UDC 547.913.5

27. **Makoto Miyazaki,**[*1] **Mieko Hashi,**[*1] **and Tyunosin Ukita**[*2] : Studies on Azulenes. IX.[*3] 3-(1-Hydroxyethyl)-S-guaiazulene.

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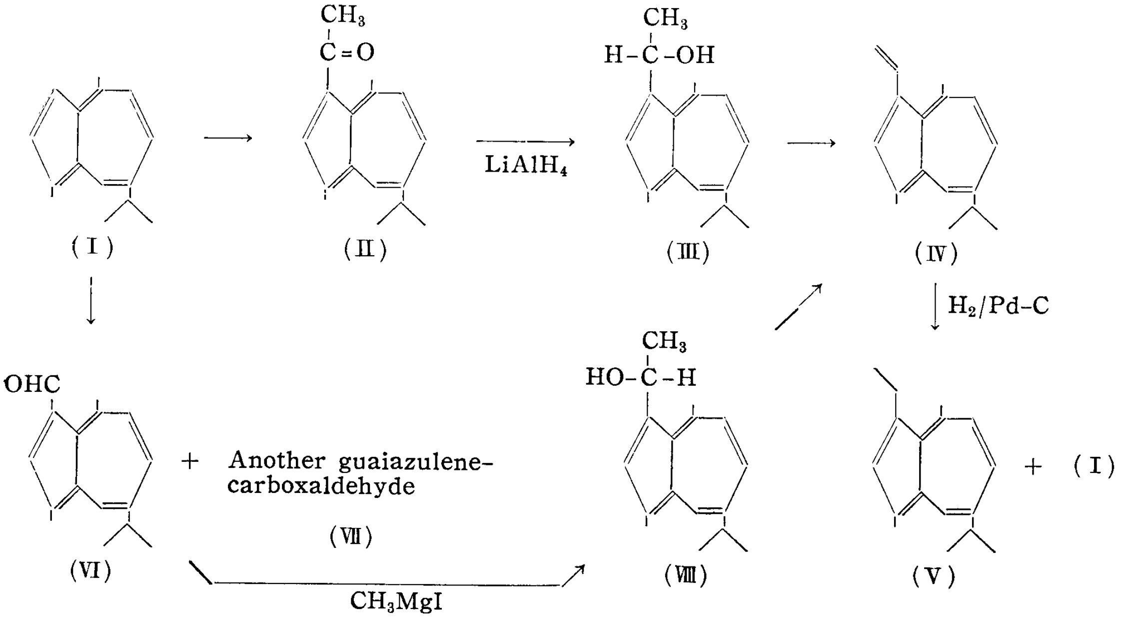
Recently, Reid, *et al.*1) reported that an attempt at the reduction of 3-acetyl-S-guaiazulene (II) with lithium aluminum hydride to 3-(1-hydroxyethyl)-S-guaiazulene (III) was unsuccessful and they assumed that such nucleophilic reagent should attack the azulene ring. In the present case, a similar reaction was successfully concluded to give the carbinol (III). This paper deals with the properties of the carbinol with its conversion to 3-ethyl-S-guaiazulene (V).



(II) was treated with lithium aluminum hydride in ether solution as usual and the reaction mixture was decomposed with saturated ammonium chloride solution. On removal of the solvent, the expected alcoholic product was obtained in 69% yield. It was purified by two recrystallizations from ligroine to form blue needles (III), $C_{17}H_{22}O$, m.p. 70~71°. The infrared spectrum of (III) showed the absorption band characteristic to OH group at 3344 cm^{-1} (in KBr). The spectra of (III) in the ultraviolet and visible regions are given in Figs. 1 and 2. This product was rather unstable to repeated recrystallization, giving a blue oily material (IV), from which a trinitrobenzene complex, $C_{23}H_{23}O_6N_3$, m.p. 99~100.5°, was obtained.

Catalytic hydrogenation of (IV) over palladium-carbon gave both S-guaiazulene (I) and a blue azulene (V), which formed a trinitrobenzene complex, $C_{23}H_{25}O_6N_3$, m.p. 141~142°. The ultraviolet and visible spectra of (V) are given in Figs. 1 and 2. The analysis of the trinitrobenzene complex suggested ethylguaiazulene for (V). As shown in Fig. 2 the maximum absorption band of (V) is at 632 mμ, showing a bathochromic shift by

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[*3] Part VIII : This Bulletin 5, 431(1957).

1) D. H. Reid, W. H. Stafford, W. L. Stafford : J. Chem. Soc., **1958**, 1118.

