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Studies on Seven-membered Ring Compounds. XXVIII.[1]
2-Imino-2*H*-cycloheptoxazole Derivatives. (2)[2]

Mitsuo Watatani

Central Research Laboratories, Sankyo Co., Ltd.[3]

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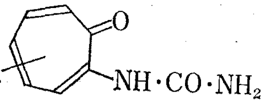
Some nucleophilic reactions of 2–imino–2*H*–cycloheptoxazoles including their hydrolysis and reactions with hydrogen sulfide, thiols, and active methylene compounds were examined. Both acid and alkaline hydrolyses of 2–imino–2*H*–cycloheptoxazole (I) gave 2–ureidotropone (III). On the other hand, a simple standing of the aqueous solution of 2–imino–2*H*–cycloheptoxazole (I) gave 2–(2–troponylamino)cycloheptimidazole (XIV). Reaction of I with hydrogen sulfide gave 2–ureidotropothione (XVI), while the reaction with thiols gave 2–alkylthiocycloheptimidazoles (XXVI—XXVIII), besides N–carbamoyl–2–alkylthiotroponeimines (XXIX—XXXI). Reactions of I with malononitrile, cyanoacetamide, and benzoylacetonitrile gave 3–substituted 2–imino–1,2–dihydrocyclohepta[*b*]pyrroles (XXXII—XXXIV), and a similar reaction with ethyl cyanoacetate gave ethyl 2–imino–1,2–dihydrocyclohepta[*b*]pyrrole–3–carboxylate (XXXV) and 2–oxo–1,2–dihydrocyclohepta[*b*]pyrrole–3–carbonitrile (XXXVI). Reactions with ethyl acetoacetate, ethyl benzoylacetate, acetylacetone, and diethyl malonate gave 3–acetyl– (XXXVIII) and 3–benzoylcyclohepta[*b*]pyrrol–2(1*H*)–one (XXXIX), 3–acetyl–2–methylcyclohepta[*b*]pyrrole (XL), and ethyl 1,2–dihydro–2–oxocyclohepta[*b*]pyrrole–3–carboxylate (XLI), respectively.

In a preceding paper of this series,[1] the formation and electrophilic reactions of 2–imino–2*H*–cycloheptoxazoles have been reported. The present paper deals with some nucleophilic reactions of 2–imino–2*H*–cycloheptoxazoles.

As reported in the preceding paper, 2–imino–2*H*–cycloheptoxazole (I) gave the sodium salt of 2–cyanaminotropone (II) on its treatment with concentrated aqueous sodium hydroxide. On the other hand, when the aqueous solution of I was allowed to stand under a slightly alkaline reaction, hydrolysis took place and 2–ureidotropone (III) was obtained. The standing of a slightly acidic aqueous solution of I also gave III. The structure of III was confirmed by the

Table I. 2–Ureidotropone Derivatives



Compound No.	R	mp (°C)	Formula	Analysis (%) Calcd. C	H	N	Found C	H	N
III	H	197 (dec)	$C_8H_8O_2N_2$	58.53	4.91	17.07	58.44	5.12	17.27
VII	5–Br	225 (dec)	$C_8H_7O_2N_2Br$	39.52	2.90	11.52	39.88	2.93	11.27
VIII	7–CN	205 (dec)	$C_9H_7O_2N_3$	57.14	3.73	22.21	56.90	3.83	22.20
IX	5–NO_2	200 (dec)	$C_8H_7O_4N_3$	45.94	3.37	20.09	45.90	3.56	20.16

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[1] Part XXVII: M. Watatani, N. Soma, and G. Sunagawa, *Chem. Pharm. Bull.* (Tokyo), **16**, 1316 (1968).

[2] Presented at the Kinki Local Meeting of the Pharmaceutical Society of Japan, Osaka, June 18, 1966 (This paper comprises a part of the dissertation submitted by the author for the doctorate degree at the Kyoto University).

[3] Location: *Hiro–machi, Shinagawa–ku, Tokyo.*

similarity of its ultraviolet (UV) spectrum to that of 2-acetamidotropone and its infrared (IR) spectrum which shows the presence of an amino and an amide groups. Similar to I, substituted 2-imino-2*H*-cycloheptoxazoles (IV to VI) were hydrolyzed and the corresponding substituted 2-ureidotropones (VII to IX) shown in Table I were obtained.

