# Studies on Seven-Membered Heterocyclic Compounds Containing Nitrogen. IV. Hexahydro-1, 2, 5-Triazazulene

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It has been found that hexahydro-1, 2-diazazulene (I)[1-3] was prepared from 2-hydroxymethylenecycloheptanone. Buchta[4] has made only a simple statement that W. Treibs succeeded in dehydrogenation of the hydroazazulene by chloranil to yield 1, 2-diazazulene (II), but no further detailed report was given. The present author has synthesized hitherto unknown hexahydro-1, 2, 5 (or 1, 2, 6)-triazazulene (XIa or XIb), having one nitrogen atom in the seven-membered ring in satisfying yield. Spectral studies have shown that the former

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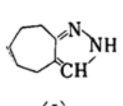
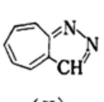
[1] O. Wallach, *Ann.*, **329**, 109 (1903).
[2] W. Treibs and H. J. Neupert, ibid., **595**, 219 (1955).
[3] E. Buchta and J. Kranz, ibid., **601**, 170 (1956).
[4] E. Buchta et al., *Angew. Chem.*, **67**, 77 (1955).

structure is more reasonable. A preliminary test of dehydrogenation was quite unsuccessful, but further attempts are in progress.


(I)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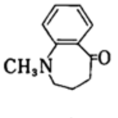
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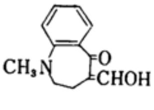
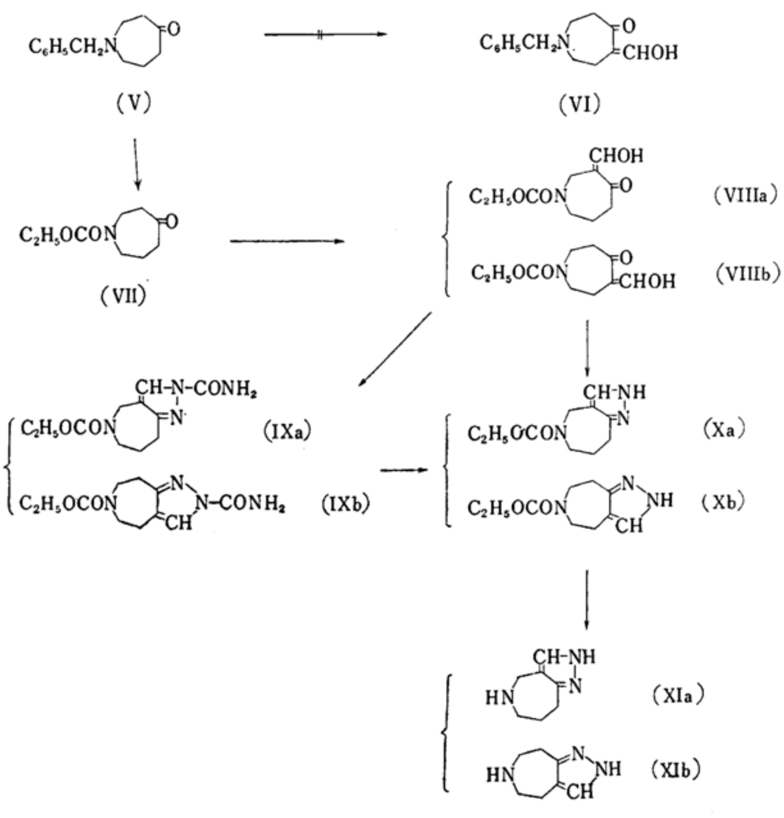

(IV)