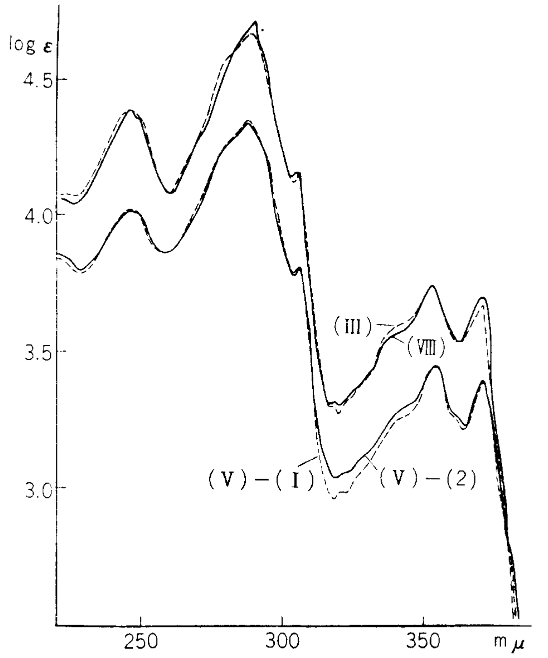

Fig. 1. Ultraviolet Absorption Spectra of Isomeric 3-(1-Hydroxyethyl)-S-guaiazulenes (III and VIII) and 3-Ethyl-S-guaiazulenes (V) (in EtOH)

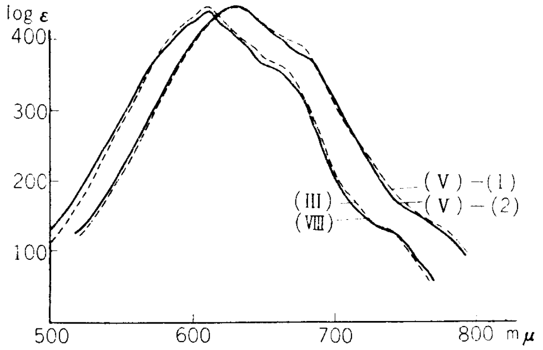

Fig. 2. Visible Absorption Spectra of Isomeric 3-(1-Hydroxyethyl)-S-guaiazulenes (III and VIII) and 3-Ethyl-S-guaiazulenes (V) (in ligroine)

(III) obtained from 3-acetylguaiazulene with $LiAlH_4$.
(VIII) obtained from S-guaiazulene-3-carboxaldehyde with CH_3MgI.
(V)-(1) obtained from (III) by dehydration and subsequent hydrogenation.
(V)-(2) obtained from (VIII) by dehydration and subsequent hydrogenation.

28 mμ from that of S-guaiazulene (I). This suggests that (V) involves an ethyl group at an odd-numbered position of (I). The series of reactions from (I) to (V) and comparison of the maximum absorpion of (V) with that of 3-methyl-S-guaiazulene[2] suggest the structure of 3-ethyl-S-guaiazulene[*4] for (V). Thus the final product (V) should be obtained by dehydration of (III) to 3-vinyl compound (IV) and its subsequent reduction.

(III) is so unstable that on gentle boiling in hexane, a gradual increase in the optical density at 620 mμ, absorption maximum characteristic for 3-isopropenyl-S-guaiazulene,[2] was observed, which is evidence of the dehydration of (III) to 3-vinyl-S-guaiazulene (IV). After boiling for 2 hours, when the optical density reached maximum at 620 mμ, the solution was reduced catalystically over palladium-carbon and from the reaction mixture, 3-ethyl-S-guaiazulene (V) was obtained in excellent yield.

[*4] Treibs[3] has reported that trinitrobenzene complex of 5-ethyl-S-guaiazulene melts at 147~148°. This ethyl-S-guaiazulene must be 3-ethyl-S-guaiazulene, as it was derived by Se-dehydrogenation of a derivative obtained from α-kessyl alcohol which has been confirmed to be 3-hydroxy-7,3a-epoxy-1,4-dimethyl-7-isopropyl-perhydrocyclopentenocycloheptene by Ukita.[4] Further, some discrepancy in melting point between his trinitrobenzene complex (147~148°) with that obtained here (141~142°) should be attributed to impurity of the former. It probably contained trinitrobenzene complex of some other azulene derivative.

2) T. Ukita, H. Watanabe, M. Miyazaki : J. Am. Chem. Soc., **76**, 4584(1954); Recently Treibs, *et al.*[5] reported that the maximum absorption of 3-methyl-S-guaiazulene in cyclohexane in visible region appeared at 622 mμ.

