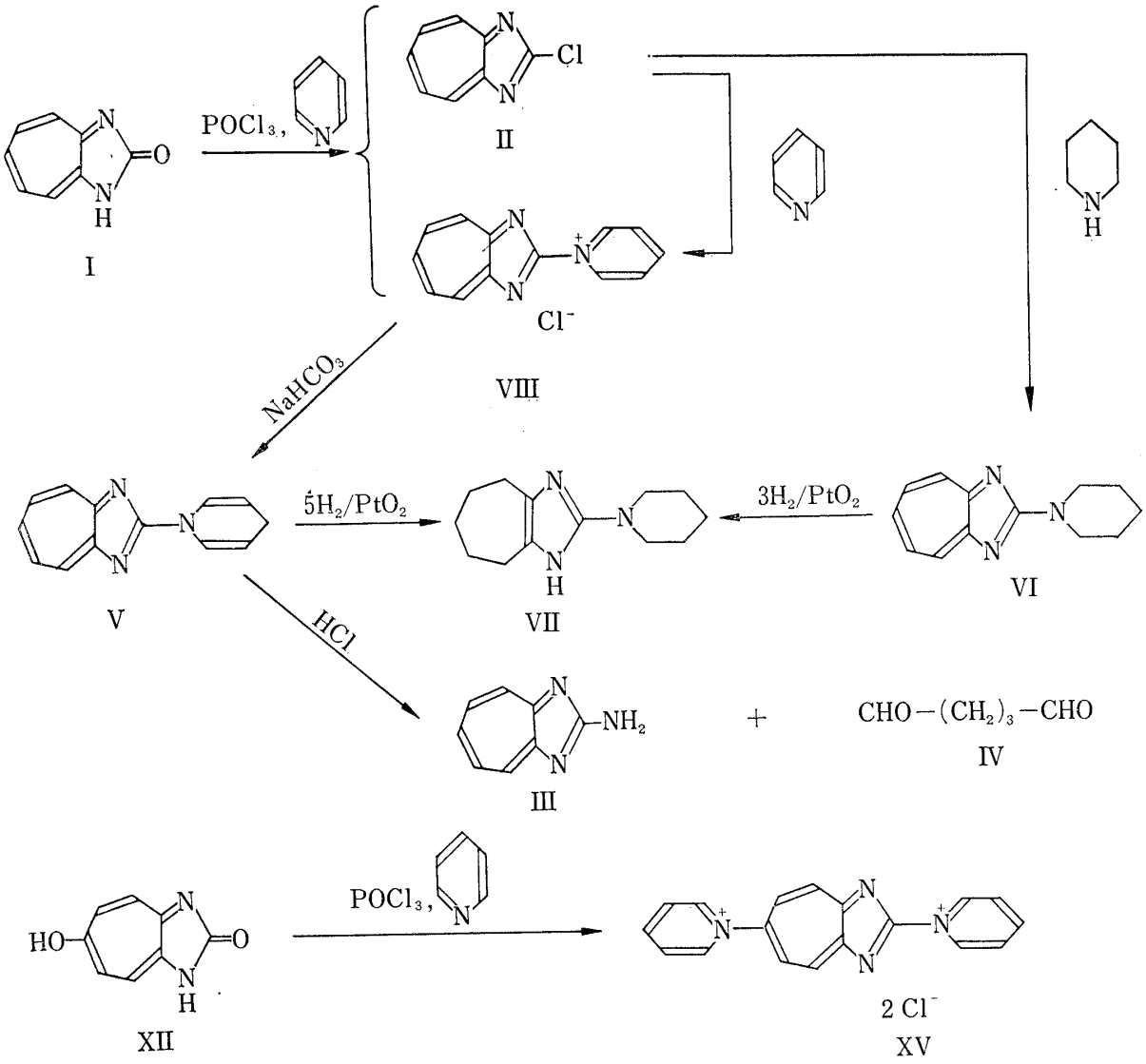

Chart 1

dihydropyridine ring, respectively. This coupling pattern agrees with the characteristics found previously for N–phenyl–1,4–dihydropyridine by Saunders, *et al.*[8]

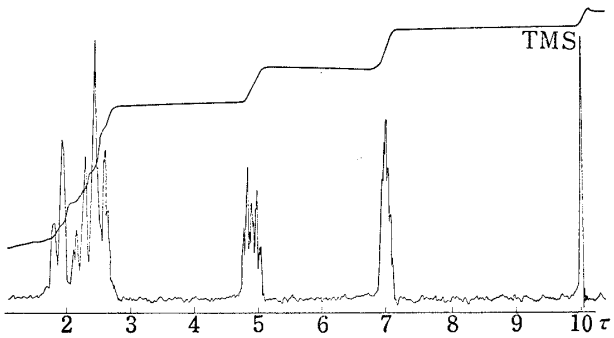

Fig. 1. Nuclear Magnetic Resonance Spectrum of V in $CDCl_3$ at 60 Mc

When the reaction product of the foregoing chlorination was isolated without neutralization, a hitherto unreported water–soluble crystals, $C_{13}H_{10}N_3Cl$, were obtained. This product was confirmed to be 1–(2–cycloheptimidazolyl)pyridinium chloride (VIII) from its satisfactory elemental analysis and its identification with the product obtained by an independent synthesis from II and pyridine. It was suspected that the above–mentioned V might have been produced from VIII by neutralization. This assumption was proved to be correct by the treatment of VIII with aqueous sodium hydrogencarbonate which gave V.

