formed in the reaction mixture was filtered by suction. Recrystallization from MeOH gave 0.3 g. of deep red needles, m.p. >320°. *Anal.* Calcd. for $C_{19}H_{13}O_6N_5$: N, 17.80. Found : N, 17.90.

1-[2-(5-Nitro)furylacryloyl]-2-isonicotinoylhydrazine (XXII)—A solution of 0.55 g. of isonicotinic acid hydrazide (m.p. 178°) and 0.75 g. of 2-(5-nitro)furylacryloyl chloride (m.p. 92~94°) in 5 cc. of pyridine was gently heated on a water bath for 30 mins. After cooling to the room temperature, the reaction mixture was poured into ice water, the pale yellow mass that formed from the reaction mixture was filtered by suction, and washed with cold water. Recrystallization from hydrous pyridine or dilution of MeOH solution with some water gave 0.4 g. of light yellow crystals, m.p. 218° (decomp.). *Anal.* Calcd. for $C_{13}H_{10}O_5N_4$: N, 17.98. Found : 17.46.

Summary

Twenty-two new nitrofuran derivatives were prepared by the condensation of 2-(5-nitro)furfural and 1-(5-nitro)furylacrolein with hydrazides. Among these compounds, 1-[2-(5-nitro)furylacrylidene]-2-isonicotinoylhydrazine (XIII) showed an excellent bacteriostatic activity for *Mycobacterium tuberculosis*.

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38. **Tyunosin Ukita, Makoto Miyazaki, and Hiroshi Watanabe** : Studies on Azulenes. II.[1] Synthesis of Polybromoazulenes.

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Besides the various alkylazulenes obtainable by dehydrogenation of naturally occurring or synthetic azulenogenes, the recent progress on electrophilic substitution reactions of azulene ring offered a great possibility for synthesizing new azulenes substituted with different kinds of radicals such as acetyl, halogen, nitro, and amino groups.[2,5] However, the electrophilic substitution of the azulene ring is limited to its 1- or 3-position, and 1,3-derivatives are the only disubstituted azulenes synthesized by this procedure.

This paper describes the synthesis and properties of three new polybromoazulenes which were obtained by a new synthetic route involving no dehydrogenation reaction in the stages.

Some years before, the occurrence of one oily and three crystalline bromoazulenes was reported by Anderson, *et al.*[3] These products were separated from a mixture obtained by the dehydrobromination of reaction product from 1,2,3,4,5,6-hexahydroazulene and N-bromosuccinimide, but because of insufficient amounts of the yield, they failed to give properties of these new derivatives.

Independent of the above authors, the present writers attempted the preparation of some bromoazulenes by the bromination of 1,2,3,4,5,6,7,8-octahydroazulene with N-bromosuccinimide and by subsequent dehydrobromination with pyridine.

The starting material 1,2,3,4,5,6,7,8-octahydroazulene (I) was prepared by the Wolff-Kishner or the Clemmensen-Martin reduction of 4-oxo-1,2,3,4,5,6,7,8-octahydroazulene which is obtainable by Hückel and Schnitzspahn's method.[4] (I) was treated

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[1] Part I : T. Ukita, H. Watanabe, M. Miyazaki : J. Am. Chem. Soc., **76**, 4584 (1954).

[2] A. G. Anderson, Jr., J. A. Nelson : *Ibid.*, **72**, 3824 (1950).

[3] *Ibid.*, **73**, 232 (1951).

[4] W. Hückel, L. Schnitzspahn : Ann., **505**, 274 (1933); see also Footnote 3.

with N-bromosuccinimide and the product was triturated with pyridine to furnish a mixture of bromoazulenes. The product was separated by chromatography over alumina. The effluent from the development of the chromatogram with petroleum ether was separated into two fractions (A and B).

The faster moving fraction (A) was treated with ethanol to separate into the ethanol-soluble and ethanol-sparingly soluble parts. On addition of trinitrobenzene, the former gave a trinitrobenzene (TNB) complex (m.p. 138~139°) of a bromoazulene, and the bromoazulene isolated from the complex salt was confirmed to be a dibromoazulene (II) with m.p. 76~78° and m.p. 88~89° (dimorph).

