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# An efficient preparation, the structure and the properties of 1-isopropyl-4-(3-guaiazulenylmethylium)benzene hexafluorophosphate and tetrafluoroborate

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**Abstract**—Reactions of guaiazulene (**1**) with 4-isopropylbenzaldehyde in acetic acid in the presence of hexafluorophosphoric acid (and tetrafluoroboronic acid) at 25°C for 2 h under aerobic conditions quantitatively give the new title monocarbocation compounds, 1-isopropyl-4-(3-guaiazulenylmethylium)benzene hexafluorophosphate (**4**) and the tetrafluoroborate (**5**), which upon reaction with sodium methoxide dissolved in methanol in acetonitrile at 0°C for 20 min, respectively, afford as high as 92% isolated yield of 1-isopropyl-4-(3-guaiazulenylmethoxymethyl)benzene (**8**). The crystal structure of **5**, as the first example of carbocations stabilized by azulenyl groups, and the characteristic and chemical properties of **4** and **5** are reported. © 2002 Elsevier Science Ltd. All rights reserved.

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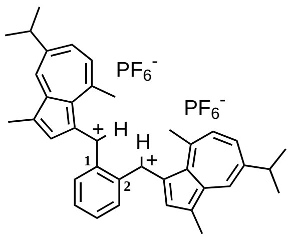
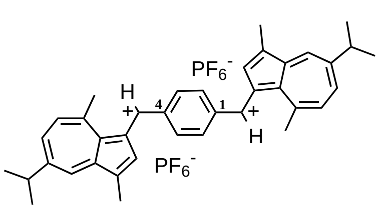
Although the chemistry of carbocations stabilized by azulenyl groups has been extensively studied and the chemical structures and the characteristic properties of a number of these compounds have been well documented, nothing has so far been achieved towards their accurate X-ray crystallographic analyses. In the previous papers, we reported an efficient preparation and the characteristic and chemical properties of two dicarbocations stabilized by two guaiazulenyl groups, 1,2- and 1,4-bis(3-guaiazulenylmethylium)benzene bis-hexafluorophosphate (**2**[1] and **3**[1,2]); however, their accurate X-ray crystallographic analyses have not yet been achieved because of difficulty in obtaining single crystals suitable for this purpose. In a series of basic studies on the above chemistry, our interest has been focused on the X-ray crystallographic analyses of carbocations stabilized by azulenyl groups, establishing the crystal (molecular) structures and their packing structures, and on the characteristic and chemical properties of those molecules in which the single crystals are formed. We now wish to report our detailed studies on a one-pot synthesis, the chemical structure and the characteristic and chemical properties of the title new monocarbocation compound, 1-isopropyl-4-(3-guaiazulenylmethylium)benzene hexafluorophosphate (**4**) with a view to comparison and discussion with those of **2** and **3**, and further, on the crystal structure of 1-isopropyl-4-(3-guaiazulenylmethylium)benzene tetrafluoroborate (**5**), which formed a π-stacking structure in the single crystal, as the first example for carbocations stabilized by azulenyl groups.



**2**



**3**

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*Keywords*: azulenes; carbonium ions; X-ray crystal structures.

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Compound **4** was prepared by the following procedure: To a solution of guaiazulene (**1**) (50 mg, 0.25 mmol) in acetic acid (0.4 mL) was added a solution of 4-isopropylbenzaldehyde (80 μL, 0.53 mmol) in acetic acid (0.3 mL) containing hexafluorophosphoric acid (60% aqueous solution, 0.18 mL). The mixture was stirred at 25°C for 2 h under aerobic conditions. After the reaction, diethyl ether (3.0 mL) was slowly added and the mixture was allowed to stand at 25°C for 24 h, affording very small single crystals of **4**. The crystals thus obtained were carefully washed with diethyl ether and dried well in a vacuum desiccator to provide pure **4** as stable crystals (113 mg, 95% yield).