8) M. Saunders and E.H. Gold, *J. Org. Chem.*, **27**, 1439 (1962).

The formation of V from VIII probably proceeds through the course shown in Chart 2, in which the disproportionation of cation A is involved. Similar to the disproportionation of a tropylium cation,[9] the cation A abstracts a hydride ion from the pseudo-base B[10] produced from cation A by the attack of a hydroxide anion. No isolation of the oxidation product from this disproportionation is probably due to its less stability. An attempt to oxidize VIII with potassium ferricyanide only gave a resinous product, indicating the unstableness of the oxidized product.

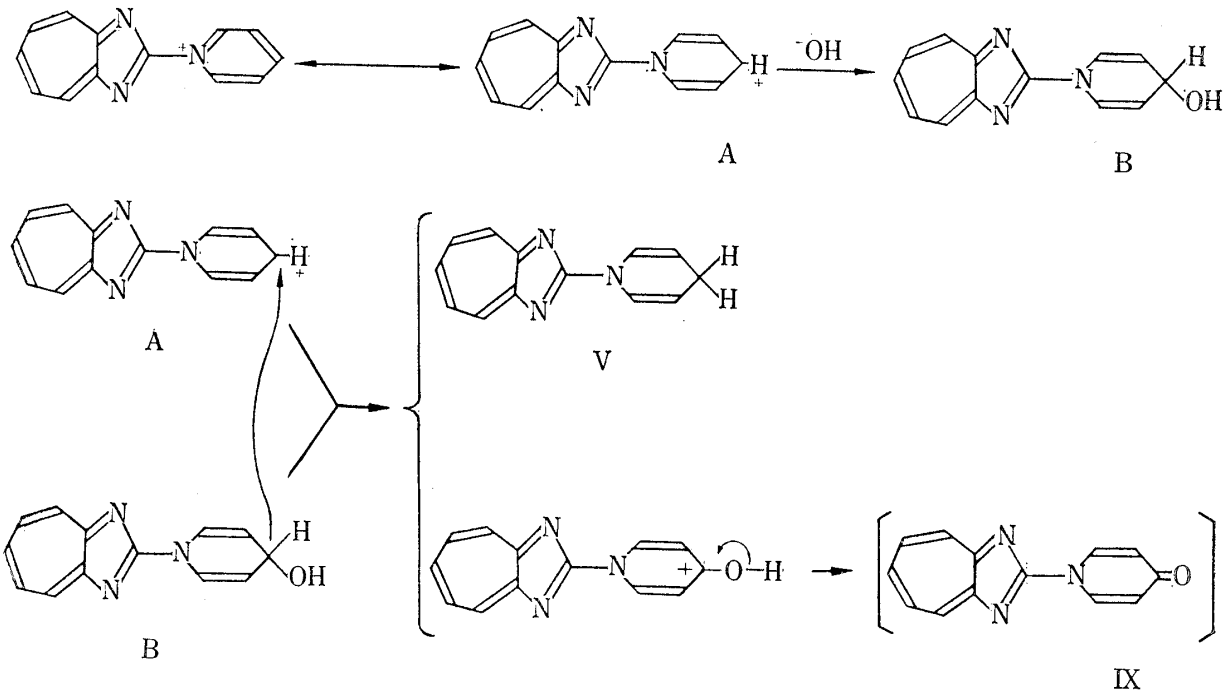

Chart 2

It has been known that the treatment of common pyridinium salts with alkali results in the formation of their pseudo-bases or in the cleavage of the pyridine ring.[11] The formation of dihydropyridine derivative from pyridinium salts by alkali, such as described above, has not been observed. In fact, when 1-(2-pyrimidinyl)pyridinium chloride (X), which can be regarded as an analog of the heterocyclic moiety of VIII, was allowed to react with alkali, the pyridine ring was cleaved to give 5-(2-pyrimidinyl)aminopenta-2,4-dien-1-al (XI).

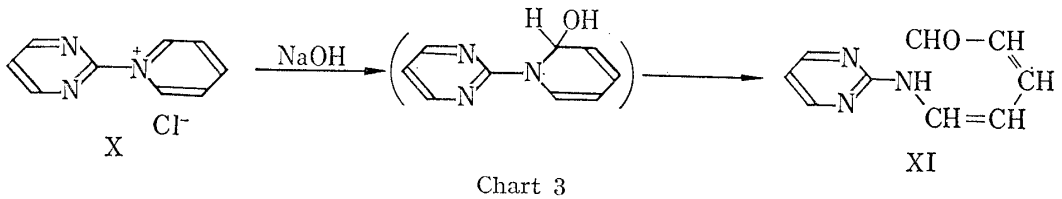

Chart 3

Next, the chlorination of 6-hydroxycycloheptimidazol-2(1*H*)-one (XII) was examined. Previous workers[12] have reported that this reaction gave 2,6-dichlorocycloheptimidazole (XIII), together with a small amount of 6-chlorocycloheptimidazol-2-(1*H*)-one (XIV).

