BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 42 1404—1407 (1969)

Reaction of Vetivazulene with Sulfur. 3,5,9-Trimethylazuleno-[1,2-*b*]thiophene

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(Received September 30, 1968)

Vetivazulene was heated with sulfur to give a new sulfur-containing azulene, 3,5,9-trimethylazuleno[1,2-*b*]thiophene. On Vilsmeier formylation, the compound normally resulted in the formation of 4-formyl derivative, while the acetylation according to the Vilsmeier procedure proceeded abnormally to produce 4-dimethylamino-3,5,9-trimethylazuleno[1,2-*b*]thiophene.

In previous papers[1,2] it has been reported that the reaction of S-guaiazulene with sulfur formed a sulfur-containing azulene, 3,5,8-trimethylazuleno-[6,5-*b*]thiophene. We will describe here how the reaction of vetivazulene with sulfur formed a new sulfur-containing azulene, whose structure was determined to be 3,5,9-trimethylazuleno[1,2-*b*]-thiophene (II). This is a condensed ring compound consisting of azulene and thiophene nuclei; an α-bond of an azulene nucleus and a *b*-bond of a thiophene nucleus were common between the two nuclei, as in the azuleno[2,1-*b*]thiophene synthesized by Matsui,[3] but the relative configurations of the two nuclei are opposite. We also attempted to compare the reactivity in the electrophilic substitution by means of Vilsmeier acylation.

Results and Discussion

The Structure of the Sulfur-containing Azulene. Vetivazulene was heated with sulfur; dark blue prisms, mp 93.5—94.0°C, with the molecular formula of $C_{15}H_{14}S$ were obtained.

When the compound was subjected to reductive desulfurization with the Raney nickel catalyst (W-2 type) and subsequent dehydrogenation by means of chloranil or 30% palladium-on-charcoal, vetivazulene, the starting material, was regenerated in a good yield. Hence, the compound is certain to retain the vetivazulene skeleton in the molecule.

In the NMR spectrum of this compound (Fig. 1-B) the isopropyl signals (methyl doublet at 1.42 ppm and methine multiplet at 3.31 ppm) which are clearly observed in that of vetivazulene (Fig. 1-A) can not be seen; the disappearnace of the isopropyl group is also observed in the IR spectrum, and the proton signals assignable to aromatic methyl groups increase from two methyl equivalents in vetivazulene to three equivalents in the compound. Such a

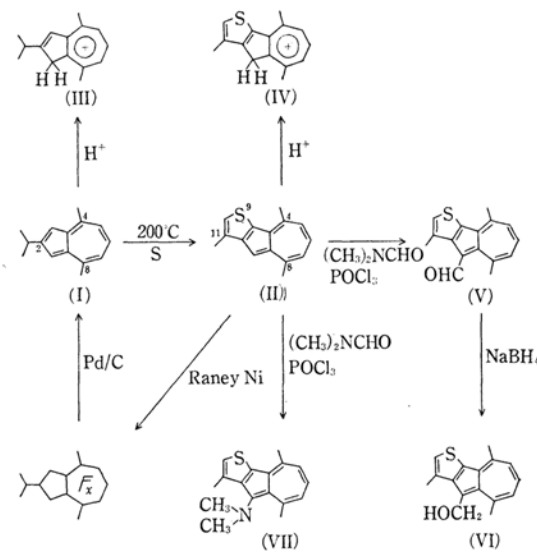

Chart 1*2

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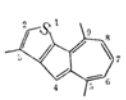
1) S. Hayashi, S. Kurokawa, M. Okano and T. Matsuura, *Tetrahedron Letters*, **1967**, 3443.

2) S. Hayashi, M. Okano, S. Kurokawa and T. Matsuura, *J. Sci. Hiroshima Univ., Ser. A-II*, **31**, 79 (1967).

3) K. Matsui, *Nippon Kagaku Zasshi* (*J. Chem. Soc. Japan, Pure Chem. Sect.*), **82**, 1520, 1665, 1667 (1961).

*2 The skeleton numbering of the compound according to the IUPAC nomenclature is:



For convenience in comparing it with vetivazulene, the numbering system in the azulene compounds was adopted in this paper, though not the name of the compound.

