b) The nucleoside (10~25 mg.) was dissolved in 1.0 ml. of 0.2*M* sodium metaperiodate and set aside at room temperature. Final rotation at 340 mμ was measured (based on the starting material) (Table Ⅲ).

The authors are grateful to Drs. M. Matsui and I. Iwai for their interest in this work. Thanks are also due to Mr. A. Saito for his assistance in the experimental work.

Summary

Anomeric arabinofuranosyl and lyxofuranosyl nucleosides are synthesized by fusion of acylhalogenosugars with trimethylsilyl derivatives of uracil and thymine followed by removal of the protecting groups. The α-anomers of the nucleosides are found to be identical with the samples prepared by the mercury procedures. Relationships of optical rotations and nuclear magnetic resonance spectra between the anomers are described.

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106. Hideo Nakao: Studies on Seven-membered Ring Compounds. XVIII.*1 Reactions of the Quaternary Ammonium Salts of Cycloheptimidazole Derivatives.

(*Research Laboratories, Sankyo Co., Ltd.**2)

As reported in the previous paper,*1 1-benzylcycloheptimidazol-2(1*H*)-one (I) was found to be an active analgesic and anti-inflammatory agent.[1] During our investigations on the better synthetic procedure of I, the quaternary ammonium salts of cycloheptimidazole derivatives have been found to show interest reactivity.

The reaction of cycloheptimidazol-2(1*H*)-one (Ⅱ) with benzyl chloride in the presence of sodium hydroxide in 50% ethanol afforded I and an orange-yellow crystalline product, $C_{21}H_{21}N_2Cl$ (A), m.p. 234° (decomp.) in about 80% and 8% yield, respectively. Treatment of A with sodium hydroxide afforded yellow crystals, $C_{21}H_{20}N_2$ (B), m.p. 84°. A was recovered on treatment of B with hydrochloric acid. Therefore, A was confirmed to be hydrochloride of B. Brasen, *et al.*[2] reported that 1-methylamino-7-methyliminocycloheptatriene showed absorption maxima at 263, 346, 360, and 418 mμ in its ultraviolet spectrum, and 1-benzylamino-7-benzyliminocycloheptatriene (Ⅲ) melted at 82°. The ultraviolet spectrum of B was similar to that of 1-methylamino-7-methyliminocycloheptatriene. Therefore, B was considered to be Ⅲ. Hydrolysis of B according to the Brasen's method[2] was unsuccessful. However, B was converted to 2-benzylaminotropone on treatment with formalin and formic acid in an attempt to prepare the methylated derivative. Likewise bromination[2] of 1-methylamino-7-methyliminocycloheptatriene, B was brominated to give a monobromo derivative, m.p. 132°, which

*1 Part XVII. This Bulletin, **13**, 473 (1965).
*2 Hiromachi, Shinagawa-ku, Tokyo (中尾英雄).
1) H. Minakami, H. Takagi, S. Kobayashi: Life Science, **3**, 305 (1964).
2) W. R. Brasen, H. E. Holmquist, R. E. Benson: J. Am. Chem. Soc., **83**, 3125 (1961).

was assumed to be 1-benzylamino-4-bromo-7-benzyliminocycloheptatriene. The structure of B was more supported by these facts.

It has been reported by Bamberger[3] that imidazole ring of quaternary ammonium salts of imidazole and benzimidazole derivatives is cleaved with alkali. Murata[4] reported that 1-benzamido-7-benzoyliminocycloheptatriene was obtained from cycloheptimidazole by the Bamberger reaction. On the basis of these findings and the fact that both I and II are not hydrolyzed with alkali, III was presumably produced by the cleavage of 2-oxo-1,3-dibenzyl-1,2-dihydrocycloheptimidazolinium chloride (IV), which was yielded from I and benzylchloride. This assumption was proved by the production of III from an authentic sample of IV, prepared from I and benzyl chloride, as shown in Chart 1.

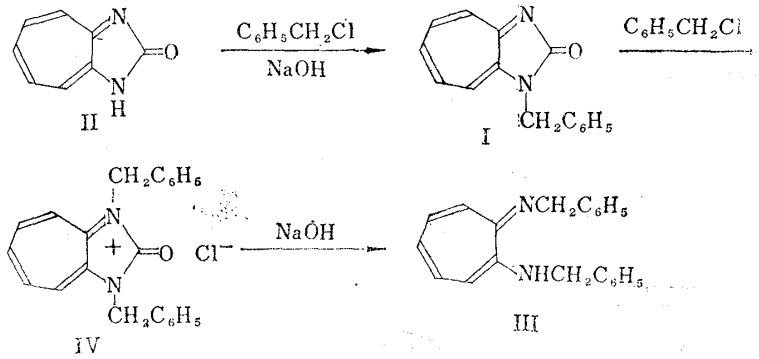
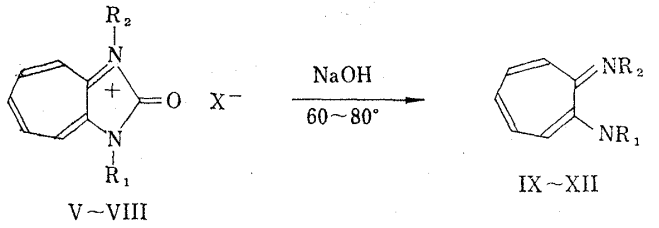


Chart 1.

Based on this result, some 1-alkylamino-7-alkyliminocycloheptatrienes were prepared from the corresponding quaternary salts of 1-alkylcycloheptimidazol-2(1*H*)-ones (Chart 2).



