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A facile preparation, spectroscopic and chemical properties, crystal structures, and electrochemical behavior of monocarbenium ion compounds stabilized by 3-guaiazulenyl and dihydroxyphenyl (or hydroxymethoxyphenyl) groups

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ABSTRACT

Reaction of guaiazulene (**8**) with 2,3-dihydroxybenzaldehyde (**9**) in methanol in the presence of hexafluorophosphoric acid (i.e., 65% aqueous solution) at 25 °C for 2 h gives (3-guaiazulenyl)(2,3-dihydroxyphenyl)methylium hexafluorophosphate (**13**) in 86% yield. Similarly, reaction of **8** with 2-hydroxy-3-methoxybenzaldehyde (**10**) [or 3,4-dihydroxybenzaldehyde (**11**) or 4-hydroxy-3-methoxybenzaldehyde (**12**)] under the same reaction conditions as for **9** affords the corresponding monocarbenium ion compound **14** (63% yield) [or **15** (43% yield) or **16** (77% yield)], respectively, each product of which is stabilized by 3-guaiazulenyl and dihydroxyphenyl (or hydroxymethoxyphenyl) groups. A facile preparation and crystal structures as well as spectroscopic, chemical, and electrochemical properties of **13**–**16**, possessing two interesting resonance structures, respectively, i.e., a protonated *o*- (or *p*-) benzoquinonemethide form and a 3-guaiazulenylium ion form, in a solution of acetonitrile and further, in a single crystal, are reported.

1. Introduction

In 1996 Atwood et al. reported a crystal and molecular structure of the $[H_3O\cdot 18\text{-crown-6}]_2[ReCl_6]$ **1** isolated from a liquid clathrate medium as the first example for the crystal structure of the oxonium ion H_3O^+ (see Chart 1),[1] while the hydrogen atoms of **1** were not refined and further, the related studies have been documented.[2–8] The hydrogen atoms of the oxonium ion H_3O^+ were refined in 2007, and the corresponding three O–H bond lengths tended to be 0.86 Å,[5] the bond length of which was characteristically shorter in comparison with that of water molecule (0.96 Å). Along with those studies, in 1997 Yamaguchi, Tamura, and Maeda reported a unique crystal structure of the phenolsulfonphthalein[9] **2**, with a zwitterionic form, whose molecular structure possesses an interesting protonated *p*-benzoquinonemethide form (see Chart 1);[10] however, the hydrogen atoms of **2** were not refined. Besides the above, Ito et al. reported synthesis and properties, with the exception of X-ray crystallographic analyses, of delocalized methylium ion compounds stabilized by azulen-1-yl (or alkyl-substituted azulen-1-yl) and 4-hydroxyphenyl (or 4-methoxyphenyl) groups.[11–13] On the other hand, we have been working on basic and systematic investigations using a naturally occurring guaiazulene[14] (=7-isopropyl-1,4-dimethylazulene) (**8**), whose compound has been widely used clinically as an anti-inflammatory and anti-ulcer agent, and have reported a facile preparation and crystal structures as well as spectroscopic, chemical, and electrochemical properties of extended π-electron systems possessing a 3-guaiazulenyl (=5-isopropyl-3,8-dimethylazulen-1-yl) group.[15–40] In relation to the study on the molecular structure of **2**,[10] in 2005 we found that the reaction of **8** with 2- (or 4-) hydroxybenzaldehyde in methanol in the presence of hexafluorophosphoric acid at 25 °C for 2 h gave the corresponding monocarbenium ion compound **3** (or **6**),[25] possessing two interesting resonance structures, respectively, i.e., a protonated *o*- (or *p*-) benzoquinonemethide form and a 3-guaiazulenylium ion form in acetonitrile (see Chart 2), while each X-ray crystallographic analysis of **3** (and **6**) could not be achieved because of difficulty in obtaining a single crystal suitable for that purpose. Furthermore, in

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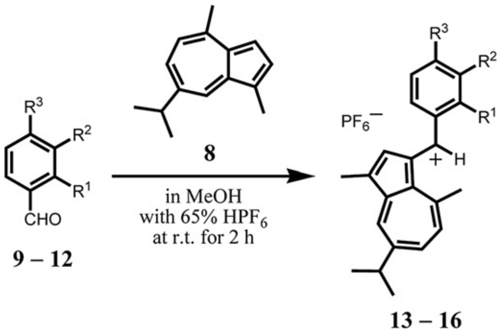
2007 we reported a comparative study on the crystal structures of (3-guaiazulenyl)(2-methoxyphenyl)methylium tetrafluoroborate[41] (**$4BF_4$**), **5**, and **7** (see Chart 2), whose hydrogen atoms could not be refined.[32] Interestingly, the structural parameters for the X-ray crystallographic analyses of **$4BF_4$** and **7** suggested the crystal structures with similar resonance structures to **3** and **6** in acetonitrile. During the course of our basic and systematic investigations on the above,[15–41] we have quite recently discovered the unique monocarbenium ion compounds **14** and **15** (see Chart 2), apparently possessing two representative resonance structures, respectively, i.e., the protonated *o*- (and *p*-) benzoquinonemethide forms **14a** (and **15a**) and the 3-guaiazulenylium ion forms **14b** (and **15b**) in a solution of acetonitrile and further, in a single crystal (see Chart 3). We now wish to report the detailed title studies: namely, a facile preparation and crystal structures as well as spectroscopic, chemical, and electrochemical properties of our systematic monocarbenium ion compounds **13–16** stabilized by 3-guaiazulenyl and dihydroxyphenyl (or hydroxymethoxyphenyl) groups with a view to comparative study (see Chart 2).