3) W. Treibs : Ann., **570**, 165(1950).

4) T. Ukita : Yakugaku Zasshi, **65**, 458(1945).

5) W. Treibs, A. Hiebsch, H. J. Neupert : Naturwissenschaften, **44**, 352(1957); W. Treibs, H. J. Neupert, J. Hiebsch : Chem. Ber., **92**, 141(1959).

Treibs, *et al.*,5) Hafner, *et al.*,6) and Reid, *et al.*1) have already found that azulenes were successfully formylated by the Vilsmeier or Gatterman reaction, introducing an aldehyde group at the 1- or 3-position at which electron density is the largest, and that the aldehyde group could be introduced by similar reaction in 1- or 3-position of several alkylated azulenes.

Independent of these works, report7) was made on the direct introduction of aldehyde group into S-guaiazulenemolecule (I) by the same type of Friedel-Crafts reaction, which gave two isomeric S-guaiazulene aldehydes (VI and VII).

These S-guaiazulene aldehydes were prepared by treatment of S-guaiazulene (I) with N-methylformanilide and phosphoryl chloride in *o*-dichlorobenzene. After completing the reaction, the mixture was hydrolysed with alkali and the product was purified through column chromatography over activated alumina, using a mixed solvent of ether and hexane. From the first eluting fraction, one of the S-guaiazulene aldehydes (VII), $C_{16}H_{18}O$, was obtained as red needles, m.p. 124.5~125.5°, in a poor yield. (VII) exhibited two absorption maxima (1642 and 2725 cm^{-1} in CCl_4) in infrared region, characteristic to aldehyde group, and gave trinitrobenzene complex of red needles, m.p. 86~87°, and oxime of violet plates, m.p. 155~156°. The spectra of (VII) in ultraviolet and visible regions are given in Figs. 3 and 4.

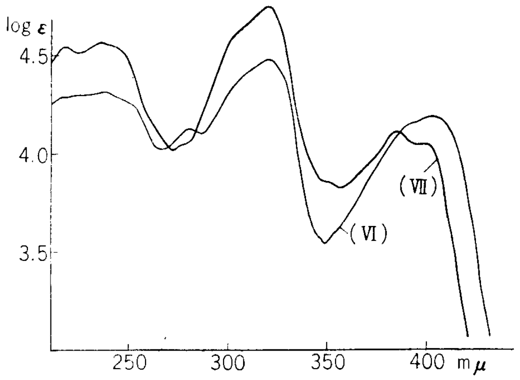

Fig. 3. Ultraviolet Absorption Spectra of S-Guaiazulene-carboxaldehydes (VI) and (VII) (in EtOH)

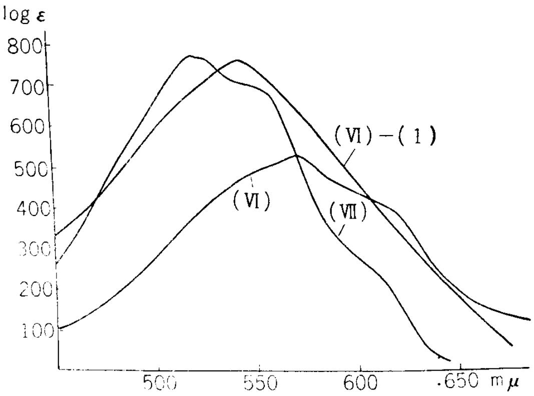

Fig. 4. Visible Absorption Spectra of S-Guaiazulene-carboxaldehydes (VI) and (VII) (in ligroine) (VI)-(1) (VI) in EtOH

From the second fraction, another S-guaiazulene-aldehyde (VI), $C_{16}H_{18}O$, dark brown needles, m.p. 84~85°, was obtained as the main product in 45% yield. (VI) showed a positive Tollen's test and two characteristic absorption maxima for aldehyde group (1631 and 2688 cm^{-1} in CCl_4) in the infrared region. It formed a trinitrobenzene complex, m.p. 92~93°; trinitrotoluene complex, m.p. 60~61° (decomp.); semicarbazone, m.p. 191~192°, oxime,*5 m.p. 128~129°. The spectra of (VI) in the ultraviolet and visible regions are given in Figs. 3 and 4.

As shown in Fig. 4, maximum absorption of (VI) in polar solution (ethanol) in visible region showed a hypsochromic shift by 51 mμ from that in nonpolar solution (ligroine), and the intensity of the maximum in ethanol is much higher than that measured in ligroine.1,8)

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*5 Reid, *et al.* obtained two aldoximes which were assigned α- (m.p. 128~130°) and β-stereo forms (m.p. 162°) by analogy with benzaldoximes.