	R_1	R_2	X		R_1	R_2
V	CH_3	CH_3	I	IX	CH_3	CH_3
VI	C_2H_5	C_2H_5	I	X	C_2H_5	C_2H_5
VII	$C_6H_5CH_2$	CH_3	I	XI	$C_6H_5CH_2$	CH_3
VIII	$C_6H_5CH_2$	*p*-$ClC_6H_4CH_2$	Cl	XII	$C_6H_5CH_2$	*p*-$ClC_6H_4CH_2$

Chart 2.

As described above, IV was converted to III on heating with sodium hydroxide. However, treatment of IV with dilute aqueous sodium hydroxide at room temperature afforded colorless crystals, $C_{44}H_{40}O_4N_4$ (C), m.p. about 90°, in good yield. C is insoluble in water, but soluble in organic solvents, and its ultraviolet spectrum is different from that of IV as shown in Fig. 1. IV was recovered on treatment of C with hydrochloric acid. Recrystallization of C from carbon tetrachloride gave colorless needles (D), m.p. 81°. The molecular formula of D agreed with $C_{48}H_{38}O_3N_4Cl_{16}$ from the results of

3) E. Bamberger : Ann., 273, 267 (1893); E. Bamberger, B. Berle : *Ibid.*, 273, 342 (1893).
4) I. Murata : Bull. Chem. Soc. Japan, 32, 841 (1959).

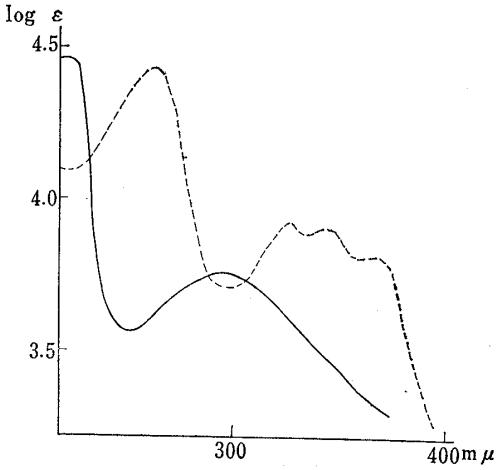
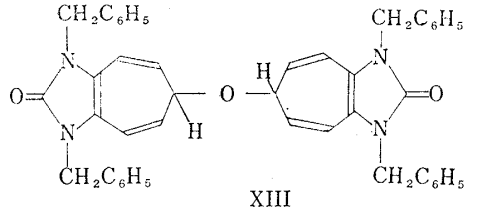


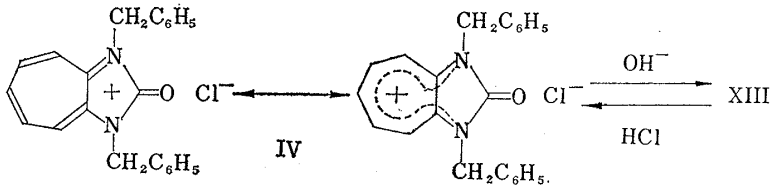
Fig. 1. Ultraviolet Spectra in Ethanol
——— C ----- Ⅳ

elementary analysis and molecular weight determination. The infrared spectrum of D showed no absorption band due to OH group. According to these facts, D was considered to be the carbon tetrachloride adduct of 6,6′-oxybis[1,3-dibenzyl-3,6-dihydrocycloheptimidazol-2(1*H*)-one] (XIII).

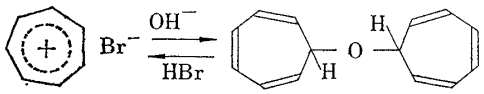


XIII

Consequently, C is considered to be the monohydrate of XIII. The formation of XIII from Ⅳ is analogous to the production of ditropyl ether[5] from tropylium bromide. This fact suggests that Ⅳ have tropylium ion structure as follows:



IV



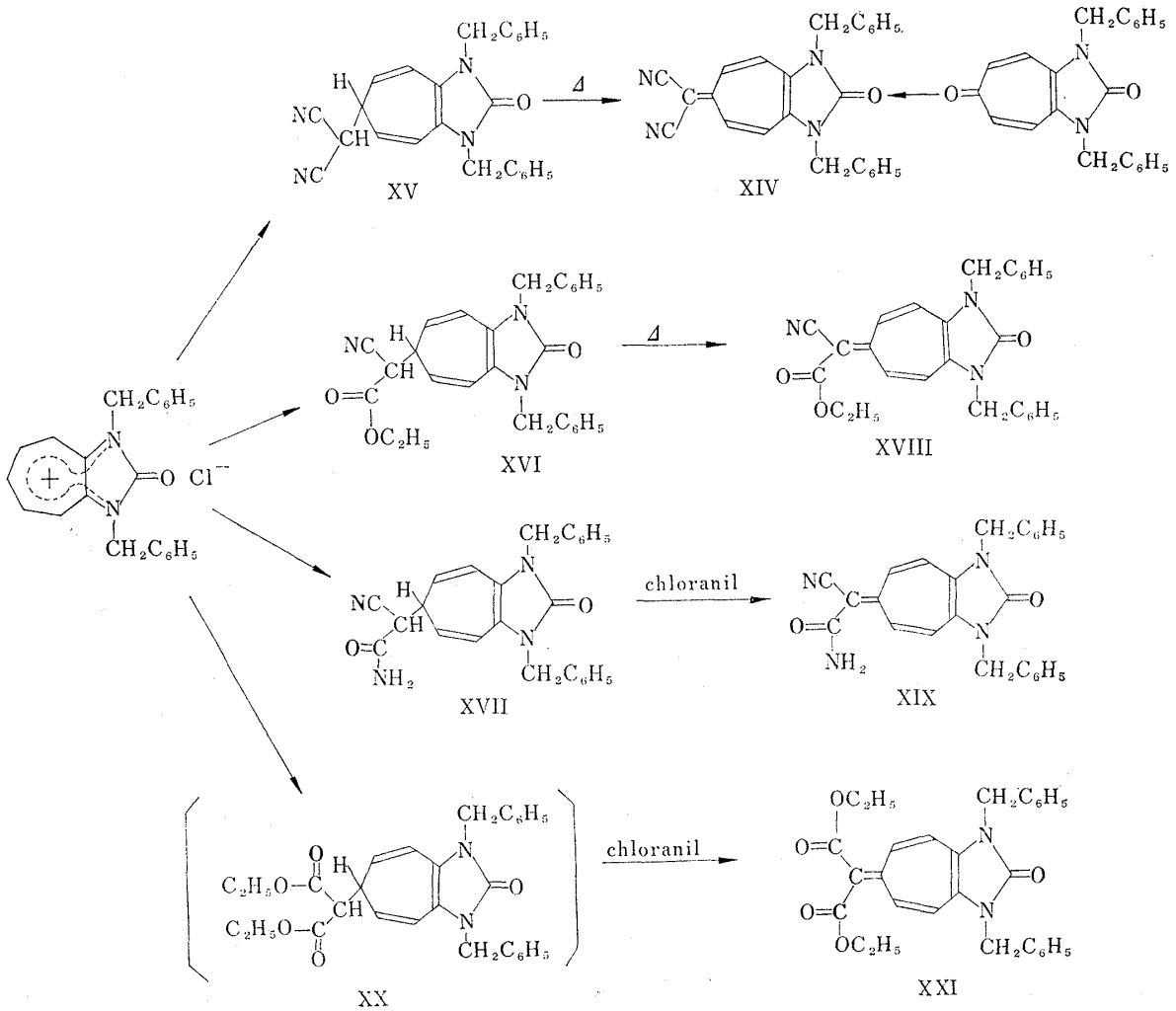
Since it was expected that Ⅳ would react with anionoid reagents, several condensation reactions of Ⅳ with active methylene compounds were attempted. The reaction of Ⅳ with malononitrile in the presence of sodium ethoxide at room temperature afforded pale orange crystals (E), whose ultraviolet spectrum was similar to that of XIII. E was converted to red crystals (F) on heating with ethanol. Since F had absorption maxima at 455 mμ (log ε 4.49) in the visible spectrum, it was assumed to be 6-dicyanomethylene-1,3-dibenzyl-3,6-dihydrocycloheptimidazol-2(1*H*)-one (XIV). An authentic specimen of XIV was synthesized from 1,3-dibenzylcycloheptimidazole-2,6(1*H*,3*H*)-dione and malononitrile according to the method of Kitahara and his coworkers.[6] The identity of the infrared and ultraviolet spectra of XIV with those of F ascertained the structure of the latter product. Consequently, E is considered to be 6-dicyanomethyl-1,3-dibenzyl-3,6-dihydrocycloheptimidazol-2(1*H*)-one (XV). Similarly, reactions of Ⅳ with ethyl cyanoacetate and 2-cyanoacetamide afforded 6-[cyano(ethoxycarbonyl)methyl]-1,3-dibenzyl-3,6-dihydrocycloheptimidazol-2(1*H*)-one (XVI) and 6-(carbamoylcyanomethyl)-1,3-dibenzyl-3,6-dihydrocycloheptimidazol-2(1*H*)-one (XVII), respectively. XVI was converted to red crystals, $C_{27}H_{23}O_3N_3$, m.p. 235° on heating with ethanol. The analytical data of this compound agreed with the formula of the corresponding dehydrogenated derivative, and its ultraviolet spectrum was similar to that of XIV. Therefore, this