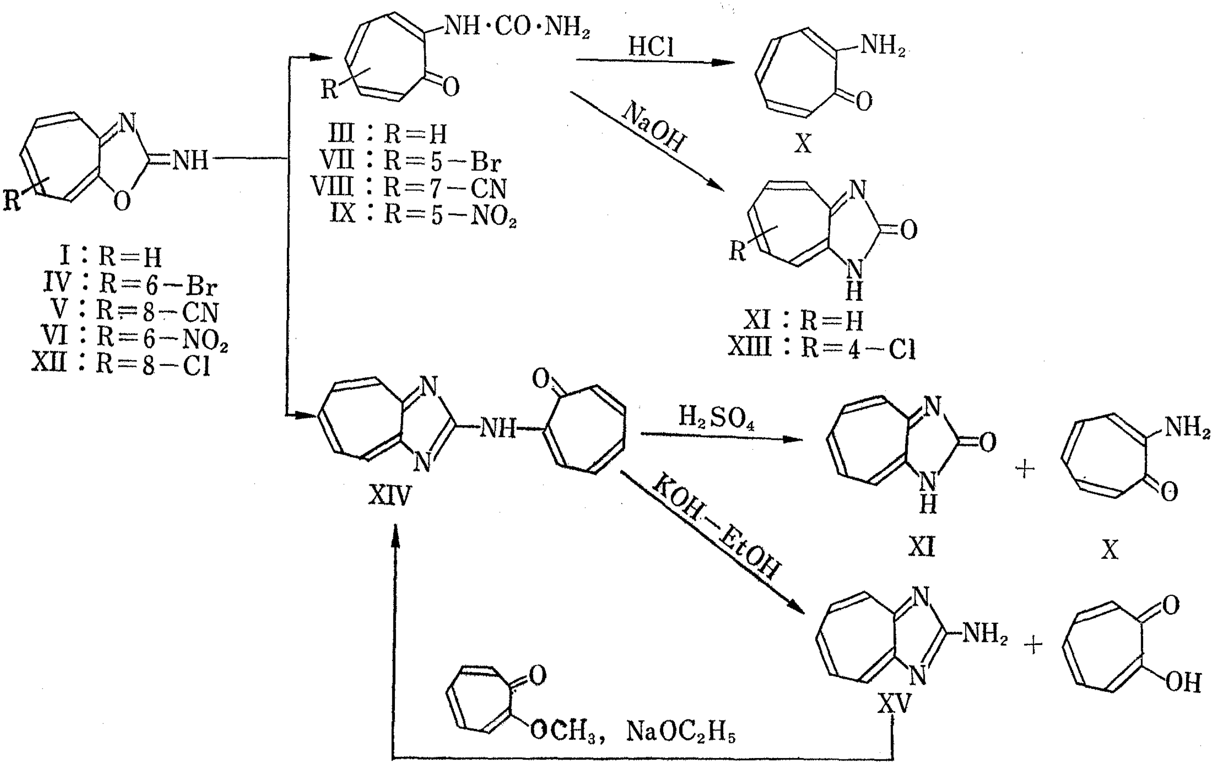

Chart 1

Acid hydrolysis of III gave 2-aminotropone (X), while the treatment of III with alkali yielded cycloheptimidazol-2(1*H*)-one (XI). In contrast to the above hydrolysis to III, standing of an aqueous solution of I without the addition of any acid or base, an interesting dimerization reaction took place which afforded 2-(2-troponylamino)cycloheptimidazole (XIV). The structure of XIV[4] was confirmed by its satisfactory elemental analysis, its identification with the product obtained by the reaction of 2-aminocycloheptimidazole (XV) with 2-methoxytropone, and the following hydrolysis experiment. Hydrolysis of XIV with 50% sulfuric acid gave X and XI, while that with ethanolic potassium hydroxide gave tropolone and XV. The formation of XIV from I probably proceeds through the course shown in Chart 2, which involves the attack of I at the C-8a of another molecule, a successive cleavage of the oxazole ring, and a ring closure to cycloheptimidazole ring accompanied by the elimination of isocyanic acid. Actual isolation of isocyanic acid as its silver salt from the reaction mixture indicates the correctness of this assumption.

Next, the reaction of I with hydrogen sulfide was examined. When I was allowed to react with hydrogen sulfide, there were obtained red crystals, $C_8H_8ON_2S$, which were assigned as 2-ureidotropothione (XVI) from the similarity of its UV spectrum to thatof 2-benzoylaminotropothione[5] and its IR spectrum which indicated the presence of amino, amide, and thiocarbonyl group of a tropothione structure. As was described above, 2-ureidotropones

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[4] Although three tautomeric forms (XIV, XIV′ and XIV″) are considered to be present for 2-(2-troponylamino)cycloheptimidazole, structure XIV is used representatively in this paper.

[5] T. Nozoe and K. Matsui, *Bull. Chem. Soc. Japan*, **34**, 1382 (1961).

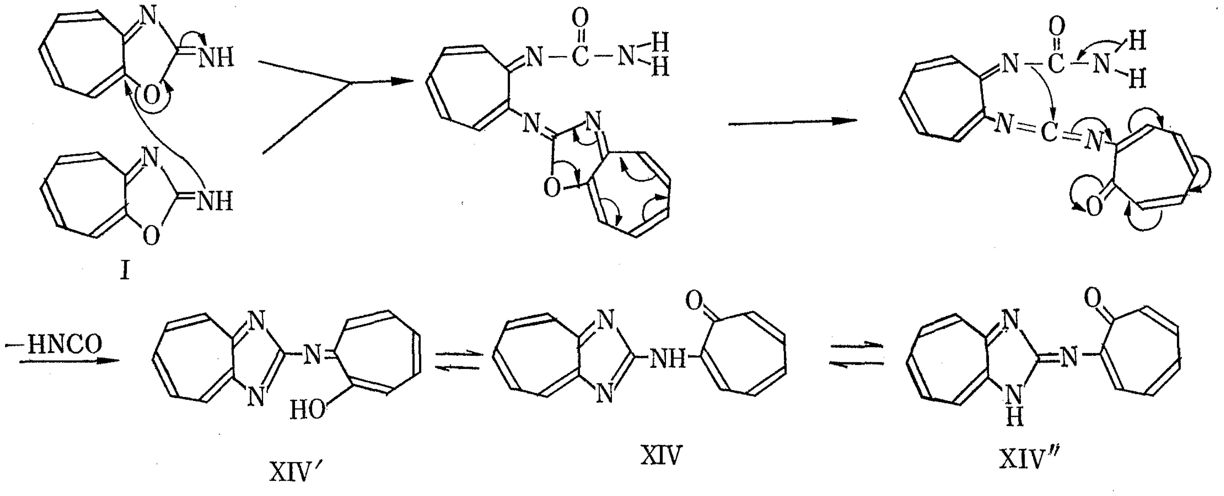

Chart 2

were hydrolyzed with dilute acid and underwent ring closure to form cycloheptimidazol-2(1*H*)-ones by the treatment with alkali. Contrast, treatment of XVI with dilute hydrochloric acid resulted in a ring closure to form 2*H*-cycloheptathiazol-2-one (XIX), whereas treatment of XVI with aqueous alkali gave 2-hydroxytropothione (XVII) and 2,2′-ditroponyl disulfide (XVIII).

The reaction of 5-isopropyl- (XX) and 7-isopropyl-2-imino-2*H*-cycloheptoxazole (XXI) with hydrogen sulfide similarly gave 4-isopropyl- (XXII) and 6-isopropyl-2-ureidotropothione (XXIII), respectively, which were converted to 5-isopropyl- (XXIV) and 7-isopropyl-2*H*-cycloheptathiazol-2-one (XXV) by treatment with hydrochloric acid.

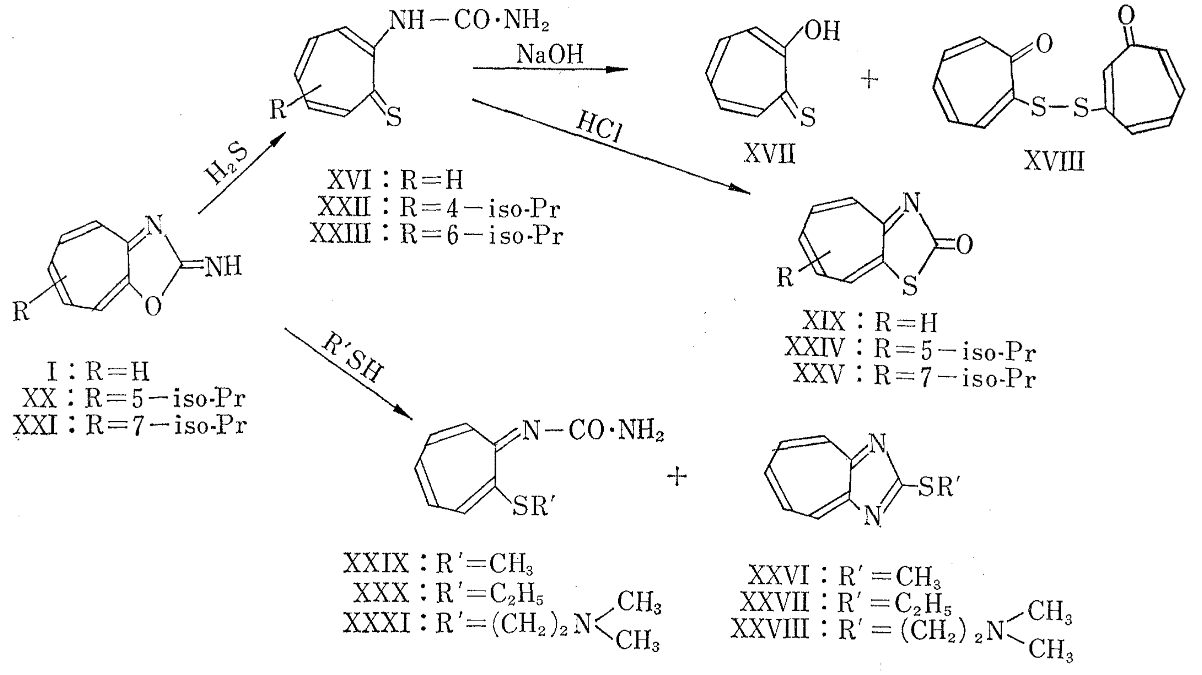

Chart 3

The reactions of I with thiols, such as methane, ethane, and 2-dimethylaminoethanethiols gave 2-methylthio- (XXVI), 2-ethylthio- (XXVII), and 2-(2-dimethylaminoethylthio)-cycloheptimidazole (XXVIII), besides 2-methylthio- (XXIX), 2-ethylthio- (XXX), and 2-(2-dimethylaminoethylthio)-N-carbamoyltroponeimine (XXXI), respectively. The structure of XXIX, XXX, and XXXI was proved from their elemental analysis, similarity of their UV