6) K. Hafner, C. Bernhard: Angew. Chem., **69**, 533(1957).

7) T. Ukita, M. Miyazaki, M. Hashi: This Bulletin, **6**, 223(1958).

8) E. Heilbronner, R.W. Schmid: Helv. Chim. Acta., **37**, 2018(1954).

If (VI) has the aldehyde group at 3-position of S-guaiazulene (I), it will give a carbinol compound, identical with (III) on reaction with methylmagnesium iodide. Although Treibs, *et al.* have tried this reaction on azulene aldehydes with unsuccessful results, the product, hydroxyethyl-S-guaiazulene (VIII), $C_{17}H_{22}O$, m.p. 72~73°, was obtained in 52% yield. The infrared spectrum of (VIII) exhibited the absorption band at 3335 cm^{-1} (in KBr) characteristic for OH group. As shown in Figs. 1 and 2, absorption spectra of (VIII) in the ultraviolet and visible regions are in good agreement with those of (III), derived from 3-acetyl-S-guaiazulene (II) by its reduction with lithium aluminum hydride. On mixed fusion of (VIII) with (III), no melting point depression was observed. However, in respect to their stability against dehydration these compounds showed a great difference, (VIII) was more stable than (III). On recrystallization from ligroine, (VIII) did not a give blue oil (IV) as in the case of (III). On adsorption of (VIII) on an alumina column followed by elution with ether, which resulted in dehydration of (III) to 3-vinyl-S-guaiazulene (IV) in measurable amounts, almost 90% of the starting compound (VIII) was recovered. Further, contrary to (III), 2 hours of boiling (VIII) in hexane caused no dehydration, recovering the starting compound.

(VIII), however, was dehydrated by additional treatment with excess of methylmagnesium iodide in ether solution. Although the product was again unstable on further isolation in the pure state, it was converted on catalytic hydrogenation to a deep blue oil which formed a trinitrobenzene complex of m.p. 141~142°, identical with that derived from 3-ethyl-S-guaiazulene (V) obtained by a similar reduction of (IV).

Because (VIII) and (III) gave the same 3-ethyl-S-guaiazulene (V), the substitutions of both 1-hydroxyethyl groups in these two isomers must have been located at the same 3-position.

As reported in previous papers of this series,[2] substitution of a group with large atomic volume, such as isopropyl or isopropenyl, at the 3-position of S-guaiazulene causes hinderance between the methyl group at 4-position of the parent azulene. Thus, in both (II) and (VI), the respective acetyl and formyl groups at 3-position are expected to have considerable restrictions in their free rotations caused by the methyl group at 4-position. If in the following respective reactions, i.e. reduction with lithium aluminum hydride and Grignard reaction with methylmagnesium iodide, the hydrogen and methyl group attack their acetyl- and formylcarbonyl groups from the same least-hindered side, the products, (III) and (VIII), must possess hydroxyethyl groups which have their hydrogen, methyl, and hydroxyl in opposite orientations as shown in Chart 1, and have greater restrictions in their free rotations.

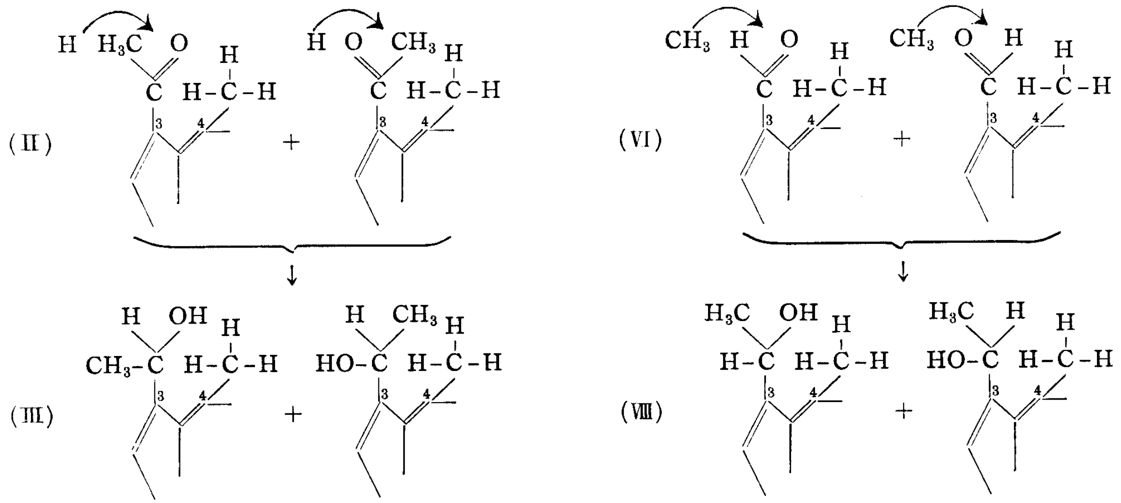

Chart 1.

