〔Chem. Pharm. Bull.
15(5) 634～643 (1967)〕

UDC 547.517.07

78. **Yasunobu Sato and Genshun Sunagawa**: Studies on Seven-membered Ring Compounds. XXIV.*[1] Syntheses of 8-Methylimino cyclohepta[*b*]pyrrole and Cyclohepta[*b*]pyrrole-8(1*H*)-thione Derivatives and Tropone Analogues of Tryptamine*[2]

(*Central Research Laboratories, Sankyo Co., Ltd.*[*3])

8-Methylimino-1,8-dihydrocyclohepta[*b*]pyrrole derivatives (XIa～d) were synthesized by cyclization of azines obtained from 2-methylaminotropone hydrazone and various carbonyl compounds. Direct methylation of cyclohepta[*b*]pyrrol-8(1*H*)-one derivatives with dimethyl sulfate resulted in O-methylation affording 8-methoxycyclohepta[*b*]pyrroles (XVa～c) which on condensation with methylamine also gave XIa～c. Cyclohepta[*b*]pyrrole-8(1*H*)-thione derivatives were synthesized by reaction of XVa～c and sodium sulfide. In addition, tropone analogues of tryptamine, 3-(2-aminoethyl)cyclohepta[*b*]pyrrole derivatives were prepared.

(Received March 29, 1966)

The previous paper in this series described the syntheses of cyclohepta[*b*]pyrrolone derivatives.[1] The present paper describes the syntheses of 8-methylimino cyclohepta-[*b*]pyrrole and cyclohepta[*b*]pyrrole-8(1*H*)-thione derivatives from 2-aminotroponeimine derivatives, and seven-membered ring compounds having a similar structure to tryptamine, 3-(2-aminoethyl)cyclohepta[*b*]pyrrole derivatives.

2-Aminotroponeimine derivatives are stable, colored compounds that exhibit a non-benzenoid aromatic character similar to that of tropolone. They were synthesized by amination of the tetrafluorocycloheptadienes accessible from cyclopentadiene and tetrafluoroethylene, and were not conveniently obtained from tropolone or its derivatives.[2]

Recently, a new convenient method of synthesis of 2-aminotroponeimine derivatives was reported from this laboratory, based on the amination of the 2-methoxytroponeimine obtained by direct methylation of 2-aminotropone with dimethyl sulfate.[3]

One of the methods of synthesis of 8-methyliminocyclohepta[*b*]pyrrole derivatives was cyclization of azines (Xa～d, XVIIa～c) accessible from 2-methylaminotropone hydrazone (IV) and various carbonyl compounds, and another was condensation of methylamine with 8-methoxycyclohepta[*b*]pyrroles (XVa～c) obtained from cyclohepta[*b*]pyrrol-8-(1*H*)-one derivatives (XIVa～c). Cyclohepta[*b*]pyrrole-8(1*H*)-thione derivatives (XVIa～c) were synthesized by the condensation of (XVa～c) with sodium sulfide.

First, 2-methylaminotropone hydrazone which was used as a starting material was prepared from 2-methylamino-N-methyltroponeimine (I) as described below.

It was reported that N,N′-disubstituted 2-aminotroponeimine derivatives were stable to hydrolysis with strong acids or bases. However, I reacted with a bifunctional amine such as hydrazine hydrate to give 2-aminotropone azine (V). Furthermore,

---

*[1] Part XXIII: N. Soma, J. Nakazawa, T. Watanabe, Y. Sato, G. Sunagawa: This Bulletin, **15**, 627 (1967).
*[2] Presented at the 5th Annual Meeting of Pharmaceutical Society of Japan, October 1965, Tokushima.
*[3] 1-2-58 Hiromachi, Shinagawa-ku, Tokyo (佐藤裕信, 砂川玄俊).

[1] G. Sunagawa, N. Soma, H. Nakao, Y. Matsumoto: Yakugaku Zasshi, **81**, 1799 (1961); G. Sunagawa, Y. Sato: *Ibid.*, **82**, 408, 414 (1962); Y. Sato: Ann. Sankyo Res. Lab., **15**, 47 (1963); *Idem*: This Bulletin, **11**, 1431, 1440 (1963).
[2] W.R. Brasen, H.E. Holmquist, R.E. Benson; J. Am. Chem. Soc., **82**, 995 (1960); *Idem*: *Ibid.*, **83**, 3215 (1961).
[3] N. Soma, J. Nakazawa, T. Watanabe, Y. Sato, G. Sunagawa: This Bulletin, **13**, 819 (1965).

bromine of 2-methylamino-5-bromo-N-methyltroponeimine (Ⅱ) was moderately labile.[2] Condensation of Ⅱ with hydrazine hydrate in refluxing ethanol for fifteen minutes gave crystals, m.p. 102~103°, which gave a Beilstein reaction contrary to our expectations.