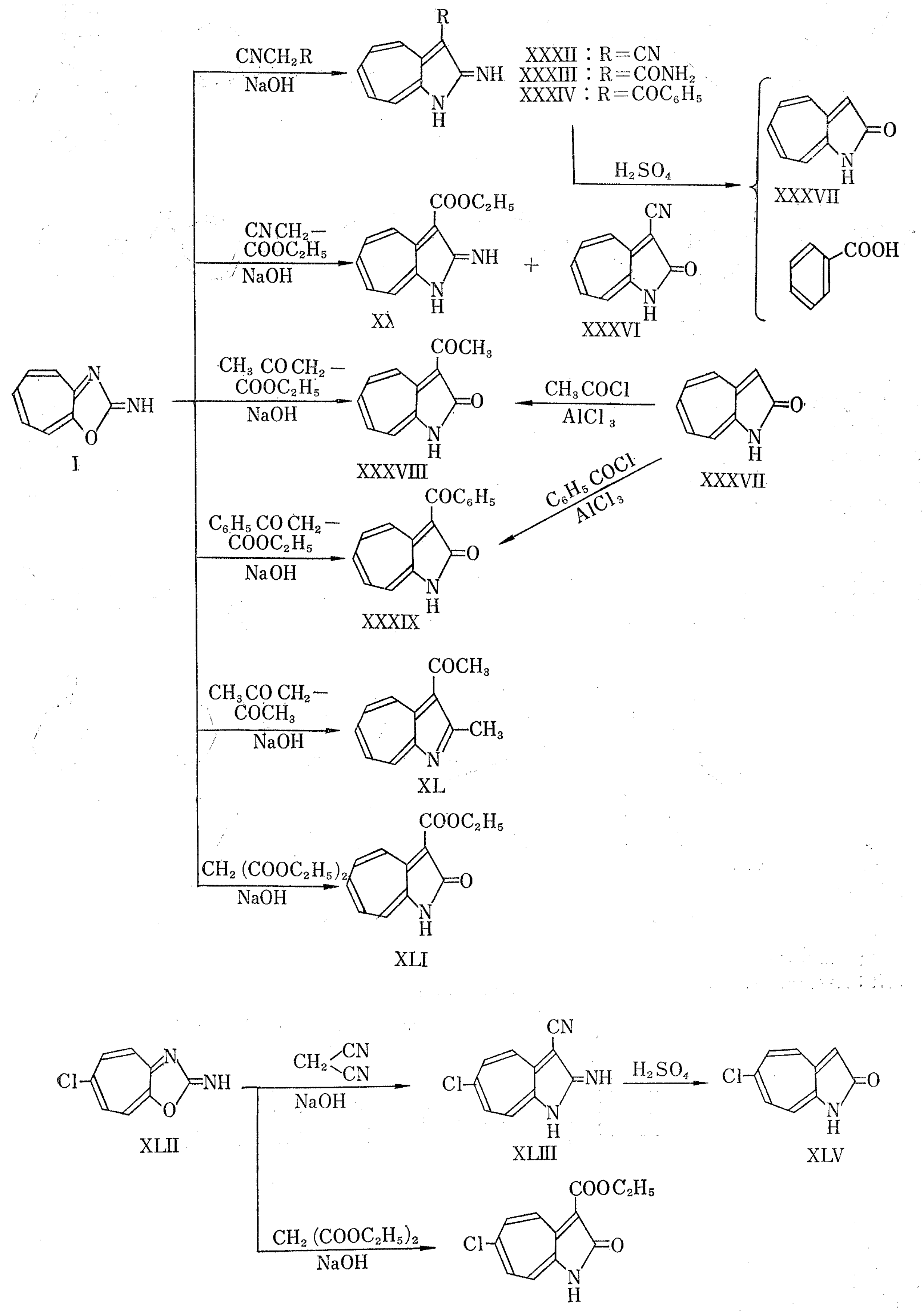
I
CNCH₂R
NaOH
R
=NH
XXXII : R=CN
XXXIII : R=CONH₂
XXXIV : R=COC₆H₅
H₂SO₄
XXXVII
COOH
CNCH₂−COOC₂H₅
NaOH
COOC₂H₅
XX
+
CN
XXXVI
CH₃COCH₂−COOC₂H₅
NaOH
COCH₃
XXXVIII
CH₃COCl
AlCl₃
XXXVII
C₆H₅COCl
AlCl₃
C₆H₅COCH₂−COOC₂H₅
NaOH
COC₆H₅
XXXIX
CH₃COCH₂−COCH₃
NaOH
COCH₃
−CH₃
XL
CH₂(COOC₂H₅)₂
NaOH
COOC₂H₅
XLI
Cl
XLII
CH₂(CN)₂
NaOH
CN
XLIII
H₂SO₄
XLV
CH₂(COOC₂H₅)₂
NaOH
COOC₂H₅

Chart 4

spectra to that of 2-methoxytroponeimine,[6] and their IR spectra which indicated the presence of an amino and a conjugate carbonyl group. The UV spectrum of the hitherto unreported XXVIII was similar to those of known XXVI and XXVII.[7]

Finally, reactions with active methylene compounds were investigated. The reactions of I with malononitrile, cyanoacetamide, benzoylacetonitrile, and ethyl cyanoacetate, in the presence of sodium hydroxide in an aqueous solution, respectively gave 2-imino-1,2-dihydrocyclohepta[*b*]pyrrole-3-carbonitrile (XXXII), 2-imino-1,2-dihydrocyclohepta[*b*]pyrrole-3-carboxamide (XXXIII), 3-benzoyl-2-imino-1, 2-dihydrocyclohepta[*b*]pyrrole (XXXIV), and ethyl 2-imino-1,2-dihydrocyclohepta[*b*]pyrrole-3-carboxylate (XXXV) in a good yield. In the reaction with ethyl cyanoacetate, a small amount of 2-oxo-1,2-dihydrocyclohepta[*b*]-pyrrole-3-carbonitrile (XXXVI) was obtained besides XXXV. The structure of the hitherto unreported XXXIV was proved from the similarity of its UV spectrum to that of XXXII and its acid hydrolysis to the known cyclohepta[*b*]pyrrol-2(1*H*)-one (XXXVII) and benzoic acid.