The crystals sparingly soluble in ethanol were combined with the filtrate of the TNB-complex and fractionated over an alumina column. The effluent was taken to make four fractions successively and the bromoazulenes isolated from each fraction were found to differ from each other. These four bromoazulenes were tetrabromoazulene (III), m.p. 247°, dibromoazulene (II), m.p. 88~89°, monobromoazulene (IV) (TNB-complex, m.p. 134~136°), and tribromoazulene (V), m.p. 113~114°, in the order of fractions from which they were isolated.

Fraction B, on removal of the solvent, gave another crystalline tetrabromoazulene (VI), m.p. 158~160°, which showed a marked depression on admixture with (III). Neither tribromoazulene nor tetrabromoazulenes (III and VI) gave complex salt with trinitrobenzene.

The absorption spectra in the ultraviolet and visible regions for the bromoazulenes are given in Figs. 1~4.

From the melting points of the two allotropic forms and the data in the absorption spectra, together with the properties of its TNB-complex, the dibromoazulene (II) must

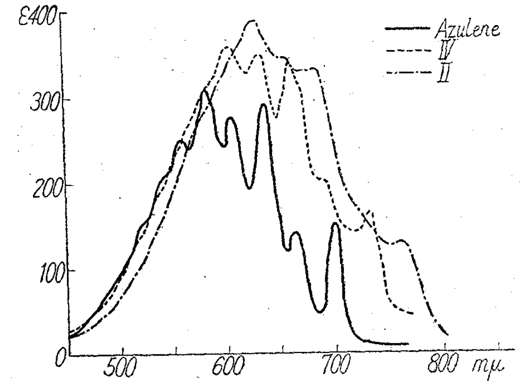


Fig. 1.

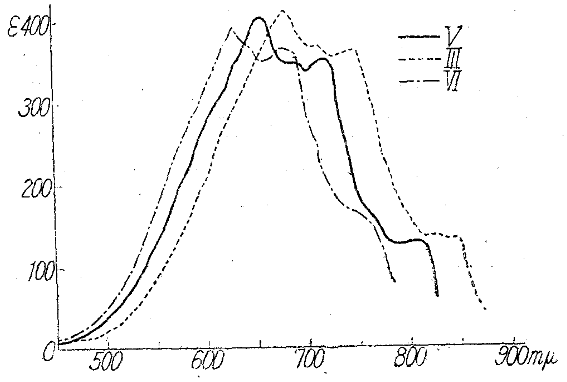


Fig. 2.

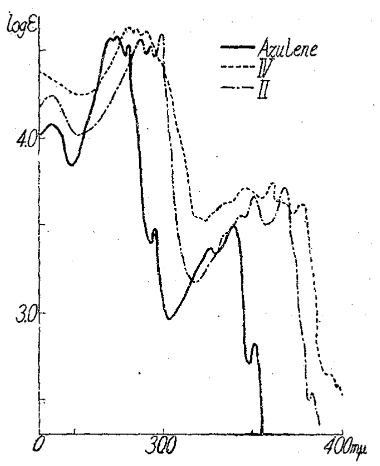


Fig. 3.

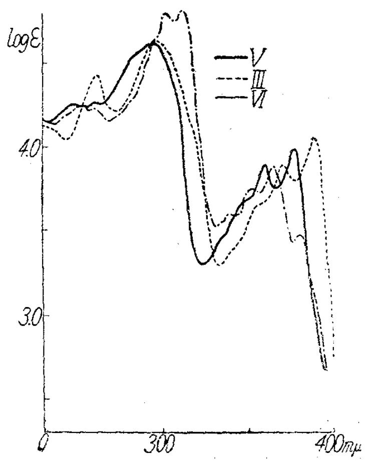


Fig. 4.

be the same compound as 1,3-dibromoazulene reported by Anderson *et al.*[5]

A melting point of 105°(decomp.) was reported by Anderson *et al.*[3] for the TNB-complex of 1-bromoazulene, but the facts that the data obtained in the absorption spectrum of (IV) was practically the same as that of Anderson's 1-bromoazulene and that a considerable amount of 1,3-dibromoazulene was isolated from the same reaction mixture cannot exclude the possibility for the identity of monobromoazulene (IV) with 1-bromoazulene.