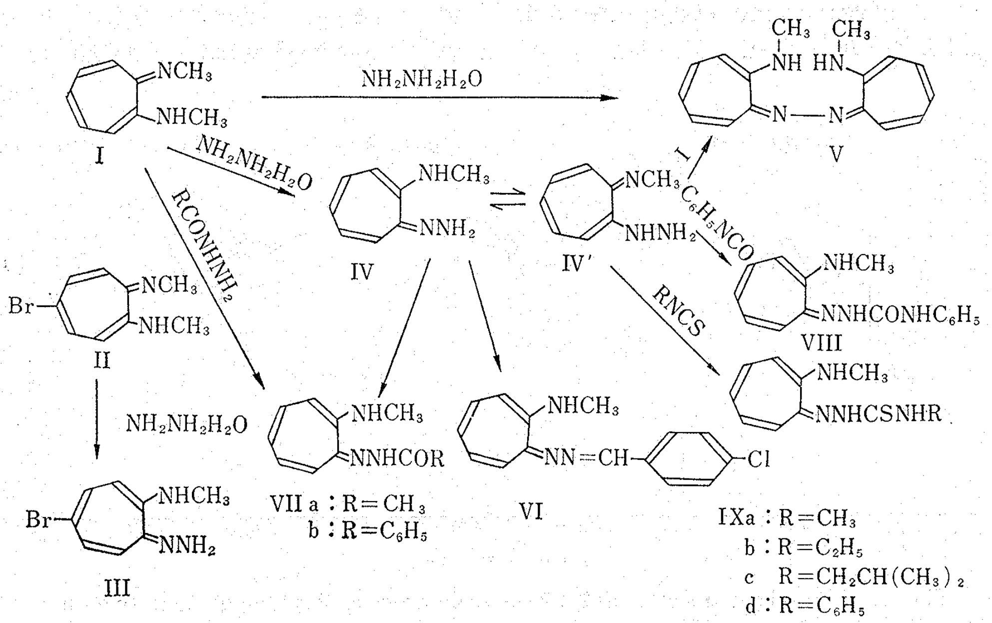


Chart 1.

Its analytical values agreed with the formula, $C_8H_{10}N_3Br$. Consequently, this was considered to be 2-methylamino-5-bromotropone hydrazone (Ⅲ) or its tautomeric form, 2-hydrazino-5-bromo-N-methyltroponeimine. A similar reaction of I with hydrazine hydrate proceeded readily to yield Ⅳ or its tautomeric form Ⅳ'. The structure was established by the following reactions: condensation of Ⅳ with *p*-chlorobenzaldehyde afforded 2-methylaminotropone *p*-chlorobenzaldehyde azine (Ⅵ). Benzoylation of Ⅳ gave a monobenzoyl compound which was considered to be 2-methylaminotropone benzoylhydrazone (Ⅶb), since Ⅶb was identical with the product obtained from I and benzoylhydrazine. Similarly, 2-methylaminotropone acetylhydrazone (Ⅶa) was obtained from I and acetylhydrazine. Semicarbazone (Ⅷ) and thiosemicarbazone (Ⅸa~d) were also prepared by an addition reaction of I with isocyanate or isothiocyanate. Furthermore, Ⅳ was converted to Ⅴ[2] by a condensation reaction with I.

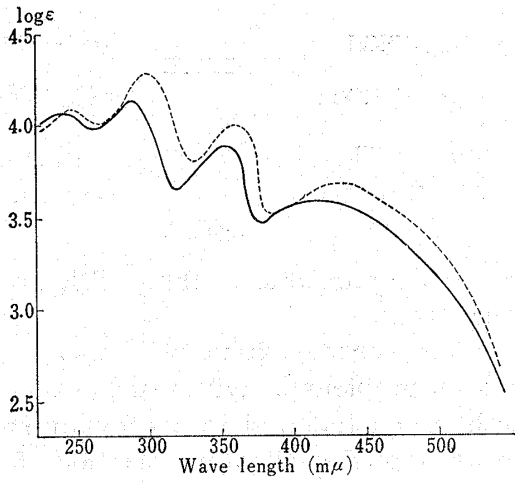


Fig. 1. Ultraviolet Spectra of 5-Bromo-(Ⅲ) and 2-methylaminotropone Hydrazone (Ⅳ) (in EtOH)

------- (Ⅲ) ——— (Ⅳ)

In contrast with I, which shows a single methyl resonance at 3.10 p.p.m., Ⅳ showed a doublet methyl resonance at 2.89 and 2.98 p.p.m., and a single one at 3.13 p.p.m. in deuterochloroform solution. This doublet methyl resonance corresponded to that observed for 2-methylaminotroponethione.[4] Therefore, the ratio of existence of

---

[4] W.R. Brasen, R.E. Benson: J. Am. Chem. Soc., 83, 3135 (1961).

Ⅳ and Ⅳ′ was approximately 9:1, based on the ratio of area of their methyl resonance. Compound (Ⅲ) showed only a doublet methyl resonance at 2.86 and 2.94 p.p.m., suggesting that Ⅲ existed in the hydrazone form. It was reported that the ultraviolet spectra of semicarbazone,[5] oxime[5] and acylhydrazone[6] of tropone changed with the acidity of the solvent, because the conjugate acid and base are formed, respectively in an acidic or alkaline solution. Similar behavior was observed with both Ⅶa and Ⅶb, as shown in Fig. 2. Namely, it was considered that tautomerization between Ⅶa,b and Ⅶa′,b′ existed in solution. This was supported by the NMR spectrum of Ⅶ which showed a doublet signal at 3.04 and 3.00 p.p.m. due to the N-CH_3 group and a singlet signal at 2.30, 2.16, and 9.24 p.p.m. due to the C-CH_3 group in keto and enol form, and hydroxy group, respectively.