Compound **4** was reddish-orange needles, mp >118°C [decomp., determined by thermal analysis (TGA and DTA)]. The UV–vis [$\lambda_{\max}$ ($CH_3CN$) nm (log $\varepsilon$)] spectrum appeared at 223 (4.51), 250sh (4.36), 295 (4.27), 328 (4.18), 393 (4.30) and 471 (4.56) (Fig. 1). Similarly, as in the cases of **2**[1] and **3**,[1,2] no characteristic absorption bands for guaiazulene were observed, indicating formation of a charge transfer (CT) complex between the 1-isopropyl-4-(3-guaiazulenylmethylium)benzene moiety with a delocalized π-electron system and the counter anion ($PF_6^-$). The absorption maximum appeared at $\lambda_{\max}$ 471 nm, which showed a hypsochromic shift (Δ 40 nm) and hypochromic effect in comparison with that of **3** ($\lambda_{\max}$ 511 nm, log $\varepsilon = 4.87$)[1] (Fig. 1). The IR (KBr) spectrum showed two specific bands based on the counter anion ($PF_6^-$) at $\nu_{\max}$ 783 and 448 $cm^{-1}$, which showed larger low wavenumber field shifts in comparison with those of **2** ($\nu_{\max}$ 837 and 556 $cm^{-1}$)[1] and **3** ($\nu_{\max}$ 841 and 559 $cm^{-1}$).[1] The MALDI-TOF-MS (3,5-dimethoxy-4-hydroxycinnamic acid matrix) spectrum showed only one ion peak at *m*/*z* 329 (100%, $[M-PF_6]^+$). The molecular formula $C_{25}H_{29}$ for the carbocation unit was determined by the exact FAB-MS (3-nitrobenzyl alcohol matrix) spectrum (found: *m*/*z* 329.2294. Calcd for $C_{25}H_{29}$: $[M-PF_6]^+$, *m*/*z* 329.2269.). The 500 MHz $^1H$ NMR ($CD_3CN$) spectrum showed signals for the 3-guaiazulenylmethylium substituent at $\delta$ 1.47 (6H, d, $J = 7.0$ Hz, $(C\underline{H}_3)_2CH$-7′), 2.54 (3H, brd s, Me-1′), 3.38 (3H, s, Me-4′), 3.51 (1H, sept, $J = 7.0$ Hz, $Me_2C\underline{H}$-7′), 8.07 (1H, brd s, $HC^+$-α), 8.43 (1H, dd, $J = 11.0$, 2.0 Hz, H-6′), 8.53 (1H, d, $J = 11.0$ Hz, H-5′), 8.61 (1H, d, $J = 2.0$ Hz, H-8′), 8.79 (1H, brd s, H-2′) and signals for the 4-1-isopropylphenyl group at $\delta$ 1.32 (6H, d, $J = 7.0$ Hz, $(C\underline{H}_3)_2CH$-1), 3.07 (1H, sept, $J = 7.0$ Hz, $Me_2C\underline{H}$-1), 7.53 (2H, ddd, $J = 8.0$, 1.5, 1.0 Hz, H-2,6), 7.82 (2H, brd ddd, $J = 8.0$, 1.5, 1.0 Hz, H-3,5). Moreover, the $^1H$–$^1H$ COSY spectrum showed cross peaks between the following signals (Me-1′ and H-2′; Me-1′ and H-8′; Me-1′ and $HC^+$-α; Me-4′ and H-5′; Me-4′ and H-2′; H-2′ and H-3,5; H-2′ and $HC^+$-α), indicating that each proton possesses a long-range coupling (*J* value: <1.0 Hz each) between them. The 125 MHz $^{13}C$ NMR ($CD_3CN$) spectrum exhibited the following 21 carbon signals assigned by the $^1H$–$^{13}C$ COSY and $^1H$–$^{13}C$ COLOC techniques: $\delta$ 171.3 (C-7′), 161.2 (C-1′), 157.9 (C-4′), 155.5 (C-3a′), 153.8 (C-8a′), 151.0 (C-2′), 150.5 (C-5′), 145.9 (C-3′), 144.9 (C-6′), 141.7 ($HC^+$-α), 139.9 (C-8′), 139.7 (C-4), 134.4 (C-3,5), 134.3 (C-1), 128.7 (C-2,6), 40.3 ($Me_2\underline{C}H$-7′), 35.1 ($Me_2\underline{C}H$-1), 29.8 (Me-4′), 23.9 ($(\underline{C}H_3)_2CH$-7′), 23.8 ($(\underline{C}H_3)_2CH$-1) and 13.8 (Me-1′). The chemical shifts ($\delta$ ppm) for the proton and carbon signals of the $HC^+$-α carbonium ion of **4** coincided with those of the $HC^+$-1,4 dicarbonium ions (8.03 for $^1H$ NMR; 141.0 for $^{13}C$ NMR) of **3**.[2] These spectroscopic data led to the structure, 1-isopropyl-4-(3-guaiazulenylmethylium)benzene hexafluorophosphate, for **4**.

