Studies of the Azulenes. V.[1] Condensation Products of Guaiazulene and 4,6,8-Trimethylazulene with Active Methylene Compounds by Means of Selenium Dioxide. Molecular Asymmetry Induced by Chelate Ring and Its Anisotropy Effect†

Kazuko KOHARA

Konan Chemical Industry, Co., Ltd., 5-21, Nakagawa-cho, Takatsuki, Osaka 569

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In the presence of selenium dioxide, guaiazulene and 4,6,8-trimethylazulene condensed with the active methylene compounds, ethyl acetoacetate and acetylacetone, to give ethyl α-(3-guaiazulenyl)acetoacetate (**3a**), α-(3-guaiazulenyl)acetylacetone, ethyl α-(4,6,8-trimethyl-1-azulenyl)acetoacetate (**5a**), and α-(4,6,8-trimethyl-1-azulenyl)acetylacetone. These α-substituted β-diketones exist exclusively in their corresponding enol forms, as evidenced by their NMR spectra. In the NMR spectra of **3a** and **5a**, the ethyl protons of the ester group show an ABX_3 pattern; the observed nonequivalence of the methylene protons is attributable to the restricted rotation between azulene and the substituent carbon atoms. From an inspection of the chemical shifts of the methyl group of metal chelate compounds of azulene derivatives, it is now reasonably concluded that there is no aromaticity associated with the chelate ring, providing further support for Musso's proposal.

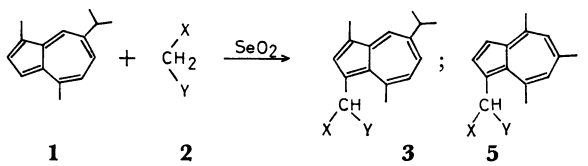
It has previously been reported[2] that guaiazulene (**1**) condensed with active methyl compounds such as acetone and ethyl methyl ketone in the presence of selenium dioxide to give the di-3-guaiazulenylmethyl ketones. The experiments described in this paper deal with similar reactions of **1** and 4,6,8-trimethylazulene (**4**) with active methylene compounds (**2**) to give the corresponding α-(3-guaiazulenyl) and α-(4,6,8-trimethyl-1-azulenyl) derivatives. The condensation products (**3a**, **3b**, **5a**, and **5b**) involve an identical structural moiety, *e.g.*, a β-dicarbonyl substituent is located at peri-position to the methyl group attached to the seven-membered ring of the azulene skeleton.

In this paper we wish to report the molecular asymmetry of **3a** and **5a** induced by restricted rotation around the bond between the azulene skeleton and 3- and 1-substituted chelate ring. The anisotropy effect of the 6π chelate ring is also discussed.

Results and Discussion

We have recently found that guaiazulene (**1**) condensed with active methylene compounds (**2**) in the presence of selenium dioxide to give the corresponding α-guaiazulenyl derivatives (**3**).[3] Furthermore, 4,6,8-trimethylazulene (**4**) can also be condensed with the active methylene compounds (**2**) to produce similar products (**5**).

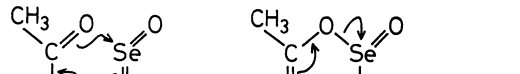
Although there are several possible mechanisms for the formation of **3a**, **3b**, **5a**, and **5b** from the reaction of guaiazulene and 4,6,8-trimethylazulene with active methylene compounds, the most likely one is *via* formation of the half ester (A) of selenious acid with the enol form of the active methylene compounds, followed by [2.3]sigmatropic shift to the intermediate (B).[4] A final nucleophilic attack of the azulene and elimination of the elements of hyposelenious acid (H_2SeO_2)[5] would account for the formation of the observed products.



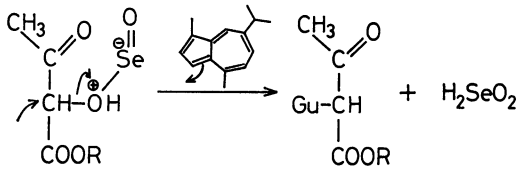
1 **2** **3** **5**

a: X=$COCH_3$, Y=$COOC_2H_5$ b: X=Y=$COCH_3$

Scheme 1.



(A)



(B) (Gu:3-guaiazulenyl group)

Scheme 2.