2. Results and discussion

2.1. Preparation and spectroscopic properties of 13–16

The target monocarbenium ion compounds **13–16** were prepared according to the procedures shown in Scheme 1, Table 1, and Sections 4.1.1–4.1.4. The structures of the products **13–16** were established on the basis of elemental analysis and spectroscopic data [UV–vis, IR, exact FABMS, and ^1H and ^{13}C NMR including 2D NMR (i.e., DQF COSY, HSQC, and HMBC)].



Scheme 1. The reactions of **8** with **9–12** in methanol in the presence of hexafluorophosphoric acid (i.e., 65% aqueous solution) at 25 °C for 2 h, yielding the corresponding monocarbenium ion compounds **13–16**.

Table 1
The isolated yields (%) of the products **13–16** obtained by the reactions of **8** with **9–12** in methanol in the presence of hexafluorophosphoric acid (i.e., 65% aqueous solution) at 25 °C for 2 h

Entry	Substituent			Temp/°C	Time/h	Product	Yield/%
	R^1	R^2	R^3				
1	OH	OH	H	25	2	**13**	86
2	OH	OCH_3	H	25	2	**14**	63
3	H	OH	OH	25	2	**15**	43
4	H	OCH_3	OH	25	2	**16**	77

Compound **13** was obtained as a dark-red powder (see Section 4.1.1). The IR spectrum showed that although a specific band (ν_{max} 3452 cm^{-1}) from two hydroxy groups of **13** revealed a low wavenumber shift in comparison with that of **3** (ν_{max} 3483 cm^{-1}),[25] two specific bands (ν_{max} 841 and 559 cm^{-1}) based on the counter anion (PF_6^-) of **13** coincided with those of **3** (ν_{max} 845 and 559 cm^{-1}).[25] The formula $C_{22}H_{23}O_2$ for the monocarbenium ion structure $[M-PF_6]^+$ was determined by exact FABMS spectrum. An elemental analysis confirmed the formula $C_{22}H_{23}O_4F_6P$ (i.e., $C_{22}H_{23}O_2+PF_6+O_2$). The ^1H NMR spectrum for **13** showed signals based on a 2,3-dihydroxyphenyl group with a similar resonance structure to the protonated quinonemethide form **14a** (see Chart 3) and further, revealed signals based on a 3-guaiazulenylmethylium ion unit with a similar resonance structure to the 3-guaiazulenylium ion form **14b** (see Chart 3), the signals of which were carefully assigned using DQF COSY and computer-assisted simulation based on first-order analysis (see Tables 2 and 3 and Section 4.1.1). The ^{13}C NMR spectrum exhibited 21 carbon signals assigned by HSQC and HMBC (see Tables 4 and 5 and Section 4.1.1), the assignments of which support a (3-guaiazulenyl)(2,3-dihydroxyphenyl)methylium ion structure. Thus, the elemental analysis and the total spectroscopic analyses for **13** led to the target monocarbenium ion structure (3-guaiazulenyl)(2,3-dihydroxyphenyl)methylium hexafluorophosphate.

Table 2
The ^1H NMR chemical shifts (δ) for the dihydroxyphenyl (and hydroxymethoxyphenyl) groups of **13–18**

Compound	H-2	H-3	H-4	H-5	H-6	CH_3O-3	HO-2	HO-3	HO-4
13	—	—	7.07	6.93	7.22	—	[a]	[a]	—
14	—	—	7.16	7.03	7.30	3.93	7.58	—	—
15	7.41	—	—	7.04	7.38	—	—	7.25	7.87
16	7.45	—	—	7.01	7.50	3.98	—	—	7.69
17	—	—	6.78	6.63	6.13	3.85	6.57	—	—
18	6.72	—	—	6.66	6.34	3.73	—	—	6.28

[a] The OH signal was included in a signal of slightly existing water molecule in CD_3CN.