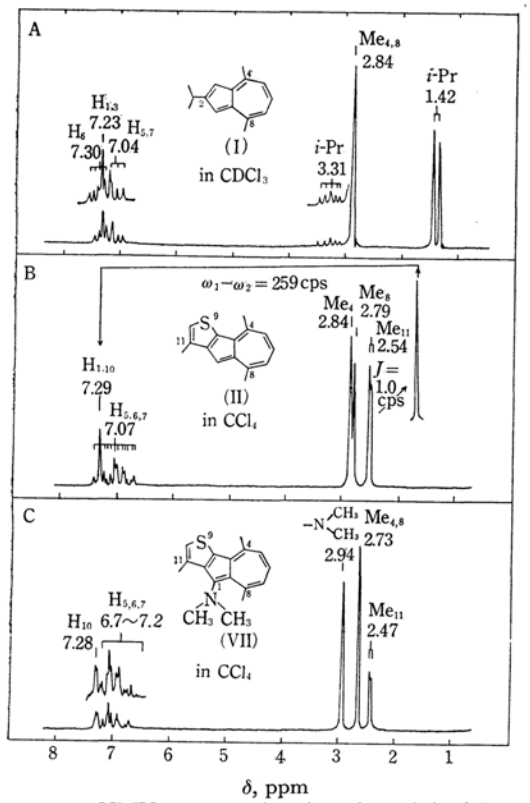


Fig. 1. NMV spectra of vetivazulene (A), 3,5,9-trimethylazuleno[1,2-*b*]thiophene (B) and 4-dimethylamino derivative (C).

change in the substituents between the starting and resulting compounds indicates that one end of the isopropyl group in vetivazulene participated in the reaction with sulfur.

The UV spectrum has an absorption maximum at 325 mμ the value of which corresponds to the bathochromic shift of 34 mμ from that of vetivazulene (291 mμ); this fact suggests that the conjugate system was elongated in the present compound. The absorption pattern of the IR spectrum in the $\nu_{C=C}$ region well resembles that of Matsui's azuleno-[2,1-*b*]thiophene.[3] The evidence of UV and IR spectroscopy thus suggests that the compound is 3,5,9-trimethylazuleno[1,2-*b*]thiophene (II).

The detailed inspection of the NMR spectrum affords reliable support for the proposed structure. An aromatic methyl doublet of 2.54 ppm (3H, J=1.0 cps) can be assigned to Me_{11} by comparison with the spectra of 3,5,8-trimethylazuleno[6,5-*b*]-thiophene,[1,2] and 3-methylbenz[*b*]thiophene,[4] and the doublet was decoupled, as expected, by irradiation upon an aromatic ring proton of 7.29 ppm (2H, singlet*[3]). The other two methyl singlets at 2.79 and 2.84 ppm are assigned to Me_8 and Me_4 respectively, because the groups overlapping at the same chemical shift in the spectrum of vetivazulene are considered to be resolved by the paramagnetic effect of the sulfur atom. Regarding the aromatic ring protons, one proton present in the singlet of 7.29 ppm (2H) can be assigned to H_{10} on the basis of the results of the above double-resonance experiment.

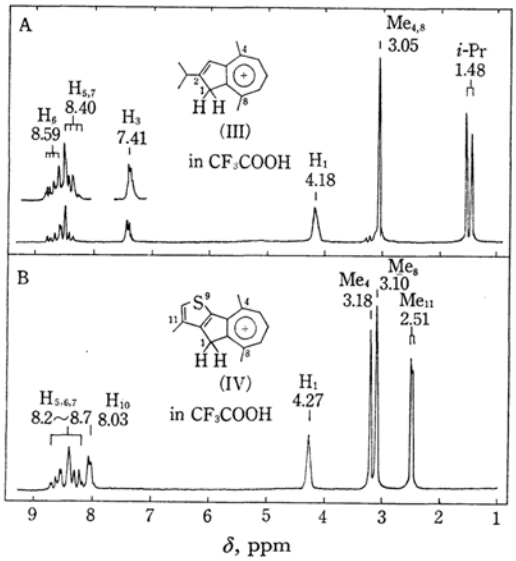


Fig. 2. NMR spectra of conjugate acids of vetivazulene (A) and 3,5,9-trimethylazuleno[1,2-*b*]thiophene (B).