9) *a*) T. Ikemi, T. Nozoe, and H. Sugiyama, *Chem. & Ind.* (London), **1960**, 932. *b*) P. ter Borg, R. von Heldern, A.F. Bickel, W. Renold, and A.S. Dreiding, *Helv. Chim. Acta*, **43**, 457 (1960).
10) The compounds B and IX might as well have the 2-oxopyridine function.
11) R.C. Elderfield, "Heterocyclic Compounds," Vol. 1, reviewed by H.S. Mosher, John Wiley & Sons, Inc., New York, 1950, 415—417.
12) T. Nozoe, T. Mukai, and T. Asao, *Bull. Chem. Soc. Japan*, **35**, 1188 (1962).

However, reëxamination of this chlorination did not give the reported XIII and XIV, and only a trace of yellow orange crystals, mp 287° (decomp.), was obtained. This product was presumed to be a dihydropyridine derivative from its ultraviolet (UV) spectral analogy to that of V. Further examination was not carried out because of the lack of the material. Treatment of this reaction mixture without neutralization, similar to the chlorination of I, also gave a pyridinium compound 1,1′-(2,6-cycloheptimidazolylene)bis(pyridinium chloride) (XV).

When the chlorination of I was carried out with dimethylaniline instead of pyridine, II was obtained, as expected, in a better yield. However, this chlorination was also accompanied by three by-products; yellow crystals (C), mp 139—140°, reddish brown crystals (D), mp 223° (decomp.), and reddish brown crystals (E), mp 235—236° (decomp.). The analytical values of (C) agreed with the formula $C_{15}H_{13}N_3$, and its UV spectrum was similar to that of 2-dimethylaminocycloheptimidazole.[5,13] Therefore, (C) was considered to be 2-(N-methylanilino)cycloheptimidazole (XVI). This was proved by the identification of (C) with the authentic sample of XVI, obtained by the reaction of II with methylaniline. The compound XVI, from the chlorination of I, was probably formed by the reaction of II with dimethylaniline accompanied by demethylation. This was confirmed by the fact that XVI was actually obtained by the reaction of II with dimethylaniline. The two by-products, (D) and (E), possessed the same composition $C_{16}H_{14}N_3Cl$. The hydrolysis product from (D) was proved to be 4-(*p*-dimethylaminophenyl)cycloheptimidazol-2(1*H*)-one (XVII) by identification with the authentic sample prepared from tropolone through the course shown in Chart 4. Consequently, (D) was confirmed to be 2-chloro-4-(*p*-dimethylaminophenyl)cycloheptimidazole (XVIII). The by-product (E) was considered to be 2-chloro-6-(*p*-dimethylaminophenyl)cycloheptimidazole (XIX) on the basis of its NMR spectrum, in which four protons of a seven-membered ring showed the A B pattern as described in the experimental. Hydrolysis of (E) gave 6-(*p*-dimethylaminophenyl)cycloheptimidazol-2(1*H*)-one (XX).

The chlorination of XII in the presence of dimethylaniline was also examined. This reaction gave XIII and XIV, which were not obtained by chlorination in the presence of pyridine described above. In addition to those, two by-products were obtained; yellow crystals (F), mp 192—193°, and red crystals (G), mp 235° (decomp.). The by-product (F) was concluded to be 2-chloro-6-(N-methylanilino)cycloheptimidazole (XXVI) on the basis of its elemental analysis and from the similarity of its UV spectrum to that of 6-amino-2-chlorocycloheptimidazole.[12,13] From elemental analysis and spectral analogy to XVIII, the structure of 2,6-dichloro-4-*p*-dimethylaminophenylcycloheptimidazole (XXVII) was assigned to (G).

Since dimethylaniline caused side reactions in the chlorination described above, the use of diethylaniline as the base for the chlorination of I was finally examined. In this case, any product corresponding to XVI was not isolated as expected and the II was obtained in a fairly good yield.

In summary, chlorination of cycloheptimidazol-2(1*H*)-one derivatives with phosphoryl chloride gave different results according to the bases used in such a reaction. The use of pyridine led to the formation of pyridinium salts, while the use of dimethylaniline produced substitution reaction in the *para* position or nitrogen to give 2-, 4-, or 6- substituted cycloheptimidazole derivatives. On the other hand, the use of diethylaniline as the base gave II in a fairly good yield.

Experimental[14]

Reaction of Cycloheptimidazol-2(1*H*)-one (I) with Phosphoryl Chloride——a) In the presence of pyridine: i) A mixture of 30 g of I, 30 ml of pyridine, and 350 ml of $POCl_3$ was heated with stirring at 110° for

13) I. Murata, *Bull. Chem. Res. Inst. Non-Aqueous Soln. Tohoku Univ.*, **9**, 102 (1960).
14) All melting points were uncorrected.