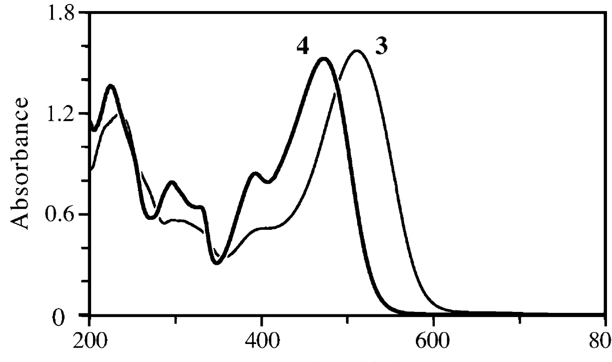


**Figure 1.** The UV–vis spectra of compounds **3**[1] and **4** in $CH_3CN$. Concentrations, **3**: 0.020 g/L; **4**: 0.020 g/L; length of the cell, 1 cm each.

Although an X-ray crystallographic analysis of compound **4** has not yet been achieved because of difficulty in obtaining a single crystal suitable for this purpose, the crystal structure of 1-isopropyl-4-(3-guaiazulenylmethylium)benzene tetrafluoroborate (**5**)[3] has been determined by means of X-ray diffraction, producing accurate structural parameters.[4,5] The ORTEP drawing and the space-filling structure of **5** are shown in Fig. 2(b)[6] together with the selected bond distances, revealing that the best plane of the 1-isopropylbenzene ring twists by 29.2° from the best plane of the 3-guaiazulenylmethylium substituent owing to the influence of steric hindrance between the hydrogen atoms of the C-5 and C-2′ positions. The 3-guaiazulenylmethylium substituent clearly indicates the bond alternation between the single and double bonds in comparison with the bond distances of the parent azulene.[7] The counter anion ($BF_4^-$) is located on the Cα carbonium ion (the distance between the B-Cα atoms: 5.647 Å). The average C–C bond distance for the seven-membered ring of the 3-guaiazulenyl group (1.401 Å) is slightly shorter than the distance observed for that of the parent azulene (1.412 Å).[7] Moreover, the distances for the five-membered ring of the 3-guaiazulenyl group appreciably vary between 1.347 and 1.470 Å; in particular, the C1′–C2′ distance (1.347 Å) is characteristically shorter than the average C–C bond distance for the five-membered ring (1.436 Å), which is slightly longer than the distance observed for that of the parent azulene (1.427 Å).[7] The Cα–C3′ distance (1.364 Å) is also characteristically shorter than the C4–Cα distance (1.451 Å), which coincides with the bond distance between the methylium carbon atom and the benzene ring for triphenylmethylium perchlorate (1.454 Å).[8] The average C–C bond distance for the benzene ring (1.388 Å) coincides with the distance observed for that of triphenylmethylium perchlorate (1.381 Å).[8] Along with the crystal structure of **5**, the two different (top and side) views for the packing (molecular) structure of **5** revealed that this molecule formed a π-stacking structure in the single crystal and that the *inter*-plane distances between the overlapping molecules (i.e. 3-guaiazulenylmethylium planes) were 3.56–3.64 Å (Fig. 2c, d). From a comparative study with the bond distances of the parent azulene,[7] the azulenium ions (i.e. the average C–C bond distance for the seven-membered rings of the azulenium ions: 1.38 Å)[9] and triphenylmethylium perchlorate,[8] it can be inferred that: (1) although the positive charge of **5** in the single crystal is mainly localized at the Cα carbon atom, forming a 3-guaiazulenylmethylium ion, the positive charge apparently is slightly transferred to the seven-membered ring, forming a 3-guaiazulenium ion; and further (2) from a result of the torsion angle between the 3-guaiazulenylmethylium plane and the 1-isopropylbenzene ring, formation of a conjugated π-electron system between them is possible. Thus, the X-ray crystallographic analysis of **5** enabled us to presume the plausible crystal (molecular) structures of **4**, **2** and **3**; namely: (1) the structural parameters for the 1-isopropyl-4-(3-guaiazulenylmethylium)benzene unit of **4** are nearly the same as those of **5**; and (2) the two 3-guaiazulenylmethylium planes of **3** twist by ca. 30° from the benzene ring, whereas in the case of **2**, the two 3-guaiazulenylmethylium planes twist by >30° from the benzene ring owing to the influence of steric hindrance between them, the repulsion between the two 3-guaiazulenylmethylium ions and so on. In addition to the X-ray