If another proton of this singlet is now assigned to H_1 on the basis of comparison with the spectrum of vetivazulene, the remaining aromatic proton signals (nine lines centered at 7.07 ppm, 3H) can be assigned to H_5, H_6, and H_7 without any difficulty, for the signal pattern in nearly identical with such a spectrum of an ABC coupling system approaching an AB_2-type pattern as seen in 3-chloro-2-toluidine.[5]

The NMR spectrum (Fig. 2-B) taken in trifluoroacetic acid also supports the structure (II). A methylene singlet (2H, 4.27 ppm) which was absent in the spectrum taken in carbon tetrachloride (Fig. 1-B) can be attributed to two protons of a C_1-methylene group of the conjugate acid (IV) expected for the structure (II) on the basis of a comparison with the spectrum (Fig. 2-A) of a vetivazulenium cation. The other signals are also easily assigned as in Fig. 2-B. Regarding the conjugate acid formula (IV), the allylic coupling is expected between Me_{11} and C_{10}-ring protons, and the homoallylic coupling, between Me_8 and $2H_1$.

*3 Since a proton-signal of H_{10} is expected to be split into a quartet as a result of its spin-coupling with Me_{11}, this singlet may be due to the overlapping of H_{10} and H_1 signals.

4) J. A. Elvidge and R. G. Foster, *J. Chem. Soc.*, **1964**, 981.

5) R. E. Richards and J. Schaefer, *Mol. Phys.*, **1**, 331 (1958).

These were confirmed by double-resonance experiments; the Me_{11}-doublet at 2.51 ppm was decoupled by the saturation of H_{10}, and the half-band width (1.5 cps) of the Me_8-singlet at 3.10 ppm was reduced to two-thirds (1.0 cps) by the irradiation of H_1.

The authors have previously pointed out that Plattner's rule regarding the calculation of the visible absorption maxima of the alkylazulenes can also be applied to alkyl-substituted azulenothiophenes by replacing the standard value (17265 cm^{-1}=579 mμ) with the absorption maximum (615 mμ) of benz[*a*]azulene which has the same condensing mode.[2] The absorption maximum (592 mμ) thus calculated of the present compound*4 is in good agreement with the observed value (593 mμ). This also supports the proposed structure (II).

Electrophilic Substitution of 3,5,9-Trimethylazuleno[1,2-*b*]thiophene. Matsui has reported that azuleno[2,1-*b*]thiophene undergoes electrophilic substitution at the same position regarding the azulene nucleus, C_1 or C_3, as in the case of alkyl azulenes.[3] For confirmation of this, Vilsmeier formylation and acetylation[6] were attempted.

Formylation: Formation of 4-Formyl-3,5,9-trimethylazuleno[1,2-*b*]thiophene (V). In the presence of phosphorus oxychloride the condensation of *N,N*-dimethylformamide with 3,5,9-trimethylazuleno[1,2-*b*]thiophene was carried out; brown needles, mp 136—141°C, were thus obtained in a nearly theoretical yield.

The compound exhibited a strong absorption band due to an aldehyde group at 1632 cm^{-1} in the IR spectrum and formed an oxime of green needles, mp 193.0—194.5°C. The formyl derivative, upon reduction with sodium borohydride, gave dark blue crystals of a primary alcohol (VI) (ν_{OH} 3408—3584 cm^{-1}), mp 122.5—123.5°C. Although the NMR spectrum of this alcohol exhibited a hydroxyl proton signal at 3.37 ppm and methylene protons attached to the hydroxyl group at 4.97 ppm the remaining portion of the spectrum had a remarkable resemblance to that of original azulenothiophene, except that the integral strength of the signal of 7.29 ppm was reduced by half. This NMR spectrum indicates the introduction of a hydroxymethyl group into a C_1- or C_{10}-position. Of these positions, the C_1-position is adopted because the signal of Me_{11} is a doublet. Accordingly, it is certain that the formylation product has the structure of 4-formyl-3,5,9-trimethylazuleno[1,2-*b*]-thiophene (V), and that Vilsmeier formylation in the azulenothiophene takes place at the same position as in Matsui's azulenothiophene.

Acetylation: Formation of 4-Dimethylamino-3,5,9-trimethylazuleno[1,2-*b*]thiophene (VII). The acetylation of the azulenothiophene was carried out by using *N,N*-dimethylacetamide in the presence of phosphorus oxychloride; a green, oily substance was thus obtained. This compound, contrary to expectations, had an empirical formula of $C_{17}H_{19}NS$ containing one nitrogen atom, and its IR spectrum had no absorption band which could be assigned to a carbonyl group. The UV and visible absorption spectra are quite similar to those of the original azulenothiophene, except that their fine structures were reduced. Hence, it may be deduced that the resulting green oil is not a normal acetyl derivative.