The structure of **3a** was established through its spectroscopic properties. Thus, in the NMR spectrum of **3a** (Fig. 1), the proton at C-2 of the azulene skeleton appears as a singlet at δ 7.34, indicating that it must be a 3-substituted guaiazulene. The singlet at δ 13.11 is assignable to a hydroxyl proton incorporated into a strong hydrogen bonding. This is also proved by its IR spectrum, which exhibits bands at 1608 cm^{-1} (C=C) and 1640 cm^{-1} (C=O) characteristic of a chelate ring. These findings accord well with the known linear relationship[6] between the chemical shift of the chelate hydroxyl proton and the stretching frequency of the carbonyl group associated with the hydrogen bonding.

† A preliminary report of this work was presented at the 7th International Congress of Essential Oils, Kyoto, Japan, October 1977.

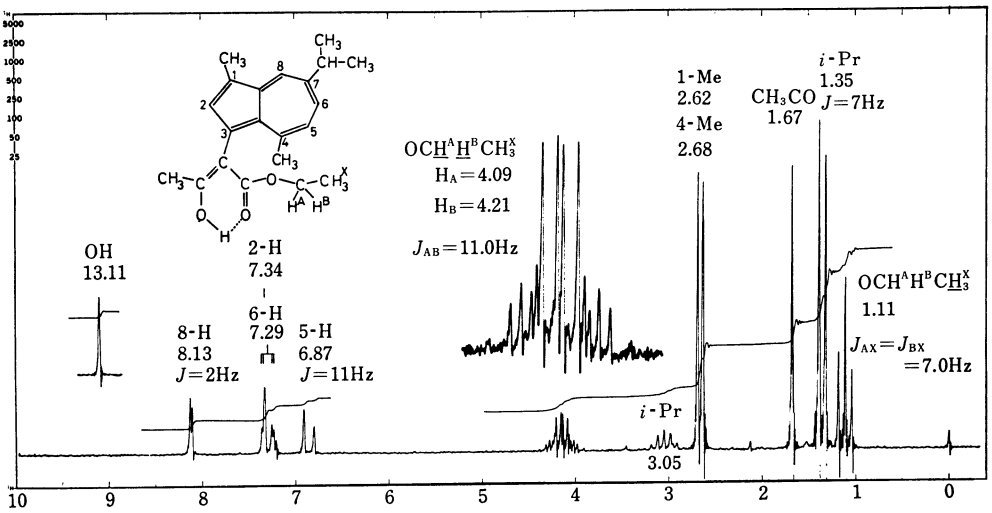


Fig. 1. 100 MHz NMR spectrum of **3a**.

The expanded spectrum of the methylene protons of **3a** is shown in Fig. 1; it could easily be analyzed as an AB-part of an ABX_3 spin system arising from the ethyl ester. The spectral parameters thus obtained are δ_A= 4.09, δ_B=4.21, δ_X=1.11 ppm, $J_{AX}=J_{BX}$=7.0, and J_{AB}=11.0 Hz. These assignments are fully confirmed by the comparison with the computer simulated spectrum, which agreed well with the experimental spectrum. Furthermore, irradiation at the site of the X-part signal at δ 1.11 assigned to the methyl protons changed the methylene protons multiplet to a broad AB-quartet, as illustrated in Fig. 2.

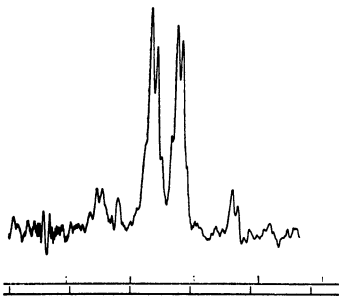


Fig. 2. Decoupled Spectrum of $-O-CH_2-$ region of **3a**.

Since the ethyl protons of the ester group of **3a** show an ABX_3 pattern, it is reasonable to assume that the nonequivalence of the methylene protons is attributable to the molecular asymmetry induced by restricted rotation about the bond between C-3 of the azulene nucleus and the substituent carbon atoms.[7-9] This is also the case for the corresponding derivative (**5a**) derived from 4,6,8-trimethylazulene (**4**). As can be seen from the NMR spectrum depicted in Fig. 3, the magnetic nonequivalence of the methylene protons is also observed.