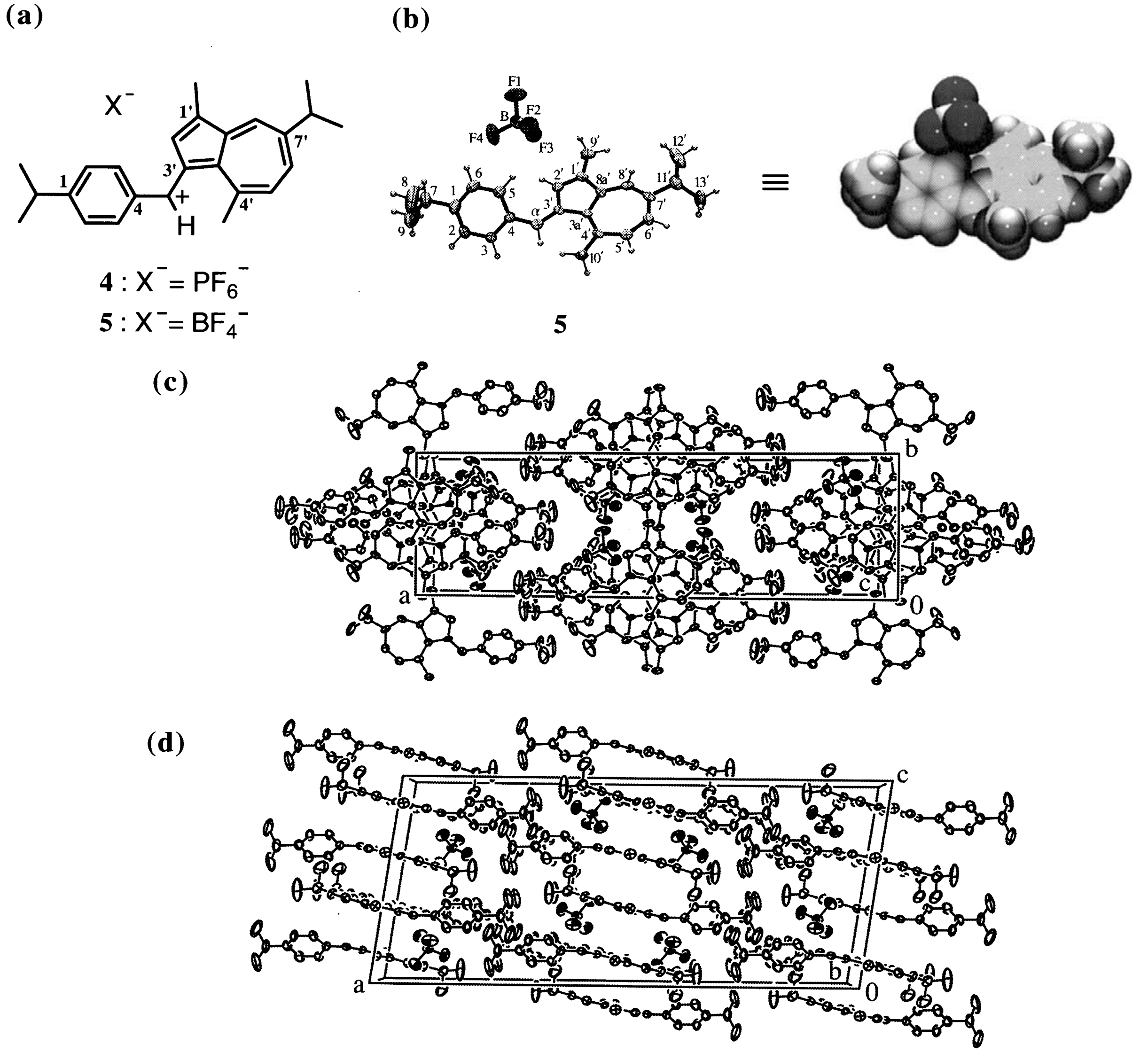


**Figure 2.** (a) Structures of 1-isopropyl-4-(3-guaiazulenylmethylium)benzene hexafluorophosphate and tetrafluoroborate (**4** and **5**). (b) The ORTEP drawing with the numbering scheme (30% probability thermal ellipsoids) and the space-filling structure of **5**. The selected bond distances (Å) of **5** are as follows: C1–C2; 1.381(9), C2–C3; 1.376(8), C3–C4; 1.408(8), C4–C5; 1.393(8), C5–C6; 1.376(9), C6–C1; 1.388(9), C4–Cα; 1.451(8), Cα–C3′; 1.364(8), C1′–C2′; 1.347(8), C2′–C3′; 1.456(8), C3′–C3a′; 1.470(8), C3a′–C4′; 1.391(8), C4′–C5′; 1.411(8), C5′–C6′; 1.383(8), C6′–C7′; 1.400(7), C7′–C8′; 1.380(8), C8′–C8a′; 1.373(8), C8a′–C1′; 1.440(8) and C8a′–C3a′; 1.466(8). (c and d) The two different (top and side) views for the packing (molecular) structure of **5**; hydrogen atoms are omitted for reasons of clarity.

crystallographic analysis of **5**, the accurate parameters for the crystal structure of **5** were transferred to a WinMOPAC program[10] and then the atomic-charges of **5** were calculated. As a result, it was suggested that a carbocation was mainly localized at the Cα carbon atom (the calculation value: +0.243).