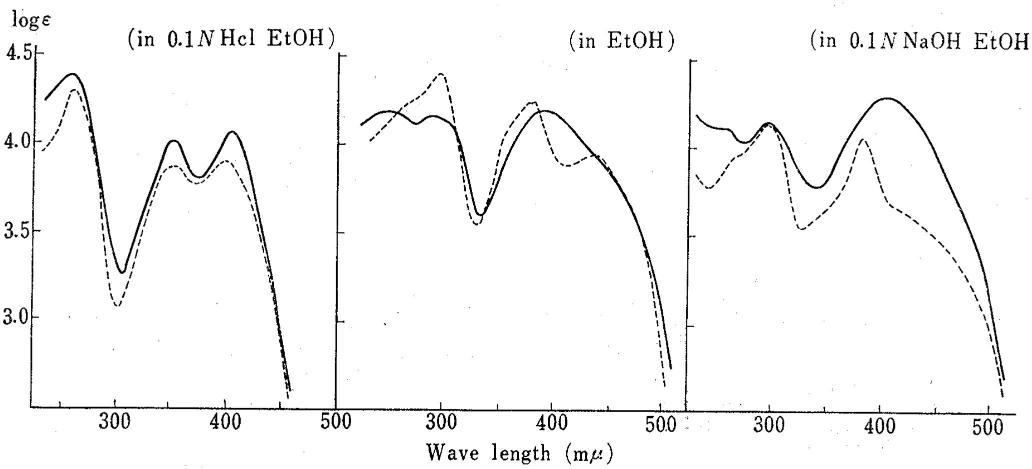
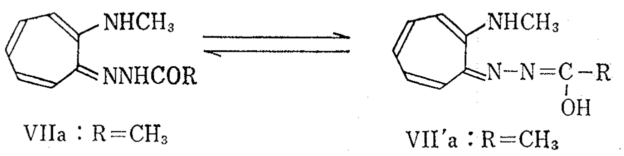


Fig. 2. Ultraviolet Spectra of 2-Methylaminotropone Acetylhydrazone (Ⅶa) and Benzoylhydrazone (Ⅶb)

------- (Ⅶa) ——— (Ⅶb)



VIIa : R=CH_3
VIIb : R=C_6H_5

VII′a : R=CH_3
VII′b : R=C_6H_5

Chart 2.

Then, condensation of Ⅳ with propionaldehyde readily afforded 2-methylaminotropone propionaldehyde azine (Xa), which was identical with the product obtained by methylation followed by methylamination of propionaldehyde 2-troponylhydrazone (Ⅻa). An attempted cyclization reaction of Xa by heating with diluted sulfuric acid ended in failure. However, this reaction was accomplished in the following manner.

Heating Xa with polyphosphoric acid gave a yellowish orange product, m.p. 146~147°, which showed a similar ultraviolet absorption curve to that of 3-methylcyclohepta[*b*]-pyrrol-8(1*H*)-one (XIVa) with a bathochromic shift. Its analytical values agreed with the formula, $C_{11}H_{12}N_2$. Therefore, it was assumed to be 3-methyl-8-methylimino-1,8-dihydrocyclohepta[*b*]pyrrole (Ⅺa), whose structure was proved by its identity with a product synthesized by another route. Direct methylation of XIVa with dimethyl sulfate resulted in O-methylation affording 3-methyl-8-methoxycyclohepta[*b*]pyrrole-(XVa) as the monomethylsulfate. A condensation reaction of XVa with methylamine yielded Ⅺa and a very small amount of yellow crystals. The analytical values of the picrate of the latter, agreed with the formula, $C_{17}H_{14}O_8N_4$, but further investigation

---

5) T. Mukai: Bull. Chem. Soc. Japan, **33**, 238 (1960).
6) G. Sunagawa, N. Soma, H. Nakao, Y. Matsumoto: Yakugaku Zasshi, **81**, 1792 (1961).

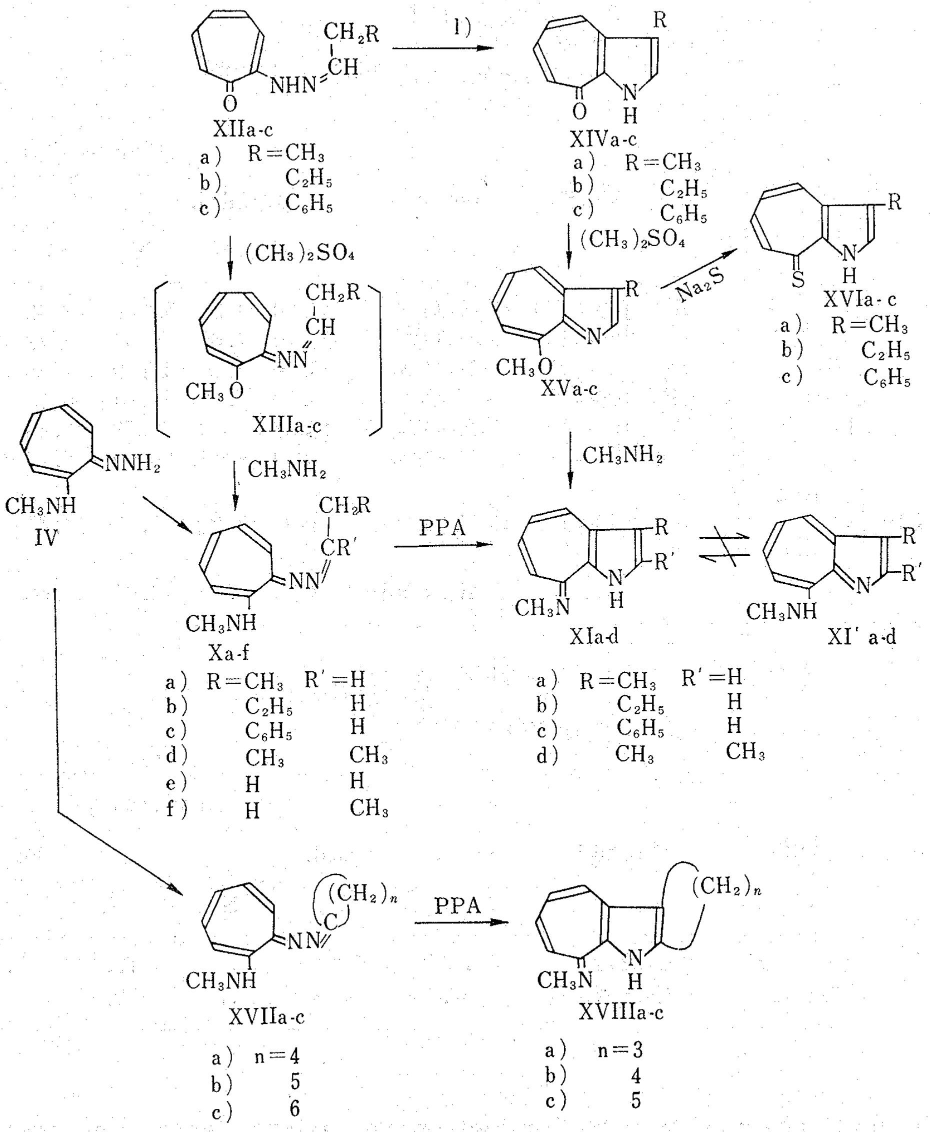


Chart 3.