The electronic spectrum of **3a** is illustrated in Fig. 4 and compared with that of guaiazulene (**1**). No appreciable differences between the spectra of **1** and **3a** could be discerned in intensities or in absorption maxima. These phenomena can reasonably be interpreted by the postulate that the six-membered chelate ring is oriented perpendicular to the plane of the azulene skeleton. This presumption is fully consistent with the afore-mentioned magnetic nonequivalence of the meth-

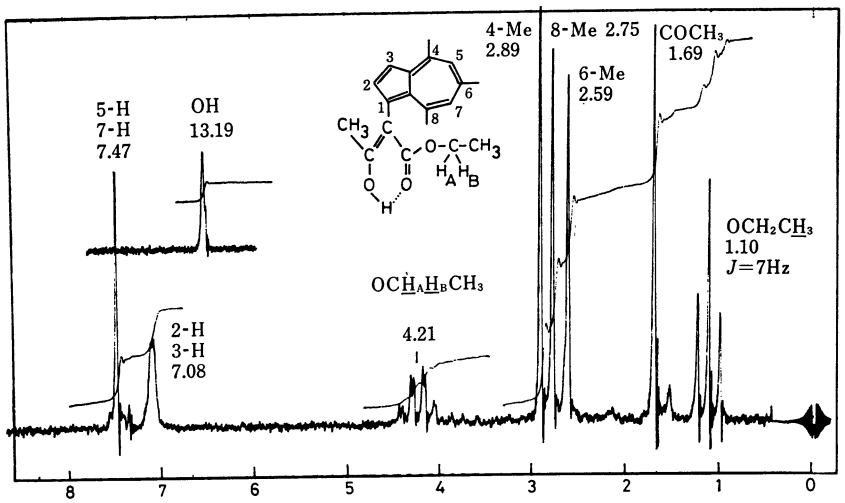


Fig. 3. 60 MHz NMR spectrum of **5a**.

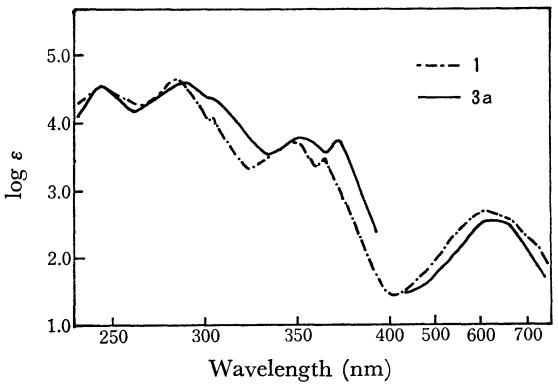


Fig. 4. Electronic spectra of **1** and **3a** in hexane.

ylene protons.

With these findings in mind, the series of compounds: **3a**, **3b**, **5a**, and **5b** provides a good model for the examination of the shielding effect of a chelate ring,[10] because one of the methyl groups attached to the azulene nucleus must be situated in a position just above the plane of the chelate ring, as shown schematically in Fig. 5.

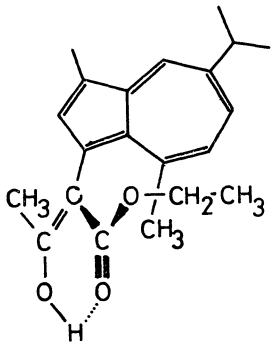
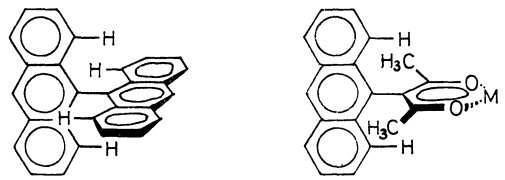


Fig. 5.

About a decade ago, Musso and coworkers[11] reported that in 9,9-bianthryl (**6**) the chemical shift of the 1- and 8-protons is more than 1 ppm higher than those at positions 4 and 5, while in the *C*-(9-anthryl)acetylacetonate salts (**7**) this difference is much smaller. Thus, these authors concluded that there is no ring current and no aromaticity in the chelate ring.



6 **7**

Fig. 6.

Our compounds (**3a**, **3b**, **5a**, and **5b**) possess several advantages over the model compounds reported by Musso *et al.*: *e.g.*, i) the methyl protons singlet in our compounds might more easily be recognized than the aromatic hydrogen multiplet in **7**; ii) the location of the methyl hydrogens of our compounds is above the plane of the chelate ring more precisely than that of the aromatic hydrogens of **7**.