Table 3
The ^1H NMR chemical shifts (δ) for the 3-guaiazulenylmethylium ion units of **13–16** and the 3-guaiazulenylmethyl groups of **17** and **18**

Compound	HC^+-α	Me-1′	H-2′	Me-4′	H-5′	H-6′	$(CH_3)_2CH$-7′	$(CH_3)_2CH$-7′	H-8′
13	9.00	2.50	7.99	3.33	8.48	8.38	3.48	1.45	8.57
14	9.02	2.50	8.00	3.33	8.47	8.38	3.48	1.45	8.57
15	8.65	2.53	8.09	3.32	8.42	8.35	3.46	1.46	8.56
16	8.72	2.54	8.12	3.34	8.42	8.35	3.46	1.44	8.57
17	4.49[a]	2.56	7.32	2.77	6.80	7.28	3.03	1.31	8.09
18	4.48[a]	2.56	7.37	2.82	6.80	7.28	3.02	1.30	8.09

[a] CH_2-3′.

Table 4
The ^{13}C NMR chemical shifts (δ) for the dihydroxyphenyl (and hydroxymethoxyphenyl) groups of **13–18**

Compound	C-1	C-2	C-3	C-4	C-5	C-6	CH_3O-3
13	145.4	148.2	124.2	120.3	121.8	125.5	—
14	149.2	148.6	123.3	116.3	121.6	125.5	57.0
15	129.2	120.1	146.6	151.8	117.4	130.3	—
16	129.0	117.1	149.2	153.2	117.2	130.9	57.0
17	130.3	143.9	147.6	109.9	120.1	122.8	56.7
18	136.2	112.9	148.1	144.9	115.4	121.7	56.6

Although a single crystal of compound **13** could not be obtained under numerous recrystallization conditions, that of compound **14** could be obtained as dark-red needles from a mixed recrystallization solvent of acetonitrile and diethyl ether (1:5, vol/vol) (see Section 4.1.2). The UV–vis spectrum showed that the longest absorption wavelength of **14** (λ_{max} 486 nm) (see Fig. 1) coincided with those of **3** (λ_{max} 489 nm)[25] and **4** (λ_{max} 487 nm);[32] however, the molar extinction coefficient ($\log \varepsilon$=4.12) of which revealed a hypochromic effect in comparison with those of **3** ($\log \varepsilon$=4.50)[25] and **4** ($\log \varepsilon$=4.44).[32] The IR

Table 5
The selected ^{13}C NMR chemical shifts (δ) for the 3-guaiazulenylmethylium ion units of **13**–**16** and the 3-guaiazulenylmethyl groups of **17** and **18**

Compound	HC^{+}-α	C-1′	C-2′	C-3′	C-3a′	C-4′	C-5′	C-6′	C-7′	C-8′	C-8a′
13	146.0	145.7	142.1	139.4	153.6	157.6	150.3	144.8	171.0	139.8	161.2
14	145.6	145.4	141.9	139.4	153.6	157.5	150.3	144.7	171.0	139.8	161.2
15	151.8	146.6	141.8	137.5	153.3	157.1	149.0	144.3	169.2	139.6	159.6
16	151.8	144.6	141.8	137.5	153.3	157.1	149.0	144.3	169.2	139.6	159.6
17	31.4[a]	125.0	141.7	126.4	133.9	146.4	126.8	135.7	139.8	134.2	138.7
18	37.1[a]	125.1	141.9	127.3	133.7	146.4	127.0	135.7	139.9	134.3	138.8

[a] CH_2-3′.

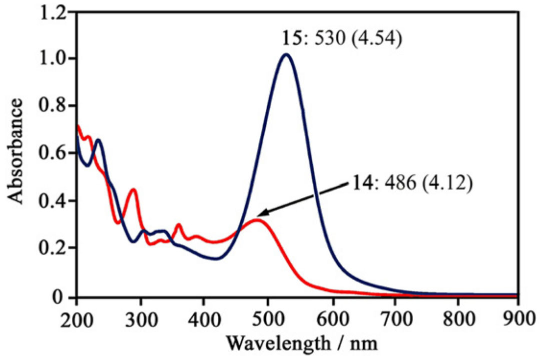


Fig. 1. The UV–vis spectra of **14** and **15** in CH_3CN. Concentrations, **14**: 0.13 g L^{-1} (242 μmol L^{-1}), **15**: 0.14 g L^{-1} (290 μmol L^{-1}). Length of cell: 0.1 cm each. Each log ε value is given in parenthesis.

