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New Azulene Derivatives Obtained by the Sulfur Dehydrogenation of Guaiene: 3,6,9-Trimethylazuleno[4,5-*b*]thiophene and 2-Methylthioguaiazulene[1)]

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Synopsis. Two new azulene derivatives, 2-methylthioguaiazulene and 3,6,9-trimethylazuleno[4,5-*b*]thiophene, have been obtained and characterized, along with known 3,5,8-trimethylazuleno[6,5-*b*]thiophene and 2,2′-biguaiazulenyl, by the sulfur dehydrogenation of guaiene.

Guaiazulene[2)] is a well-known azulene derivative and is readily accessible as a major product of the sulfur dehydrogenation of guaiene. In our factory, guaiazulene was produced in large quantities as a precursor for sodium salt of guaiazulene-3-sulfonic acid. During the production of the guaiazulene, several products retaining an azulene skeleton were obtained as minor ingredients. This paper will deal with the isolation and structural elucidation of these minor products.

Experimental

All the melting points are uncorrected. The infrared spectra were determined with a Hitachi Model EPI-G2 spectrometer. The proton nuclear magnetic resonance spectra were recorded as a solution in chloroform-*d*, with internal tetramethylsilane, on a Varian T-60, a Varian A-60D, or a Varian XL-100-15 spectrometer. The mass spectra were measured at 70 eV. The guaiene was prepared by the dehydration of guaiol with formic acid.[3)]

The dehydrogenation of guaiene was performed with sulfur at 200—260 °C for 2—3 h. After the separation of guaiazulene by extraction with sulfuric acid, followed by distillation, the mother liquor of the recrystallization of guaiazulene from methanol was extracted again with 55% sulfuric acid. The extract was diluted with water, and the products were taken into benzene and washed with an aqueous solution of sodium carbonate. The solvent was removed by distillation, and the residue was subjected to fractional vacuum distillation. Seven fractions; i) bp 155 °C/3.5 Torr, ii) bp 155—160 °C/3.5 Torr, iii) bp 160—170 °C/3.5 Torr, iv) bp 170—185 °C/3.5 Torr, v) bp 185—190 °C/3.5 Torr, vi) bp 190—195 °C/3.5 Torr, vii) bp 195—203 °C/3.5 Torr, were thus obtained. Fractions i, ii, and iii contain mainly guaiazulene. From the latter fractions, four kinds of crystalline products were obtained through repeated column chromatography on alumina and/or silica gel as follows:

*Product **A***: Fraction iii was dissolved in hexane and they allowed to stand in a refrigerator. The crystals thus separated were recrystallized from hexane and benzene (10 : 1) to give purple crystals; mp 116—117 °C (≈1%).[4)] Found: C, 79.34; H, 6.14%. Calcd for $C_{15}H_{14}S$: C, 79.60; H, 6.23%.

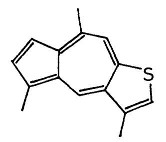
*Product **B***: After the separation of a small quantity of Product **A** from Fraction vii, the residue was extracted with 40% sulfuric acid. The usual work-up of the extract afforded blue crystals with a mp of 73—74 °C (recrystallized from hexane) in a 0.3% yield.[4)] $\lambda_{\max}^{\text{c-hexane}}$ nm (log ε) 235 (4.24), 259 (4.46), 300 (sh, 4.18), 321 (4.37), 335 (4.34), 365 (3.52), 383 (3.58), 403 (3.12), 622 (2.72), 650 (sh, 2.67), 683 (2.59), 725 (sh, 2.28). Found: C, 79.54; H, 6.21%. Calcd for $C_{15}H_{14}S$: C, 79.60; H, 6.23%.

*Product **C***: Products **A** and **B** were removed from Fraction v in the usual manner, and the residue was dissolved in hexane and allowed to stand in a refrigerator. The crystals thus separated were purified by repeated column chromatography on silica gel containing 3% of water eluted with hexane. Product **C** was thus obtained as blue crystals with a mp of 58.5—59 °C in a 0.1% yield.[4)] $\lambda_{\max}^{\text{c-hexane}}$ nm (log ε) 254 (4.28), 307 (4.70), 316 (4.74), 348 (3.45), 365 (3.66), 383 (3.89), 403 (4.03), 570 (2.60), 605 (2.58), 670 (sh, 2.18). Found: C, 78.63; H, 8.24; S, 12.74%. Calcd for $C_{16}H_{20}S$: C, 78.63; H, 8.25; S, 13.12%.