The reaction of I with ethyl acetoacetate gave 3-acetylcyclohepta[*b*]pyrrol-2(1*H*)-one (XXXVIII), which was identical with the product obtained from XXXVII and acetyl chloride. On the other hand, when I was allowed to react with ethyl benzoylacetate, white crystals,

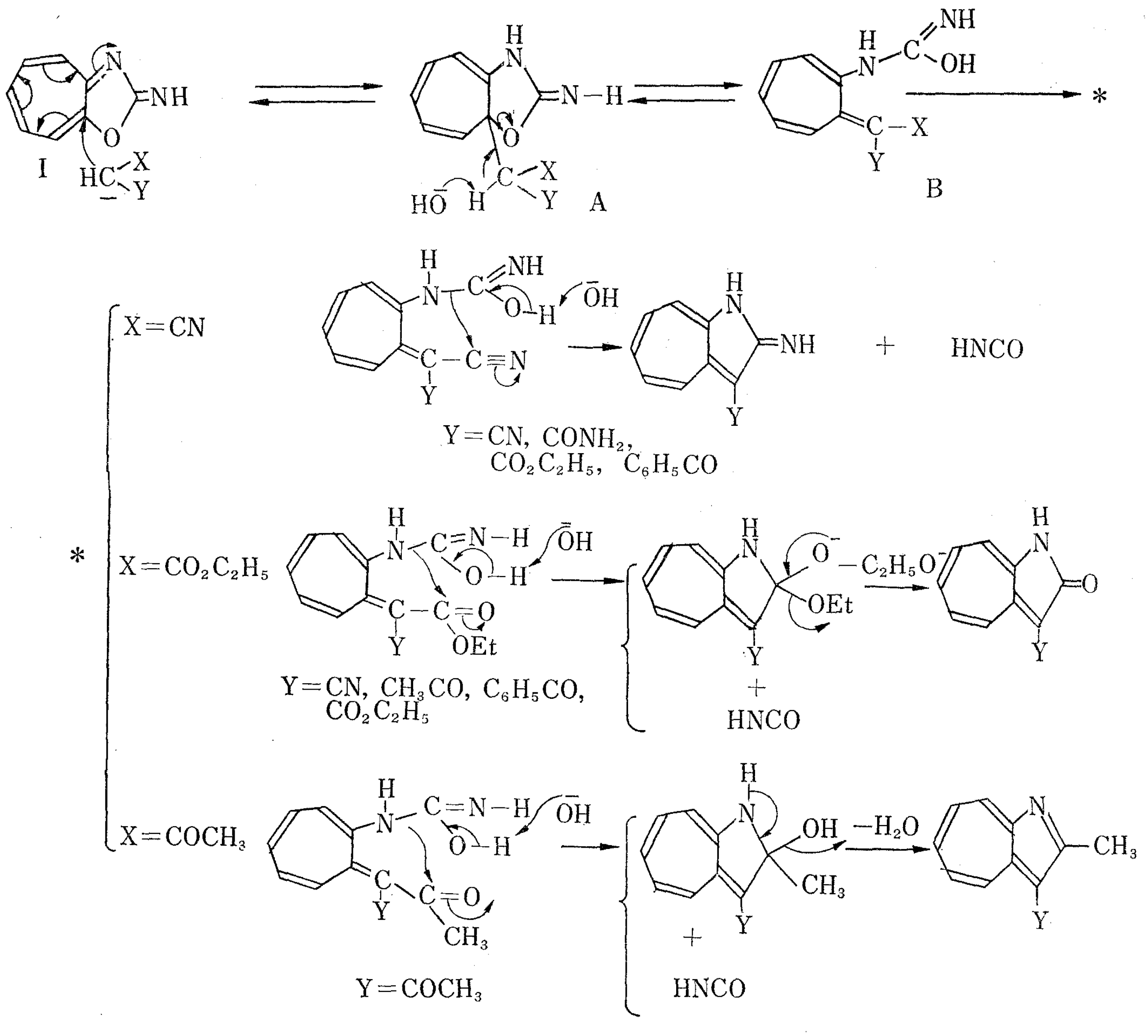

Chart 5

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[6] N. Soma, J. Nakazawa, T. Watanabe, Y. Sato and G. Sunagawa, *Chem. Pharm. Bull.* (Tokyo), **13**, 457 (1965).

[7] I. Murata, *Bull. Chem. Soc. Japan*, **33**, 56 (1960).

mp 120—121° (decomp.), separated out, and a further treatment of the latter with alkali produced 3–benzoylcyclohepta[*b*]pyrrol–2(1*H*)–one (XXXIX) which was identical with the product obtained from XXXVII and benzoyl chloride. The definite structure of the intermediary separated crystals has not been assigned due to its unstability, especially, in the state of a solution, but its elemental analysis agreed with the composition, $C_{19}H_{18}O_4N_2$, corresponding to the addition product of I and ethyl benzoylacetate, and the IR spectrum (in Nujol mull) showed two ν_{NH} at 3401 and 3125 cm^{-1}. The reactions with acetylacetone and diethyl malonate proceeded in a similar manner and 3–acetyl–2–methylcyclohepta[*b*]pyrrole (XL) and ethyl 2–oxo–1,2–dihydrocyclohepta[*b*]pyrrole–3–carboxylate (XLI) were finally obtained, respectively. The structure of XL was confirmed by the similarity of its UV spectrum to that of 3–acetyl–2–chlorocyclohepta[*b*]pyrrole[8] and from the IR spectrum which shows no ν_{NH} or ν_{OH} but $\nu_{C=O}$ at 1621 cm^{-1}. This extremely low frequency value of $\nu_{C=O}$ resembles that of carbonyl in 3–acetyl–2–chlorocylohepta[*b*]pyrrole[8] indicating the correctness of the assumed structure of XL.

The formation of the above–mentioned cyclohepta[*b*]pyrrole derivatives is elucidated by the mechanism shown in Chart 5.

The attack of the carbanion of active methylene compound at the C–8a of I and successive cleavage of the oxazole ring may lead to the formation of the heptafulvene intermediate (B). The ring closure of (B) accompanied by the liberation of isocyanic acid forms the various type of cyclohepta[*b*]pyrrole derivatives according to the functional groups in (B). Ring closure became less facile with the functional group in the intermediate (B) in the order of cyano, ester, and then ketone. This is probably due to their electrophilic nature. The liberation of isocyanic acid was proved by the isolation of its silver salt from the reaction mixture. In addition to the route shown in Chart 5, the formation of cyclohepta[*b*]pyrrole derivatives may be illustrated by the attack of the carbanion in the active methylene compounds at C–4 of I followed by the hydrogen shift as had been shown in the reaction of 2–chlorotropone or 2–tosyloxytropone with active methylene compounds[9] (Chart 6). However, this route was excluded by the fact that the reaction of 6–chloro–2–imino–2*H*–cycloheptoxazole (XLII) with malononitrile and diethyl malonate did not give 5–chloro–2–imino–1,2–dihydrocyclohepta[*b*]pyrrole–3–carbonitrile and ethyl 5–chloro–2–oxo–1,2–dihydrocyclohepta[*b*]pyrrole–3–carboxylate but did respectively give 6–chloro–2–imino–1,2–dihydrocyclohepta[*b*]pyrrole–3–carbonitrile (XLIII) and ethyl 6–chloro–2–oxo–1,2–dihydrocyclohepta[*b*]pyrrole–3–carboxylate