was not carried out. As shown in Table III, XIa showed a single N-methyl resonance at 3.18 p.p.m., and infrared absorption due to ν_{NH} at 3356 cm^{-1}, indicating that tautomerization to 3-methyl-8-methylaminocyclohepta[*b*]pyrrole (XI'-a) was not favorable. Moreover, its ultraviolet spectrum was different from that of cyclohepta[*b*]pyrrole (λ_{max}^{MeOH} mμ (log ε): 224 (4.15), 263 (4.60), 316 (3.40), 460 (3.05) as shown in Fig. 3. Similarly, cyclization of azines which were prepared by the condensation of IV with *n*-butyraldehyde, phenylacetaldehyde, ethyl methylketone, cyclopentanone, cyclohexanone, and cycloheptanone gave 3- or 2,3-disubstituted and tricyclic system cyclohepta[*b*]pyrrole derivatives (XIb~d and XVIIIa~c). However, efforts to obtain cyclization of

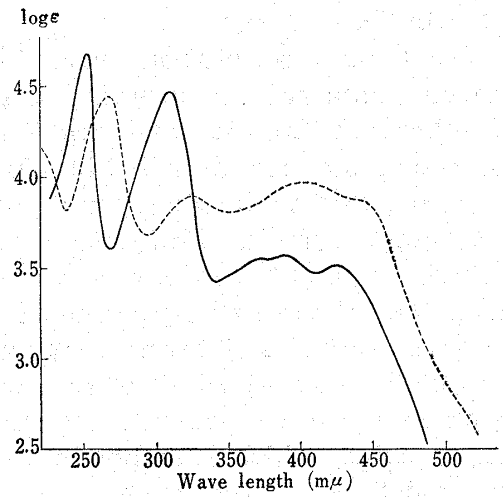
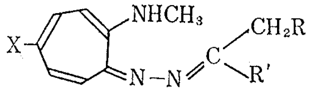


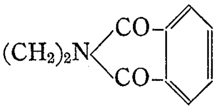
Fig. 3. Ultraviolet Spectra of 8-Methylimino-(XIa) and 8-Thioxo-3-methyl-1,8-dihydrocyclohepta[*b*]pyrrole (XVIa) (in EtOH)

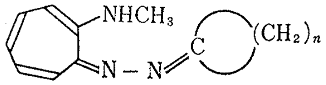
——— (XIa) - - - - - (XVIa)

TABLE I.



picrate

Compound	X	R	R'	m.p. (°C)	Formula	Analysis (%) Calcd. C	H	N	Found C	H	N
Xa	H	CH_3	H	169～170	$C_{17}H_{18}O_7N_6$	48.80	4.34	20.09	48.42	4.40	19.78
Xb	〃	C_2H_5	〃	166～167	$C_{18}H_{20}O_7N_6$	50.00	4.66	19.44	49.79	4.85	19.70
Xc	〃	C_6H_5	〃	155～156	$C_{22}H_{20}O_7N_6$	55.00	4.20	17.49	54.53	4.15	17.41
Xd	〃	CH_3	CH_3	103～104	$C_{18}H_{20}O_7N_6$	50.00	4.66	19.44	50.21	4.86	19.64
Xe	〃	H	H	163～164	$C_{16}H_{16}O_7N_6$	47.52	3.99	20.79	47.64	3.94	20.54
Xf	〃	〃	CH_3	120～121	$C_{17}H_{18}O_7N_6$	48.80	4.34	20.09	48.74	4.40	19.92
XIXb	〃	 $(CH_2)_2N$ CO CO	〃	176～177	$C_{27}H_{25}O_9N_7$	54.81	4.26	16.57	54.41	4.31	16.20
XIXc	Br	〃	〃	173～174	$C_{27}H_{24}O_9N_7Br$	48.36	3.60	14.62	47.68	3.59	14.69



Compound	n	m.p. (°C)	Formula	Analysis (%) Calcd. C	H	N	Found C	H	N
XVIIa	4	94～ 95	$C_{13}H_{17}N_3$	72.52	7.96	19.52	72.32	7.91	19.10
XVIIb$^{a)}$	5	132～133	$C_{20}H_{22}O_7N_6$	52.40	4.84	18.33	52.45	4.90	18.37

a) picrate

acetaldehyde and acetone 2-methylaminotropone azines were unsuccessful. The synthesized azines and 8-methylimino-1,8-dihydrocyclohepta[*b*]pyrrole derivatives are listed in Table I and II.

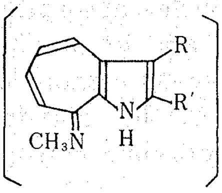
Next, the condensation reaction of XVa with sodium sulfide was attempted. The following data gave confirmation that the product was 3-methylcyclohepta[*b*]pyrrole-8-(1*H*)-thione (XVIa). Its analytical values agreed with the formula, $C_{10}H_9NS$. It showed absorption maxima at 267, 320, 405, and 440 (shoulder) mμ in the ultraviolet spectrum indicating that the product could possibly have another structure, 3-methyl-8-mercapto-cyclohepta[*b*]pyrrole. However, in general, the ultraviolet absorption of troponthione derivatives shift to a longer wave length than that of tropone derivatives.[7] Furthermore, the infrared absorption bands due to ν_{NH} and $\nu_{C=S}$ were found at 3205 and 1051 cm^{-1}, respectively. Therefore, it existed in the thione form (XVIa).

