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A Facile Preparation of 5-Isopropylidene-3,8-dimethyl-1(5*H*)-azulenone and Its Crystal Structure

Shin-ichi Takekuma,* Syougo Jyoujima,
Masato Sasaki, Takuya Matsumoto,
Hideo Fukunaga, Hideko Takekuma,
and Hiroshi Yamamoto†

Department of Applied Chemistry, Faculty of Science and Engineering, Kinki University,
3-4-1 Kowakae, Higashi-Osaka 577-8502

†Department of Chemistry, Okayama University,
3-1-1 Tsushima-naka, Okayama 700-8530

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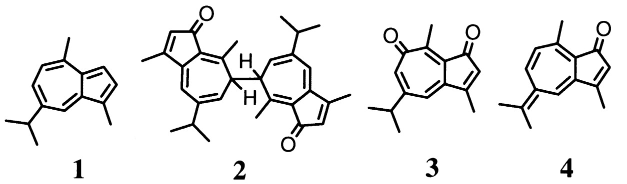
Oxidation of 5,5′-biguaiazulene-3,3′(5*H*,5′*H*)-dione (**2**) with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) in CH_2Cl_2 at 25 °C under aerobic conditions rapidly gives the title compound, 5-isopropylidene-3,8-dimethyl-1(5*H*)-azulenone (**4**), in 52% isolated yield. The crystal structure of **4** is reported as the first example for azulenequinonemethides.

In a previous paper,[1] we reported that oxidation of naturally occurring guaiazulene (**1**) with *m*-chloroperbenzoic acid in ethanol at 0 °C for 1 h under aerobic conditions quantitatively gave a mixture (2 : 1 : 1) of meso and two enantiomeric forms of 5,5′-biguaiazulene-3,3′(5*H*,5′*H*)-dione (**2** biguaiazulenone), which upon recrystallization from a mixed solvent of CH_2Cl_2 and hexane provided single crystals of the meso form only. The first X-ray crystallographic analysis and the electrochemical behavior were then described for the meso form, (5*R*,5′*S*)-5,5′-biguaiazulene-3,3′(5*H*,5′*H*)-dione (**2′**), in comparison with those of 3,5-guaiazulenedione (**3**).[2] Meanwhile, biguaiazulenone **2** was found[2–5] to be a highly important key intermediate for the various air-oxidation products of **1**. For example, air-oxidation of **2** in pyridine at 25 °C provided as high as 46% yield of **3**,[2,4] along with 2,2′-bi(3,5-guaiazulenedione) (1%),[2,5] whereas air-oxidation of **2** in $CHCl_3$ (or CH_2Cl_2) at 25 °C afforded the title compound, 5-isopropylidene-3,8-dimethyl-1(5*H*)-azulenone (**4**), as a major product (< 30% yield), which was a reactive substance under aerobic conditions.[3,5] We now wish to report the detailed studies on a facile preparation method and the crystal structure of **4** possessing a π-conjugate, fused heptafulvene-cyclopentenone bicyclic aromatic ring system. This structure is compared with the crystal structures of heptafulvenes, biguaiazulenone **2′**, and guaiazulenequinone **3** (Chart 1).

Compound **4** was prepared according to the following method: Oxidation of **2** (100 mg, 0.23 mmol) with DDQ (55 mg, 0.24 mmol) in CH_2Cl_2 (8 mL) at 25 °C under aerobic conditions rapidly gave **4** (51 mg, 52% yield), which was isolated by careful chromatographic purification. Although TLC monitoring of the reaction products indicated its formation in a much larger proportion, **4** was isolable only in 52% yield, apparently because of its instability during the repeated purification. Indeed, when **4** was dissolved in an organic solvent (e.g., MeOH, $CHCl_3$, CH_2Cl_2, or hexane) and allowed to stand at 25 °C, it was gradually converted into several 1*H*-inden-1-ones on exposure to the air.[3,5] Compound **4** was recrystallized from diethyl ether under argon for about one month in a freezer (−20 °C) to provide the single crystals[6] suitable for the X-ray crystallographic analysis.



1 **2** **3** **4**

Chart 1. Structural formulas.