The difference between (II) and (VIII) can most reasonably be explained by their isomerism caused by restricted rotation of each hydroxyethyl group at 3-position hindered by the methyl group at 4-position. As the occurrence of such type of isomers has not hitherto been encountered in azulene derivatives, the final conclusion and explanations can only be obtained after further experiments which are now in progress.

Experimental

3-(1-Hydroxyethyl)-S-guaiazulene (III) from 3-Acetyl-S-guaiazulene (II)—Into a solution of 20 mg. of $LiAlH_4$ in 300 cc. of ether, 300 mg. of (II) in 15 cc. of ether was added dropwise under cooling and stirring, the mixture was stirred for another 20 min., and then decomposed with satd. NH_4Cl solution. After washing the ether layer with H_2O, the solvent was removed by distillation in N_2 to give 210 mg. of blue crystals. Two recrystallizations from ligroine gave 3-(1-hydroxyethyl)-S-guaiazulene (III) as blue needles, m.p. 70~71°. *Anal.* Calcd. for $C_{17}H_{22}O$: C, 84.25; H, 9.15. Found : C, 83.91; H, 9.09. UV λ_{max}^{EtOH} mμ (log ε) : 247(4.39), 291(4.68), 306(4.16), 319(3.33), 353(3.76), 371(3.68); Visible spectrum : $\lambda_{max}^{ligroine}$ mμ (ε) : 612(438), 642(387), 660(357), 738(138).

3-Vinyl-S-guaiazulene (IV)—The filtrate obtained after repeated recrystallization of pure (III) from hexane was distilled at 40° in N_2, leaving a blue oily (IV). TNB-complex of (IV) was recrystallized from EtOH to dark needles, m.p. 99~100.5°. *Anal.* Calcd. for $C_{23}H_{23}O_6N_3$: C, 63.15; H, 5.30. Found : C, 62.77; H, 5.17.

(IV) was unstable and on standing for a few days in cool conditions gave blue needles, m.p. 120~125°.

3-Ethyl-S-Guaiazulene (V) from (IV)—a) A solution of 50 mg. of (IV) in 10 cc. of EtOH was shaken in H_2 stream over 15 mg. of 10% Pd-C and the solvent was removed under reduced pressure in N_2 to leave a blue oil. It was put on a column of alumina (1 × 12 cm.) and eluted with hexane. Blue eluate was collected and rechromatographed through alumina column (1.3 × 23 cm.) with hexane. From the 1st blue fraction (30 cc.), the solvent was removed in N_2 atmosphere to leave 10 mg. of blue oil (V). Its TNB-complex was recrystallized from EtOH to 8 mg. of black needles, m.p. 141~142°. *Anal.* Calcd. for $C_{23}H_{25}O_6N_3$: C, 62.86; H, 5.73. Found : C, 63.15; H, 5.60. UV of (V) recovered from the complex : λ_{max}^{EtOH} mμ (log ε) : 248(4.03), 288(4.34), 306(3.81), 354(3.44), 371(3.38); Visible spectrum: $\lambda_{max}^{ligroine}$ mμ (ε) : 632(444), 692(358), 775(125).

The 2nd blue fraction (20 cc.) furnished a few mg. of blue oil. Its TNB-complex melted at 149~150°, undepressed on admixture with an authentic sample of TNB-complex, m.p. 149°, of S-guaiazulene.

b) A solution of 40 mg. of (III) in 5 cc. of hexane was gently boiled for 2 hr. and measurements of the optical density of the solution were performed at intervals of 30 min. The results were as follows : λ_{max}^{EtOH} mμ (min.) : 612(0), 612(30), 611~616(60), 618~620(90), 620(120). After boiling, 10 cc. of EtOH and 60 mg. of 10% Pd-C were added and the solution was hydrogenated catalytically (5.1 cc. of H_2). Purification of the product through alumina column (1.2 × 15 cm.) using hexane, gave 30 cc. of a blue fraction, from which 30 mg. of blue oil was obtained. The TNB-complex of the blue oil melted at 141~141.5° and showed no depression on mixed fusion with that of 3-ethyl-S-guaiazulene (V) described in (a). From additional effluent a small amount of blue material was obtained but was not identified.