*N*-Methyl type azasuberenone, 1-methyl-2, 3, 4, 5-tetrahydro-5-keto-1-benzazepine (III)[5] has been reported to afford 4-hydroxymethylene derivative (IV) in 72% yield by the reaction with ethyl formate in the presence of sodium methoxide in benzene. Under the same condition, however, *N*-benzyl type azasuberone, 1-benzyl-1-azacycloheptan-4-one (V)[6] gave only a trace of hydroxymethylene compound, which certified as bis-2, 4-dinitrophenylhydrazone, leaving much residue on distillation. 1-Ethoxycarbonyl-1-azacycloheptan-4-one (VII) derived from V was subjected to the similar treatment and 1-ethoxycarbonyl-3 (or 5)-hydroxymethylene-1-azacycloheptan-4-one (VIIIa or VIIIb)*, b. p. 127∼130°C/0.7 mmHg was obtained in 72.5% yield as a colorless oil. Reaction of hydrazine hydrate with VIII in ether gave a stable pyrazole derivative (Xa or Xb), b. p. 183∼185°C/0.3 mmHg in 87.6% yield. X was also derived from VIII cyclic semicarbazone (IXa or IXb), m. p. 159∼159.5°C by hydrolysis. X afforded a picrate of m. p. 136.5∼137.5°C and a chloroplatinate of m. p. 184°C (decomp.) respectively. Deethoxycarbonylation of X by hydrogen bromide in glacial acetic acid gave hydrobromide of XIa or XIb in 84% yield as hygroscopic colorless long prisms which softened at above 260°C. Free base, XIa or XIb, was liberated almost quantitatively from the hydrobromide with alkali as hygroscopic, colorless hexagonal prisms of m. p. 155.5∼156.5°C. XI formed a picrate of m. p. 220∼221°C (decomp.), which was unstable to light and turned brown on standing.

As a preliminary examination of dehydrogenation 4, 5-cyclohepteno-7-methylthiazole (XIV), b. p. 109∼111°C/15 mmHg which was prepared from cycloheptanone** (XII) by NBS bromination and condensation with thioacetamide was subjected to the dehydrogenation



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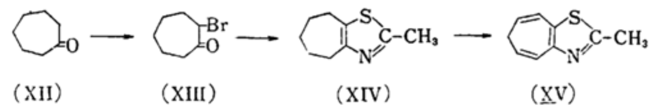
5) B. D. Astill and V. Beokelheide, *J. Am. Chem. Soc.*, 77, 4079 (1955).

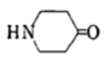
6) (a) A. Yokoo and S. Morosawa, This Bulletin, 29, 631 (1956); (b) S. Morosawa, ibid., 31, 418 (1958).

* Degradative studies will be reported later.

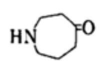
** The author wishes to thank Professor Tetsuo Nozoe (Tohoku University) for donating the sample.



(XII) (XIII) (XIV) (XV)



(XVI)



(XVII)

with 10% palladium on carbon at elevated temperature. Thus 4,5-cycloheptatrieno-7-methylthiazole (XV) was obtained as a colorless oil, b. p. 104°C/12 mmHg, XV gave a picrate of m. p. 147∼148°C. XI, however, was decomposed under the same condition with evolution of hydrogen. Ultraviolet absorption spectra of XI, XIV and XV are given in Fig. 1, together with that of the condensation product of XIV ethiodide with *p*-dimethylaminobenzaldehyde.

It appeared of interest to obtain a unique product in the formation of the hydroxymethylene compound (VIII) from the asymmetrical ring ketone (VII). The structure of the pyrazole derivative (XI) was estimated by the following spectral studies. It has already been recognized[7] that the band arising from the hydrogen bending vibrations of methylene appeared near the 1450 cm$^{-1}$ region and shifted in some degree higher when attached to the nitrogen atom and somewhat lower to carbon-carbon or carbon-oxygen double bond. As shown in Fig. 2, 1-azacyclohexane-4-one (XVI)[8],* gave rise to only two bands near the region at 1469 and 1428 cm$^{-1}$, presumably arising from 2 (or 6)- and 3 (or 5)-methylene of the ring respectively. 1-Azacycloheptan-4-one (XVII)**, on the other hand, indicated at least three bands at 1464, 1452 and 1431 cm$^{-1}$, probably due to 2 (or 7)-, 6- and 3 (or 5)-methylene respectively. Hydrochlorides of XVI and XVII also gave rise to two and three bands respectively, corresponding to the above absorption bands. XV was expected to show two bands near the region arising from methyl*** at 2-position of the thiazole ring and methylene in the seven-membered ring, and in fact two bands at 1457 and 1437 cm$^{-1}$ were observed. From a consideration of these facts it became clear that the methylenes in the nitrogen containing ring ketone were distinguishable from each other in the infrared