In order to confirm the identity, 1-bromoazulene was synthesized according to the method reported by Anderson *et al.*[5] and it was found that the only monobromoazulene obtained by this method gave a TNB-complex with m.p. 134~136°, after repeated recrystallization from ethanol. A mixed fusion of this TNB-complex with that of monobromoazulene (IV) showed no depression of the melting point, and further, a small amount of 1,3-dibromoazulene was also isolated from the reaction mixture.

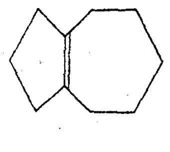
The bromoazulene obtained in the present experiments should result from repeated bromination and subsequent dehydrobromination which occurred in some of the methylene groups activated by the double bond in the starting compound (I).

There are no conclusive evidences as to the substituted positions of the bromine atom in the azulene ring of the tribromoazulene (V) and two tetrabromoazulenes (III and VI), but in the visible spectra of these bromoazulenes, especially in 1-bromo- and 1,3-dibromoazulenes, a regular increasing shift of the maximal absorption, 25 mμ each to a longer wave length, is observed for each additional substitution of bromine on the odd-numbered position of the azulene ring. This tendency is very similar to the results found by Plattner[6] that substitutions of alkyl groups in the odd-numbered positions cause a shift toward longer wave lengths and substitutions of alkyl groups on even-numbered positions, a shift toward shorter wave lengths in the spectra.

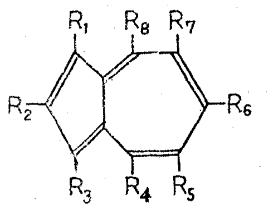
These shifts must result by changes in the electron distributions of the azulene ring by the groups substituted and the directions of the shifts should depend on the nature and positions of the substituted groups.

As both *ortho-para* directing alkyl and halogen groups are reported to cause a similar effect on absorption spectra when substituted in the benzene ring,[7] it is not unlikely that they also cause a parallel shift in the spectra when substituted in the corresponding positions of the azulene ring.

From the fact that the maximal absorption of 1,3-dibromoazulene (628 mμ), tribromoazulene (V) (656 mμ), and tetrabromoazulene (III) (680 mμ) show a regular increasing shift of the maximal absorption towards longer wave lengths by each additional substitution of bromine, and together with the above assumptions, it is very probable



(I)



(IV) $R_1=Br$, $R_2\sim R_8=H$
(II) $R_1, R_3=Br$, $R_2, R_4\sim R_8=H$
(V) $R_1, R_3, R_5=Br$, $R_2, R_4, R_6\sim R_8=H$
(III) $R_1, R_3, R_5, R_7=Br$, $R_2, R_4, R_6, R_8=H$
(VI) $R_1, R_3, R_5, R_6=Br$, $R_2, R_4, R_7, R_8=H$
or $R_1, R_2, R_3, R_5=Br$, $R_4, R_6, R_7, R_8=H$

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5) A. G. Anderson, Jr., J. A. Nelson, J. Tazuma: J. Am. Chem. Soc., **75**, 4980(1953).
6) M. Gordon: Chem. Revs., **50**, 127(1951).
7) L. Doud, J. M. Vandenbelt.: J. Am. Chem. Soc., **69**, 2714(1947).

that in the molecules of bromoazulenes (V and III), all bromine groups are substituted in the odd-numbered positions of the azulene ring (Table I).

TABLE I.

Compound	Max. absorption in visible spectra	
	ε	λ(mμ)
Azulene	307	580
1-Bromoazulene (IV)	362	605
1,3-Dibromoazulene (II)	388	628
Tribromoazulene (V)	403	656
Tetrabromoazulene (III)	413	680
Tetrabromoazulene (VI)	391	628

Then, the structure of tetrabromoazulene (III) must be 1,3,5,7-substituted bromoazulene, because there are only four odd-numbered positions in the azulene ring.