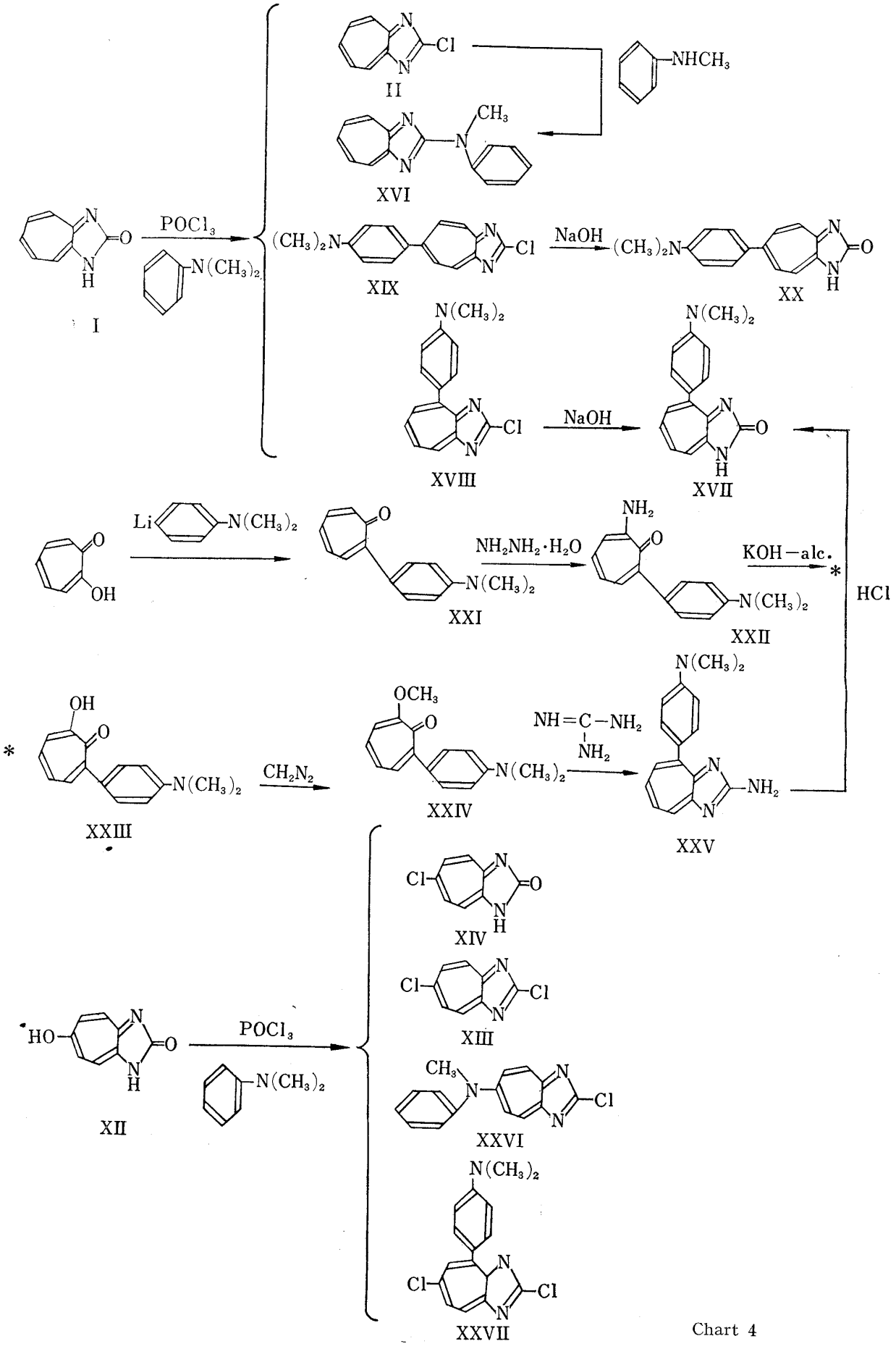

Chart 4

2.5 hr. The excess of $POCl_3$ was distilled off in a reduced pressure and the residue was poured on crushed ice. The aqueous solution was neutralized with solid $NaHCO_3$ and extracted with $CHCl_3$. The extract, dried over Na_2SO_4, was evaporated to dryness and the residue was chromatographed on alumina with benzene as a developer. Concentration of the initial eluate gave 3.95 g of 2-chlorocycloheptimidazole (II) as yellow needles, mp 162—163°. The latter eluates on concentration gave 2.5 g of 2-(1,4-dihydropyridino)cycloheptimidazole (V) as red needles (from benzene), mp 165—166° (decomp.), *Anal.* Calcd. for $C_{13}H_{11}N_3$: C, 74.62; H, 5.30; N, 20.08. Found: C, 74.74; H, 5.35; N, 20.16. UV λ_{max}^{EtOH} mμ (log ε): 224 (4.28), 253 (4.79), 319 (3.58), 425 (4.34). IR ν_{max}^{Nujol} 1689 cm^{-1}.