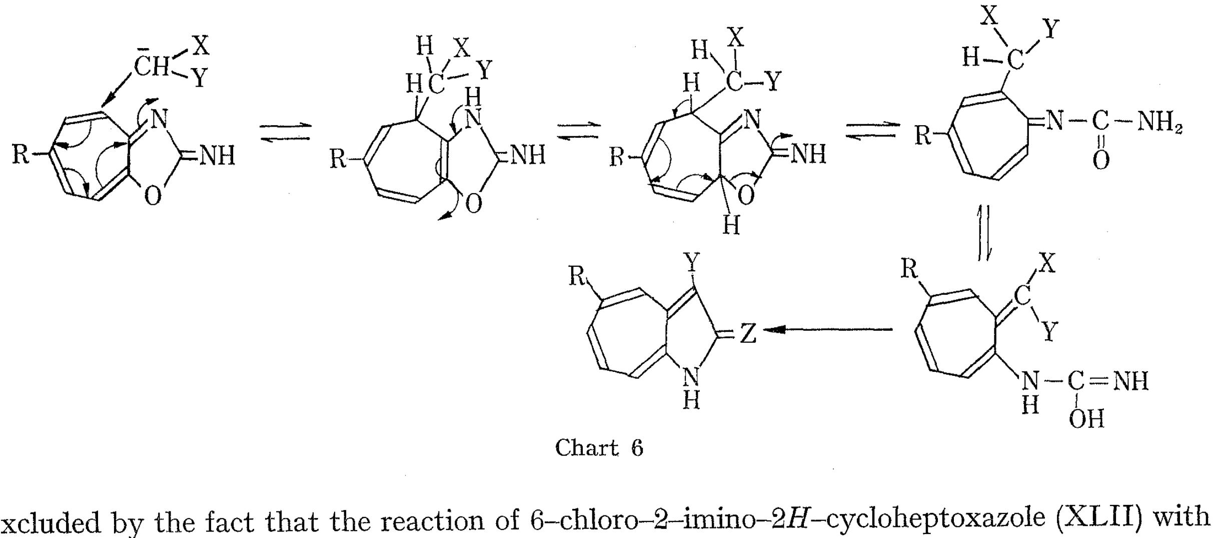

Chart 6

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[8] K. Ogura, H. Sasaki, and S. Seto, *Bull. Chem. Soc. Japan*, **38**, 306 (1965).
[9] T. Nozoe, S. Seto, K. Takase, S. Matsumura, and T. Nakazawa, *Nippon Kagaku Zasshi*, **86**, 346 (1965).

(XLIV).[10] The structure of XLIII was proved by its hydrolysis followed by decarboxylation to 6-chlorocyclohepta[*b*]pyrrol-2(1*H*)-one (XLV).[10]

Further work is now in progress on the reaction of 2-imino-2*H*-cycloheptoxazoles and will be reported in the follwoing paper.

Experimental[11]

2-Ureidotropone (III)——An aqueous soluiton (30 ml) of 2-imino-2*H*-cycloheptoxazole (I), prepared from 500 mg of Na salt of 2-cyanaminotropone (II), was adjusted to pH 10.25—10.5 with aqueous NaOH solution and allowed to stand overnight at room temperatures. The separated crystals were collected and recrystallized from EtOH to 310 mg of yellow needles, mp 196—197° (decomp.). The analytical data are given in Table I. UV $\lambda_{\max}^{\text{EtOH}}$ mμ (log ε): 236 (4.38), 255 (shoulder), 331 (4.05), 366 (3.97), 383 (3.92). IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 3378, 3289, 3226, 1724.

When an aqueous solution (2 ml) of I was adjusted to pH 3 with dil. AcOH, III was also obtained.

Acid Hydrolysis of III——A mixture of 100 mg of III and 5 ml of 10% HCl was heated on a water bath for 5 min. The reaction mixture was neutralized with dil. NaOH and extracted with $CHCl_3$. The extract was dried over Na_2SO_4 and evaporated to dryness. The residue was recrystallized from benzene to 52 mg of yellow needles, mp 104—105°, which were identified with an authentic sample of 2-aminotropone (X) by mixed mp determination and comparison of their UV and IR spectra.

Treatment of III with Alkali: Preparation of Cycloheptimidazol-2(1*H*)-one (XI)——A mixture of 300 mg of III and 10 ml of 10% NaOH was heated on a water bath for 2 hr. The reaction mixture was neutralized with dil. HCl and concentrated. Filtration of the separated crystals gave 200 mg of pale yellow needles, mp 245°, which were identified with an authentic sample of XI by mixed mp determination and comparison of their UV and IR spectra.

Substituted 2-Ureidotropones (VII—IX)——Substituted 2-ureidotropones listed in Table I were prepared from the corresponding substituted 2-imino-2*H*-cycloheptoxazoles (IV—VI) by the same procedure as for the preparation of III. The analytical data are also given in Table I.

4-Chlorocycloheptimidazol-2(1*H*)-one (XIII)——An aqueous solution (20 ml) of 8-chloro-2-imino-2*H*-cycloheptoxazole (XII), prepared from 500 mg of Na salt of 7-chloro-2-cyanaminotropone, was adjusted to pH 10.7 with dil. NaOH. The mixture was heated on a water bath for 5 hr and filtered. The filtrate, after charcoal treatment, was adjusted to pH 4—5 and concentrated. The separated crystals were collected and recrystallization from EtOH gave 131 mg of XIII as pale yellow needles, mp above 280°.

2-(2-Troponylamino)cycloheptimidazole (XIV)——i) An aqueous solution (30 ml) of I, prepared from 0.5 g of II and 268 mg of conc. HNO_3, was allowed to stand overnight at room temperature. The separated crystals were collected and recrystallized from EtOH to orange needles, mp 226—227°. Yield, 190 mg. *Anal.* Calcd. for $C_{15}H_{11}ON_3$: C, 72.27; H, 4.45; N, 16.86. Found: C, 72.44; H, 4.61; N, 16.77. UV $\lambda_{\max}^{\text{EtOH}}$ mμ (log ε): 240.5 (4.56), 318 (4.00), 449 (4.62). IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 3279, 1618, 1600.

To the filtrate, after washing with $CHCl_3$, an aqueous $AgNO_3$ was added. The separated white crystals were identified as AgNCO by comparison of its IR spectrum with that of an authentic sample.

ii) To an EtOH solution of NaOEt obtained from 0.126 g of Na and 20 ml of EtOH, 0.725 g of 2-aminocycloheptimidazole (XV) and 0.7 g of 2-methoxytropone were added. The mixture was refluxed for 5 hr. The crystals which separated on cooling were collected and recrystallization from EtOH gave 0.712 g of orange crystals, mp 226—227°, which were identified with the product obtained in i) by mixed mp determination and comparison of their UV and IR spectra.