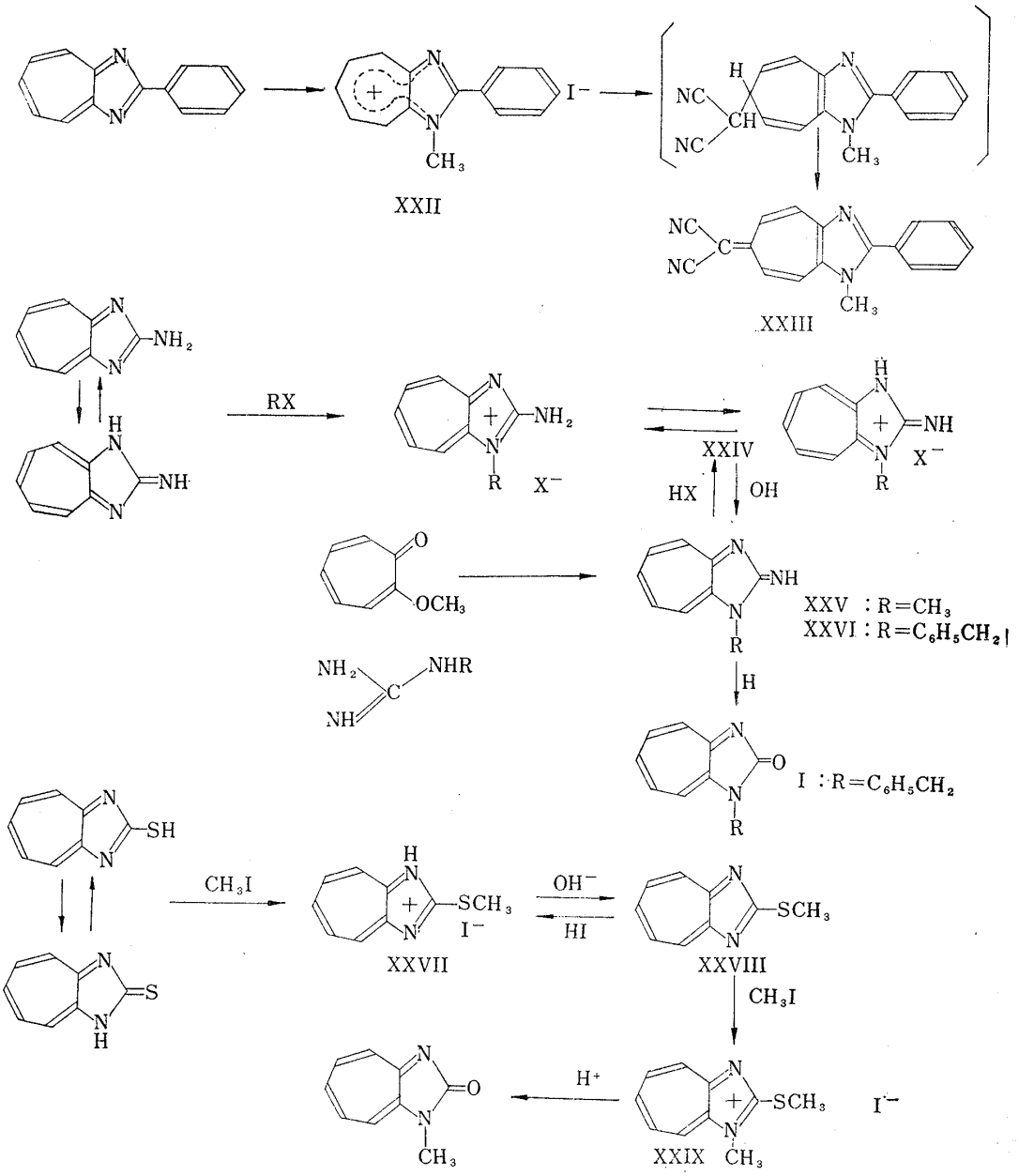
5) W. E. Deerung, L. H. Knox: J. Am. Chem. Soc., **76**, 3203 (1954).
6) Y. Kitahara: This work was presented at the 12th Annual Meeting of the Chemical Research Institute of Non-Aqueous Solutions. Tohoku Univ.

compound was suggested to be the corresponding 6-[cyano(ethoxycarbonyl)methylene]-1,3-dibenzyl-3,6-dihydrocycloheptimidazol-2(1*H*)-one (XVIII). On the other hand, XVII was not affected on heating with ethanol, but changed to red crystals by dehydrogenation with chloranil. This product is apparently 6-(carbamoylcyanomethylene)-1,3-dibenzyl-3,6-dihydrocycloheptimidazol-2(1*H*)-one (XIX) as evidenced from its ultraviolet spectrum and analytical data. Similar reaction of IV with diethyl malonate afforded a condensation product (XX) whose structure was proved by dehydrogenation of XX with chloranil to give red-brown crystals which are considered to be 6-bis(ethoxycarbonyl)-methylene-3,6-dihydrocycloheptimidazol-2(1*H*)-one (XXI).

In order to ascertain whether the quaternary ammonium salt of other cycloheptimidazole derivative can undergo such reaction, the reaction of 2-phenylcycloheptimidazole methiodide (XXII) with malononitrile was carried out. XXII reacted with malononitrile in the presence of sodium ethoxide on heating in ethanol to give red-orange needles, m.p. above 280°. The analytical values of this compound agreed with the formula $C_{18}H_{12}N_4$ and its ultraviolet spectrum was similar to that of XIV. Therefore, this compound is considered to be 1-methyl-2-phenyl-6-dicyanomethylene-1,6-dihydrocycloheptimidazole (XXIII).

Furthermore, the reactions of 2-amino- and 2-mercaptocycloheptimidazole methiodides were examined. Reaction of 2-aminocycloheptimidazole with excess methyl iodide afforded the corresponding monomethiodide (XXIV). Treatment of XXIV with aqueous





sodium hydroxide at room temperature gave 1-methyl-2-imino-1,2-dihydrocycloheptimidazole (XXV), which was identified by comparison of its infrared spectrum with that of an authentic sample.[7] Similarly, the reaction of 2-aminocycloheptimidazole with benzyl chloride afforded 1-benzyl-2-imino-1,2-dihydrocycloheptimidazole (XXVI), which was identified with an authentic sample prepared from 2-methoxytropone and benzylguanidine according to the previously reported method.[7] Hydrolysis of XXVI yielded 1-benzylcycloheptimidazol-2(1*H*)-one (I). Reaction of 2-mercaptocycloheptimidazole with excess methyl iodide afforded also the corresponding monomethiodide (XXVII). Treatment of XXVII with aqueous sodium hydroxide at room temperature gave 2-methylthiocycloheptimidazole (XXVIII), which was identified by comparison of its infrared spectrum with that of an authentid sample.[8] Moreover, action of methyl iodide on XXVIII gave the corresponding monomethiodide (XXIX). Although alkaline hydrolysis of

7) H. Nakao, G. Sunagawa : This Bulletin, **13**, 465 (1965).
8) T. Nozoe, T. Mukai, I. Murata : J. Am. Chem. Soc., **76**, 3352 (1954).

XXIX was unsuccessful to obtain pure product, acid hydrolysis gave 1-methylcycloheptimidazol-2(1*H*)-one.