The crystal structure of compound **4** was determined by means of X-ray diffraction.[7] The calculation of maximum atomic deviation from the least-squares plane indicated that the molecular frame of **4** was planar. This result is noteworthy because some X-ray crystal structures of heptafulvenes had revealed that those molecules assumed a symmetrical shallow boat conformation, except when electron-accepting groups (as C=O groups) at the C-8 position of heptafulvene induced a planarization of the seven-membered ring.[8,9] The C-5 carbonyl group of 3,5-guaiazulenedione (**3**) is slightly deviated (4°) from the best plane of the seven-membered ring, while the C-3 carbonyl group remains on the best plane of the five-membered ring.[2] In the case of **4**, one can infer that the heptafulvene unit forms a plane structure owing to the influence of a C=O group substituted at the C-8a position and the formation of a π-conjugate, fused heptafulvene-cyclopentenone bicyclic aromatic ring system. An ORTEP drawing of **4** and its packing structure are shown in Fig. 1 together with the selected bond distances, which clearly indicate the bond alternation between single and double bonds. The distances corresponding to the five double bonds in **4** are within a close range of their average lengths (1.350 Å), which coincide with the distances observed for those of **2′** (1.349 Å),[1] and are slightly shorter than those of **3** (1.364 Å).[2] The C_1=O distance of **4** (1.230 Å) coincides with the C_3=O distances of **2′** (1.227 Å) and **3** (1.225 Å). Moreover, the packing (molecular) structure of **4** revealed that this molecule formed a π-stacking structure in the single crystal and that the *inter*-plane distances between the overlapping molecules were 3.45–3.50 Å.

In addition to the X-ray crystallographic analysis on **4**, the accurate parameters for the crystal structure of **4** were transferred to a WinMOPAC program.[10] Its dipole moment was calculated to be 3.53351 D. Thus, one can infer that the heptafulvene unit of **4** forms a plane structure owing to influence of its large dipole moment.

We have been interested further in the electrochemical properties of compound **4**. The electrochemical behavior of **4** was

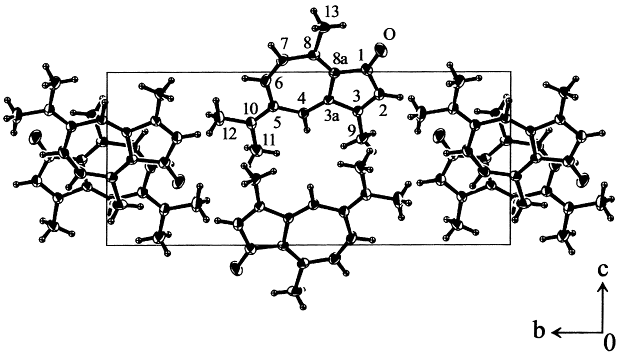


Fig. 1. An ORTEP drawing of **4** with the numbering scheme (30% probability thermal ellipsoids) and its packing (π-stacking) structure. The selected bond distances (Å) are as follows: C1–C2; 1.457(3), C2–C3; 1.339(3), C3–C3a; 1.477(3), C3a–C4; 1.345(3), C4–C5; 1.449(3), C5–C6; 1.460(3), C6–C7; 1.344(3), C7–C8; 1.446(3), C8–C8a; 1.359(3), C8a–C3a; 1.475(3), C3–C9; 1.491(3), C5–C10; 1.365(3), C10–C11; 1.501(4), C10–C12; 1.505(4), C8–C13; 1.504(3), C1–O; 1.230(3).

therefore measured by means of CV and DPV (Potential/V vs SCE) in 0.1 M Et_4NClO_4, CH_3CN at a glassy carbon working electrode. Platinum wire served as the auxiliary electrode.[11] Three redox potentials observed by DPV were positioned at the E_p values of +0.94, −1.53, and −2.28 V, while the corresponding three irreversible redox potentials determined by CV were located at the values of $+0.93(E_{pa})$, $-1.59(E_{pc})$, and $-2.36(E_{pc})$ V. From a comparative study with the redox potentials of **2′**,[1] **3**,[2] and 2,2′-bi(3,5-guaiazulenedione),[2] two points can be inferred; (1) **4** undergoes one-electron reduction at the potential of -1.59 (E_{pc}) V by CV (corresponding to −1.53 V by DPV), giving the radical anion generated by reduction of the C-1 carbonyl group of the π-conjugate five-membered ring, which is further reduced to the di-anion at the potential of $-2.36(E_{pc})$ V by CV (corresponding to −2.28 V by DPV); and further, (2) **4** undergoes one-electron oxidation at the potential of $+0.93(E_{pa})$ V by CV (corresponding to +0.94 V by DPV), giving the radical cation generated by oxidation of the heptafulvene unit. These ion species generated are presumed to be unstable and thus show the corresponding irreversible cyclic voltammograms.

