X-Ray Crystal Structure and Electrochemical Behavior of (5*R*,5'*S*)-5,5'-Biguaiazulene-3,3'(5*H*,5'*H*)-dione

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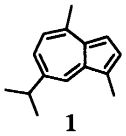
Oxidation of guaiazulene (**1**) with a 2.5 molar amount of *m*-chloroperbenzoic acid in ethanol at 0 °C for 1 h under aerobic conditions gives a *ca.* 2:1:1 mixture of meso and two enantiomeric forms of 5,5'-biguaiazulene-3,3'(5*H*,5'*H*)-dione (**2**), which upon recrystallization from dichloromethane-hexane selectively provides the single crystals of its meso form only. The first X-ray crystallographic analysis and the electrochemical behavior on the title meso form are reported.

5,5'-Biguaiazulene-3,3'(5*H*,5'*H*)-dione (**2**, biguaiazulenone) obtained exclusively by the peracetic acid oxidation of naturally occurring guaiazulene (**1**) in hexane has been found to be a highly important key intermediate for the various air-oxidation products of **1**.[1-4] For example, air-oxidation of biguaiazulenone **2** in pyridine at 25 °C provides as high as 46% yield of 3,5-guaiazulenedione (**3**),[2] along with 2,2'-bi(3,5-guaiazulenedione) (1%),[3,4] whereas air-oxidation of **2** in $CHCl_3$ (or CH_2Cl_2) at 25 °C affords 5-isopropylidene-3,8-dimethyl-1(5*H*)-azulenone (**4**) as a major product (~30% yield).[1,3] The primary air-oxidation step of biguaiazulenone **2** was presumed to be an equilibration, in organic solvents, of **2** with the monomeric 3-guaiazulenone radical **5**, from which various types of the air-oxidation products are derived. This is because, on setting aside a $CHCl_3$ (or CH_2Cl_2) solution of biguaiazulenone at 25 °C under anaerobic conditions, a well-resolved, hyperfine ESR spectrum became observable.[1,5] We now wish to describe on the first X-ray single crystal structure and the electrochemical behavior of the title meso form, (5*R*,5'*S*)-5,5'-biguaiazulene-3,3'(5*H*,5'*H*)-dione (**2a**), which enabled us to provide the single crystals.



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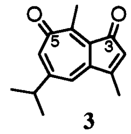

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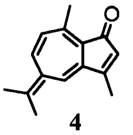

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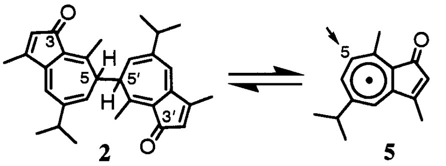


2 **5**

A *ca.* 2:1:1 mixture of meso and two enantiomeric forms of 5,5'-biguaiazulene-3,3'(5*H*,5'*H*)-dione (**2**) was prepared according to the following method: Oxidation of guaiazulene (**1**) (100 mg, 0.51 mmol) with a 2.5 molar amount of *m*-chloroperbenzoic acid (216 mg, 1.25 mmol) in ethanol (2 mL) at 0 °C for 1 h under aerobic conditions gave compound **2** (85 mg, 80% yield), indicating the same results as the peracetic acid oxidation of **1**.[1,2] Biguaiazulenone **2** obtained was recrystallized from dichloromethane-hexane (1:20, vol/vol) to provide the single crystals of only its meso form, (5*R*,5'*S*)-5,5'-biguaiazulene-3,3'(5*H*,5'*H*)-dione (**2a**) (46 mg, 43% yield) suitable for the X-ray crystallographic analysis.