Finally, attempted synthesis of seven-membered ring compounds analogous to tryptamine was carried out. Heating 2-methylaminotropone 4-phthalimido-*n*-butyraldehyde azine, which was obtained by the condensation of IV and 4-phthalimido-*n*-butyraldehyde yielded crystals, m.p. 250°. This product was assumed to be 3-(2-phthalimidoethyl)-8-methylimino-1,8-dihydrocyclohepta[*b*]pyrrole (XXa) which was subjected to hydrolysis without purification. The ultraviolet spectrum of the hydrolysis product

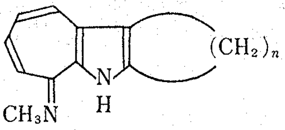
---

[7] T. Nozoe, K. Matsui: Bull. Chem. Soc. Japan, **34**, 616 (1961).

TABLE II.



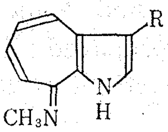
Compound	R	R′	m.p. (°C)	Formula	Analysis (%) Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
XIa	CH_3	H	146∼147	$C_{11}H_{12}N_2$	76.71	7.02	16.27	76.88	6.98	16.43
XIb	C_2H_5	〃	101∼102	$C_{12}H_{14}N_2$	77.38	7.58	15.04	77.12	7.20	15.24
XIc	C_6H_5	〃	154∼155	$C_{16}H_{14}N_2$	82.02	6.02	11.96	81.83	6.02	11.96
XId	CH_3	CH_3	145∼146	$C_{12}H_{14}N_2$	77.38	7.58	15.04	77.29	7.69	15.08



Compound	*n*	m.p. (°C)	Formula	Analysis (%) Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
XVIIIa	3	124∼125	$C_{13}H_{14}N_2$	78.75	7.12	14.13	78.54	7.11	14.29
XVIIIb(a)	4	232∼233	$C_{20}H_{19}O_7N_5$	54.42	4.34	15.87	54.09	4.37	15.83
XVIIIc	5	131∼132	$C_{15}H_{18}N_2$	79.60	8.02	12.38	79.34	7.92	12.16

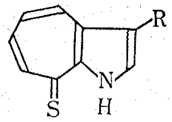
a) picrate

TABLE III.



R	IR ν_{N-H} (cm^{-1})	NMR N-CH_3 (in $CDCl_3$) (p.p.m.)
CH_3	3356	3.18
C_2H_5	3356	3.12
C_6H_5	3333	3.08

TABLE IV.



Compound	R	m.p. (°C)	Formula	Analysis (%) Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
XVIa	CH_3	167∼168	$C_{10}H_9NS$	68.53	5.17	7.99	68.54	5.52	8.03
XVIb	C_2H_5	114∼115	$C_{11}H_{11}NS$	69.80	5.85	7.40	69.91	5.50	7.45
XVIc	C_6H_5	159∼160	$C_{15}H_{11}NS$	75.19	4.67	5.90	75.62	4.80	5.98

showed the characteristic ultraviolet absorption spectra of 8-methylimino-1,8-dihydrocyclohepta[*b*]pyrrole derivatives, and its analytical values agreed with a composition of $C_{12}H_{17}N_3Cl_2$. Consequently, it was established to be 3-(2-aminoethyl)-8-methylimino-1,8-dihydrocyclohepta[*b*]pyrrole (XXIIIa) dihydrochloride. Similarly, the cyclization, followed by hydrolysis of 2-methylaminotropone and 2-methylamino-5-bromotropone

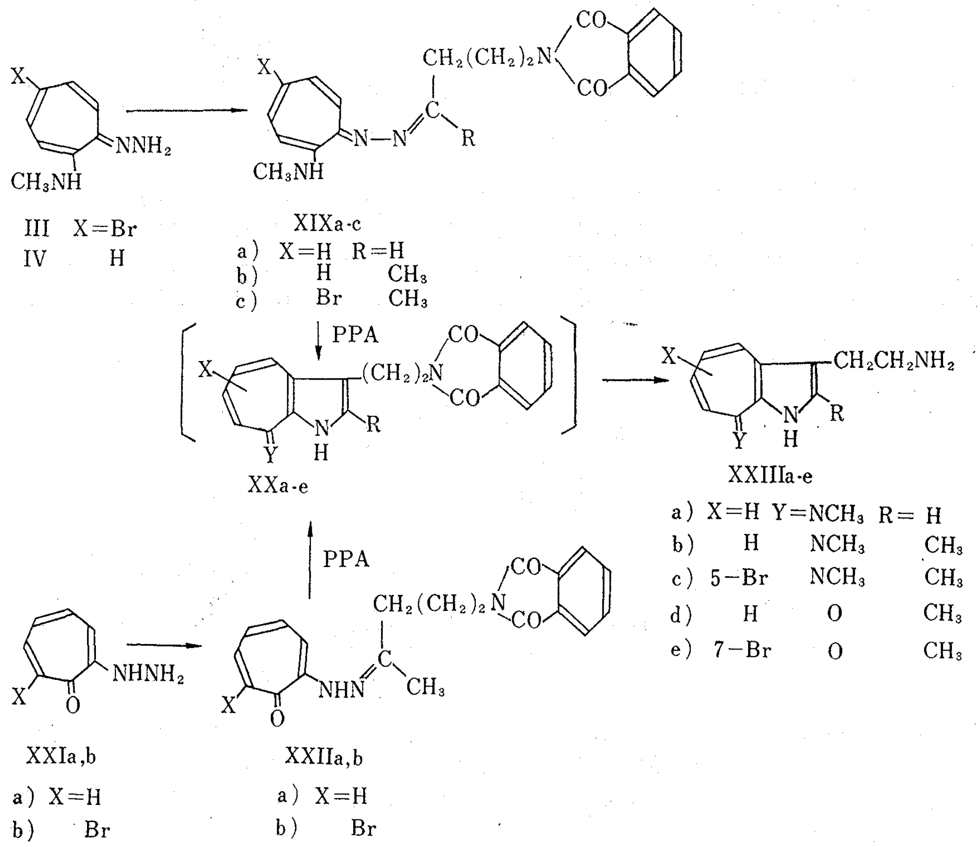
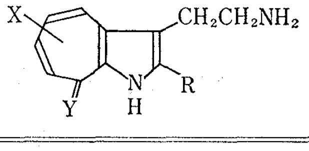