As 1-bromo- and 1,3-dibromoazulenes are the only mono- and disubstituted azulenes isolated from the reaction mixture, one of the positions 1 and 3 is very likely to have preferentially been brominated during the reaction. The tribromoazulene (V) which contains all bromine groups on the odd-numbered positions should, therefore, have a structure of 1,3,5- (or 1,3,7-)-tribromoazulene.

In the case of another tetrabromoazulene (VI), which gives a maximal absorption at 628 mμ, the same wave length as that of dibromoazulene (II), the three of the four bromine atoms should be substituted in the odd-numbered and the remaining one in the even-numbered position. The tentative and most probable structure for (VI) is 1,2,3,5- (or 1,2,3,7-) or 1,3,6,7- (or 1,3,5,6-)-tetrabromoazulene. The structure of (VI) would also be supported by the above assumption that 1- and 3-positions are the commonly substituted positions for these polybromoazulenes and further by the reason that a simultaneous substitution of bromine atoms in 1,8 or 3,4 is difficult by structural hindrances of the azulene molecule.

The authors are indebted to Prof. S. Akiya for his encouragement, and wish to thank Misses R. Ohta and E. Kondo, and Mr. B. Kurihara for carrying out the microanalyses. A part of the expenses for the present study was defrayed by grants from both the Ministry of Education and the Ministry of Agriculture and Forestry.

Experimental

1,2,3,4,5,6,7,8-Octahydroazulene (I)—3.0 g. of 4-oxo-1,2,3,4,5,6,7,8-octahydroazulene, 4.5 g. of semicarbazide hydrochloride, and 4.5 g. of AcONa were dissolved in 30 cc. EtOH, and the solution was boiled for 1 hr. After removal of the solvent from the reaction mixture, 5.0 g. of KOH was added, and the mixture was heated in a Claisen flask at 240° in an oil bath. The distillate was taken up in ether and the solution was dried. An oily residue obtained, after removal of the ether, gave colorless oil with $b.p_{11}$ 66~67°; yield, 1.0 g. (37%). The same compound was obtained by the Clemmensen-Martin reduction in a yield of 60%.

Bromination of 1,2,3,4,5,6,7,8-Octahydroazulene—1.0 g. of 1,2,3,4,5,6,7,8-octahydroazulene and 6.3 g. of N-bromosuccinimide were dissolved in 30 g. CCl_4, and the mixture was boiled for 1.75 hrs. After cooling, the reaction mixture was filtered, the filtrate was washed successively with thiosulfate solution and water, and dried. The solvent was removed and to the residue 30 cc. dry pyridine was added. The solution was heated for 2 hrs. at 100°, the cooled reaction mixture was acidified, and extracted 6 times with petr. ether containing a small amount of EtOH. From a deep greenish blue-colored extract, the solvent was removed after drying over $CaCl_2$. A blue oil obtained on evaporation of the solvent was adsorbed on the top of a column (1×10 cm.) prepared with activated alumina and eluted with petroleum ether. 108 cc. of the effluent, colored deep greenish blue, was collected. After removal of the solvent, 470 mg. of blue oily mixture of bromoazulenes was obtained.

Separation of bromoazulenes—900 mg. of the above mixture of bromoazulenes was adsorbed on the top of an activated alumina column (2.5×30 cm.) and developed with petroleum ether. The first effluent of 210 cc. (Fraction A) and the second one of 80 cc. (Fraction B) were taken. Fraction A gave 490 mg. of a crude bromoazulene after removal of the solvent. This crude product contained a small amount of crystals with m.p. 224~240° which were separated from the main oily portion.

1,3-Dibromoazulene (II)—To EtOH solution of the oil was added 0.1 g. of trinitrobenzene (TNB) to furnish black violet needles which were filtered and recrystallized from EtOH to a TNB-complex, m.p. 138~139°. *Anal.* Calcd. for $C_{10}H_6Br_2 \cdot C_6H_3O_6N_3$: C, 38.50; H, 1.82; N, 8.42; Br, 32,04. Found: C, 38.30; H, 1.69; N, 8.08; Br, 32.25.