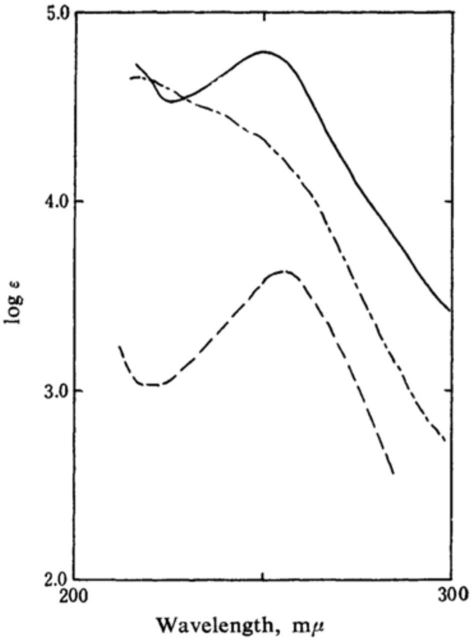


Fig. 1. (in methanol)

—— XI, – – – XIV, – · – · – XV

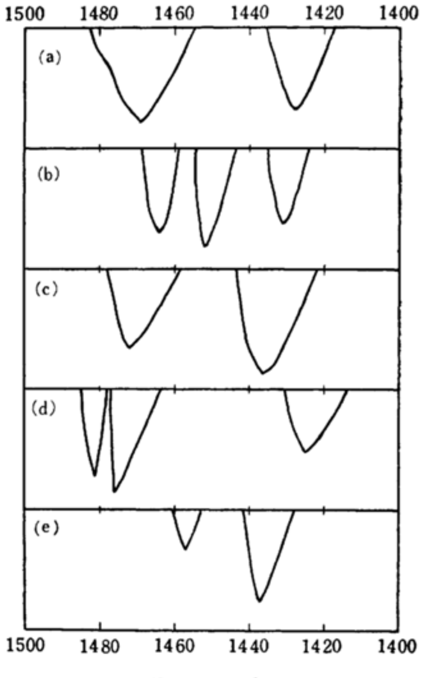


Fig. 2.

(a) XVI; (b) XVII; (c) XVI hydrochloride; (d) XVII hydrochloride; (e) XV

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7) L. J. Bellamy, "The Infra-red Spectra of Complex Molecules", Methuen & Co. Ltd., London (1958), p. 20.

8) E. Königs and L. Neumann, *Ber.*, **48**, 956 (1915).

* Prepared from 1-benzyl-1-azacyclohexan-4-one[6b] by catalytic reduction in the presence of palladous oxide, b. p. 56∼57°C/6 mmHg. It began to polymerize into a white solid within an hour after distillation.

** Liberated by potassium carbonate from its hydrochloride[6a], b. p. 95∼96°C/15 mmHg.

*** According to Bellamy[7], the band arising from the methyl group adjacent to the carbon atom appeared near 1450 cm$^{-1}$ in relatively low intensity.

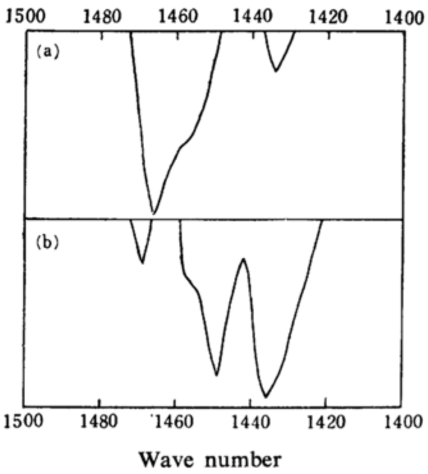

Fig. 3.

(a) XI; (b) XI hydrobromide

absorption spectra. The pyrazole derivative (XI) indicated, as seen in Fig. 3, three bands at 1466, 1458 (shoulder) and 1434 cm$^{-1}$. It may be assumed that the former band is due to 6-methylene and the latter to 8, the shoulder being due to overlapping of bands arising from 4- and 7-methylene. Hydrobromide of XI distinctly showed three principal bands at 1469, 1449 and 1436 cm$^{-1}$ together with a shoulder at 1456 cm$^{-1}$ which probably arose from 4-methylene. From these spectral data it may be concluded that XI has an angular form (XIa) rather than a linear one (XIb) and therefore the hydroxymethylene compound is in the form of VIIIa.