Experimental

Reaction of Cycloheptimidazol-2(1*H*)-one with Benzyl Chloride——To a solution of 14.6 g. of cycloheptimidazol-2(1*H*)-one in 50 ml. of 10% NaOH was added a solution of 13.9 g. of benzyl chloride in 60 ml. of EtOH. The mixture was stirred under reflux for 8.5 hr. After cooling, 200 ml. of water was added to the reaction mixture, and the separated crystals were poured into 100 ml. of 10% HCl. The mixture was filtered off to remove insoluble matter. The filtrate was neutralized with 10% NaOH, and the precipitate was collected and recrystallized from MeOH to give 18 g. of 1-benzylcycloheptimidazol-2(1*H*)-one.

The insoluble matter was recrystallized from EtOH to give 1 g. of 1-benzylamino-7-benzyliminocycloheptatriene hydrochloride, m.p. 234° (decomp.). *Anal.* Calcd. for $C_{21}H_{21}N_2Cl$: C, 74.87; H, 6.28; N, 8.32. Found: C, 74.67; H, 6.19; N, 8.53. UV λ_{max}^{EtOH} mμ (log ε): 260 (4.44), 346 (4.04), 412 (4.15).

1-Benzylamino-7-benzyliminocycloheptatriene (III)——To a mixture of 5 ml. of 10% NaOH and 8 ml. of EtOH was added 500 mg. of the above described hydrochloride. The mixture was warmed for 10 min. After cooling, the separated crystals were collected and recrystallized from EtOH to give 200 mg. of yellow needles, m.p. 84°. *Anal.* Calcd. for $C_{21}H_{20}N_2$: C, 83.96; H, 6.71; N, 9.33. Found: C, 83.45; H, 6.87; N, 9.21. UV λ_{max}^{EtOH} mμ (log ε): 259 (4.33), 344 (4.05), 357 (4.08), 413 (3.98). IR ν_{max}^{Nujol} cm^{-1}: 3300, 1590.

1-Benzylamino-4-bromo-7-benzyliminocycloheptatriene——To a solution of 300 mg. of III in 1 ml. of $CHCl_3$ was added dropwise a solution of 160 mg. of bromine in 0.5 ml. of $CHCl_3$. The mixture was allowed to stand at room temperature for 10 min., then concentrated to dryness *in vacuo*. To the residue was added 5 ml. of 5% aqueous NH_3. The resulting crystals were collected and recrystallized from EtOH to give 250 mg. of orange-yellow needles, m.p. 132°. *Anal.* Calcd. for $C_{21}H_{19}N_2Br$: C, 66.49; H, 5.05; N, 7.39. Found: C, 66.43; H, 4.99; N, 7.25.

Action of Formalin and Formic Acid to III——A mixture of 500 mg. of III, 300 mg. of 97% formic acid and 300 mg. of 37% formalin was heated on a steam bath for 30 min. After cooling, 5 ml. of water was added to the reaction mixture, and separated crystals were collected and recrystallized from EtOH to give 80 mg. of 2-benzylaminotropone, m.p. 127°, identified by comparison of its infrared spectrum with that of an authentic sample. *Anal.* Calcd. for $C_{14}H_{13}ON$: C, 79.59; H, 6.20; N, 6.63. Found: C, 79.36; H, 6.15; N, 6.29.

2-Oxo-1,3-dibenzyl-1,2-dihydrocycloheptimidazolinium Chloride (IV)——A mixture of 1 g. of 1-benzylcycloheptimidazol-2(1*H*)-one and 1.2 ml. of benzyl chloride was heated at 130~140° for 10 min. After cooling, 10 ml. of benzene was added to the reaction mixture. The resulting crystals were collected and recrystallized from water containing a small amounts of hydrochloric acid to give colorless needles, m.p. 237° (decomp.). Yield, 1 g. *Anal.* Calcd. for $C_{22}H_{19}ON_2Cl$: C, 72.82; H, 5.28; N, 7.72. Found: C, 72.80; H, 5.26; N, 7.89. UV λ_{max}^{EtOH} mμ (log ε): 260 (4.45), 325 (3.90), 345 (3.90), 370 (3.80).

Reaction of IV with Sodium Hydroxide——a) To a solution of 1 g. of IV in 5 ml. of EtOH was added 5 ml. of 3% NaOH. The mixture was heated at 70° for 1 hr. After cooling, the separated oil was extracted with $CHCl_3$ and chromatographed on alumina. Evaporation of the first eluate gave yellow crystals, m.p. 83° which did not depress the melting point of an authentic sample of 1-benzylamino-7-benzyliminocycloheptatriene. Yield, 100 mg.

b) To a cold solution of 1 g. of IV in 30 ml. of water was added 20 ml. of 1% NaOH. The separated crystals were collected and washed with water to give monohydrate of 6,6′-oxybis[1,3-dibenzyl-3,6-dihydrocycloheptimidazol-2(1*H*)-one] (XIII), m.p. 90°. Yield, 0.8 g. *Anal.* Calcd. for $C_{44}H_{38}O_3N_4 \cdot H_2O$: C, 76.72; H, 5.85; N, 8.13. Found: C, 76.97; H, 5.88; N, 8.01. UV λ_{max}^{EtOH} mμ (log ε): 220 (4.45), 290 (3.75).

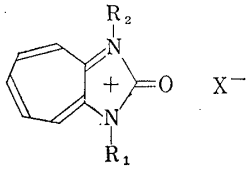
A solution of 0.5 g. of this monohydrate in 10 ml. of CCl_4 was allowed to stand at room temperature overnight. The separated crystals were collected and recrystallized from CCl_4 to give 0.4 g. of CCl_4 adduct of XIII as colorless needles, m.p. 82°. *Anal.* Calcd. for $C_{44}H_{38}O_3N_4 \cdot 4CCl_4$: C, 44.82; H, 2.98; N, 4.36; mol. wt., 1286. Found: C, 45.11; H, 3.05; N, 4.66; mol. wt., 1260. UV λ_{max}^{EtOH} mμ (log ε): 220 (4.74), 290 (4.08).