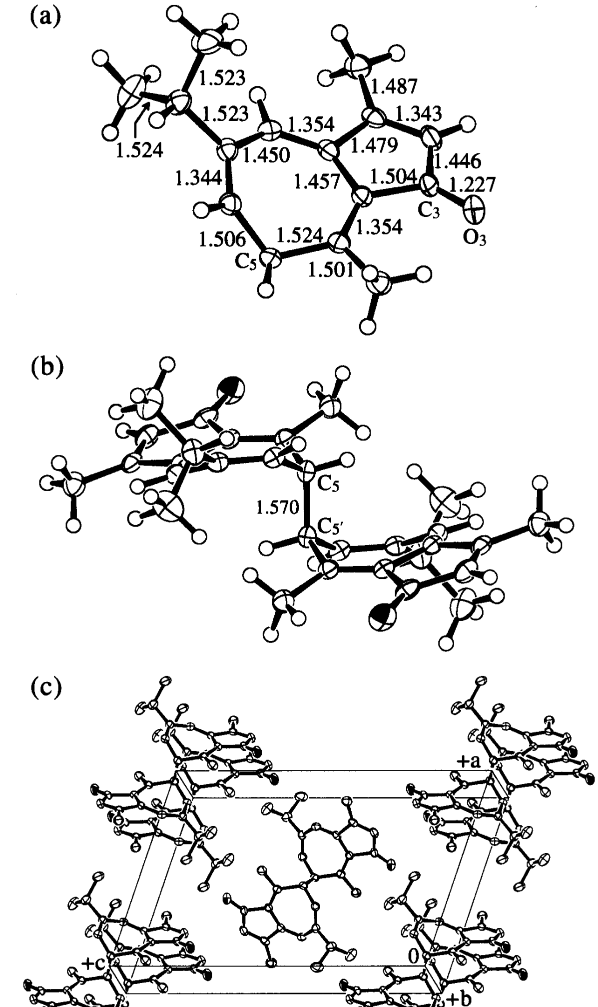


Figure 1. An ORTEP drawing of the partial structure of (5*R*,5'*S*)-5,5'-biguaiazulene-3,3'(5*H*,5'*H*)-dione (**2a**) with the numbering scheme and bond distances (Å) (a), the side view of the ORTEP drawing of **2a** (50% probability thermal ellipsoids) (b), and the packing (molecular) structure of **2a**; hydrogen atoms are omitted for reasons of clarity (c).

The meso compound **2a** was pale yellow needles. The TGA/DTA (thermal analysis) indicated that compound **2a** decomposed around 120 °C.[6] The elemental analysis confirmed the molecular formula $C_{30}H_{34}O_2$ (Found: C, 83.26; H, 8.07%. Calcd for $3C_{30}H_{34}O_2{\cdot}H_2O$: C, 83.29; H, 8.08%.). The crystal structure of compound **2a** was determined by means of X-ray diffraction,[7] indicating the molecular structure of the title meso form. The ORTEP drawing of compound **2a** is shown in Figures 1a,b together with the bond distances, which clearly indicate the bond alteration between single and double bonds.[8] The distances corresponding to the four double bonds in the partial structure of **2a** are within a close range of their average lengths (1.349(1) Å), which is slightly shorter than the distances observed for those of 3,5-guaiazulenedione (**3**) (1.364 Å).[4] However, the distances corresponding to the single bonds in the partial structure of **2a** appreciably vary between 1.446(4) and 1.524(3) Å; in particular, the C_5–$C_{5'}$ distance (1.570(5) Å) is characteristically the longest in every single bond distance. The C_3=O (1.227(3) Å) distance coincides with the C_3=O distance of 3,5-guaiazulenedione (**3**) (1.225 Å).[4] Along with the crystal structure of compound **2a**, the packing (molecular) structure of **2a** revealed that this molecule formed a unique accumulation (π stacking structure) in the single crystal (Figure 1c) and the *inter*-plane distances between the overlapping molecules were 5.46 Å (average lengths), suggesting the *inter*-molecular π–π* transition (*inter*-molecular photo-induced electron transfer) can be generated.

We have been interested further in the electrochemical property of compound **2a**. The electrochemical behavior (*E*/V vs. SCE) of compound **2a** was then measured by means of CV in 0.1 M (TBA)ClO_4, CH_2Cl_2 (Figure 2).[9] One irreversible electroreduction and one irreversible electrooxidation potentials were located at the values of -1.64 (E_{pc}), -0.73 (E_{pa}), +1.19 (E_{pa}) and +0.32 (E_{pc}) V. A plausible electron transfer mechanism for compound **2a** based on the results of the ESR spectrum[5] and the cyclic voltammogram for **2a** is illustrated in Scheme 1; the monomeric 3-guaiazulenone radical **5**, derived from **2a** in an equilibrium, undergoes one electron reduction, giving the hitherto unisolated guaiazulene-3-oxido anion **6**. This anion is presumed to be highly unstable and thus shows an irreversible voltammogram, since 3-hydroxyguaiazulene has been shown[2,10] too unstable to be isolated as a pure form at room temperature. Moreover, the monomeric 3-guaiazulenone radical **5** undergoes one electron oxidation, giving the unstable 3-guaiazulenone cation **7** showed an irreversible voltammogram. Thus, the CV for compound **2a** revealed one irreversible electroreduction and one irreversible electrooxidation potentials.