These facts and the NMR spectrum (Fig. 1-C) can be reasonably explained when the dimethylamino group is directly introduced into an azulenothiophene nucleus. The methyl signals observed in the aromatic methyl region (2.47 ppm, doublet, 3H; 2.73 ppm, singlet, 6H; 2.94 ppm, singlet, 6H) can be assigned to three methyl groups located originally and two methyl groups of the dimethylamino group[7] newly introduced. The aromatic-ring-proton region of the spectrum shows a remarkable resemblance to that of the preceding formylated product. Accordingly, the obtained compound may be certainly said to have the structure of 4-dimethylamino-3,5,9-trimethylazuleno[1,2-*b*]thiophene(VII). Thus, the Vilsmeier acetylation of the azulenothiophene does not result in the introduction of an acetyl group, but the substituion of a dimethylamino group at the C_1-position in the azulene moiety. This is the first example of a dimethylamino derivative being produced in the Vilsmeier acetylation procedure.

Experimental

The melting points in this paper were uncorrected. The UV and visible absorption spectra were taken in cyclohexane. The gas chromatography was carried out at 170°C, using a column (1 m in length) of Diasolid-L impregnated by DEGS (10%).

Reaction of Vetivazulene (I) and Sulfur. A mixture of 2.50 g of vetivazulene and 1.25 g of powdered sulfur was heated at 200°C, for 4 hr with shaking under a nitrogen atomosphere. The reaction mixture, after being cooled at room temperature to solidify it, was crushed into small fragments. The fragments were then thoroughly ground together with petroleum ether in a mortar; 1.03 g of a dark violet, oily substance were extracted and chromatographed on a silica-gel column with petroleum ether. From a quickly-eluted fraction, 450 mg (18%) of unchanged vetivazulene were re-

*4 The contribution of the substituents held in the thiophene moiety is neglected (*cf.* Ref. 2).

Benz[*a*]azulene	16260 cm^{-1} (615 mμ)
4,8-Me	318×2 cm^{-1}
11-Me	0 cm^{-1}
Sum	16896 cm^{-1} (592 mμ)

6) K. Hafner and C. Bernhard, *Ann.*, **625**, 108 (1959).

7) Varian Associates, "High Resolution NMR Spectra Catalog," National Press, California (1962), No. 238.

covered, and from a slowly-eluted fraction, 310 mg (12.4%) of 3,5,9-trimethylazuleno[1,2-*b*]thiophene (II) were obtained as dark blue prisms, mp 93.5—94.0°C, after being purified by repeated recrystallizations from methanol.

Found: C, 79.54; H, 6.36; S, 14.16%. Calcd for $C_{15}H_{14}S$: C, 79.60; H, 6.23; S, 14.17%. Mass spectrum: $M^+=226$.

Desulfurization of 3,5,9-Trimethylazuleno[1,2-*b*]thiophene (II). A solution of 30 mg of the azulenothiophene (II) in 20 m*l* of absolute methanol was mixed with 0.6 mg of a W-2 Raney nickel catalyst freshly prepared; the mixture was then warmed at 60°C for 30 min under stirring. During this warming procedure the original blue color of the solution faded away. The reaction mixture was then filtered, and the nickel catalyst was repeatedly washed with ether. The filtrate and the washing were then combined; when the solvent was distilled off under reduced pressure, 20 mg of a colorless oily substance were obtained.

Dehydrogenation of the Desulfurized Product. *a) Dehydrogenation with Chloranil.* A solution of 20 mg of the desulfurized substance in 2 m*l* of isoamyl alcohol was mixed with 50 mg of chloranil, and then the mixture was refluxed in an oil bath for 2 hr. After the dark brown reaction mixture had been diluted by adding 30 m*l* of *n*-hexane, the solution was washed with water, dried, and the solvent distilled off under reduced pressure. The dark brown oil (60 mg) thus obtained was then eluted over silica gel with *n*-hexane to separate it into 20 mg of a colorless oil which eluted quickly and 0.7 mg of a violet oil which eluted slowly. The latter oil was confirmed through thin layer and gas chromatography to be identical with authentic vetivazulene.

b) Catalytic Dehydrogenation. The colorless oil (20 mg) eluted quickly in the preceding chromatography was sealed along with 20 mg of 50% palladized charcoal in a glass tube, and the mixture was heated at 300°C for 10 min. The dehydrogenated mixture was treated with 85% phosphoric acid in the usual manner; a violet oil (10 mg) was isolated which was found to be identical with vetivazulene by gas chromatography and by UV and visible absorption spectroscopy.