Treatment of Monohydrate of XIII with Hydrochloric Acid——A mixture of 0.5 g. of monohydrate of XIII and 19 ml. of 10% HCl was stirred at room temperature for 1 hr. Insoluble substance was collected and recrystallized from water containing a small amounts of HCl to give 0.3 g. of colorless crystals, which were identified as IV.

Treatment of Monohydrate of XIII with Sodium Hydroxide——By the same procedure as described in (a) of the reaction of IV with NaOH, III was obtained from 0.5 g. of monohydrate of XIII. Yield, 30 mg.

2-Oxo-1,3-dialkyl-1,2-dihydrocycloheptimidazolinium Halide (V, VI, VII)——Heating 1-alkylcycloheptimidazol-2(1*H*)-one with excess alkyl halide in a sealed tube at 100° for 7 hr. gave corresponding quaternary ammonium halide (Table I).

Table I. 2-Oxo-1,3-dialkyl-1,2-dihydrocycloheptimidazolinium Halides

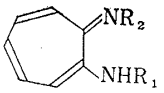


No.	R_1	R_2	m.p. (°C)	Formula	Analysis (%) Calcd. C	Calcd. H	Found C	Found H
V	CH_3	CH_3	259	$C_{10}H_{11}ON_2I$	39.75	3.67	39.79	3.62
VI	C_2H_5	C_2H_5	271	$C_{12}H_{15}ON_2I$	43.65	4.58	44.00	4.49
VII	$C_6H_5CH_2$	CH_3	233	$C_{16}H_{15}ON_2I$	50.81	4.00	50.60	3.99
VIII	〃	p-$ClC_6H_4CH_2$	236	$C_{22}H_{18}ON_2Cl_2 \cdot 3H_2O$	58.54	5.36	58.70	5.25

1-Benzyl-2-oxo-3-(*p*-chlorobenzyl)-1,2-dihydrocycloheptimidazolinium Chloride (VIII)——By the same procedure as described in preparation of IV, VIII was obtained from I and *p*-chlorobenzyl chloride.

1-Alkylamino-7-alkyliminocycloheptatriene (IX~XII)——To a solution of 1 g. of ammonium salt (V~VIII) in 5 ml. of EtOH was added 5 ml. of 3% NaOH. The mixture was heated at 70° for 40 min. on a water bath. After cooling, the mixture was extracted with $CHCl_3$. The $CHCl_3$ extract was concentrated *in vacuo* and the residue was chromatographed on alumina. The first eluate gave 1-alkylamino-7-alkyliminocycloheptatriene (Table II).

Table II. Alkylamino-7-alkyliminocycloheptatrienes



No.	R_1	R_2	m.p. (°C)	Formula	Analysis (%) Calcd. C	Calcd. H	Found C	Found H
IX	CH_3	CH_3	67	$C_9H_{12}N_2$	72.94	8.16	73.04	8.12
X[a]	C_2H_5	C_2H_5	179	$C_{17}H_{19}O_7N_5$	50.37	4.72	50.39	4.78
XI[b]	$C_6H_5CH_2$	CH_3	196	$C_{15}H_{17}N_2Cl$	69.08	6.57	69.19	6.53
XII	〃	p-$ClC_6H_4CH_2$	84.5	$C_{21}H_{19}N_2Cl$	75.32	5.72	75.33	5.66

a) Picrate. *b*) Hydrochloride.

Reaction of IV with Malononitrile——To a solution of 70 mg. of Na and 200 mg. of malononitrile in 10 ml. of EtOH was added a solution of 1 g. of IV in 40 ml. of EtOH. The mixture was stirred at room temperature for 8 hr. The separated crystals were collected and washed with water. This compound is considered to be 6-dicyanomethyl-1,3-dibenzyl-3,6-dihydrocycloheptimidazol-2(1*H*)-one (XV). Yield, 800 mg. UV λ_{max}^{EtOH} mμ (log ε): 295 (3.80).

On recrystallization from EtOH, this compound was converted to red needles, m.p. >280°, which were identified as 6-dicyanomethylene-1,3-dibenzyl-3,6-dihydrocycloheptimidazol-2(1*H*)-one by comparison of its infrared and ultraviolet spectra with those of an authentic sample. *Anal.* Calcd. for $C_{25}H_{18}ON_4$: C, 76.90; H, 4.65; N, 14.35. Found: C, 76.67; H, 4.67; N, 14.47. UV λ_{max}^{EtOH} mμ (log ε): 264 (4.14), 455 (4.49).

6-Dicyanomethylene-1,3-dibenzyl-3,6-dihydrocycloheptimidazol-2(1*H*)-one (XIV)——A mixture of 130 mg. of 1,3-dibenzylcycloheptimidazole-2,6 (1*H*, 3*H*)-dione, 40 ml. of malononitrile and 2.5 ml. of Ac_2O was heated at 120~130° for 30 min. After cooling, separated crystals were collected and recrystallized from AcOH to give 100 mg. of red needles, m.p. >280°.