## Experimental

**1-Ethoxycarbony-1-azacycloheptan-4-one (VII).**—A solution of 15 g. of V hydrochloride[6a,b] in 200 cc. of water was shaken with hydrogen in the presence of 0.2 g. of palladous oxide under normal temperature and pressure. After the theoretical amount of hydrogen was consumed the catalyst was filtered off and evaporated to a smaller volume under reduced pressure. To this were added a solution of 2.7 g. of sodium hydroxide in 5 cc. of water and 14.7 g. of anhydrous potassium carbonate. The mixture was kept at 10°C and 15 g. of ethyl chlorocarbonate was added dropwise during 45 minutes with stirring, followed by further stirring for 1 hour at the same temperature. Precipitates were collected and washed well with ether, and the filtrate was thoroughly extracted with ether. The water layer was evaporated under reduced pressure until precipitation began and treated as before. The ethereal solutions were combined and dried over anhydrous potassium carbonate. Evaporation of ether and vacuum distillation gave 11. 5 g. (99.1%) of a colorless oil, b. p. 117°C/1 mmHg The oil was fairly soluble in water and did not give a bisulfite addition compound.

Found: N, 7.66. Calcd. for $C_9H_{15}O_3N$: N, 7.56%.

**1-Ethoxycarbonyl-3(or 5)-hydroxymethylene-1-azacycloheptan-4-one (VIIIa or VIIIb).**—A solution of 6 g. of VII and 9.5 g. of ethyl formate in 50 cc. of dry benzene was added with swirling to an ice cold suspension of crushed methanol-free sodium methoxide[9] (from 1.6 g. of sodium) in 50 cc. of dry benzene, and the whole was evacuated and filled with nitrogen. After the mixture had been allowed to stand at room temperature for 3 hours, it was boiled under gentle reflux for 1 hour. After cooling, 10 cc. of water was added and the aqueous layer was separated. The benzene solution was washed twice with 10% sodium hydroxide solution. The combined water layer was washed with ether and adjusted to pH 3.4 by adding hydrochloric acid. A reddish orange oil deposited was extracted three times with benzene. The acidic water layer was evaporated to a smaller volume under reduced pressure and nitrogen atmosphere and extracted with benzene. The benzene extracts were united, washed three times with small portions of saturated sodium chloride solution and dried over anhydrous magnesium sulfate. Evaporation of benzene and vacuum distillation of the residue under nitrogen gave 5 g. of a colorless oil, b.p. 127~130°C/0.7 mmHg in 72.5% yield. It gave a deep purple coloration with ferric chloride solution.

Found: N, 6.80. Calcd. for $C_{10}H_{15}O_4N$: N, 67.5%.

**2, 4-Dinitrophenylhydrazone,** orange prisms, m.p. 172°C (from methanol).

Found: N, 19.24. Calcd. for $C_{15}H_{19}O_6N_5$: N, 19.17%.

**VIII Cyclic Semicarbazone (IXa or IXb).**—A solution of 2.2 g. of VIII in 9 cc. of glacial acetic acid was added to a separately prepared solution of 1.7 g. of semicarbazide hydrochloride and 1.7 g. of anhydrous sodium acetate in as small an amount of water as possible. After the mixture was allowed to stand for a few days with 1 cc. of concentrated sulfuric acid, 50 cc. of water was added to deposit gradually 1.0 g. of cyclic semicarbazone in colorless needles, m. p. 155°C. Recrystallization from ethanol raised the m. p. to 159~159.5°C.

Found: N, 22.16. Calcd. for $C_{11}H_{16}O_3N_4$: N, 22.21%.