Formylation of S-Guaiazulene (I)—A solution of 4 g. of (I) in 20 cc. of *o*-dichlorobenzene was added dropwise into a reagent prepared from 8 g. of N-methylformanilide, 8 g. of $POCl_3$, and 20 cc. of *o*-dichlorobenzene, under ice-cooling and stirring. The reaction mixture was stirred at 32~35° for 6.5 hr. The mixture was decomposed with 150 cc. of 10% aqueous NaOH solution containing 200 g. of ice, in an ice bath, and extracted with 300 cc. of hexane. The upper layer was washed with H_2O and extracted with 300 cc. of 60% H_3PO_4. The red-colored acid layer was separated, diluted with H_2O, and shaken twice with 200 cc. of hexane. The extracts were collected, washed with H_2O, dried over Na_2SO_4, and concentrated to 30 cc. under reduced pressure in N_2. The concentrate solidified on cooling and, on filtration, 1.12 g. of brown needles was obtained. Successive concentration of the filtrate gave 0.64 g. of additional needles. The combined crystals were recrystallized from hexane to S-guaiazulene-3-carboxaldehyde (VI) as brown needles, m.p. 84~85°. *Anal.* Calcd. for $C_{16}H_{18}O$: C, 84.91; H, 8.02. Found : C, 84.75; H, 7.96. UV λ_{max}^{EtOH} mμ (log ε) : 237(4.23), 280(4.15), 319(4.51), 402(4.23); Visible spectrum : $\lambda_{max}^{ligroine}$ mμ (ε) : 535(440), 570(525), 604(427), 623(384); λ_{max}^{EtOH} mμ (ε) : 540 (757).

Both filtrates obtained above were combined, passed through an alumina column (1.5 × 40 cm.) and the column was eluted with a mixture (1:1) of ether and hexane to afford three fractions. On distillation of the 1st blue fraction (300 cc.), 1.5 g. of unreacted (I) was recovered. On concentration of the 2nd fraction (80 cc.) to 5 cc., 110 mg. of red needles was obtained. This was recrystallized from hexane to red needles (VII), m.p. 124～125.5°. *Anal.* Calcd. for $C_{16}H_{18}O$: C, 84.91; H, 8.02. Found : C, 84.90; H, 7.87. UV λ_{max}^{EtOH} mμ (log ε) : 216(4.55), 233(4.57), 319(4.76), 385(4.15), 400(4.09); Visible spectrum : $\lambda_{max}^{ligroine}$ mμ (ε) : 519(776), 555(686), 610(238).

The 3rd fraction (600 cc.) was concentrated to 10 cc. and filtered to give additional 250 mg. of (VI). The filtrates left after removal of (VII) and (VI) were combined and rechromatographed through alumina column with the same mixture (1:1) of ether and hexane to give additional 50 mg. of (VI) and 40 mg. of (VII). Total yield of (VI) and (VII) amounted to 2.06 and 0.15 g., respectively.

TNB-complex of (VI) : Into a solution of 100 mg. of (VI) in 2 cc. of EtOH, 90 mg. of trinitrobenzene was added and the mixture was warmed slightly on a water bath. TNB-complex was collected and recrystallized from EtOH to 160 mg. of brown needles, m.p. 92～93°. *Anal.* Calcd. for $C_{22}H_{21}O_7N_3$: C, 60.13; H, 4.82. Found : C, 60.12; H, 4.70.

TNT-complex of (VI) : From 20 mg. of (VI) and 20 mg. of trinitrotoluene, 28 mg. of TNT-complex was obtained as brown needles, m.p. 60～61°(decomp.). *Anal.* Calcd. for $C_{23}H_{23}O_7N_3$: C, 60.92; H, 5.11. Found : C, 61.05; H, 5.13.

Semicarbazone of (VI) : Into an aqueous solution of 50 mg. of semicarbazide hydrochloride and 50 mg. of AcOK in 0.7 cc. of H_2O, 50 mg. of (VI) and a minimum amount of MeOH were added. After standing the mixture for 24 hr. at room temperature, a small amount of H_2O was added and 40 mg. of the semicarbazone so formed was recrystallized from EtOH to green needles, m.p. 191～192°(decomp.). *Anal.* Calcd. for $C_{17}H_{21}ON_3$: C, 72.05; H, 7.47. Found : C, 72.08; H, 7.67.