Table 1. Chemical shifts of 4-methyl (guaiazulene series) and 8-methyl (trimethylazulene series)

	R=H	R = 3a	3b	8	9
4-CH_3	2.76	2.68	2.67	2.72	2.80
$\Delta\delta^{a)}$		+0.08	+0.09	+0.04	−0.04
	R=H	R = 5a	5b	10	
8-CH_3	2.82	2.75	2.73	2.77	
$\Delta\delta^{a)}$		+0.07	+0.09	+0.05	

a) + and − denote upfield and downfield shifts, respectively.

In order to gain further evidence for the aromaticity of the chelate ring, we have examined the chemical shifts of the methyl groups being considered. These values are summarized in Table 1. Although the chemical shifts of the 4-methyl protons of **3a** and **3b** are shifted upfield compared with that of guaiazulene,[12] the difference (0.08—0.09 ppm) in chemical shifts cannot be regarded as significant. The same is true for compounds **5a** and **5b**. No appreciable upfield shift can be observed even in the palladium and beryllium salts of **3b** and the palladium salt of **5b**.

These results provide further confirmation of Musso's proposal.

Experimental

IR spectra were obtained on a Hitachi Model EPI-G2 spectrophotometer. NMR spectra were taken in $CDCl_3$ or CCl_4 solution with a Varian XL-100-15, A-60D, or T-60 spectrometer and are reported in δ-values with tetramethylsilane as the internal standard.

4,6,8-Trimethylazulene (**4**) was prepared according to the literature.[13]

Reaction of Azulenes with Ethyl Acetoacetate or Acetylacetone. General Procedure: To a solution of azulene (4 g) in 60 g of ethyl acetoacetate or acetylacetone was added a solution containing 2 g of selenium dioxide in 4 ml of water. The solution was stirred for 3 days at room temperature. Work-up was made in a similar manner with that of the literature.[2] All products, obtained in 15—20% yield, were recrystallized from methanol. These condensation products are sensitive to air and are converted gradually to unidentified, variously colored products.

*Ethyl α-(3-guaiazulenyl)acetoacetate (**3a**)*: Blue needles; mp 70—72 °C. IR (Nujol): 1608 (C=C), 1640 (C=O) cm^{-1}. UV (hexane): λ_{max} (log ε) 247 (4.51), 287 (4.61), 306^{sh} (4.30), 354 (3.79), 372 (3.78), 612 (2.62), 666^{sh} nm (2.51). NMR ($CDCl_3$, 100 MHz): δ 1.11 (3H, t, X_3-part of an ABX_3, $J_{AX}=J_{BX}=7.0$ Hz, $CH_2C\underline{H}_3$), 1.35 and 3.05 (6H, d, and 1H, septet, $J=7.0$ Hz, 7-*i*-Pr), 1.67 (3H, s, $COCH_3$), 2.62 (3H, s, 1-Me), 2.68 (3H, s, 4-Me), 4.15 (2H, m, AB-part of an ABX_3, $J_{AX}=J_{BX}=7.0$, $J_{AB}=11.0$ Hz; $\delta_A=4.09$, $\delta_B=4.21$, $C\underline{H}_2CH_3$), 6.87 (1H, d, $J=11.0$ Hz, 5-H), 7.29 (1H, dd, $J=11.0$, 2.0 Hz, 6-H), 7.34 (1H, s, 2-H), 8.13 (1H, d, $J=2.0$ Hz, 8-H), 13.11

ppm (1H, s, chelate OH). Found: C, 77.28; H, 7.96%. Calcd for $C_{21}H_{26}O_3$: C, 77.27; H, 8.03%.

*α-(3-Guaiazulenyl)acetylacetone (**3b**)*: Blue needles; mp 58 °C. IR (Nujol): 1600, br (C=O, C=C) cm^{-1}. UV (hexane): λ_{max} (log ε) 245 (4.42), 287 (4.65), 307^{sh} (4.34), 354 (3.82), 372 (3.76), 612 (2.69), 666^{sh} nm (2.60). NMR (CCl_4, 100 MHz): δ 1.39 and 3.05 (6H, d, and 1H, septet, J=7.0 Hz, 7-*i*-Pr), 1.75 (6H, s, $COCH_3$), 2.63 (3H, s, 1-Me), 2.67 (3H, s, 4-Me), 6.82 (1H, d, J=11.0 Hz, 5-H), 7.26 (1H, dd, J=11.0, 2.0 Hz, 6-H), 7.30 (1H, s, 2-H), 8.04 (1H, d, J=2.0 Hz, 8-H), 16.36 ppm (1H, s, chelate OH). Found: C, 80.80; H, 8.09%. Calcd for $C_{20}H_{24}O_2$: C, 81.04; H, 8.16%.