We have been interested further in a comparative study of the electrochemical properties of the previously obtained dicarbonium hexafluorophosphates **2**,[1] **3**[1] and the title monocarbonium hexafluorophosphate **4**. The electrochemical behavior of **4** was, therefore, measured by means of CV and DPV (potential/V versus SCE) in 0.1 M [*n*-$Bu_4N$]$PF_6$, $CH_3CN$ (Fig. 3).[11] Three reduction potentials observed by DPV were positioned at the $E_p$ values of −0.22, −1.80 and −1.94sh V, while five redox potentials determined by CV were located at the values of +0.65 ($E_{pa}$), +0.57sh ($E_{pa}$), −0.29 ($E_{pc}$), −1.85 ($E_{1/2}$) and −1.99 ($E_{pc}$) V. From a comparative study with the redox potentials of **1**,[12] **3**[1,13] (Fig. 3) and 1-isopropyl-4-(3-guaiazulenylmethyl)benzene (**6**)[14] obtained by the reduction of **4** with $NaBH_4$, it can be inferred that: (1) **4** undergoes one-electron reduction at a potential of −0.29 ($E_{pc}$) V by CV (corresponding to −0.22 V by DPV), generating the corresponding 3-(4-1-isopropylphenyl)guaiazulenylmethyl radical species, which is rapidly converted into the radical homo-coupling product **7**; (2) the dimer **7** yielded is stepwise reduced to the di-anion at the potentials of −1.85 ($E_{1/2}$) and −1.99 ($E_{pc}$) V by CV (corresponding to −1.80 and −1.94sh V by DPV); and further; (3) **7** stepwise undergoes two-electron oxidation at the potentials of +0.57sh ($E_{pa}$) and +0.65 ($E_{pa}$) by CV. The two oxidation and two reduction potentials [+0.65 ($E_{pa}$) and +0.57sh ($E_{pa}$) V; −1.85 ($E_{1/2}$) and −1.99 ($E_{pc}$) V] observed by CV are based on the redox potentials of the two 3-guaiazulenyl groups of **7**, which are supported by the corresponding redox potentials of **1**,[12] **2**,[1] **3**[1,13] and **6**.[14]

In addition to the above investigations, we studied the chemical properties of **4** and **5** in which the single crystals were formed, and have found that the reactions of **4** and **5** with sodium methoxide dissolved in methanol in acetonitrile at 0°C for 20 min, respectively, afforded as high as 92% isolated yield of 1-isopropyl-4-(3-guaiazulenylmethoxymethyl)benzene (**8**),[15] indicating that the nucleophilic substitution reactions readily occur at the Cα carbon atoms of **4** and **5** (Scheme 1). Thus, similarly as the above computation for the atomic-charges of the crystal structure **5**, the present work also bears out that the carbonium ions of **4** and **5** in acetonitrile are mainly localized at their Cα carbon atoms. Moreover, when dissolved in a mixed solvent of acetonitrile and water and allowed to stand at room temperature for 2 weeks under aerobic conditions, **8** was gradually converted into 1-isopropyl-4-[bis(3-guaiazulenyl)methyl]benzene (**9**) and the starting 4-isopropylbenzaldehyde, quantitatively (Scheme 1).[4,16] Application of the nucleophilic substitution reactions by using types of the title carbocation compounds as the starting materials is currently under intensive investigation.

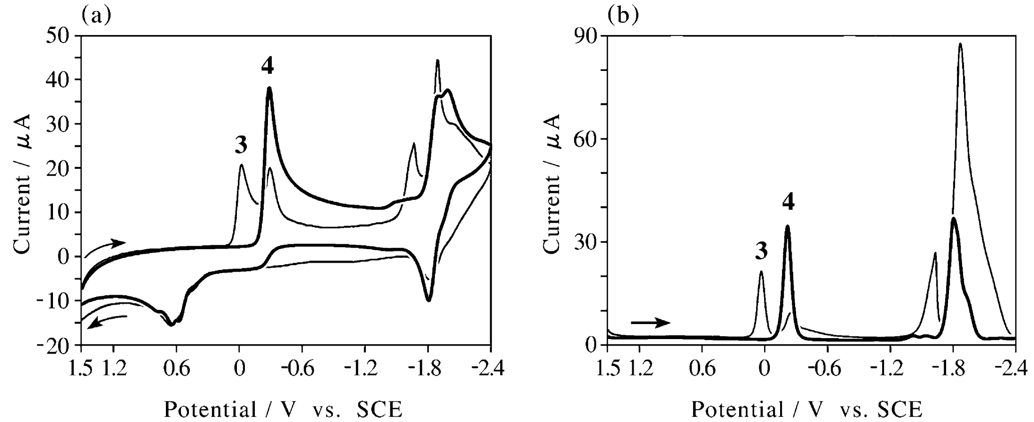
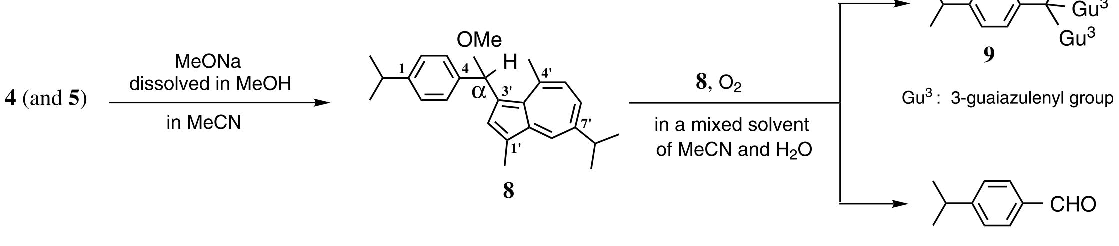