spectrum showed that although a specific band (ν_{max} 3452 cm^{-1}) from a hydroxy group of **14** revealed a low wavenumber shift in comparison with that of **3**,[25] the wavenumber of which coincided with that of **13**, and further, that two specific bands (ν_{max} 841 and 559 cm^{-1}) based on the counter anion (PF_6^-) of **14** coincided with those of **3**,[25] **4** (ν_{max} 841 and 559 cm^{-1}),[32] and **13**. The formula $C_{23}H_{25}O_2$ for the monocarbenium ion structure $[M-PF_6]^+$ was determined by exact FABMS spectrum. An elemental analysis confirmed the formula $C_{25}H_{28}O_3NF_6P$ (i.e., $C_{23}H_{25}O_2+PF_6+CH_3CN+1/2O_2$). The ^1H NMR spectrum for **14** showed signals based on a 2-hydroxy-3-methoxyphenyl group with the resonance structure **14a** (see Chart 3) and further, revealed signals based on a 3-guaiazulenylmethylium ion unit with the resonance structure **14b** (see Chart 3), the signals of which were carefully assigned using similar analyses to those of **13** (see Tables 2 and 3 and Section 4.1.2). The ^{13}C NMR spectrum exhibited 22 carbon signals assigned using similar analyses to those of **13** (see Tables 4 and 5 and Section 4.1.2), the assignments of which support a (3-guaiazulenyl)(2-hydroxy-3-methoxyphenyl) methylium ion structure. Thus, the elemental analysis and the total spectroscopic analyses for **14** led to the target monocarbenium ion structure (3-guaiazulenyl)(2-hydroxy-3-methoxyphenyl)methylium hexafluorophosphate.

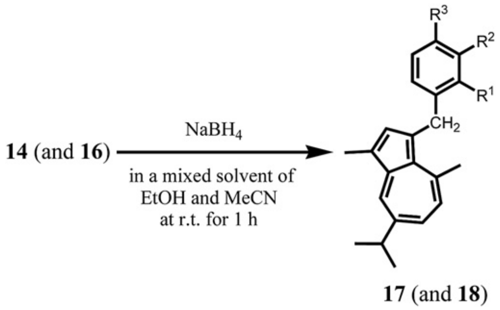
A single crystal of compound **15** was obtained as dark-red blocks under the same recrystallization conditions as for **14** (see Section 4.1.3). The UV–vis spectrum showed that the longest absorption wavelength of **15** (λ_{max} 530 nm, log ε=4.54) revealed a bathochromic shift and a hyperchromic effect in comparison with that of **14** (see Fig. 1) and further, that the wavelength of which revealed a bathochromic shift and a hypochromic effect in comparison with that of **6** (λ_{max} 510 nm, log ε=4.67).[25] The IR spectrum showed that although two specific bands (ν_{max} 3444 and 3274 cm^{-1}) from two hydroxy groups of **15** revealed low wavenumber shifts in comparison with that of **6** (ν_{max} 3476 cm^{-1}),[25] two specific bands (ν_{max} 844 and 559 cm^{-1}) based on the counter anion (PF_6^-) of **15** coincided with those of **6** (ν_{max} 837 and 556 cm^{-1}).[25] The formula $C_{22}H_{23}O_2$ for the monocarbenium ion structure $[M-PF_6]^+$ was determined by exact FABMS spectrum. An elemental analysis confirmed the formula $C_{22}H_{23}O_3F_6P$ (i.e., $C_{22}H_{23}O_2+PF_6+1/2O_2$). The ^1H NMR spectrum for **15** showed signals based on a 3,4-dihydroxyphenyl group with the resonance structure **15a** (see Chart 3) and further, revealed signals based on a 3-guaiazulenylmethylium ion unit with the resonance structure **15b** (see Chart 3), the signals of which were carefully assigned using similar analyses to those of **13** (see Tables 2 and 3 and Section 4.1.3). The ^{13}C NMR spectrum exhibited 21 carbon signals assigned using similar analyses to those of **13** (see Tables 4 and 5 and Section 4.1.3), the assignments of which support a (3-guaiazulenyl)(3,4-dihydroxyphenyl)methylium ion structure. Thus, the elemental analysis and the total spectroscopic analyses for **15** led to the target monocarbenium ion structure (3-guaiazulenyl)(3,4-dihydroxyphenyl)methylium hexafluorophosphate.