Acid Hydrolysis of XIV——A mixture of 1 g of XIV and 5 ml of 50% H_2SO_4 was refluxed for 14 hr. When cooled, the reaction mixture was made alkaline with NaOH solution and extracted with $CHCl_3$. The extract was dried over Na_2SO_4 and evaporated to dryness. Sublimation of the residue gave 0.4 g of yellow needles, mp 107—108°, which were identified with an authentic sample of X by mixed mp determination and comparison of their UV and IR spectra. The aqueous solution from the extraction was adjusted to pH 5—6 and concentrated. The crystals that separated on cooling were collected giving 0.514 g of pale yellow needles, mp 245°, which were identified with an authentic sample of XI by mixed mp determination and comparison of their UV and IR spectra.

Alkali Hydrolysis of XIV——To an EtOH solution (30 ml) of 0.847 g of XIV, 10 ml of 20% KOH was added and the mixture was refluxed for 20 hr. After removal of EtOH, the residue was washed with water and recrystallized from EtOH to 130 mg of yellow crystals, mp 295° (decomp.), which were identified with an authentic sample of XV by mixed mp determination and comparison of their UV and IR spectra.

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[10] T. Toda: Ph. D. Thesis, 1958. The author is indebted to Dr. T. Toda for supplying the authentic samples of XLIV and XLV.

[11] All melting points are uncorrected.

The washings were adjusted to pH 4 and extracted with $CHCl_3$. The extract was dried over Na_2SO_4 and evaporated to dryness. Sublimation of the residue gave 0.3 g of white needles, mp 51—52°, which were identical with an authentic sample of tropolone by mixed mp determination and comparison of their IR spectra.

2-Ureidotroponethione (XVI)——H_2S was passed through 300 ml of $CHCl_3$ solution of I, prepared from 1.7 g of II. After removal of $CHCl_3$ and excess H_2S, the residue was recrystallized from EtOH to 1.3 g of red needles, mp 154—155°. *Anal.* Calcd. for $C_8H_8O_3N_2$: C, 53.33; H, 4.48; N, 15.55. Found: C, 53.30; H, 4.50; N, 15.64. UV $\lambda_{\max}^{\text{EtOH}}$ mμ(log ε): 242 (4.08), 284 (4.38), 422 (4.17). IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 3344, 3289 (broad), 3185, 1681, 1106, 1029.

Alkali Hydrolysis of XVI——A mixture of 1.0 g of XVI and 10 ml of 20% NaOH was heated on a water bath for 20 min. The reaction mixture was neutralized with dil. HCl and filtered. The solid product was recrystallized from petr. ether and gave 0.45 g of reddish orange crystals, mp 54—55°, which were identified with an authentic sample of 2–hydroxytroponethione (XVII) by mixed mp determination and comparison of their UV and IR spectra.

The filtrate was adjusted to pH 4 and allowed to stand overnight. The separated crystals were collected and recrystallized from EtOH to 0.2 g of yellow scales, mp 200° (decomp.), which were identical with an authentic sample of 2,2′–ditroponyl disulfide (XVIII) by comparison of their IR spectra.

2*H*-Cycloheptathiazol-2-one (XIX)——A mixture of 0.6 g of XVI and 10 ml of 10% HCl was stirred at room temperatures for 15 min. The reaction mixture was neutralized with dil. NaOH and crystals that separated were collected to 0.4 g of pale yellow needles, mp 155—156°, which were identified with an authentic sample by mixed mp determination and comparison of their UV and IR spectra.

5-Isopropyl- (XXIV) and 7-Isopropyl-2*H*-cycloheptathiazol-2-one (XXV)——To an EtOH solution of NaOEt prepared from 0.64 g of Na and 30 ml of EtOH, 1.16 g of cyanamide and 4.5 g of a mixture of 4–(and 6–)isopropyl–2–methoxytropone were added. The mixture was refluxed for 3 hr. When cooled, the separated crystals were collected and wasned with a small amount of EtOH. The obtained yellow crystals were dissolved in 100 ml of water and neutralized with 1.45 g of AcOH. H_2S was passed through this aqueous solution and the reaction mixture was extracted with $CHCl_3$. The extract, after drying over Na_2SO_4, was evaporated and the residue was dissolved in 50 ml of 10% HCl. The acid solution was heated on a water bath for 30 min and then neutralized with 20% NaOH. The resultant solution was extracted with $CHCl_3$. The extract was dried over Na_2SO_4 and evaporated, and the residue was chromatographed on alumina, eluted with benzene and then AcOEt. The benzene eluate was evaporated to dryness and the residue was recrystallized from Et_2O to yellow crystals of mp 126—127°. Yield, 1.88 g. The mp of this product agreed with that reported for XXIV. *Anal.* Calcd. for $C_{11}H_{11}ONS$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.22; H, 5.39; N, 6.91.

The AcOEt eluate was evaporated to dryness. Recrystallization of the residue from ether gave 0.5 g of yellow crystals, melting at 132—133°, the value of which agreed with that reported[12] for XXV. *Anal.* Calcd. for $C_{11}H_{11}ONS$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.24; H, 5.37; N, 7.30.

Reactions of I with Thiols——An example is cited for the reaction with EtSH as follows. To an aqueous solution of I, prepared from 1.7 g of II, 0.65 g of EtSH was added and the mixture was stirred at room temperatures for 2 hr. The reaction mixture was extracted with $CHCl_3$, the extract was dried over Na_2SO_4, and evaporated to dryness. To the residue, a small amount of benzene was added and the mixture was allowed to stand overnight. The crystals that separated were collected and recrystallization from AcOEt gave 0.31 g of N–carbamoyl–2–ethylthiotroponeimine (XXX) as yellow crystals, mp 131—133°. *Anal.* Calcd. for $C_{10}H_{12}ON_2S$: C, 57.68; H, 5.81; N, 13.46; S, 15.37. Found: C, 57.55; H, 5.60; N, 13.41; S, 15.36. UV $\lambda_{\max}^{\text{EtOH}}$ mμ (log ε): 245 (4.20), 350 (3.87). IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 3390, 3205, 1634, 1603.

The filtrate was evaporated and the residue was chromatographed on alumina with benzene. Removal of benzene and sublimation of the residue gave 0.11 g of 2–ethylthiocycloheptimidazole (XXVII) as pale yellow crystals, mp 97—98°, which were identified with an authentic sample by mixed mp determination and comparison of their UV and IR spectra. The reactions of I with MeSH and 2–dimethylaminoethanethiol were carried out in the same manner as described above. The reaction with MeSH gave the following two products.

N–Carbamoyl–2–methylthiotroponeimine (XXIX): Pale yellow crystals, mp 136—136.5° (decomp.). *Anal.* Calcd. for $C_9H_{10}ON_2S$: C, 55.66; H, 5.19; N, 14.43; S, 16.48. Found: C, 55.48; H, 5.26; N, 14.33; S, 16.10.

2–Methylthiocycloheptimidazole (XXVI): Pale yellow prisms, mp 101—102°, undepressed on admixture with an authentic sample.

The reaction with 2–dimethylaminoethanethiol gave the following two products.