**Figure 3.** Cyclic (a) and differential pulse (b) voltammograms of compounds **3**[13] (6.0 mg, 7.6 µmol) and **4** (6.0 mg, 12.6 µmol) in 0.1 M [*n*-$Bu_4N$]$PF_6$, $CH_3CN$ (10 mL) at a glassy carbon (ID: 3 mm) and platinum wire served as the working and auxiliary electrodes; scan rates 100 mV $s^{-1}$ at 25°C under argon, respectively.



**Scheme 1.**

## Acknowledgements

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3. The same procedure as the preparation method of compound **4** was employed: reaction of guaiazulene (**1**) (50 mg, 0.25 mmol) with 4-isopropylbenzaldehyde (80 μL, 0.53 mmol) in acetic acid (0.7 mL) containing tetrafluoroboronic acid (42% aqueous solution, 0.18 mL) at 25°C for 2 h under aerobic conditions afforded **5** as stable single crystals (60 mg, 58% isolated yield). Compound **5**: Reddish-orange needles, mp 160.8°C [determined by thermal analysis (TGA and DTA)]; UV–vis $\lambda_{\max}$ ($CH_3CN$) nm (log $\varepsilon$), 226 (4.41), 250sh (4.25), 295 (4.16), 326 (4.08), 392 (4.21) and 472 (4.47); IR $\nu_{\max}$ (KBr) $cm^{-1}$, 1080, 1049 and 521 ($BF_4^-$); found: H, 6.89; C, 72.09%; calcd for $C_{25}H_{29}BF_4$: H, 7.02; C, 72.13%. The $^1H$ and $^{13}C$ NMR spectral data of **5** coincided with those of **4**.
4. Details will be reported elsewhere.
5. Crystallographic data for compound **5**: $C_{25}H_{29}BF_4$ (FW = 416.31), reddish-orange needle (the crystal size, 0.20×0.25×0.08 mm), monoclinic, *C*2/*c* (#15), $a$ = 33.348(7), $b$ = 9.856(4), $c$ = 14.272(3) Å, $\beta$ = 98.61(3)°, $V$ = 4638(2) Å$^3$, $Z$ = 8, $D_{\text{calcd}}$ = 1.192 g/cm$^3$, $\mu$(Mo-K$\alpha$) = 0.89 cm$^{-1}$, measured reflections = 3610, observed reflections = 3376, $R_1$ = 0.066, $wR_2$ = 0.092. A total 3610 reflections with $2\theta_{\max}$ = 50.0° were collected on a Rigaku AFC-5R automated four-circle diffractometer with graphite monochromated Mo-K$\alpha$ radiation ($\lambda$ = 0.71069 Å, rotating anode: 50 kV, 180 mA) at 296 K. The structure was solved by direct methods (SIR97) 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.
6. The ORTEP drawing and the space-filling structure of **5** in Fig. 2(b) were drawn using the following softwares, Ortep-3 for Windows Ver. 1.06 and POV-Ray for Windows Ver. 3.1g.
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10. This computer program (Ver. 3.0) was developed by Fujitsu Ltd., Japan. A keyword (1SCF) was used. Moreover, the π-HOMO (corresponding to the ionization potential), π-LUMO (corresponding to the electron affinity) and the dipole moment were calculated to be −9.693 and −3.555 eV (i.e. the gap between them: 6.138 eV) and 24.94649 D, respectively.
11. For comparative purposes, the oxidation potential using ferrocene as a standard material showed +0.42 ($E_p$) V by DPV and +0.40 ($E_{1/2}$) V by CV under the same electrochemical conditions as **4**.
12. **1**: DPV ($E_p$), +0.59 and −1.77 V; CV, +0.69 ($E_{pa}$) and −1.83 ($E_{1/2}$) V.
13. **3**: DPV ($E_p$), +0.04, −0.25, −1.63 and −1.87 V; CV, +0.64 ($E_{pa}$), −0.02 ($E_{pc}$), −0.29 ($E_{pc}$), −1.67 ($E_{pc}$), −1.89 ($E_{pc}$), −2.07sh ($E_{pc}$) and −1.84 ($E_{pa}$) V.