Chart 4.

5-phthalimido-2-pentanone azine (XIXb,c) gave 2-methyl-3-(2-aminoethyl)-8-methylimino- and 2-methyl-3-(2-aminoethyl)-5-bromo-8-methylimino-1,8-dihydrocyclohepta[*b*]pyrrole (XXIIIb,c), respectively. Furthermore, 2-methyl-3-(2-aminoethyl)- and 2-methyl-3-(2-aminoethyl)-7-bromocyclohepta[*b*]pyrrol-8(1*H*)-one (XXIIId,e) were prepared from the corresponding hydrazones (XXIIa,b). The synthesized 3-(2-aminoethyl) cyclohepta[*b*]-pyrrole derivatives are listed in Table V.

TABLE V.



Compound	X	Y	R	Salt	m.p. (°C)	Formula	Analysis (%) Calcd. C	Calcd. H	Calcd. N	Calcd. Cl	Found C	Found H	Found N	Found Cl
XXIIIa	H	NCH_3	H	2HCl	305	$C_{12}H_{17}N_3Cl_2$	52.56	6.24	15.33		52.54	6.16	15.04	
XXIIIb	〃	〃	CH_3	〃	280	$C_{13}H_{19}N_3Cl_2\cdot H_2O$	50.98	6.91	13.72	23.15	51.38	6.82	13.81	23.17
	〃	〃	〃	2HBr	295	$C_{13}H_{19}N_3Br_2\cdot H_2O$	39.51	5.35	10.63		39.87	5.45	10.32	
XXIIIc	5-Br	〃	〃	2HCl	300	$C_{13}H_{18}N_3BrCl$	42.52	4.94	11.44		42.33	4.95	11.52	
XXIIId	H	O	〃	〃	300	$C_{12}H_{16}N_2OCl_2$	52.37	5.86	10.18	25.77	51.93	5.77	10.37	26.07
XXIIIe	7-Br	〃	〃	HCl	300	$C_{12}H_{14}N_2OBrCl$	45.37	4.44	8.82		45.58	4.51	8.82	

Experimental

2-Methylamino-5-bromotropone Hydrazone (III)——In 15 ml. of hot EtOH, 1.1 g. of Ⅱ was dissolved. To this solution was added 1 ml. of 90% hydrazine hydrate, and the mixture was refluxed for 20 min. on a water bath. Ethanol was removed under reduced pressure, and the residue was chromatographed on alumina with $CHCl_3$ as a solvent to give, after recrystallization from 50% aq. EtOH, 600 mg. of dark violet needles, m.p. 102~103°. *Anal.* Calcd. for $C_8H_{10}N_3Br$: C, 42.12; H, 4.41; N, 18.42. Found: C, 42.00; H, 4.46; N, 18.80. UV λ_{max}^{EtOH} mμ (log ε): 245 (4.09), 299 (4.29), 364 (4.01), 430 (3.64).

2-Methylaminotropone Hydrazone (IV)——In 14 ml. of hot EtOH, 3 g. of I was dissolved. To this solution was added 2 ml. of 90% hydrazine hydrate, and the mixture was refluxed for 30 min. Ethanol was removed under reduced pressure, and the residue was chromatographed on alumina with $CHCl_3$ to give 1.9 g. of dark violet needles, m.p. 43~45°. Yield 63.4%. The sample was recrystallized from 45% aq. EtOH to give dark violet needles, m.p. 45°. *Anal.* Calcd. for $C_8H_{11}N_3$: C, 64.40; H, 7.43; N, 28.17. Found: C, 64.49; H, 7.44; N, 28.25. UV λ_{max}^{EtOH} mμ (log ε): 239 (4.08), 288 (4.13), 355 (3.88), 415 (3.57). This compound was gradually decomposed in air to a tarry material.

2-Methylaminotropone Azine (V)——A mixture of 1.5 g. of I, 1.5 g. of Ⅳ and 14 ml. of EtOH was refluxed for 38 hr. After cooling the reaction mixture, the separated crystals were collected and chromatographed on alumina with $CHCl_3$ as the solvent. Evaporation of the first eluate gave a crude product, which was recrystallized from $CHCl_3$-EtOH (8:2) to give 220 mg. of dark violet needles, m.p. 221~222° (decomp.). *Anal.* Calcd. for $C_{16}H_{18}N_4$: C, 72.15; H, 6.81; N, 21.04. Found: C, 72.03; H, 6.68; N, 20.96. This product was identical with an authentic sample of 2-methylaminotropone azine (V).[2] The compound (V) was also prepared by heating Ⅳ and I in dioxane for 38 hr., and in the presence of little amount of AcOH, the reaction time was shortened to 24 hr.