Vilsmeier Formylation of 3,5,9-Trimethylazuleno[1,2-*b*]thiophene (II). To a mixture of 30 mg of 3,5,9-trimethylazuleno[1,2-*b*]thiophene and 1 m*l* of *N,N*-dimethylformamide, 0.5 m*l* of *N,N*-dimethylformamide containing 0.1 g of phosphorus oxychloride was added, drop by drop, under ice cooling; the mixture was then allowed to stand overnight. The reaction mixture was then poured into 50 m*l* of water, kept slightly alkaline (*ca.* pH 9) by the addition of powdered potassium carbonate, and extracted with benzene. The 40 mg of a 4-formyl derivative (V) in the form of brown needles, mp 136—141°C, thus obtained showed a single brown spot ($R_f=2.5$) in thin-layer chromatography carried out using methylene chloride as the solvent. This spot turned yellow when sprayed with an acidic solution of 2,4-dinitrophenylhydrazine in alcohol.

Oxime. From 10 mg of 4-formyl-3,5,9-trimethylazuleno[1,2-*b*]thiophene, 10 mg of crude oxime was prepared using pyridine as a solvent; it was recrystallized from methanol to give green needles, mp 193.0—194.5°C.

Reduction of 4-Formyl-3,5,9-trimethylazuleno-[1,2-*b*]thiophene (V). Twenty-five milligrams of the 4-formyl derivative (V) were reduced with 50 mg of sodium borohydride in 5 m*l* of methanol by stirring at room temperature for 40 min. When the reaction mixture turned from brown to blue, a large amount of water was added; 30 mg of the 4-hydroxymethyl derivative (VI) were thus obtained as blue crystals. The crystals thus obtained were purified by recrystallization from ethanol to dark blue needles (3.0 mg), mp 122.0—123.5°C, which showed one blue-colored spot ($R_f=3.2$) in thin-layer chromatography using a *n*-hexane-ether (2 : 3) mixture.

$\delta_{TMS}^{CCl_4}$: Me_{11}, 2.65 (3H, doublet, $J=1.0$ cps); Me_4, 2.90 (3H, singlet); Me_8, 3.06 (3H, singlet); –OH, 3.37 (1H, singlet); $-CH_2(OH)$, 4.97 (2H, singlet); $H_{5,6,7}$, 6.88—7.16 (3H); H_{10}, 7.27 (1H, multiplet).

Acetylation of 3,5,9-Trimethylazuleno[1,2-*b*]thiophene (II). To 100 mg of azuleno[1,2-*b*]thiophene and 110 mg of *N,N*-dimethylacetamide dissolved in 1 m*l* of dry tetrahydrofuran, there was slowly added 1 m*l* of a dry tetrahydrofuran solution containing 200 mg of phosphorus oxychloride. The mixture was then refluxed on a water bath for 3 hr and treated in the same manner as in the formylation to afford 170 mg of a green oil, 39.3 mg of which was then chromatographed over an alumina column (Merck II-III) using an ether-*n*-hexane (1 : 9) mixture. The 4-dimethylamino derivative (VII) (19.3 mg) was thus obtained as a greenish-blue oil.

Found: N, 5.17; S, 11.80%. Calcd for $C_{17}H_{19}NS$: N, 5.20; S, 11.90%.

$\lambda_{max}^{cyclohexane}$ mμ (log ε): 240 (3.68), 288.5 (4.30), 310 sh (4.42), 318 (4.49), 330 sh (4.36), 364.5 (3.62), 382 (3.65), 398.2 (3.43). $\lambda_{max}^{cyclohexane}$ mμ (ε): 552 sh (371), 559 (460), 630 (405), 690 (189), 710 (158).

The authors are indebted to Professor Shô Itô of Tohoku University for his kind measurement of the mass spectra and to Dr. Hitoshi Minato of Shionogi Research Laboratory of Shionogi & Co., Ltd. for his measurement of the NMR spectra.