14. Compound **6** was prepared by the following procedure: To a solution of $NaBH_4$ (5 mg, 132 μmol) in ethanol (1 mL) was added a solution of **4** (30 mg, 63 μmol) in acetonitrile (2 mL). The mixture was stirred at 25°C for 20 min under aerobic conditions and then evaporated in vacuo. The residue thus obtained was dissolved in hexane and filtered. The hexane filtrate was evaporated in vacuo, giving pure **6** as a blue paste (20 mg, 96% yield). Compound **6**: $R_f$ = 0.51 on silica gel TLC (hexane/AcOEt = 96/4, vol/vol); UV–vis $\lambda_{\max}$ (hexane) nm (log $\varepsilon$), 213 (4.30), 247 (4.36), 291 (4.66), 306 (4.21), 353 (3.80), 371 (3.76), 623 (2.62), 678sh (2.52) and 754sh (2.05); exact EI-MS, found: $m/z$ 330.2359; calcd for $C_{25}H_{30}$: M$^+$, $m/z$ 330.2348; $^1H$ NMR ($CD_3CN$), $\delta$ 1.14 (6H, d, $J$ = 7.0 Hz, $(C\underline{H}_3)_2CH$-1), 1.28 (6H, d, $J$ = 7.0 Hz, $(C\underline{H}_3)_2CH$-7′), 2.54 (3H, s, Me-1′), 2.77 (3H, s, Me-4′), 2.80 (1H, sept, $J$ = 7.0 Hz, $Me_2C\underline{H}$-1), 3.00 (1H, sept, $J$ = 7.0 Hz, $Me_2C\underline{H}$-7′), 4.50 (2H, s, $CH_2$-4), 6.78 (1H, d, $J$ = 11.0 Hz, H-5′), 6.88 (2H, brd ddd, $J$ = 8.0, 1.5, 1.0 Hz, H-2,6), 7.07 (2H, ddd, $J$ = 8.0, 1.5, 1.0 Hz, H-3,5), 7.27 (1H, dd, $J$ = 11.0, 2.0 Hz, H-6′), 7.36 (1H, brd s, H-2′) and 8.07 (1H, d, $J$ = 2.0 Hz, H-8′); DPV ($E_p$), +0.63 and −1.82 V; CV, +0.63 ($E_{pa}$) and −1.84 ($E_{1/2}$) V.
15. (a) Compound **8** was prepared by the following procedure: To a solution of sodium methoxide (5 mg, 93 μmol) in methanol (1 mL) was added a solution of **4** (30 mg, 63 μmol) in acetonitrile (2 mL). The mixture was stirred at 0°C for 20 min under aerobic conditions and then evaporated in vacuo. The residue thus obtained was dissolved in hexane and filtered to remove the yielded $NaPF_6$. The hexane filtrate was evaporated in vacuo, giving pure **8** as a blue paste (21 mg, 92% yield). Compound **8**: $R_f$ = 0.28 on silica gel TLC (hexane/AcOEt = 96/4, vol/vol); UV–vis $\lambda_{\max}$ (hexane) nm (log $\varepsilon$), 218 (4.27), 247 (4.38), 285sh (4.59), 290sh (4.64), 293 (4.65), 306sh (4.25), 340sh (3.59), 354 (3.77), 371 (3.76), 610 (2.59), 665sh (2.49) and 738sh (1.99); exact FAB-MS (3-nitrobenzyl alcohol matrix), found: $m/z$ 360.2422; calcd for $C_{26}H_{32}O$: M$^+$, $m/z$ 360.2453; $^1H$ NMR ($CD_3CN$), $\delta$ 1.21 (6H, d, $J$ = 7.0 Hz, $(C\underline{H}_3)_2CH$-1), 1.33 (6H, d, $J$ = 7.0 Hz, $(C\underline{H}_3)_2CH$-7′), 2.56 (3H, s, Me-1′), 2.89 (1H, sept, $J$ = 7.0 Hz, $Me_2C\underline{H}$-1), 2.95 (3H, s, Me-4′), 3.07 (1H, sept, $J$ = 7.0 Hz, $Me_2C\underline{H}$-7′), 3.33 (3H, s, $-OCH_3$), 6.22 (1H, s, CH-4), 6.97 (1H, d, $J$ = 11.0 Hz, H-5′), 7.20 (4H, s, H-2,3,5,6), 7.38 (1H, dd, $J$ = 11.0, 2.0 Hz, H-6′), 7.49 (1H, brd s, H-2′) and 8.16 (1H, d, $J$ = 2.0 Hz, H-8′); $^{13}C$ NMR ($CD_3CN$), $\delta$ 148.7 (C-3′), 146.0 (C-4′), 142.0 (C-8a′), 141.3 (C-3a′), 139.5 (C-7′), 139.3 (C-2′), 135.7 (C-6′), 134.6 (C-8′), 134.1 (C-4), 128.9 (C-1), 128.6 (C-3,5), 128.0 (C-5′), 127.1 (C-2,6), 125.4 (C-1′), 81.4 (CH-4), 57.0 ($-OCH_3$), 38.3 ($Me_2\underline{C}H$-7′), 34.5 ($Me_2\underline{C}H$-1), 27.8 (Me-4′), 24.7 ($(\underline{C}H_3)_2CH$-7′),