N–Carbamoyl–2–(2–dimethylaminoethylthio)troponeimine (XXXI): Yellow crystals, mp 123—124°. *Anal.* Calcd. for $C_{12}H_{17}ON_3S$: C, 57.35; H, 6.82; N, 16.72; S, 12.73. Found: C, 56.98; H, 6.72; N, 16.67; S, 12.86.

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12) I. Murata and K. Tezuka, *Bull. Chem. Res. Inst. Non–Aqueous Soln., Tohoku Univ.*, **10**, 257 (1961).

2-(2-Dimethylaminoethylthio)cycloheptimidazole (XXVIII): Pale yellow oil. Dipicrate, mp 200—202°. *Anal.* Calcd. for $C_{24}H_{21}O_{14}N_9S$: C, 41.68; H, 3.06; N, 18.23; S, 4.63. Found: C, 41.66; H, 2.92; N, 18.17; S, 4.86.

Reaction of I with Malononitrile, Cyanoacetamide, and Benzoylacetonitrile——An example is cited for the reaction with malononitrile as follows. To an aqueous solution (30 ml) of I, prepared from 1 g of II, were added 0.59 g of malononitrile and 2.5 ml of 10% NaOH. The mixture was stirred at room temperatures for 1 hr and filtered. Recrystallization of the separated crystals from EtOH gave 1.1 g of yellow needles, mp 238°, which were identified with an authentic sample of 2-imino-1,2-dihydrocyclohepta[*b*]pyrrole-3-carbonitrile (XXXII) by mixed mp determination and comparison of their UV and IR spectra.

The filtrate was neutralized with dil. HNO_3 and aqueous $AgNO_3$ was added. The separated crystals were collected and washed with water to give white crystals which were identified with an authentic sample of AgNCO.

The reactions of I with cyanoacetamide and benzoylacetonitrile were carried out in the same manner as described above to give 2-imino-1,2-dihydrocyclohepta[*b*]pyrrole-3-carboxamide (XXXIII), mp 275° (decomp.), undepressed on admixture with an authentic sample, and 3-benzoyl-2-imino-1,2-dihydrocyclohepta[*b*]pyrrole (XXXIV) as yellow needles, mp 216° (decomp.), respectively. *Anal.* Calcd. for $C_{16}H_{12}ON_2$: C, 77.40; H, 4.87; N, 11.28. Found: C, 77.03; H, 4.91; N, 11.63. UV $\lambda_{\max}^{\text{EtOH}}$ mμ (log ε): 277 (4.50), 308 (4.37), 365 (shoulder), 444 (3.98). IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 3356, 3125, 1629 (broad), 1618.

AgNCO was also obtained from both reaction similarly as in the reaction with molononitrile.

Hydrolysis of XXXIV——A solution of 1 g of XXXIV in 5 ml of 50% H_2SO_4 was heated at 150—160° for 3 hr. The reaction mixture was poured into ice water and the aqueous solution was extracted with ether. Evaporation of the extract gave 0.5 g of benzoic acid, mp 120—121°, undepressed on admixture with an authentic sample. The aqueous layer left after extraction was neutralized with dil. NaOH and the separated crystals were collected by filtration. Recrystallization from EtOH gave 0.25 g of yellow needles, mp 163—164°, which were identified with an authentic sample of cyclohepta[*b*]pyrrol-2(1*H*)-one (XXXVII) by mixed mp determination and comparison of their UV and IR spectra.

Reaction of I with Ethyl Cyanoacetate——By the same procedure as for the reaction of I with malononitrile, a mixture of I, prepared from 1 g of II, 1 g of ethyl cyanoacetate, and 0.25 g of NaOH was allowed to react. $CHCl_3$ was added to the reaction mixture and the mixture was filtered. Recrystallization of the crystals from EtOH gave 0.2 g of yellow needles, mp 318° (decomp.), which were identified with an authentic sample of 3-cyanocyclohepta[*b*]pyrrol-2(1*H*)-one (XXXVI) by comparison of their UV and IR spectra.

The $CHCl_3$ layer of the filtrate was dried over Na_2SO_4, evaporated, and the residue (0.95 g) was chromatographed on alumina. The eluate with benzene—$CHCl_3$ (2:1) was evaporated to dryness and the residue was recrystallized from EtOH to 0.646 g of yellow needles of mp 150—151°, which were identified with an authentic sample of ethyl 2-imino-1,2-dihydrocyclohepta[*b*]pyrrole-3-carboxylate (XXXV) by mixed mp determination and comparison of their UV and IR spectra. AgNCO was obtained from the aqueous layer of the filtrate of XXXVI similarly as in the reaction of I with malononitrile.

Reaction of I with Ethyl Acetoacetate——To an aqueous solution (80 ml) of I, prepared from 3.4 g of II, were added 0.8 g of NaOH and a solution of 2.9 g of ethyl acetoacetate in 5 ml of EtOH. The mixture was stirred at room temperatures for 5 hr and filtered to give 1.4 g of a crystalline product. The filtrate was neutralized with dil. HNO_3 and extracted with $CHCl_3$. The extract was dried over Na_2SO_4, evaporated and the residue (2.6 g) was chromatographed on acidic alumina. Elution with $CHCl_3$—EtOH (1:1) gave additional 0.4 g of a crystalline product. The combined crystals were recrystallized from EtOH and gave 3-acetylcyclohepta[*b*]pyrrol-2(1*H*)-one (XXXVIII) as yellow needles, which changed to black from around 265° and decomposed at 270°. *Anal.* Calcd. for $C_{11}H_9O_2N$: C, 70.58; H, 4.85; N, 7.48. Found: C, 70.40; H, 4.71; N, 7.53. UV $\lambda_{\max}^{\text{EtOH}}$ mμ (log ε); 226 (4.22), 252 (4.26), 286.5 (4.39), 436 (4.29). IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 3100—2500 (broad), 1675, 1634. AgNCO was obtained from the aqueous layer left after extraction similarly as in the reaction of I with malononitrile.

Reaction of XXXVII with Acetyl Chloride——To a solution of 3 g of XXXVII in 70 ml of CS_2, 2.76 g of powdered $AlCl_3$ and 1.62 g of acetyl chloride were added and the mixture was stirred under reflux for 4 hr. After removal of CS_2 by decantation, the residue was poured on ice. The separated crystals (1.1 g) were recrystallized from EtOH to 0.51 g of XXXVIII as yellow needles, which were identical with the product obtained by the reaction of I with ethyl acetoacetate by mixed mp determination and comparison of their IR spectra. *Anal.* Calcd. for $C_{11}H_9O_2N$: C, 70.58; H, 4.85; N, 7.48. Found: C, 70.70; H, 4.67; N, 7.55.

Reaction of I with Ethyl Benzoylacetate——To an aqueous solution of I, prepared from 4 g of II, were added 1.0 g of NaOH and a solution of 6.8 g of ethyl benzoylacetate in 10 ml of EtOH. The mixture was stirred at room temperatures and filtered to 5.8 g of a crystalline product, mp 120—121° (decomp.). *Anal.* Calcd. for $C_{19}H_{18}O_4N_2$: C, 67.44; H, 5.36; N, 8.28. Found: C, 67.43; H, 5.54; N, 8.23. UV $\lambda_{\max}^{\text{dioxane}}$: 334 m$\mu$ (log ε: 3.19). IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 3401, 3125, 1721, 1689.