**5(or 6)-Ethoxycarbonyl-1, 2, 5(or 1, 2, 6)-triazazulene (Xa or Xb).**—(a) To a solution of 5 g. of VIII in 50 cc. of ether was added dropwise under stirring and ice-water cooling 1.2 g. of hydrazine hydrate (100%), followed by an additional stirring for 1 hour. After decantation of the ethereal solution, a large excess of anhydrous potassium carbonate was added to the viscous water layer in order to remove the water completely. Ether was added, agitated well and decanted repeatedly. The combined ethereal solution was dried over anhydrous potassium carbonate and the ether was removed by distillation. Vacuum distillation of the residue gave 4.3 g. of a colorless viscous oil, b. p. 183~185°C/0.3 mmHg in 87.6% yield.

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[9] W. S. Johnson and H. Posvic, *J. Am. Chem. Soc.*, **69**, 1361 (1947).

Found: N, 20.15. Calcd. for $C_{10}H_{15}N_2O_3$: N, 20.08%.

A **picrate** derived from the above oil showed, after several recrystallizations from ethanol, m. p. 136.5~137.5°C with sintering at about 80°C.

Found: N, 17.53. Calcd. for $C_{10}H_{15}O_2N_3 \cdot C_6H_3O_7N_3 \cdot C_2H_6O$: N, 17.35%.

After drying at 100°C for 1 hour the nitrogen content varied to 19.38%. (Calcd. for $C_{10}H_{15}O_2N_3 \cdot C_6H_3O_7N_3$: N, 19.17%).

The oil also afforded a cream yellow **chloroplatinate,** m. p. 184°C (decomp.) (from aqueous ethanol containing 1 drop of concentrated hydrochloric acid).

Found: N, 10.50. Calcd. for $(C_{10}H_{15}O_2N_3)_2 \cdot H_2PtCl_6$: N, 10.14%.

(b) A mixture of 1.35 g. of IX, 1.7 cc. of concentrated sulfuric acid and 5.1 cc. of water was heated under reflux for 15 minutes. After cooling it was made alkaline by adding aqueous ammonia, extracted with benzene and dried over anhydrous potassium carbonate. Benzene was removed and the residue was distilled in vacuo to give 1.0 g. of colorless viscous oil, b.p. 201°C/0.7 mmHg in 89.3% yield. (Found: N, 19.79%). The **picrate** formed was not depressed on admixture with that described above, m. p. and mixed m. p. 137°C. (Found: N, 17.61%).

**Hexahydro-1, 2, 5 (or 1, 2, 6)-triazazulene (XIa or XIb).**—A solution of 1.5 g. of X in 15 cc. of glacial acetic acid was saturated with dry hydrogen bromide under ice-water cooling. After standing overnight at room temperature, the solution was heated slowly to 90°C and kept for 2 hours at the same temperature, followed by refluxing for 1 hour. The hydrobromide deposited during the refluxing was separated by decantation, washed twice with a small amount of ethanol and recrystallized from methanol and ether to yield 1.4 g. of hygroscopic, colorless long prisms, which softened at above 260°C, and the second crop of the crystal, 0.4 g. was obtained from the filtrate. The total yield was 84%.

Found: N, 13.83. Calcd. for $C_7H_{11}N_3 \cdot 2HBr$: N, 14.05%.

To a solution of 7.5 g. of the hydrobromide in a small amount of water anhydrous potassium carbonate was added to make it sufficiently alkaline and the mixture was evaporated to dryness under reduced pressure. The residual mass was dried in a desiccator and extracted in the Soxhlet apparatus with isopropyl ether for 15 hours to give 3.4 g. of somewhat hygroscopic, hexagonal **free base,** m. p. 155.5~156.5°C in 99% yield. An analytical specimen was recrystallized from benzene and ethanol.

Found: C, 61.40; H, 8.22; N, 30.75. Calcd. for $C_7H_{11}N_3$: C, 61.29; H, 8.08; N, 30.63%.

The free base and a saturated ethanolic solution of picric acid formed a picrate, which was recrystallized from ethanol to yellow rhombo prisms, m. p. 220~221°C (decomp.). These gradually turned brown on standing.

Found: N, 23.04. Calcd. for $C_7H_{11}N_3 \cdot C_6H_3O_7N_3$: N, 22.94%.