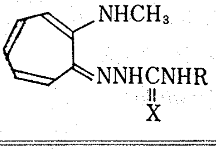
2-Methylaminotropone *p*-Chlorobenzaldehyde Azine (VI)——A mixture of 149 mg. of Ⅳ, 140 mg. of *p*-chlorobenzaldehyde and 15 ml. of EtOH was refluxed for 3 hr. Ethanol was removed under reduced pressure, and an EtOH solution of picric acid was added to the oily residue. The separated crystals were filtered and crystallized from EtOH to give yellow needles, m.p. 205°. *Anal.* Calcd. for $C_{21}H_{17}O_7N_6Cl$: C, 50.36; H, 3.42; N, 16.78. Found: C, 50.12; H, 3.38; N, 17.28.

2-Methylaminotropone Acetylhydrazone (VIIa)——A mixture of 1.5 g. of I, 0.74 g. of acetylhydrazine and 14 ml. of EtOH was refluxed for 10 hr. After cooling, the reaction mixture was diluted with H_2O. The separated crystals were recrystallized from 30% aq. EtOH or benzene to give orange silky needles, m.p. 157~158°. *Anal.* Calcd. for $C_{10}H_{13}ON_3$: C, 62.80; H, 6.85; N, 21.98. Found: C, 62.76; H, 6.95; N, 22.01.

2-Methylaminotropone Benzoylhydrazone (VIIb)——i) A mixture of 1.5 g. of I, 1.4 g. of benzoylhydrazine and 14 ml. of EtOH was refluxed for 8 hr. The separated crystals were crystallized from 70% aq. EtOH to give 1.6 g. of orange silky needles, m.p. 199~201°. *Anal.* Calcd. for $C_{15}H_{15}ON_3$: C, 71.12; H, 5.97; N, 16.59. Found: C, 71.02; H, 5.89; N, 16.96.

ii) To a suspension of 150 mg. of Ⅳ in a 10% NaOH aq. solution, 0.2 ml. of benzoylchloride was added with stirring. After 30 min., the separated crystals were collected and recrystallized from 50% aq. EtOH to give 30 mg. of orange silky needles, m.p. 199~201°. *Anal.* Calcd. for $C_{15}H_{15}ON_3$: C, 71.12; H, 5.97; N, 16.59. Found: C, 71.12; H, 6.12; N, 16.77. The infrared and ultraviolet spectra of the product were identical with those of Ⅶb obtained in i).

TABLE Ⅵ.



Compound	X	R	m.p. (°C) (decomp.)	Formula	Analysis (%)					
					Calcd.			Found		
					C	H	N	C	H	N
Ⅷ	O	C_6H_5	173~174	$C_{15}H_{16}N_4O$	67.14	6.01	20.88	27.08	6.00	20.52
Ⅸa	S	CH_3	199~200	$C_{10}H_{14}N_4S$	54.02	6.34	25.20	54.06	6.41	25.76
Ⅸb	〃	C_2H_5	201~202	$C_{11}H_{16}N_4S$	55.90	6.83	23.71	55.90	6.98	23.61
Ⅸc	〃	$CH_2CH(CH_3)_2$	210~212	$C_{13}H_{20}N_4S$	59.05	7.62	21.19	59.11	7.62	20.69
Ⅸd	〃	C_6H_5	161~162	$C_{15}H_{16}N_4S$	63.35	5.67	19.70	62.99	5.64	19.38

2-Methylaminotropone Phenylsemicarbazone (**VIII**)——In 30 ml. of dry benzene, 6 g. of Ⅳ was dissolved. To this solution was added 4.8 g. of phenyl isocyanate, and the mixture was refluxed for 1 hr. on a water bath. After cooling the reaction mixture, the separated crystals were collected and recrystallized from 85% aq. EtOH to give 8 g. of reddish brown needles, m.p. 173~174°. The analytical data are shown in Table Ⅵ.

2-Methylaminotropone Thiosemicarbazones (**IXa~d**)——A mixture of 1 mole of Ⅳ, 1.1 mole of isothiocyanate and dry benzene was refluxed for 1 hr. and treated in a similar manner to that described for Ⅷ. The products are listed in Table Ⅵ.

Azines (**Xa~f, XVIIa~c and XIXa~c**)——i) A mixture of 1 g. of Ⅳ, 450 mg. of propionaldehyde and 15 ml. of EtOH was refluxed for 4 hr. Ethanol was removed under reduced pressure to give a dark brown oil whose picrate was prepared by the usual method yielding yellowish brown needles, m.p. 169~170° (from dichloroethane). The same procedure was applied to other cases. Azine (Xa) was obtained as crystals, and recrystallized from 70% aq. EtOH. The products are listed in Table Ⅰ.

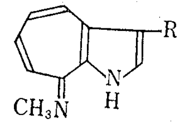
ii) A mixture of 1 g. of Ⅻa and 2 g. of dimethylsulfuric acid was heated at 100° for 5 min. The resulting dark brown solution was diluted with H_2O, and the excess of dimethylsulfuric acid was removed with benzene. To the aq. layer was added 2 ml. of 30% aq. CH_3NH_2 to separate the dark brown oil whose picrate was prepared by the usual method as yellowish brown needles, m.p. 169~170°. *Anal.* Calcd. for $C_{17}H_{18}O_7N_6$: C, 48.80 ; H, 4.34; N, 20.09. Found : C, 48.81 ; H, 4.57; N, 20.01. The infrared and ultraviolet spectra of the product were identical with those of the picrate of Xa obtained in i).