6-[Cyano(ethoxycarbonyl)methyl]-1,3-dibenzyl-3,6-dihydrocycloheptimidazol-2(1*H*)-one (XVI)——To a solution of 70 mg. of Na and 350 mg. of ethyl cyanoacetate in 30 ml. of EtOH was added a solution of

1 g. of IV in 50 ml. of EtOH. The mixture was stirred at room temperature for 15 min. The separated colorless crystals were collected and washed with EtOH. Yield, 1 g., m.p. 153° (decomp.). *Anal.* Calcd. for $C_{27}H_{25}O_3N_3$: N, 9.56. Found : N, 9.28.

6-(Carbamoylcyanomethyl)-1,3-dibenzyl-3,6-dihydrocycloheptimidazol-2(1*H*)-one (XVII)——To a solution of 70 mg. of Na and 260 mg. of cyanoacetamide in 30 ml. of EtOH was added 1 g. of IV. The mixture was refluxed on a steam bath for 15 min. The separated crystals were collected, washed with water, and recrystallized from EtOH to give 500 mg. of colorless crystals, m.p. 203° (decomp.). *Anal.* Calcd. for $C_{25}H_{22}O_2N_4$: C, 73.15; H, 5.40; N, 13.65. Found : C, 72.91; H, 5.27; N, 13.68. UV λ_{max}^{EtOH} mμ (log ε) : 295 (3.71).

6-[Cyano(ethoxycarbonyl)methylene]-1,3-dibenzyl-3,6-dihydrocycloheptimidazol-2(1*H*)-one (XVIII)——A mixture of 200 mg. of XVI and 10 ml. of EtOH was refluxed for 10 hr. During the reaction, XVI was converted to red crystals. After cooling, the red crystals were collected and recrystallized from EtOH to give red needles, m.p. 235° (decomp.). Yield, 50 mg. *Anal.* Calcd. for $C_{27}H_{23}O_3N_3$: C, 74.12; H, 5.30; N, 9.61. Found : C, 73.73; H, 5.15; N, 9.50. UV λ_{max}^{EtOH} mμ (log ε) : 265 (4.16), 465 (4.66).

6-(Carbamoylcyanomethylene)-1,3-dibenzyl-3,6-dihydrocycloheptimidazol-2(1*H*)-one(XIX)——A mixture of 400 mg. of XV, 250 mg. of chloranil and 10 ml. of xylene was heated under reflux 20 min. After removing separated tary substance, the reaction solution was cooled and then the separated crystals were collected and recrystallized from EtOH to give 50 mg. of red-brown crystals, m.p. 243°. *Anal.* Calcd. for $C_{25}H_{20}O_2N_4$: C, 73.51; H, 4.94; N, 13.72. Found : C, 73.30; H, 4.88; N, 13.98. UV λ_{max}^{EtOH} mμ (log ε) : 264 (4.09), 452 (4.48).

6-Bis(ethoxycarbonyl)methylene-1,3-dibenzyl-3,6-dihydrocycloheptimidazol-2(1*H*)-one (XXI)——To a solution of 70 mg. of Na and 500 mg. of diethyl malonate in 20 ml. of EtOH was added 1 g. of IV. The mixture was refluxed for 8 hr. After removal of the solvent under reduced pressure, 20 ml. of xylene and 560 mg. of chloranil were added to the residue. The mixture was refluxed for 20 min., and filtered off to remove insoluble matter. The filtrate was cooled, and separated crystals were purified by alumina chromatography. The eluate gave 50 mg. of red-brown crystals, m.p. 148°. *Anal.* Calcd. for $C_{29}H_{28}O_5N_2$: C, 71.88; H, 5.83; N, 5.78. Found : C, 71.98; H, 5.71; N, 5.95.

1-Methyl-2-phenyl-6-dicyanomethylene-1,6-dihydrocycloheptimidazole (XXIII)——To a solution of 70 mg. of Na and 204 mg. of malononitrile in 20 ml. of EtOH was added 960 mg. of 2-phenylcycloheptimidazole methiodide. The mixture was refluxed for 8 hr. and then separated crystals were collected and recrystallized from AcOH to give 400 mg. of red-orange needles, m.p. >280°. *Anal.* Calcd. for $C_{18}H_{12}N_4$: C, 76.04; H, 4.25; N, 19.71. Found : C, 75.73; H, 4.25; N, 19.51. UV λ_{max}^{EtOH} mμ (log ε) : 257 (4.42), 437 (4.62).

2-Phenylcycloheptimidazole Methiodide——A mixture of 1 g. of 2-phenylcycloheptimidazole and 4 ml. of methyl iodide was heated at 100° for 6 hr. in a sealed tube. The reaction product was recrystallized from EtOH to give 1 g. of red-orange needles, m.p. 185° (decomp.). *Anal.* Calcd. for $C_{15}H_{13}N_2I$: C, 51.74; H, 3.76; N, 8.05. Found : C, 51.70; H, 4.01; N, 8.31.

2-Aminocycloheptimidazole Methiodide (XXIV)——A mixture of 1 g. of 2-aminocycloheptimidazole and 5 ml. of methyl iodide was heated at 120° for 7 hr. in a sealed tube. After cooling, separated crystals were recrystallized from MeOH to give 1 g. of orange-yellow crystals, m.p. 289° (decomp.). *Anal.* Calcd. for $C_9H_{10}N_3I$: C, 37.65; H, 3.51; I, 44.20. Found : C, 37.83; H, 3.70; I, 44.27. UV λ_{max}^{EtOH} mμ (log ε) : 256 (4.46), 345 (3.96). 385 (4.00).