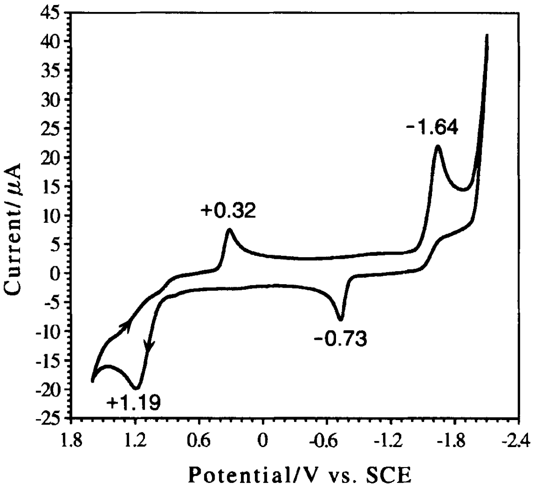
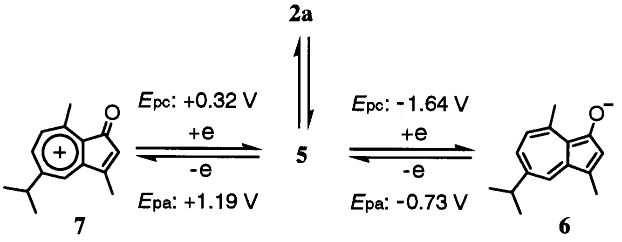


Figure 2. Cyclic voltammogram of compound **2a** (2.0 mg, 4.7 μmol) dissolved in 0.1 M (TBA)ClO_4, CH_2Cl_2 (10 mL) at a glassy carbon (ID: 3 mm) and platinum wire served as the working and auxiliary electrodes; scan rate 100 mV s^{-1} at -7 °C under argon.



Scheme 1. A plausible electron transfer mechanism for compound **2a** based on the results of the ESR spectrum[5] and the cyclic voltammogram for **2a**.

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References and Notes

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4 H. Takekuma, S. Takekuma, Y. Matsubara, H. Yamamoto, and T. Nozoe, *Chem. Lett.*, **1995**, 465.
5 The assignments of all signals of a well-resolved, hyperfine ESR spectrum of the monomeric 3-guaiazulenone radical **5** by using a computer-assisted simulation analysis are currently in progress. Details will be reported elsewhere.
6 Compound **2** [lit:[1,2] pale yellow powder, mp 138–142 °C (decomp)].
7 Crystallographic data for compound **2b**: $C_{30}H_{34}O_2$ (FW = 426.60), pale yellow needle (the crystal size, 0.20 × 0.10 × 0.05 mm), monoclinic, $P2_1/n$ (#14), a = 12.177(3) Å, b = 5.455(1) Å, c = 18.407(2) Å, β = 105.631(3)°, V = 1177.5(4) $Å^3$, Z = 2, D_{calcd} = 1.203 g/cm^3, μ (Mo-Kα) = 0.73 cm^{-1}, measured reflections = 2962, observed reflections = 2674, $R1$ = 0.073 , $wR2$ = 0.161. The X-ray measurement of compound **2b** was made with graphite monochromated Mo-Kα radiation (λ = 0.71069 Å) on a Quantum CCD area detector coupled with a Rigaku AFC-7 diffractometer at 123 K. The structure was solved by direct methods (SIR92) and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. The final cycle of full-matrix least-squares refinement was based on F^2 using the program SHELXL 97. All calculations were performed using the teXsan crystallographic software package.
8 It is expected that the X-ray crystallographic data of compound **2a** assist a computer-assisted simulation analysis for the assignments of all signals of a well-resolved, hyperfine ESR spectrum of the monomeric 3-guaiazulenone radical **5**, and this study is currently in progress. Furthermore, separation of the two enantiomeric forms of 5,5'- biguaiazulene-3,3'(5*H*,5'*H*)-dione (**2**) by using a HPLC equipped with a chiral column and their recrystallization to provide a respective specimen suitable for X-ray crystallographic analysis are currently under intensive investigation.
9 For a comparative purpose, the oxidation potential (*E*/V vs. SCE) using ferrocene as a standard material showed +0.49 V ($E_{1/2}$) by CV under the same electrochemical conditions as compound **2a**.
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