Compound **16** was obtained as dark-red blocks under the same recrystallization conditions as for **15**, while a single crystal suitable for X-ray crystallographic analysis of **16** could not be obtained (see Section 4.1.4). The UV–vis spectrum showed that the longest absorption wavelength and the molar extinction coefficient of **16** (λ_{max} 527 nm, log ε=4.59) coincided with those of **15**. The IR spectrum showed that although a specific band (ν_{max} 3468 cm^{-1}) from a hydroxy group of **16** revealed a high wavenumber shift in comparison with those of **15**, two specific bands (ν_{max} 841 and 559 cm^{-1}) based on the counter anion (PF_6^-) of **16** coincided with those of **15**. The formula $C_{23}H_{25}O_2$ for the monocarbenium ion structure $[M-PF_6]^+$ was determined by exact FABMS spectrum. An elemental analysis confirmed the formula $C_{25}H_{28}O_4NF_6P$ (i.e., $C_{23}H_{25}O_2+PF_6+CH_3CN+O_2$). The ^1H NMR spectrum for **16** showed signals based on a 4-hydroxy-3-methoxyphenyl group with a similar resonance structure to the protonated quinonemethide form **15a** (see Chart 3) and further, revealed signals based on a 3-guaiazulenylmethylium ion unit with a similar resonance structure to the 3-guaiazulenylium ion form **15b** (see Chart 3), the signals of which were carefully assigned using similar analyses to those of **13** (see Tables 2 and 3 and Section 4.1.4). The ^{13}C NMR spectrum exhibited 22 carbon signals assigned using similar analyses to those of **13** (see Tables 4 and 5 and Section 4.1.4), the assignments of which support a (3-guaiazulenyl)(4-hydroxy-3-methoxyphenyl)methylium ion structure. Thus, the elemental analysis and the total spectroscopic analyses for **16** led to the target monocarbenium ion structure (3-guaiazulenyl)(4-hydroxy-3-methoxyphenyl)methylium hexafluorophosphate.

The HC^{+}-α proton NMR signals of **13** and **14** (δ 9.00 and 9.02) showed larger down-field shifts in comparison with those of **15** and **16** (δ 8.65 and 8.72), suggesting the formation of the $C\alpha{-}H{\cdots}O{-}C2$ hydrogen bond. Similarly, the HC^{+}-α proton NMR signals of the previously reported compounds **3**[25] and **4**[32] (δ 9.01 and 9.04) revealed larger down-field shifts in comparison with those of **6**[25] and **7**[32] (δ 8.72 and 8.74), owing to the same influence as for **13** and **14**.

2.2. Hydride-reductions of 14 and 16 with $NaBH_4$

Although the hydride-reductions of the (3-guaiazulenyl)-(dihydroxyphenyl)methylium hexafluorophosphates **13** and **15** with $NaBH_4$ in a mixed solvent of ethanol and acetonitrile at 25 °C for 1 h gave several products simultaneously, the hydride-reductions of the 1-hydroxy-2-methoxybenzene derivatives **14** and **16** with $NaBH_4$ under the same reaction conditions as for **13** and **15** afforded **17** and **18** quantitatively (94% yield each) (see Scheme 2 and Table 6). Thus, a hydride-ion attached to each HC^+-α position of **14** and **16** selectively.



Scheme 2. The hydride-reductions of **14** (and **16**) with $NaBH_4$ in a mixed solvent of ethanol and acetonitrile at 25 °C for 1 h, yielding **17** (and **18**) quantitatively.

Table 6
The isolated yields (%) of the products **17** (and **18**) obtained by the hydride-reductions of **14** (and **16**) with $NaBH_4$ in a mixed solvent of ethanol and acetonitrile at 25 °C for 1 h

Entry	Substituent			Temp/°C	Time/h	Product	Yield/%
	R^1	R^2	R^3				
1	OH	OCH_3	H	25	1	**17**	94
2	H	OCH_3	OH	25	1	**18**	94

The product **17** was obtained as blue needles (see Section 4.1.5). The molecular formula $C_{23}H_{26}O_2$ was determined by exact FABMS spectrum. The IR spectrum showed that a specific band (ν_{max} 3436 cm^{-1}) from a hydroxy group of **17** revealed a low wavenumber shift in comparison with that of **14** (ν_{max} 3452 cm^{-1}). The ^1H NMR spectrum showed signals based on a 2-hydroxy-3-methoxyphenyl and 3-guaiazulenylmethyl group, the signals of which were carefully assigned using similar analyses to those of **13** (see Tables 2 and 3 and Section 4.1.5). The ^{13}C NMR spectrum exhibited 22 carbon signals assigned using similar analyses to those of **13** (see Tables 4 and 5 and Section 4.1.5). Thus, the total spectroscopic analyses for **17** led to the molecular structure (3-guaiazulenyl)(2-hydroxy-3-methoxyphenyl)methane. From comparative studies of the chemical shifts (δ) for the ^1H and ^{13}C NMR signals of **14** with those of **17** (see Tables 2–5), it can be inferred that a positive charge of the 3-guaiazulenylmethylium ion unit of **14** is transferred to the 2-hydroxy-3-methoxybenzene and guaiazulene rings, generating two representative resonance structures of the protonated quinonemethide form **14a** and the 3-guaiazulenylium ion form **14b** (see Chart 3). From the detailed comparative NMR studies of **13** with **14** (see Tables 2–5), it can be inferred that **13** also possesses similar resonance structures to **14** in acetonitrile-d_3.