**NBS Bromination of Cycloheptanone.**—A mixture of 12.4 g. of cycloheptanone (b. p. 174~181°C), 25 g. of NBS and 1.5 g. of benzoyl peroxide in 600 cc. of carbon tetrachloride was boiled under reflux for 5 hours on a water bath. Initially the mixture was gradually colored, and reaction suddenly started to make it colorless with the evolution of much hydrogen bromide. After cooling in ice-water succinimide was separated, and the filtrate was washed with 50 cc. of 40% potassium carbonate solution and with 10 cc. of water and finally dried over anhydrous potassium carbonate. The solvent was removed and the residue was distilled in vacuo to yield 11 g. of 2-bromocycloheptanone (XIII) as a colorless oil, b. p. 90~130°C/5 mmHg. This was fractionated into three parts, b. p. 90~101°C/5 mmHg, 101~111°C/5 mmHg and 111~128°C/5 mmHg. These, however, gave the same thiazole derivative as described below.

**Condensation of XIII with Thioacetamide.**—A solution of 11 g. of XIII and 6 g. of thioacetamide in 20 cc. of ethanol was refluxed on a water bath for 5 hours. After removing ethanol and heating the residue for 5 hours in an oil bath kept at 160°C, 40 cc. of 4 N hydrochloric acid was added and extracted three times with each 20 cc. portion of ether. The combined ethereal solution was washed with 10 cc. of 4N hydrochloric acid. Acidic solutions were united, made alkaline by adding anhydrous potassium carbonate and 5 cc. of 5N sodium hydroxide solution, and extracted three times with each 20 cc. portion of ether. After drying over anhydrous potassium carbonate, the ether was expelled and the residue was distilled in vacuo to yield 1.4 g. of **4, 5-cyclohepteno-2-methylthiazole** (XIV) as a colorless oil, b. p. 109~111°C/15 mmHg.

Found: N, 8.06. Calcd. for $C_9H_{13}NS$: N, 8.38%.

Ethanolic solution of XIV was boiled with an excessive picric acid to form a **picrate,** which was recrystallized three times from ethanol to yellow crystals, m. p. 129~131°C.

Found: N, 13.84. Calcd. for $C_9H_{13}NS \cdot C_6H_3O_7N_3$: N, 14.15%.

**Ethiodide** of XIV was obtained as an oily substance by refluxing an ethanolic solution of 0.2 g. of XIV with an excessive ethyl iodide for 8 hours, followed by the addition of ether. This, however, gave a crystalline condensation product assumed to be **4, 5-cyclohepteno-2-(*p*-dimethylaminostyryl)-3-ethylthiazolium iodide** by refluxing with *p*-dimethylaminobenzaldehyde for 8 hours in the presence of a small amount of piperidine and adding ether. The condensation product was recrystallized from ethanol to afford 50 mg. of red crystals, m. p. 219~220°C (decomp.).

Found: N, 5.88. Calcd. for $C_{20}H_{27}N_2SI$: N, 6.17%.

The red crystals showed absorption maximum at 480 m$\mu$.

**Dehydrogenation of XIV.**—In a 25 cc. hard ground glass flask jointed with an air condenser, the top of which was connected to a measuring bottle, were placed 1.5 g. of XIV, 1.5 g. of 10% palladium on carbon and 1 g. of roughly crushed boiling stone, and heated in an electric oven. Hydrogen began to evolve when the temperature of the oven indicated about 390°C. About 450 cc. of hydrogen had been collected after heating for 6 hours at 440~460°C. The reaction mixture was first washed out with hot benzene and then with ether. After drying the combined organic solution over anhydrous magnesium sulfate, the solvent was removed and the residue was distilled in vacuo to yield 0.7 g. of **4, 5-cycloheptatrieno-2-methylthiazole** (XV) as a colorless liquid, b. p. 104°C/12 mmHg.

Found: C, 65.95; H, 5.66; N, 8.70. Calcd. for $C_9H_9NS$: C, 66. 24; H, 5.56; N, 8.58%.

A **picrate** derived from the liquid was recrystallized three times from ethanol in yellow crystals, m. p. 147~148°C.

Found: N, 14.50. Calcd. for $C_9H_9NS \cdot C_6H_3O_7N_3$: N, 14.27%.

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