24.3 ($(\underline{C}H_3)_2$CH-1) and 13.1 (Me-1′); (b) similarly, the reaction of compound **5** with sodium methoxide provided the same results as **4**.

16. Compound **8** (30 mg, 83 μmol) was dissolved in a mixed solvent (6 mL) of acetonitrile and water (70:30, vol/vol) and allowed to stand at room temperature for 2 weeks under aerobic conditions, providing only crystals of 1-isopropyl-4-[bis(3-guaiazulenyl)methyl]benzene (**9**) (18 mg, 34 μmol, 41% yield) in the solution. Another product of 4-isopropylbenzaldehyde was identified by TLC and HPLC analyses of the solution compared with those of the authentic sample. Compound **9**: Dark-blue prisms, mp 201°C [determined by thermal analysis (TGA and DTA)]; $R_f = 0.44$ on silica gel TLC (hexane/AcOEt = 96/4, vol/vol); UV–vis $\lambda_{max}$ (hexane) nm (log $\varepsilon$), 219 (4.48), 248 (4.61), 284sh (4.81), 291 (4.81), 310 (4.62), 344sh (3.98), 358 (4.09), 375 (4.13), 580sh (2.82), 628 (2.94), 664sh (2.87), 686sh (2.84), 736sh (2.47) and 768sh (2.34); exact EI-MS, found: $m/z$ 526.3620; calcd for $C_{40}H_{46}$: $M^+$, $m/z$ 526.3600; $^1$H NMR ($CD_3CN$), $\delta$ 1.24 (6H, d, $J = 7.0$ Hz, $(C\underline{H}_3)_2$CH-1), 1.34 (12H, d, $J = 7.0$ Hz, $(C\underline{H}_3)_2$CH-7′,7″), 2.51 (6H, s, Me-1′,1″), 2.88 (1H, sept, $J = 7.0$ Hz, $Me_2C\underline{H}$-1), 2.89 (6H, s, Me-4′,4″), 3.02 (2H, sept, $J = 7.0$ Hz, $Me_2C\underline{H}$-7′,7″), 6.76 (2H, d, $J = 11.0$ Hz, H-5′,5″), 6.85 (2H, ddd, $J = 8.0$, 1.5, 1.0 Hz, H-2,6), 7.02 (2H, s, H-2′,2″), 7.09 (2H, ddd, $J = 8.0$, 1.5, 1.0 Hz, H-3,5), 7.24 (2H, dd, $J = 11.0$, 2.0 Hz, H-6′,6″), 7.28 (1H, s, CH-4) and 8.08 (2H, d, $J = 2.0$ Hz, H-8′,8″); $^{13}$C NMR ($CD_3CN$), $\delta$ 146.43, 146.39, 145.4, 141.6 (C-2′,2″), 139.4, 138.1, 135.1 (C-6′,6″), 134.0 (C-8′,8″), 132.7, 132.2, 129.7 (C-2,6), 126.8 (C-5′,5″), 126.5 (C-3,5), 124.4, 47.5 (CH-4), 38.0 ($Me_2\underline{C}H$-7′,7″), 34.0 ($Me_2\underline{C}H$-1), 27.3 (Me-4′,4″), 24.7 ($(\underline{C}H_3)_2$CH-7′,7″), 24.2 ($(\underline{C}H_3)_2$CH-1) and 13.1 (Me-1′,1″); found: H, 8.64; C, 91.14%; calcd for $C_{40}H_{46}$: H, 8.80; C, 91.20%.