*Product **D***: This product was separated from Fraction vii through repeated column chromatography on alumina with hexane. Pure Product **D** was obtained as blue crystals with a mp of 176 °C (recrystallized from hexane) in a ≈0.05% yield.[4)]

Results and Discussion

Product **A** was easily identified as 3,5,8-trimethylazuleno[6,5-*b*]thiophene (**1**) on the basis of a comparison of its melting point and ^{1}H-NMR spectrum with those of the authentic sample reported by Hayashi *et al.*[5)]



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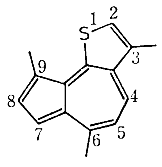
The structure of Product **B** was unambiguously established by an examination of its ^{1}H-NMR spectrum, which exhibited two sets of AB-quartets at δ 6.94 and 7.68 (J=11 Hz) and 7.29 and 7.57 (J=4.5 Hz), indicating the presence of vicinal hydrogens on both seven- and five-membered rings. Along with the resonance of two methyl groups at δ 2.88 (6H, s), a signal at δ 2.42 (3H, d, J=1.5 Hz) and a broad singlet at δ 7.07 (1H, bs) indicate that the condensed thiophene ring is substituted with the methyl group at the β-position.[6)] In trifluoroacetic acid, Product **B** exists as its conjugate acid (**2′**), showing three methyl groups at δ 2.92 (3H, d, J=1.0 Hz, 3-CH_3), 3.04 (3H, q, J=1.5 Hz, 9-CH_3), and 3.22 (3H, s, 6-CH_3), a two-proton multiplet at δ 4.15 (7,7′-H), a one-proton multiplet at δ 7.85 (8-H), a one-proton broad singlet at δ 8.65 (2-H), and an AB-quartet at δ 8.58 and 9.11 (J=10.5 Hz, 5-, 4-H). These NMR data are fully consistent with the formulation of Product **B** as 3,6,9-trimethylazuleno[4,5-*b*]thiophene (**2**). To the best of



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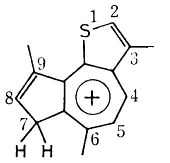
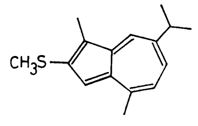


2′

our knowledge, Compound **2** is the second example of an azulene derivative in which a thiophene ring is annulated to the seven-membered ring of an azulene skeleton.

The fact that Product **C** retained a guaiazulene structure was confirmed by the absorption in the ^{1}H-NMR spectrum at δ 1.33 (6H, d, J=7 Hz, $-CH(\mathbf{CH_3})_2$), 3.07 (1H, septet, J=7 Hz, $-\mathbf{CH}(CH_3)_2$), 2.76 (3H, s, 4-CH_3), and 2.63 (3H, s, 1-CH_3). Furthermore, seven-membered ring protons appeared as a doublet at 7.97 (1H, d, J=2.0 Hz, 8-H) and AB-quartet, with further small doublet splittings in the lower-field half of the signals at 6.98 (1H, d, J=10.0 Hz, 5-H), 7.26 (1H, dd, J=10.0, 2.0 Hz, 6-H). In addition, a one-proton singlet attributable to 3-H appeared at δ 6.99. Since the methyl protons characteristic of the methylthio group were observed at δ 2.49 as a singlet,[7] it may be concluded that Product **C** is to be identified as 2-methylthioguaiazulene (**3**). Further support for the structure of **3** was obtained from the sodium periodate oxidation of **3**. The sulfoxide (**4**) was easily obtained in a pure form by chromatography on alumina eluted with benzene as a blue oil. The 4-CH_3 hydrogen resonance in the NMR spectrum of **4** appeared as a singlet at δ 2.68 which is comparable to that of **3**. As expected, 1-CH_3, S-CH_3, and 3-H resonated at δ 2.89 (6H, bs) and 7.72 (1H, s) respectively, points lower than those for the corresponding signals of **3**. The spectrum of **3** taken in trifluoroacetic acid can also be interpreted as supporting the assignment as a conjugate acid (**3′**) of **3**.



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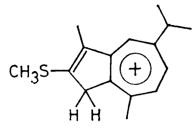
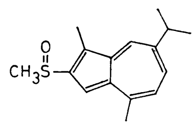


3′



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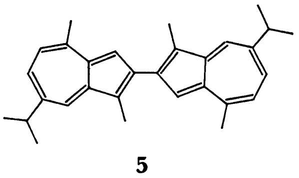
Product **D** was identified as 2,2′-biguaiazulenyl since its physical and spectral data are identical with those of the reported values for 2,2′-biguaiazulenyl.[8]



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