ii) A mixture of 15 g of I, 150 ml of $POCl_3$, and 16.2 g of pyridine was refluxed for 3 hr. The separated crystals were collected by filtration and washed with benzene. The crude product (19.1 g) was recrystallized from EtOH to pale yellow needles, which gradually black from around 255°. *Anal.* Calcd. for $C_{13}H_{10}N_3Cl$ [1-(2-cycloheptimidazolyl)pyridinium chloride (VIII)]: C, 64.07; H, 4.14; N, 17.24; Cl, 14.55. Found: C, 63.55; H, 4.25; N, 17.25; Cl, 13.89. UV λ_{max}^{EtOH} mμ (log ε): 252 (4.57), 318 (4.28), 390 (3.79).

b) In the presence of dimethylaniline: A mixture of 20 g of I, 200 ml of $POCl_3$, and 20 g of dimethylaniline was heated at 80—90° for 4 hr. The reaction mixture was treated as described in a) i), except that benzene and then AcOEt were used as the solvent for the chromatography. The initial benzene eluate, on concentration and recrystallization of the residue from benzene–cyclohexane, gave 6.2 g of 2-(N-methylanilino)cycloheptimidazole (XVI) as yellow needles, mp 139—140°, which were identified with XVI obtained by the reaction of II with methylaniline by mixed melting point determination, and comparison of infrared (IR) and UV Spectra. *Anal.* Calcd. for $C_{15}H_{13}N_3$: C, 76.57; H, 5.57; N, 17.86. Found: C, 76.34; H, 5.45; N, 17.47. UV λ_{max}^{EtOH} mμ (log ε): 246 (4.42), 260 (4.51), 372 (4.32).

The second benzene eluate gave 4.5 g of II, mp 162—163°. The third fraction eluted with AcOEt was concentrated and recrystallization of the residue from benzene gave 2-chloro-4-(*p*-dimethylaminophenyl)cycloheptimidazole (XVIII) as red-brown crystals, mp 223° (decomp.). Yield, 3.1 g. *Anal.* Calcd. for $C_{16}H_{14}N_3Cl$: C, 67.72; H, 4.97; N, 14.81. Found: C, 67.83; H, 5.00; N, 14.97. UV λ_{max}^{EtOH} mμ (log ε): 257 (4.65), 314 (4.04), 394 (3.79), 485 (4.27).

The fourth fraction eluted with AcOEt, after removal of AcOEt and recrystallization from benzene, afforded 2-chloro-6-(*p*-dimethylaminophenyl)cycloheptimidazole (XIX) as red-brown crystals, mp 235—236° (decomp.). Yield, 2.8 g. *Anal.* Calcd. for $C_{16}H_{14}N_3Cl$: C, 67.72; H, 4.97; N, 14.81. Found: C, 67.88; H, 5.16; N, 14.95. UV λ_{max}^{EtOH} mμ (log ε): 224 (4.36), 269 (4.43), 320 (3.90), 493 (4.54). NMR (in $CDCl_3$) τ: 6.89 (3H, singlet), 3.12 (2H, doublet, J=9 cps), 2.3 (2H, doublet, J=9 cps), 1.62 (2H, doublet, J=11 cps), 1.27 (2H, doublet, J=11 cps).

c) In the presence of diethylaniline: A mixture of 100 g of I, 1500 g of $POCl_3$, and 120 g of diethylaniline was heated at 70—80° for 4 hr. The reaction mixture was worked up as described in a) i) to give 30 g of II.

Reaction of II with Pyridine: Preparation of VIII——A mixture of 0.5 g of II and 0.5 g of pyridine was heated on a water bath for 20 min. The separated crystals were collected washed with benzene, and recrystallized from BuOH to 0.6 g of VIII as pale yellow needles, which gradually changed to black from around 255°. *Anal.* Calcd. for $C_{13}H_{10}N_3Cl$: C, 64.07; H, 4.14; N, 17.24; Cl, 14.55. Found: C, 64.17; H, 4.13; N, 17.21; Cl, 13.89.

Treatment of VIII with $NaHCO_3$——An aqueous solution (50 ml) of 14 g of VIII was made alkaline (pH 8—9) by the addition of solid $NaHCO_3$. Then, benzene was added and the mixture was stirred for 5 hr. The aqueous layer was separated from benzene layer and extracted with benzene. The combined benzene solution was dried over Na_2SO_4 and passed through a column of alumina. After removal of benzene from the effluent, the residue was recrystallized from benzene to 0.9 g of V as red needles, mp 165—166° (decomp.), which were identified with the product obtained by the chlorination of I in the presence of pyridine [a) i)] by mixed melting point determination and spectral comparison.

Hydrolysis of V——In 20 ml of 10% HCl, 0.5 g of V was dissolved, this solution was heated on a water bath for 3 hr, and extracted with ether. The aqueous layer was made alkaline with NaOH solution. The separated crystals were collected and recrystallized from EtOH to 0.25 g of yellow prisms, mp 295° (decomp.), which were identified with an authentic sample of 2-aminocycloheptimidazole (III) by mixed melting point determination and comparison of their IR spectra.