The product **18** was obtained as a blue paste (see Section 4.1.6). The molecular formula $C_{23}H_{26}O_2$ was determined by exact EIMS spectrum. The ^1H NMR spectrum showed signals based on a 4-hydroxy-3-methoxyphenyl and 3-guaiazulenylmethyl group, the signals of which were carefully assigned using similar analyses to those of **13** (see Tables 2 and 3 and Section 4.1.6). The ^{13}C NMR spectrum exhibited 22 carbon signals assigned using similar analyses to those of **13** (see Tables 4 and 5 and Section 4.1.6). Thus, the total spectroscopic analyses for **18** led to the molecular structure (3-guaiazulenylmethyl)(4-hydroxy-3-methoxyphenyl)methane. The chemical shifts (δ) for the ^1H and ^{13}C NMR signals of **16** compared with those of **18** are shown in Tables 2–5, leading to the formation of **16** with two representative resonance structures of the protonated *p*-benzoquinonemethide form and the 3-guaiazulenylium ion form. From the detailed comparative NMR studies of **16** with **15** (see Tables 2–5), it can be inferred that **16** possesses similar resonance structures to **15** (see Chart 3) in acetonitrile-d_3.

2.3. X-ray crystal structure of 14 compared with that of the related carbenium ion compound (3-guaiazulenyl)(2-methoxyphenyl)methylium tetrafluoroborate (4BF$_4$)

Although it was very difficult to obtain a single crystal of **13** suitable for X-ray crystallographic analysis, the recrystallization of **14** from a mixed solvent of acetonitrile and diethyl ether (1:5, vol/vol) provided a stable single crystal suitable for that purpose. Thus, the crystal structure of **14** could be determined by means of X-ray diffraction, producing accurate structural parameters (see Section 4.1.7). Non-hydrogen atoms were refined anisotropically and further, hydrogen atoms could be refined isotropically. The ORTEP drawing of **14** with a numbering scheme, indicating the structure illustrated in Chart 2, is shown in Fig. 2a along with the selected bond lengths (see Table 7). The results are as follows. The plane of the benzene ring of **14** twisted by 5.3° from that of the 3-guaiazulenylmethylium ion unit, owing to the influence of steric hindrance and steric repulsion between the hydrogen atoms of the C6 and C2′ positions (see the space-filling structure of **14** shown in Fig. 2c), the torsion angle of which was smaller than that of **4BF$_4$** (35.4°).[32] Similar to **4BF$_4$**, the 3-guaiazulenylmethylium ion unit of **14** clearly underwent bond alternation between single and double bonds as shown in Table 7. The 2-hydroxy-3-methoxybenzene ring of **14** also clearly underwent bond alternation between single and double bonds as shown in Table 7. The average C–C bond length for the seven-membered ring of the 3-guaiazulenyl group of **14** (1.405 Å) coincided with that of **4BF$_4$** (1.401 Å). The bond lengths for the five-membered ring of the 3-guaiazulenyl group of **14** appreciably varied between 1.345 and 1.451 Å; in particular, the C1′–C2′ bond length (1.345 Å) was characteristically shorter than the average C–C bond length for the five-membered ring (1.435 Å), the bond alternation pattern of which coincided with those of **4BF$_4$**. The C3′–Cα bond length of **14** (1.363 Å) was also characteristically shorter than the C1–Cα bond length of **14** (1.452 Å). The C3′–Cα bond length of **14** coincided with that of **4BF$_4$** (1.370 Å). The C–C bond alternation pattern of the 2-hydroxy-3-methoxybenzene ring of **14** coincided with that of the 2-methoxybenzene ring of **4BF$_4$**. The C1–Cα bond length of **14** was slightly longer than that of **4BF$_4$** (1.443 Å). The C1–C2, C2–C3, C6–C1, and C1–Cα bond lengths of **14** were longer than the C3–C4, C4–C5, and C5–C6 bond lengths of **14**. The C2–O bond length (1.354 Å) of **14** was slightly shorter than the C3–O bond length of **14** (1.363 Å). The Cα–H bond length of **14** (0.92 Å) coincided with the average C–H bond length for the azulene and benzene rings of **14** (0.91 Å). The O–H bond length at the C2 position was 0.76 Å, the bond length of which was characteristically shorter than that of the oxonium ion H_3O^+ (0.86 Å),[5] and the Cα–H···O–C2 and C2–OH···O–C3 distances of **14** (2.24 and 2.19 Å)[42] and the space-filling structure of **14** shown in Fig. 2c, along with the ^1H NMR chemical shifts of **14**, were suggested to form an intramolecular C–H···O–H···O–CH_3 hydrogen bond between them (see Fig. 2a). In conclusion, it can be inferred that the total structural parameters based on the X-ray crystallographic analysis of **14**, compared with those based on the related crystal structure of **4BF$_4$**, apparently led to the crystal structure (3-guaiazulenyl)(2-hydroxy-3-methoxyphenyl)methylium hexafluorophosphate together with two representative resonance structures, i.e., the protonated quinonemethide structure **14a** and the 3-guaiazulenylium ion structure **14b**, illustrated in Chart 3.