The dibromoazulene was separated from the TNB-complex by passing its petr. ether solution through an alumina column and removal of the solvent. The green needles thus obtained, on microscopic determination of the melting point, changed to blue needles at 52~53° and melted at 76~78°. Then the melt solidified to blue platelets which showed another melting point 88~89° on further heating. The ultraviolet and visible spectra are given in Figs. 1 and 3.*

The crystals (m.p. 224~240°) separated from the residue after evaporation of the solvent from Fraction A was combined with the mother liquor of above TNB-complex, the mixture was put on the top of an activated alumina column (2.5×25 cm.), and developed with petr. ether. The following four effluents a, b, c, and d were taken successively.

Tetrabromoazulene (III)—The faint bluish green effluent (a), on removal of the solvent, gave ca. 20 mg. of fine green needles. This was recrystallized from benzene to fine green needles, m.p. 247°. *Anal.* Calcd. for $C_{10}H_4Br_4$: C, 27.06; H, 0.91. Found : C, 26.96; H, 1.20.

The ultraviolet and visible spectra are given in Figs. 2 and 4.

The blue-colored fraction (b), after concentration of the solution, gave no crystals but gave a TNB-complex which was recrystallized from EtOH to a deep violet needles, m.p. 138~139°. A mixed fusion of these crystals with 1,3-dibromoazulene obtained above showed no depression of the melting point. The total yield of 1,3-dibromoazulene, 90 mg.

Monobromoazulene (IV)—The faint blue fraction (c), after removal of the solvent, gave a blue oil mixed with green crystals. The crystals were separated from the oily product by filtration. A TNB-complex obtained by the addition of trinitrobenzene to the filtrate was recrystallized several times from EtOH to a few mgs. of brown needles, m.p. 134~136°. *Anal.* Calcd. for $C_{10}H_7Br \cdot C_6H_3O_6N_3$: N, 10.00. Found : N, 10.63.

The ultraviolet and visible spectra are given in Figs. 1 and 3.

1-Monobromoazulene—To 6.6 mg. of azulene dissolved in 0.65 cc. of benzene, 9.4 mg. of N-bromosuccinimide was added and the solution was heated at 90° for 15 mins. After filtration of succinimide, the solvent was removed and the residual product was fractionated over an alumina column with petr. ether to separate 9.1 mg. of deep greenish blue oil. A TNB-complex obtained from this oil was recrystallized from EtOH to brown needles, m.p. 134~136°; yield, 5.5 mg. A mixed fusion of this complex with that of monobromoazulene (IV) showed no depression of the melting point.

From the filtrate of the TNB-complex of 1-monobromoazulene, another complex, m.p. 138~139°, was isolated which was identified as the TNB-complex of 1,3-dibromoazulene.

Tribromoazulene (V)—The blue-colored fraction (d) gave crystals after removal of the solvent. On recrystallization from petr. ether 300 mg. of green needles, m.p. 113~114°, was obtained. This bromoazulene does not give TNB-complex by the usual method. *Anal.* Calcd. for $C_{10}H_5Br_3$: C, 32.91; H, 1.38; Br, 65.73. Found : C, 33.03; H, 1.57; Br, 65.92.

The ultraviolet and visible spectra are given in Figs. 2 and 4.

Tetrabromoazulene (VI)—The fraction (B) colored deep bluish green. On evaporation of the solvent, 110 mg. of green needles, m.p. 158~160°, were obtained, which also gave no TNB-complex. *Anal.* Calcd. for $C_{10}H_4Br_4$: C, 27.06; H, 0.91; Br, 72.05. Found : C, 26.92; H, 1.07; Br, 71.66.

The ultraviolet and visible spectra are given in Figs. 2 and 4.

Summary

One tribromo- (V) and two tetrabromo-azulenes (III and VI), together with 1-bromo- (IV) and 1,3-dibromoazulenes (II), were isolated from a reaction mixture obtained by the bromination and subsequent dehydrobromination of 1,2,3,4,5,6,7,8-octahydroazulene. The probable structures for the new polybromoazulenes (V, III, and VI) were proposed as 1,3,5 (or 1,3,7)-tri-, 1,3,5,7-tetra- and 1,2,3,5- or 1,3,5,6-tetrabromoazulenes.

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* All the ultraviolet and visible spectra were taken in EtOH and ligroine solutions of the compounds, respectively.