The ether extract, after being dried over Na_2SO_4 and removal of ether, gave 0.2 g of colorless oil, which displayed an absorption peak at 1730 cm^{-1} in the IR spectrum. The 2,4-dinitrophenylhydrazone of this oil was recrystallized from AcOEt to orange needles, mp 192—193°. *Anal.* Calcd. for $C_{17}H_{16}O_8N_8$: C, 44.35; H, 3.50; N, 24.34. Found: C, 44.49; H, 3.53; N, 24.24. UV $\lambda_{max}^{CHCl_3}$ mμ (log ε): 256 (4.39), 356 (4.68). This was found to be identical with the authentic sample of glutaraldehyde bis(2,4-dinitrophenylhydrazone) by mixed melting point and IR spectra.

2-Piperidinocycloheptimidazole (VI)——A mixture of 1.65 g of II and 1.7 g of piperidine in 20 ml of EtOH was refluxed for 1 hr. After removal of EtOH, the residue was dissolved in benzene. The benzene solution was washed with water, dried over Na_2SO_4, and evaporated to give 2.1 g of yellow crystalline mass which, upon recrystallization from cyclohexane, afforded pale yellow needles, mp 125—126°. *Anal.* Calcd.

for $C_{13}H_{15}N_3$: C, 73.21; H, 7.09; N, 19.70. Found: C, 72.98; H, 7.30; N, 19.66. UV λ_{max}^{EtOH} mμ (log ε): 240 (4.44), 264 (4.47), 300 (3.88), 373 (4.36).

2-Piperidino-1,4,5,6,7,8-hexahydrocycloheptimidazole (VII)——i) A solution of 0.4 g (0.00188 mole) of VI in 20 ml of EtOH was hydrogenated with H_2 in the presence of 40 mg of PtO_2 at room temperature. When hydrogen was no longer absorbed, after the uptake of 3.3 molar equivalents of H_2, the catalyst and solvent were removed and 400 mg of colorless residue, mp 205—207° (decomp.), was immediately dissolved in EtOH and derived to the picrate. The picrate was recrystallized from EtOH to yellow needles, mp 208—210° (decomp.). *Anal.* Calcd. for $C_{19}H_{24}O_7N_6$: C, 50.88; H, 5.40; N, 18.74. Found: C, 50.96; H, 5.78; N, 18.54.

ii) Hydrogenation of 400 mg of V in 40 ml of EtOH over 40 mg of PtO_2 was carried out with the uptake 5.5 molar equivalents of H_2. Removal of the catalyst and EtOH gave 470 mg of colorless crystals, mp 205—207° (decomp.), undepressed on admixture with the hydrogenation product of VI from i). Its picrate, mp 211—213° (decomp.), also was identical with the picrate obtained in i) by mixed melting point determination and comparison of IR spectra. *Anal.* Calcd. for $C_{19}H_{24}O_7N_6$: C, 50.88; H, 5.40; N, 18.74. Found: C, 50.65; H, 5.50; N, 18.76.

Attempted Oxidation of VIII with $K_3[Fe(CN)_6]$——To 20 ml of aqueous solution containing 4.87 g of VIII, 26 ml of aqueous solution of 13.2 g of $K_3[Fe(CN)_6]$ and 10 ml of aqueous solution containing 3.2 g of NaOH were added at the same time under cooling (0—10°). After stirring for 2 hr, the separated solid was collected to 5.6 g of dark brown product which was sensitive to air and became black on standing, and easily formed a resinous material.

1-(2-Pyrimidinyl)pyridinium Chloride (X)——A mixture of 8 g of 2-chloropyrimidine and 40 ml of pyridine was heated on a water bath for 5 hr. Filtration of the separated crystals and washing with benzene gave 7.4 g of a crude product, whose recrystallization from *n*-PrOH afforded colorless cubic crystals, mp 132—133° (decomp.). *Anal.* Calcd. for $C_9H_8N_3Cl\cdot\frac{1}{4}H_2O$: C, 54.55; H, 4.32; N, 21.21. Found: C, 54.68; H, 4.27; N, 21.74. UV λ_{max}^{EtOH} 250 mμ (log ε 4.01).

5-(2-Pyrimidinyl)aminopenta-2,4-dien-1-al (XI)——To 5 ml of an aqueous solution containing 0.5 g of X, was added an aqueous solution of 0.15 g of NaOH. The separated crystals (0.4 g) were dissolved in $CHCl_3$ and chromatographed on alumina. The eluate, after removal of $CHCl_3$ and recrystallization of the residue from EtOH, gave pale orange-yellow needles, mp 154° (decomp.). *Anal.* Calcd. for $C_9H_9ON_3$: C, 61.70, H, 5.18; N, 23.99. Found: C, 61.38; H, 5.23; N, 23.93. UV λ_{max}^{EtOH} mμ (log ε): 240 (3.87), 360 (4.76). IR ν_{max}^{Nujol} cm^{-1}: 3185, 1669, 1629, 1605.