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6 **4**: Reddish-orange blocks, mp 84 °C [determined by thermal analysis (TGA and DTA)], R_f = 0.23 on silica-gel TLC (AcOEt/hexane = 15/85, vol/vol); UV/vis λ_{max}(MeOH) nm (log ε), 206 (4.11), 245 (3.98), 265 (4.00), 371sh (3.64), 393 (3.75), and 418sh (3.68); IR (KBr) ν_{max} 1666 cm^{-1} (C=O, st); ^1H NMR (CD_3OD, determined by a 2D NMR technique and computer-assisted simulation analysis) δ 1.89 (3H, brd d, J = 0.2 Hz, Me_EC=5), 1.93 (3H, brd d, J = 0.5 Hz, Me_ZC=5), 2.19 (3H, d, J = 0.9 Hz, Me-3), 2.30 (3H, s, Me-8), 5.62 (1H, d, J = 12.5 Hz, H-7), 6.09 (1H, qd, J = 0.9, 0.8 Hz, H-2), 6.52 (1H, ddd, J = 12.5, 2.0, 0.5 Hz, H-6), and 6.62(1H, dd, J = 2.0, 0.8 Hz, H-4); ^{13}C NMR (CD_3OD, determined by 2D NMR techniques) δ 196.7 (C-1), 163.9 (C-3), 146.5 (C-8), 140.2 (C-3a), 137.1 (Me_2C=5), 136.5 (C-6), 132.2 (C-2), 130.7 (C-7), 130.4 (C-8a or C-5), 130.3 (C-5 or C-8a), 126.4 (C-4), 21.8 (Me_ZC=5), 21.7 (Me_EC=5), 20.8 (Me-8), and 14.0 (Me-3); EI-MS m/z 212 (M^+, 94%), 197 (100), 183 (5), 169 (14), 165 (7), 153 (12), 141 (14), 128 (12), 115 (11), 102 (1), 91 (2), 77 (5), 63 (3), 51 (2), and 39 (2).

7 Crystallographic data for **4** (Document No. 75001 deposited at the office of the Editor of Bull. Chem. Soc. Jpn.): $C_{15}H_{16}O$ (FW = 212.29), reddish-orange block (the crystal size, 0.40 × 0.42 × 0.31 mm), monoclinic, $P2_1/n$ (#14), a = 8.165(2) Å, b = 18.368(1) Å, c = 8.615(1) Å, β = 113.48(1)°, V = 1185.0(3) Å^3, Z = 4, D_{calcd} = 1.190 g cm^{-3}, μ(Mo-$K\alpha$) = 0.73 cm^{-1}, measured reflections = 2998, observed reflections = 2716, $R1$ = 0.064, $wR2$ = 0.227. A total 2998 reflections with $2\theta_{max}$ = 55.0° were collected on a Rigaku AFC-5R automated four-circle diffractometer with graphite monochromated Mo-$K\alpha$ radiation (λ = 0.71069 Å, rotating anode: 50 kV, 180 mA) at 296 K. The structure was solved by direct methods (SIR88) and expanded using Fourier techniques (DIRDIF94). 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. All calculations were performed using the teXsan crystallographic software package. Crystallographic data have been deposited at the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK and copies can be obtained on request, free of charge, by quoting the publication citation and the deposition number CCDC 171962.

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10 This computer program (Ver. 3.0) was developed by Fujitsu Ltd., Japan. A keyword (1SCF) was used.

11 For comparative purposes, the oxidation potential using ferrocene as a standard material showed +0.43 V (E_p) by DPV and +0.44 V ($E_{1/2}$) by CV under the same electrochemical conditions as **4**.