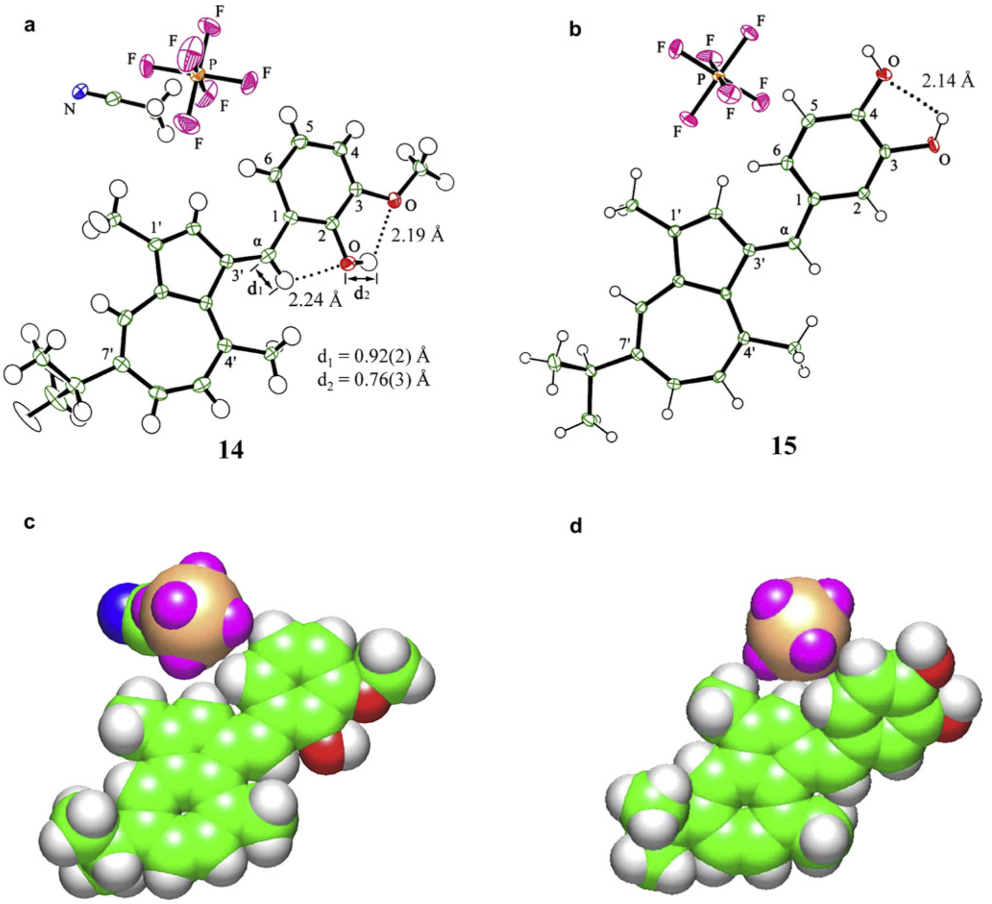


Fig. 2. (a, b) The ORTEP drawings with numbering schemes of **14**, with an equivalent of CH_3CN, and **15**: 30% probability thermal ellipsoids, respectively. **14**: Hydrogen atoms were refined isotropically. **15**: Hydrogen atoms were included but not refined. (c, d) The space-filling structures of **14**, with an equivalent of CH_3CN, and **15**.

Table 7
The selected C–C and C–O bond lengths (Å) for the 3-guaiazulenylmethylium ion units of **14** and **15**, the 2-hydroxy-3-methoxyphenyl group of **14**, and the 3,4-dihydroxyphenyl group of **15**