Reaction of 6-Hydroxycycloheptimidazol-2(1*H*)-one (XII) with Phosphoryl Chloride——a) In the presence of pyridine: i) A mixture of 3.2 g of XII, 83 ml of $POCl_3$, and 10.7 ml of pyridine was heated at 110° for 3 hr. The reaction mixture was treated as described in a) i) of the reaction of I with $POCl_3$, except that $CHCl_3$ was used as the solvent for the alumina chromatography. The $CHCl_3$ eluate, on concentration gave 5 mg of orange-yellow crystals, mp 287°. UV λ_{max}^{EtOH} mμ: 255, 335, 405.

ii) A mixture of 1.5 g of XII of pyridine, and 39 ml of $POCl_3$ was stirred at 80° for 3 hr. The separated crystals were collected and washed with benzene, then dissolved in a minimum amount of EtOH. After treatment with charcoal, benzene was added to the EtOH solution. There separated 1.6 g of 1,1′-(2,6-cycloheptimidazolylene)bis(pyridinium chloride) (XV) as pale yellow needles, which changed to black from around 200°. *Anal.* Calcd. for $C_{18}H_{14}N_4Cl_2\cdot 2H_2O$: C, 54.97: H, 4.61; N, 14.25. Found: C, 55.30; H, 4.05; N, 14.23. UV λ_{max}^{EtOH} mμ (log ε): 257 (4.65), 271 (4.65), 342 (4.53), 392 (3.84). Chloroplatinate: *Anal.* Calcd. for $C_{18}H_{14}N_4PtCl_6\cdot 2H_2O$: C, 29.60; H, 2.48; N, 7.67. Found: C, 29.34; H, 2.49; N, 7.83.

b) In the presence of dimethylaniline: A mixture of 3.0 g of XII, 9.0 g of dimethylaniline, and 80 ml of $POCl_3$ was heated at 40—50° for 1.5 hr. The separated crystals were filtered, washed with benzene, and recrystallized from EtOH to 0.23 g of 6-chlorocycloheptimidazol-2(1*H*)-one (XIV) as pale yellow needles, mp above 280°.

The benzene washings were concentrated to give 0.52 g of 2,6-dichlorocycloheptimidazole (XIII), mp 226—227° (decomp.). The $POCl_3$ filtrate was evaporated *in vacuo* and the residue was treated as described in a) i), except that benzene and then AcOEt were used as the solvent for chromatography. Elution with benzene gave 0.24 g of 2-chloro-6-(N-methylanilino)cycloheptimidazole (XXVI) as yellow crystals (from cylohexane), mp 192—193°. *Anal.* Calcd. for $C_{15}H_{12}N_3Cl$: C, 66.79; H, 4.48; N, 15.58. Found: C, 66.36; H, 4.38; N, 15.40. UV λ_{max}^{EtOH} mμ (log ε): 262.5 (4.56), 390 (4.35).

Elution with AcOEt afforded 70 mg of 2,6-dichloro-4-(*p*-dimethylaminophenyl)cycloheptimidazole (XXVII) as red crystals, mp 235° (decomp.). *Anal.* Calcd. for $C_{16}H_{13}N_3Cl_2$: C, 60.39; H, 4.12; N, 13.21. Found: C, 60.62; H, 4.02; N, 13.12. UV λ_{max}^{EtOH} mμ (log ε): 262.5 (4.62), 332 (4.17), 415 (3.83), 515 (4.27).

Reaction of II with N-methylaniline: Preparation of XVI——To a solution of 0.5 g of II in 10 ml of EtOH, 0.66 g of N-methylaniline was added and the solution was refluxed for 2 hr. After removal of EtOH, the residue was dissolved in water, the aqueous solution was neutralized with $NaHCO_3$ solution, and extracted with benzene. Removal of benzene gave 0.71 g of a crude product, mp 136—139°, which were recrystallized from cyclohexane to 0.61 g of XVI as yellow crystals, mp 139—140°. *Anal.* Calcd. for $C_{15}H_{13}N_3$: C, 76.57; H, 5.57; N, 17.86. Found: C, 76.05; H, 5.63; N, 17.53.

2-(*p*-Dimethylaminophenyl)tropone (XXI)——To ether solution of *p*-dimethylaminophenyllithium prepared from 6.94 g of Li and 99.95 g of *p*-dimethylaminobromobenzene, ether solution of 12.2 g of tropolone was added under cooling. After refluxing for 1 hr, water was added cautiously and the mixture was extracted with benzene. The extract was dried over Na_2SO_4, and evaporated. The residue, on addition of ether, gave 14.9 g of orange crystals, mp 145—150°, which were recrystallized from EtOH. mp 148—150°, *Anal.* Calcd. for $C_{15}H_{15}ON$: C, 79.97; H, 6.71; N, 6.22. Found: C, 79.73; H, 6.58; N, 6.38.

2-Amino-7-(*p*-dimethylaminophenyl)tropone (XXII)——A mixture of 14.3 g of XXI and 4.38 g of NH_2-$NH_2 \cdot H_2O$ in 200 ml of EtOH was refluxed for 30 hr. After removal of EtOH, addition of benzene and filtration gave 5.1 g of orange-brown crystals. The filtrate was chromatographed on alumina with AcOEt. From AcOEt eluate was obtained additional 1.65 g of crystals. The combined crystals were recrystallized from benzene. mp 192—193°. *Anal.* Calcd. for $C_{15}H_{16}ON_2$: C, 74.97; H, 6.71; N, 11.66. Found: C, 75.03; H, 6.68; N, 11.55.