To a solution of 3.4 g of the above crystals in 80 ml of EtOH, 60 ml of aqueous solution of 0.44 g of NaOH was added and the mixture was refluxed for 4 hr. After removal of EtOH, the reaction mixture was extracted with $CHCl_3$. The extract was dried over Na_2SO_4, evaporated, and the residue was chromatographed on acidic alumina. The fraction eluted with $CHCl_3$—EtOH (1:1) was evaporated and the residue was recrystallized from

EtOH to 0.27 g of 3-benzoylcyclohepta[*b*]pyrrol-2(1*H*)-one (XXXIX) as yellow fibrous crystals, mp 208°. *Anal.* Calcd. for $C_{16}H_{11}O_2N$: C, 77.07; H, 4.45; N, 5.62. Found: C, 77.13; H, 4.84; N, 5.60. UV λ_{max}^{EtOH} mμ (log ε): 265.5 (4.57), 441 (4.31). IR ν_{max}^{Nujol} cm^{-1}: 3100—2600 (broad), 1672, 1631.

Reaction of XXXVII with Benzoyl Chloride——To a solution of 3.0 g of XXXVII in 100 ml of CS_2, were added 2.76 g of $AlCl_3$ and 2.9 g of benzoyl chloride. The mixture was stirred under reflux for 6 hr, poured into ice-water, and neutralized with dil. NaOH. The separated crystalline product (0.8 g) were collected by filtration. The aqueous layer of the filtrate was separated from the CS_2 layer and extracted with $CHCl_3$. The $CHCl_3$ extract and the CS_2 layer were combined, evaporated, and the residue was chromatographed on acidic alumina. Elution with $CHCl_3$—EtOH (1:1) gave 1.6 g of crystalline product and recrystallization of the combined crude product from EtOH gave 1.5 g of orange-yellow crystals, mp 208°, which were identical with the product obtained from I and ethyl benzoylacetate by mixed mp determination and comparison of their UV and IR spectra.

Reaction of I with Acetylacetone——By the same procedure as for the reaction of I with ethyl benzoylacetate, a mixture of I, prepared from 16.8 g of II, 11 g of acetylacetone, and 4 g of NaOH was allowed to react and 4.22 g of pale yellow crystals, mp 91—92° (decomp.), were obtained. *Anal.* Calcd. for $C_{13}H_{14}O_3N_2$: C, 63.40; H, 5.73; N, 11.38. Found: C, 63.40; H, 5.86; N, 11.49. UV $\lambda_{max}^{dioxane}$: 338 mμ (log ε 3.88). IR ν_{max}^{Nujol} cm^{-1}: 3378, 3145, 1724, 1678.

To a solution of 2 g of the above crystals in 40 ml of EtOH, 20 ml of 2% NaOH was added and the mixture was stirred at 50—60° for 5 hr. The reaction mixture was treated as described for the formation of XXXIX, except that the chromatography was carried out on neutral alumina with benzene. The eluate with benzene was evaporated to dryness and recrystallization of the residue from ether gave 0.2 g of 3-acetyl-2-methylcyclohepta[*b*]pyrrole (XL) as greenish yellow crystals, mp 101—102° (decomp.). *Anal.* Calcd. for $C_{12}H_{11}ON$: C, 77.81; H, 5.99; N, 7.56. Found: C, 77.44; H, 6.00; N, 7.61. UV λ_{max}^{EtOH} mμ (log ε): 290.5 (4.76), 321 (4.03), 352 (3.88), 447 (2.94), 580 (1.88). IR ν_{max}^{Nujol}: 1621 cm^{-1}.

Reaction of I with Diethyl Malonate——By the same procedure as for the reaction of I with ethyl benzoylacetate, a mixture of I, prepared from 2.1 g of II, 2.2 g of diethyl malonate, and 0.5 g of NaOH was allowed to react and 2.06 g of oily product separated (UV $\lambda_{max}^{dioxane}$: 335 mμ. IR ν_{max}^{liq} cm^{-1}: 3378, 3145, 2994, 1701, 1656).

In the same manner as described for the formation of XXXIX, treatment of this oil with aqueous NaOH gave 0.3 g of orange crystals of mp 188—190°, which were identified with an authentic sample of ethyl 1,2-dihydro-2-oxocyclohepta[*b*]pyrrole-3-carboxylate (XLI) by mixed mp determination and comparison of their UV and IR spectra.

Reaction of XLII with Malononitrile——By the same procedure as for the reaction of I with malononitrile, a mixture of XLII, prepared from 2.05 g of Na salt of 5-chloro-2-cyanaminotropone, 0.73 g of malononitrile, and 0.4 g of NaOH was allowed to react and filtered to 1.38 g of crude crystals. Recrystallization of the crystals from EtOH gave 0.7 g of 6-chloro-2-imino-1,2-dihydrocyclohepta[*b*]pyrrole-3-carbonitrile (XLIII) as orange scales, mp 260° (decomp.). *Anal.* Calcd. for $C_{10}H_6N_3Cl$: C, 58.98; H, 2.97; N, 20.64. Found: C, 59.09; H, 3.11; N, 21.33. UV λ_{max}^{EtOH} mμ (log ε): 222 (4.17), 239 (4.11), 288 (4.63), 297 (4.63), 320 (shoulder), 380 (3.98), 447.5 (3.80).

Hydrolysis of XLIII——A solution of 400 mg of XLIII in 5 ml of 50% H_2SO_4 was heated at 150—160° for 2.5 hr. The reaction mixture was poured into ice-water and the aqueous solution was neutralized with 10% NaOH. The separated crystals were collected by filtration and the filtrate was extracted with $CHCl_3$. Evaporation of the extract gave a additional crystalline product and the combined crystals were recrystallized from EtOH to 170 mg of orange needles, mp 230° (decomp.), which were identified with an authentic sample of 6-chlorocyclohepta[*b*]pyrrol-2(1*H*)-one (XLV) by mixed mp determination and comparison of their UV and IR spectra.

Reaction of XLII with Diethyl Malonate——A solution of 2.82 g of diethyl malonate in 10 ml of EtOH was added to an aqueous solution of XLII, prepared from 3.4 g of Na salt of 5-chloro-2-cyanaminotropone in 650 ml of water and 100 ml of EtOH, and the mixture was stirred at room temperature for 1 hr. Then, separated crystals were dissolved by addition of 300 ml of EtOH and the reaction mixture was refluxed for 8 hr. After removal of EtOH, the reaction mixture was extracted with $CHCl_3$. The extract was dried over Na_2SO_4, evaporated, and benzene was added to the residue. The separated crystals were collected by filtration and recrystallization from EtOH to 0.2 g of orange crystals, mp 222—224°, which were identified with an authentic sample of ethyl 6-chloro-1,2-dihydro-2-oxocyclohepta[*b*]pyrrole-3-carboxylate (XLIV) by mixed mp determination and comparison of their UV and IR spectra.

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