Oxime of (VI) : Into an aqueous solution of 8 mg. of $NH_2OH{\cdot}HCl$ and 5 mg. Na_2CO_3 in 0.5 cc. of H_2O, 25 mg. of (VI) in 2 cc. of EtOH was added and the mixture was boiled gently for 3 min. On addition of a small amount of H_2O and filtration, 20 mg. of blue needles was obtained and was recrystallized from hexane to deep green needles, m.p. 128～129°. *Anal.* Calcd. for $C_{16}H_{19}ON$: C, 79.63; H, 7.94. Found : C, 79.55; H, 7.66.

TNB-complex of (VII) : From 30 mg. of (VII), 35 mg. of its TNB-complex, red needles, m.p. 86～87°, was prepared similarly as described above. *Anal.* Calcd. for $C_{22}H_{21}O_7N_3$: C, 60.13; H, 4.82. Found: C, 59.92; H, 4.61.

Oxime of (VII) : 60 mg. of $NH_2OH{\cdot}HCl$, 170 mg. of NaOH in 1 cc. of H_2O, and 50 mg. of (VII) in 15 cc. of EtOH were combined, and the product was purified through alumina column chromatography giving 20 mg. of violet plates, m.p. 155～156°. *Anal.* Calcd. for $C_{16}H_{19}ON$: C, 79.63; H, 7.94. Found: C, 79.89; H, 7.94.

3-(1-Hydroxyethyl)-S-guaiazulene (VIII) from S-Guaiazulene-3-carboxaldehyde (VI)—A solution of 200 mg. of (VI) in 25 cc. of ether was added dropwise, under cooling and stirring, into a Grignard reagent prepared from 0.2 g. of Mg and 1.3 g. of MeI in 2.7 cc. of ether. The reaction mixture was stirred for additional 1 hr. and decomposed with a satd. NH_4Cl solution. The ether layer was washed with H_2O, dried over Na_2SO_4, and distilled under reduced pressure in N_2 to leave 0.21 g. of blue residue. It was dissolved in a small amount of petr. ether and the solution was cooled to give 130 mg. of blue crystals which were recrystallized from ligroine to 3-(1-hydroxyethyl)-S-guaiazulene (VIII) as blue needles, m.p. 72～73°. *Anal.* Calcd. for $C_{17}H_{22}O$: C, 84.25; H, 9.15. Found : C, 84.21; H, 9.26. UV λ_{max}^{EtOH} mμ (log ε) : 247(4.38), 291(4.71), 306(4.16), 3.18(3.32), 353(3.76), 370(3.70); Visible spectrum : $\lambda_{max}^{ligroine}$ mμ (ε) : 611(445), 644(390), 660(365), 740(132).

A solution of 2.1 mg. of (VIII) in 2 cc. of hexane was gently boiled for 2 hr., during which optical densities were measured every 30 min. The results were as follows: λ_{max}^{hexane} mμ (mins.) : 611(30), 612(60), 611～613(90), 612～613(130).

Dehydration of (VIII) with Grignard Reagent and Subsequent Catalytic Hydrogenation—2.3 cc. of Grignard reagent, prepared from 60 mg. of Mg, 300 mg. of MeI, and 3 cc. of ether was added dropwise into a solution of 40 mg. of (VIII) dissolved in 5 cc. of ether while cooling with ice. After standing for 0.5 min., the reaction mixture was decomposed with a satd. cold NH_4Cl solution and extracted with 10 cc. of hexane. The hexane layer was washed with H_2O, dried over Na_2SO_4, and concentrated to 5 cc. under reduced pressure in N_2. Maximum absorption of the resulting solution was observed at 619～620 mμ.

After addition of 5 cc. of EtOH, the solution was catalytically hydrogenated over 60 mg. of 10% Pd-C (6.7 cc. H_2). Residual blue oil on removal of solvent was passed through an alumina column (1 × 17 cm.) and the column eluted with hexane. Two blue eluates were obtained with a small blue band remaining at the top of the column (presumably unreacted (VIII)). On removal of the solvent from the 1st blue eluate (5 cc.) by distillation in N_2, small amount of greenish blue gummy material was obtained. From the 2nd fraction (30 cc.), 10 mg. of blue oil was obtained which gave a TNB-complex of black needles with m.p. 141～142°. The complex was identified with that of 3-ethyl-S-guaiazulene by mixed fusion. *Anal.* Calcd. for $C_{23}H_{25}O_6N_3$: C, 62.86; H, 5.73. Found : C, 63.02; H, 5.69. UV λ_{max}^{EtOH} mμ (log ε) : 247(4.02), 288(4.23), 306(3.80), 354(3.44), 371(3.40); Visible spectrum: $\lambda_{max}^{ligroine}$ mμ (ε) : 632(446), 692(352), 775(125).