*Ethyl α-(4,6,8-Trimethyl-1-azulenyl)acetoacetate (**5a**)*: Purple needles; mp 86 °C. UV (cyclohexane): λ_{max} (log ε) 246 (4.54), 291 (4.64), 339 (3.70), 349^{sh} (3.74), 353.5 (3.76), 557 (2.70), 604^{sh} (2.60), 661 nm (2.13). NMR ($CDCl_3$, 60 MHz): δ 1.10 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 1.69 (3H, s,$COCH_3$) 2.59 (3H, s, 6-Me), 2.75 (3H, s, 8-Me), 2.89 (3H, s, 4-Me), 4.21 (2H, m, $C\underline{H}_2CH_3$), 7.08 (2H, br s, 2- and 3-H), 7.47 (2H, s, 5- and 7-H), 13.19 ppm (1H, s, chelate OH). Found: C, 76.02; H, 7.30%. Calcd for $C_{19}H_{22}O_3$: C, 76.48; H, 7.43%.

*α-(4,6,8-Trimethyl-1-azulenyl)acetylacetone (**5b**)*: Purple needles; mp 106—108 °C. UV (cyclohexane): λ_{max} (log ε) 246.5 (4.48), 293 (4.70), 339 (3.78), 349^{sh} (3.76), 354 (3.73), 556 (2.72), 603^{sh} (2.63), 660 nm (2.14). NMR ($CDCl_3$, 60 MHz): δ 1.80 (6H, s, $COCH_3$), 2.61 (3H, s, 6-Me), 2.73 (3H, s, 8-Me), 2.89 (3H, s, 4-Me), 6.99 and 7.04 (each 1H, s, 2- and 3-H), 7.38 (1H, s, 5-H), 16.52 ppm (1H, s, chelate OH). Found: C, 80.13; H, 7.46%. Calcd for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51%.

*Metal Chelates **8**, **9**, and **10***. Preparation of **8**, **9**, and **10** was carried out according to Musso's procedure[10b] at room temperature.

*α-(3-Guaiazulenyl)acetylacetonate Palladium(II) (**8**)*: Blue crystals; mp >280 °C. NMR ($CDCl_3$, 60 MHz): δ 1.37 and 3.08 (6H, d, and 1H, septet, J=7 Hz, 7-*i*-Pr), 1.77 (6H, s, $COCH_3$), 2.66 (3H, s, 1-Me), 2.72 (3H, s, 4-Me), 6.90 (1H, d, J=11 Hz, 5-H), 7.33 (1H, s, 2-H), 7.34 (1H, dd, J=11, 2 Hz, 6-H), 8.16 ppm (1H, d, J=2 Hz, 8-H).

*α-(3-Guaiazulenyl)acetylacetonate Beryllium(II) (**9**)*: Blue crystals; mp 213—214 °C. NMR ($CDCl_3$, 60 MHz): δ 1.37 and 3.08 (6H, d, and 1H, septet, J=7 Hz, 7-*i*-Pr), 1.85 (6H, s, $COCH_3$), 2.68 (3H, s, 1-Me), 2.80 (3H, s, 4-Me), 6.95 (1H, d, J=11 Hz, 5-H), 7.40 (1H, dd, J=11, 2 Hz, 6-H), 7.48 (1H, s, 2-H), 8.21 ppm (1H, d, J=2 Hz, 8-H).

*α-(4,6,8-Trimethyl-1-azulenyl)acetylacetonate Palladium (II) (**10**)*: Purple crystals; mp 269 °C. NMR ($CDCl_3$, 60 MHz): δ 1.77 (6H, s, $COCH_3$), 2.60 (3H, s, 6-Me), 2.77 (3H, s, 8-Me), 2.88 (3H, s, 4-Me), 7.05 (2H, br s, 2- and 3-H), 7.42 ppm (2H, s, 5- and 7-H).

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