3-(*p*-Dimethylaminophenyl)tropolone (XXIII)——To 150 ml of EtOH solution of 2.95 g of XXII, 3 ml of an aqueous solution containing 1.6 g of KOH was added and the mixture was refluxed for 40 hr. After removal of EtOH, the residue was dissolved in water and 0.87 g of unchanged XXII was recovered by filtration. Neutralization of the filtrate with 10% HCl gave 1.5 g of orange crystals, mp 165—168°, whose recrystallization from EtOH raised their mp to 167—169°. *Anal.* Calcd. for $C_{15}H_{15}O_2N$: C, 74.66; H, 6.27; N, 5.81. Found: C, 74.30; H, 6.28; N, 5.82.

Methyl Ether of 3-(*p*-Dimethylaminophenyl)tropolone (XXIV)——To a suspension of 1.85 g of XXIII in ether excess ether solution of CH_2N_2 was added and the mixture was allowed to stand overnight. After filtration, the etheral solution was concentrated to give 0.8 g of yellow crystals, mp 135—136°, and its mother liquor was chromatographed on alumina with AcOEt. The AcOEt eluate gave additional 0.44 g of the same product. The combined crystals were recrystallized from ether to yellow needles, mp 136—137°. *Anal.* Calcd. for $C_{16}H_{17}O_2N$: C, 75.27; H, 6.71; N, 5.49. Found: C, 74.65; H, 6.55; N, 5.52.

2-Amino-4-(*p*-dimethylaminophenyl)cycloheptimidazole (XXV)——To a solution of 80 mg of metallic Na dissolved in 20 ml of EtOH, 335 mg of guanidine hydrochloride and 74 mg of XXIV were added and the mixture was refluxed for 9 hr. Filtration and washing with water gave 574 mg of orange-yellow crystals, which were recrystallized from EtOH, mp 269—270° (decomp.). *Anal.* Calcd. for $C_{16}H_{16}N_4$: C, 72.70; H, 6.10; N, 21.20. Found: C, 72.61; H, 6.23; N, 21.10. UV λ_{max}^{EtOH} mμ (log ε): 257 (4.58), 340 (4.27), 400 (4.17).

4-(*p*-Dimethylaminophenyl)cycloheptimidazol-2(1*H*)-one (XVII)——i) From XXV: A solution of 474 mg of XXV in 10 ml of conc. HCl was heated in a sealed tube at 110° for 36 hr. The HCl solution was concentrated and neutralized with NaOH solution. The separated crystals were collected and recrystallized from EtOH to 262 mg of reddish brown crystals, mp 258—260° (decomp.). *Anal.* Calcd. for $C_{16}H_{15}ON_3$: C, 72.43; H, 5.70; N, 15.84. Found: C, 71.95; H, 5.78; N, 15.97. UV λ_{max}^{EtOH} mμ (log ε): 252 (4.55), 349 (4.12), 420 (4.10). IR ν_{max}^{Nujol}: 1692 cm^{-1}.

ii) From XVIII: To an EtOH solution of 0.3 g of XVIII, 6 ml of 20% NaOH solution was added and the mixture was heated on a water bath for 4 hr. After removal of EtOH, water was added to the residue and the aqueous solution was neutralized with dil. H_2SO_4 to give 0.27 g of red crystals, which were recrystallized from EtOH, mp 260° (decomp.). This product was identified with the product obtained from XXV in i) by mixed melting point determination and comparison of their IR and UV spectra.

6-(*p*-Dimethylaminophenyl)cycloheptimidazol-2(1*H*)-one (XX)——A mixture of 0.3 g of XIX and 6 ml of 20% NaOH solution in 20 ml of EtOH was refluxed for 3 hr. The crystals that separated on cooling were collected and recrystallized from EtOH to give the sodium salt of XX as yellow crystals, mp above 300°. Yield, 0.28 g. *Anal.* Calcd. for $C_{16}H_{14}ON_3Na \cdot H_2O$: C, 62.94; H, 5.28; N, 13.76. Found: C, 62.28; H, 5.38; N, 13.71.

The aqueous solution of 193 mg of the sodium salt of XX was made slightly acid with dil. H_2SO_4 and gave 190 mg of XX as reddish brown crystals, which were recrystallized from EtOH. mp 292° (decomp.). *Anal.* Calcd. for $C_{16}H_{15}ON_3 \cdot 2H_2O$: C, 63.77; H, 6.36; N, 13.95. Found: C, 63.45; H, 6.29; N, 13.40. UV λ_{max}^{EtOH} mμ (log ε): 245.5 (4.46), 264 (4.48), 445 (4.42). IR ν_{max}^{Nujol} cm^{-1}: 1742. NMR (in conc. H_2SO_4) ppm (from cyclohexane): 2.1 (6H, doublet, J=4 cps), 6.5 (2H, doublet, J=9 cps), 6.8 (2H, doublet, J=9 cps), 7.8 (4H, singlet).

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