8-Methylimino-1,8-dihydrocyclohepta[*b*]pyrrole Derivatives (**XIa~d and XVIIIa~c**)——i) The preparation of Ⅺa is described as an example. A similar procedure applied to other cases. The products are listed in Table Ⅱ. To the azine (Xa) obtained from 1 g. of Ⅳ, 10 g. of polyphosphoric acid was added and the mixture was carefully heated at 150° for 3 min. The exothermic reaction took place at about 60°. After cooling, the reaction mixture was diluted with H_2O, and then adjusted to pH 8~9 with a NaOH aq. solution. The tarry material that gradually crystallized was purified by chromatography on alumina with $CHCl_3$, and recrystallized from 60% aqueous EtOH to give yellow scales, m.p. 231~232°. *Anal.* Calcd. for $C_{17}H_{15}O_7N_5$: C, 50.87; H, 3.77; N, 17.45. Found : C, 51.09; H, 4.24; N, 17.30.

ii) A mixture of 2 g. of XIVa and 4 g. of dimethylsulfuric acid was heated at 100° for 3 min. on an oil bath. After cooling the reaction mixture, the separated crystals were collected and washed with benzene. The product was recrystallized from iso-PrOH to give 1.1 g. of 3-methyl-8-methoxycyclohepta[*b*]pyrrole monomethyl sulfate (XVa). *Anal.* Calcd. for $C_{12}H_{15}O_5NS$: C, 50.51; H, 5.29; N, 4.90. Found : C, 49.88; H, 5.56; N, 4.97.

To a solution of XVa in 5 ml. of H_2O, was added 10 ml. of 30% aqueous CH_3NH_2 solution. The separated crystals were collected and purified by chromatography on alumina with $CHCl_3$ as a solvent. The initial eluate gave 10 mg. of yellow crystals, whose picrate was prepared by the usual method as yellow needles, m.p. 191~192°. *Anal.* Calcd. for $C_{17}H_{14}O_8N_4$: C, 50.75; H, 3.51; N, 13.93. Found : C, 50.54; H, 3.51; N, 14.00. The later eluates gave 765 mg. of 3-methyl-8-methylimino-1,8-dihydrocyclohepta[*b*]pyrrole, m.p. 146~147°, whose infrared and ultraviolet spectra were identical with those of Ⅺa obtained in i). Similarly, Ⅺb and Ⅺc were preparated from XIVb and XIVc, respectively. The analytical data of Ⅺa~c obtained in ii) are shown in Table Ⅶ.

Table Ⅶ.



Compound	R	m.p. (°C)	Formula	Analysis (%) Calcd. C	H	N	Found C	H	N
Ⅺa	CH_3	146~147	$C_{11}H_{12}N_2$	76.11	7.02	16.27	76.11	6.96	16.07
Ⅺb	C_2H_5	101~102	$C_{12}H_{14}N_2$	77.38	7.58	15.04	77.32	7.55	15.17
Ⅺc	C_6H_5	154~155	$C_{16}H_{14}N_2$	82.02	6.02	11.96	81.83	6.12	12.01

Cyclohepta[*b*]pyrrole-8-(1*H*)-thione Derivatives (**XVIa~c**)——To an aqueous solution of XVa obtained from 1 g. of XIVa, was added an aqueous solution of sodium sulfide until the pH reached 9~10. The separated oil gradually crystallized. The crystals were recrystallized from EtOH to give 500 mg. of yellowish brown needles, m.p. 167~168°. Similarly, XVIb and XVIc were prepared from the corresponding cyclohepta[*b*]pyrrolones, respectively. The products are listed in Table Ⅳ.

5-Phthalimidopentan-2-one 2-Troponylhydrazone (XXIIa)——A mixture of 3 g. of XXIa, 5 g. of 5-phthalimidopentan-2-one and 20 ml. of EtOH was refluxed for 3 hr. After cooling the reaction mixture, the separated crystals were collected and recrystallized from dioxane to give 5 g. of yellow needles, m.p. 188~190°. *Anal.* Calcd. for $C_{20}H_{19}O_3N_3$: C, 68.75; H, 5.48; N, 12.03. Found : C, 68.38; H, 5.93; N, 11.72.

5-Phthalimidopentan-2-one 7-Bromo-2-troponylhydrazone (XXIIb)——Hydrazone (XXIIb) was prepared from XXIb and 5-phthalimidopentan-2-one in a similar manner to the preparation of XXIIa. The product was recrystallized from EtOH to give yellow silky needles, m.p. 170~171°. *Anal.* Calcd. for $C_{20}H_{18}O_3N_3Br$: C, 56.08; H, 4.24; N, 9.81. Found : C, 56.18; H, 4.26; N, 9.47.

3-(2-Aminoethyl)cyclohepta[*b*]pyrrole Derivatives (XXIIIa~e)——The preparation of XXIIIb is described as an example. A similar procedure was applied to other cases. The products are listed in Table V.

A mixture of azine (XIXa) obtained from 4 g. of IV and 6.15 g. of 5-phthalimidopentan-2-one, and 60 g. of polyphosphoric acid was heated at 180° for 5 min. After cooling, the reaction mixture was diluted with H_2O. The separated crystals were collected by filtration. Yield, 13 g. The crude cyclization products was refluxed in 80 ml. of 10% aqueous KOH for 30 min. The reaction mixture was filtered while hot, and 100 g. of 50% sulfuric acid was added to the filtrate. Then, the resulting mixture was heated for 2.5 hr. on a water bath, adjusted to pH 9 by the addition of sodium carbonate, and extracted with $CHCl_3$. The $CHCl_3$ extract, after concentration, was passed through an alumina column. The first eluate was concetrated under reduced pressure, and the residue was dissolved in 10% aqueous HCl. The acidic solution was evaporated *in vacuo* to give a crude product. Yield, 2.7 g. Recrystallization from MeOH gave pale yellow crystals, m.p. 280° (decomp.).

The authors are grateful to Prof. T. Nozoe and Prof. Y. Kitahara of Tohoku University for their interest in this work. Thanks are also due to Mr. T. Tanaka for his assistance in the experimental work.