Summary

3-(1-Hydroxyethyl)-S-guaiazulene (III) was prepared by reduction of 3-acetyl-S-guaiazulene (II) with lithium aluminum hydride. (III) was converted into 3-vinyl-S-guaiazulene (IV) by dehydration and further into 3-ethyl-S-guaiazulene (V) by catalytic hydrogenation. An isomeric carbinol (VIII) was also produced from S-guaiazulene-3-carboxaldehyde (VI) by its treatment with methylmagnesium iodide, and (VIII) was confirmed to be 3-(1-hydroxyethyl)-S-guaiazulene by its derivation to (V). The remarkably different stability against dehydration observed between the two isomeric 3-(1-hydroxyethyl)-S-guaiazulenes (III and VIII) is discussed from the structural point of view.

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28. **Makoto Miyazaki** : Studies on Azulenes. X.*1
3-Aminomethyl-S-guaiazulenes.

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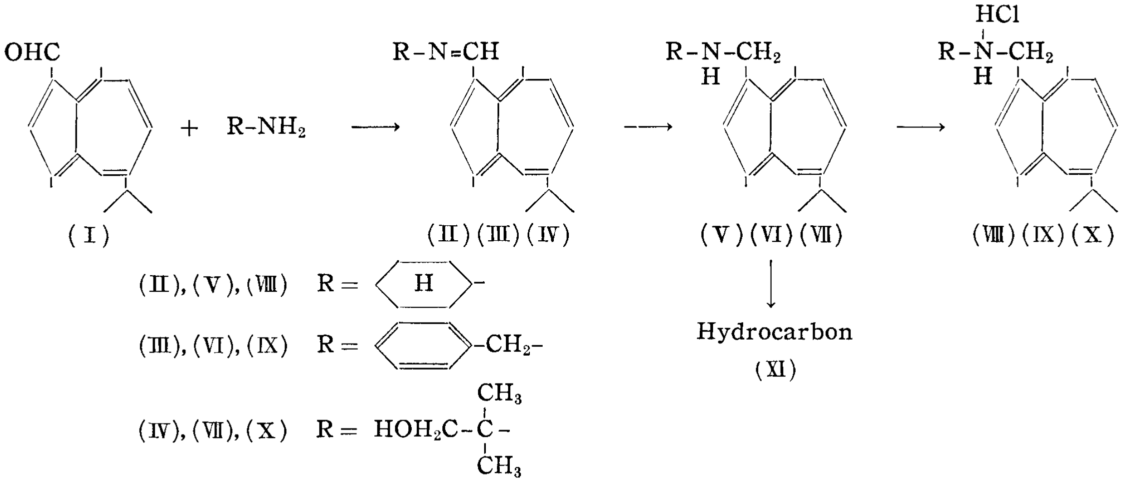
Although syntheses of several azulenes involving amino groups substituted in the ring1) or contained in their side chains2) have hitherto been reported, no attempt has been made to prepare 3-aminomethyl-S-guaiazulene derivatives from S-guaiazulene-3-carboxaldehyde (I) via the Schiff bases of the latter, a method which seems to be the simplest to introduce an amino group in the side chain of azulenoid compounds.

Recently, a brief communication2) on aminomethylation of azulene appeared and it involves treatment of the latter with bis(dimethylamino)methane, paraformaldehyde, and acetic acid in benzene. This procedure, however, does not pass through the Schiff base as intermediate which is readily attainable from azulene-aldehyde with several primary amines.



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*1 Part IX : This Bulletin, 8, 140(1960).

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1) A.G. Anderson, Jr., J.A. Nelson, J.J. Tazuma : J. Am. Chem. Soc., **75**, 4980(1953); A.G. Anderson, Jr., R. Scotonii, Jr., E.J. Cowels, G.G. Fritz : J. Org. Chem., **22**, 1193(1957); T. Nozoe, S. Matsumura, Y. Murase, S. Seto : Chem. & Ind. (London), **1955**, 1257; D.H. Reid, W.H. Stafford, J.P. Ward : J. Chem. Soc., **1958**, 1100.

2) K. Nafner : Angew. Chem., **70**, 412(1958); Ann., **606**, 79(1957); K. Hafner, H. Weldes : Ann., **606**, 90(1957).