1-Methyl-2-imino-1,2-dihydrocycloheptimidazole (XXV)——To a solution of 1.2 g. of XXIV in 20 ml. of water was added 2 ml. of 10% NaOH. The mixture was extracted with $CHCl_3$. Concentration of the extract under reduced pressure gave 0.5 g. of crude product, which was purified by alumina chromatography. The eluate gave yellow crystals, m.p. 143° (decomp.). *Anal.* Calcd. for $C_9H_9N_3$: C, 67.90; H, 5.70; N, 26.40. Found : C, 67.78; H, 5.79; N, 26.60.

Hydrolysis of XXIV——To a solution of 1 g. of XXIV in 10 ml. of water was added 6 ml. of 10% NaOH. The mixture was refluxed for 3 hr. After cooling, the reaction mixture was extracted with $CHCl_3$. The extract was concentrated to small volume and chromatographed on alumina. The eluate gave pale yellow crystals, m.p. 192°, which were identified as 1-methylcycloheptimidazol-2(1*H*)-one by comparison of its infrared spectrum with that of an authentic sample.

1-Benzyl-2-imino-1,2-dihydrocycloheptimidazole (XXVI)——a) To a solution of 338 mg. of Na in 20 ml. of EtOH was added 2.9 g. of benzylguanidine sulfate. After the mixture was stirred at room temperature for 1 hr., 2 g. of 2-methoxytropone was added. Then the mixture was stirred under reflux for 1 hr. After cooling, separated crystals were poured into 30 ml. of $CHCl_3$. The mixture was filtered off to remove insoluble matter, and the filtrate was concentrated to dryness *in vacuo*. Recrystallization of the residue from EtOH gave 0.7 g. of orange-yellow needles, m.p. 203° (decomp.). *Anal.* Calcd. for $C_{15}H_{13}N_3$: C, 76.57; H, 5.57; N, 17.86. Found : C, 76.33; H, 5.69; N, 17.79.

b) A mixture of 2 g. of 2-aminocycloheptimidazole and 3 ml. of benzyl chloride was heated at 165° for 5 hr. After cooling, 20 ml. of benzene was added and the reaction product was collected, washed with benzene and poured into 20 ml. of 2% NaOH. The mixture was warmed on a water bath for a

short time and extracted with $CHCl_3$. The extract was purified by alumina chromatography. The eluate gave 1 g. of orange-red crystals, m.p. 203° (decomp.), which was identical with the compound obtained by the (a) method.

Hydrolysis of XXVI——A mixture of 0.5 g. of XXVI and 8 ml. of 15% HCl was refluxed for 4 hr. After cooling, the mixture was made alkaline with 10% NaOH, then extracted with $CHCl_3$. Concentration of the extract gave a crude product, which, after recrystallization from benzene, gave pale yellow needles, m.p. 181°. This compound was identical with 1-benzylcycloheptimidazol-2(1*H*)-one in all respects.

Reaction of 2-Mercaptocycloheptimidazole with Methyl Iodide——A mixture of 2 g. of 2-mercaptocycloheptimidazole, 8 g. of methyl iodide and 30 ml. of MeOH was refluxed for 2 hr. After cooling, separated crystals were collected and recrystallized from MeOH to give 1.5 g. of 2-methylthiocycloheptimidazole hydroiodide, m.p. 194° (decomp.). *Anal.* Calcd. for $C_9H_{10}N_2IS$: C, 35.54; H, 2.94; N, 9.21. Found: C, 35.70; H, 3.01; N, 9.24.

2-Methylthiocycloheptimidazole Methiodide (XXVII)——A mixture of 200 mg. of 2-methylthiocycloheptimidazole, 1 ml. of methyl iodide and 4 ml. of MeOH was refluxed for 3 hr. The reaction mixture was concentrated under reduced pressure, and the resulting residue was recrystallized from EtOH to give red crystals, m.p. 186° (decomp.). *Anal.* Calcd. for $C_{10}H_{11}N_2IS$: C, 37.75; H, 3.49; N, 8.81. Found: C, 37.81; H, 3.63; N, 9.27.

Hydrolysis of XXVII——A mixture of 500 mg. of XXVII and 5 ml. of 10% HCl was heated under reflux for 2 hr. After cooling, the reaction mixture was made alkaline with 10% NaOH, and then extracted with $CHCl_3$. The extract was concentrated under reduced pressure, and the resulting residue was purified by alumina chromatography to give pale yellow crystals, m.p. 192°. This compound was identical with 1-methylcycloheptimidazol-2(1*H*)-one in all respects.

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Summary

The quaternary ammonium salt of 1-alkylcycloheptimidazol-2(1*H*)-one afforded 1-alkylamino-7-alkyliminocycloheptatriene on heating with alkali. However, treatment of this salt with dilute aqueous sodium hydroxide at room temperature gave a ditropyl ether derivative. Action of active methylene compounds on the ammonium salt in the presence of sodium ethoxide yielded 6-substituted derivatives, which were easily dehydrogenated to the corresponding heptafulvene derivatives. As an example, the reaction of 2-oxo-1,3-dibenzyl-1,2-dihydrocycloheptimidazolinium chloride with ethyl cyanoacetate afforded 6-[cyano(ethoxycarbonyl)methyl]-1,3-dibenzyl-3,6-dihydrocycloheptimidazol-2(1*H*)-one, which was dehydrogenated to 6-[cyano(ethoxycarbonyl)methylene]-1,3-dibenzyl-3,6-dihydrocycloheptimidazol-2(1*H*)-one on heating with ethanol. This reaction made it clear that the quaternary ammonium salt has tropylium ion structure. Such reaction occurred also in case of 2-phenylcycloheptimidazole methiodide. The quaternary ammonium salts of 2-amino- and 2-methylthiocycloheptimidazole afforded 1-alkylcycloheptimidazol-2(1*H*)-one on treatment with acid.

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