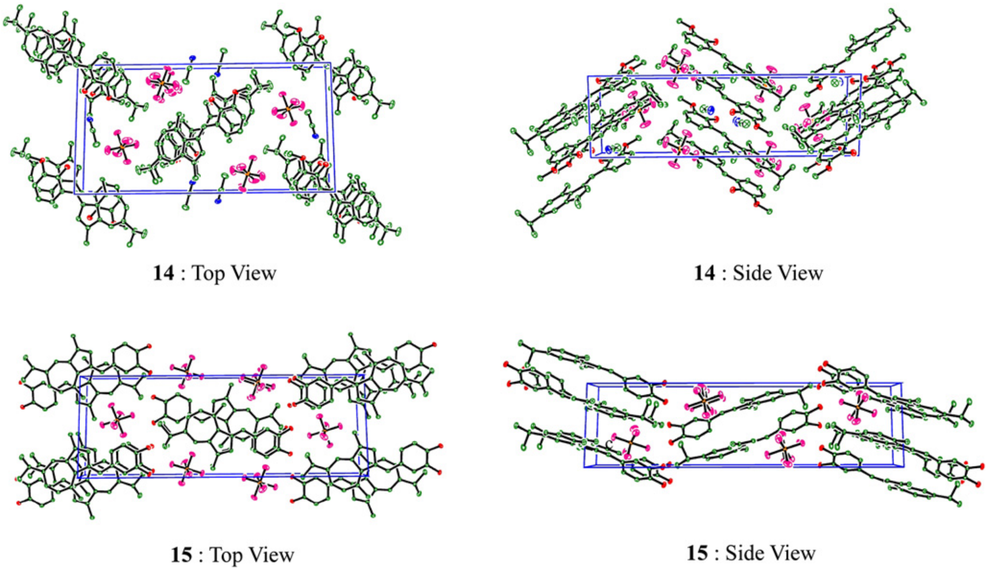
Atom	**14**	**15**	Atom	**14**	**15**
C1′–C2′	1.345(3)	1.349(3)	C1–C2	1.406(3)	1.411(3)
C2′–C3′	1.443(4)	1.457(3)	C2–C3	1.405(3)	1.378(3)
C3′–C3a′	1.486(3)	1.479(3)	C3–C4	1.382(4)	1.402(2)
C3a′–C4′	1.411(3)	1.396(3)	C4–C5	1.383(4)	1.383(3)
C4′–C5′	1.419(3)	1.411(3)	C5–C6	1.374(4)	1.380(3)
C5′–C6′	1.378(3)	1.384(3)	C6–C1	1.422(3)	1.408(2)
C6′–C7′	1.403(4)	1.398(3)	C1–Cα	1.452(3)	1.450(3)
C7′–C8′	1.380(4)	1.395(3)	C2–O	1.354(3)	—
C8′–C8a′	1.394(3)	1.392(3)	C3–O	1.363(2)	1.375(2)
C8a′–C1′	1.450(3)	1.456(3)	C4–O	—	1.354(2)
C3a′–C8a′	1.451(3)	1.456(3)	C3O–CH_3	1.430(3)	—
C3′–Cα	1.363(3)	1.374(3)	—	—	—

2.4. X-ray crystal structure of 15 compared with those of the related compounds 2, 7, 19, and 20

Although it was very difficult to obtain a single crystal of **16** suitable for X-ray crystallographic analysis, the recrystallization of **15** from a mixed solvent of acetonitrile and diethyl ether (1:5, vol/vol) provided a stable single crystal suitable for that purpose. Thus, the crystal structure of **15** could be determined by means of X-ray diffraction, producing accurate structural parameters (see Section 4.1.8). Non-hydrogen atoms were refined anisotropically and hydrogen atoms were included but not refined. The ORTEP drawing of **15** with a numbering scheme, indicating the structure illustrated in Chart 2, is shown in Fig. 2b along with the selected bond lengths (see Table 7). The results are as follows. The plane of the benzene ring of **15** twisted by 29.5° from that of the 3-guaiazulenylmethylium ion unit, owing to the influence of steric hindrance and steric repulsion between the hydrogen atoms of the C6 and C2′ positions (see the space-filling structure of **15** shown in Fig. 2d), the torsion angle of which was larger than that of **7** (22.7°).[32] Similar to **7**, the 3-guaiazulenylmethylium ion unit of **15** clearly underwent bond alternation between single and double bonds as shown in Table 7. The 3,4-dihydroxybenzene ring of **15** also underwent bond alternation between single and double bonds as shown in Table 7. The average C–C bond length for the seven-membered ring of the 3-guaiazulenyl group of **15** (1.405 Å) coincided with that of **7** (1.403 Å). The bond lengths for the five-membered ring of the 3-guaiazulenyl group of **15** appreciably varied between 1.349 and 1.456 Å; in particular, the C1′–C2′ bond length (1.349 Å) was characteristically shorter than the average C–C bond length for the five-membered ring (1.440 Å), the bond alternation pattern of which coincided with that of **7**. The C3′–Cα bond length of **15** (1.374 Å) was also characteristically shorter than the C1–Cα bond length of **15** (1.450 Å). The C3′–Cα bond length of **15** was slightly longer than those of **7** and **19**[43] (1.364 Å each); however, the bond length of which was characteristically shorter than the C3′–C7 bond length of **20**[43] (1.433 Å) (see Chart 4). The C1–Cα bond length of **15** coincided with those of **7** (1.448 Å) and **19** (1.443 Å); however, the bond length of which was longer than that of **2**[10] (1.412 Å) and the C4–C7 bond length of **20** (1.374 Å). The bond alternation pattern of the 3,4-dihydroxyphenyl group of **15** coincided with that of the 4-methoxyphenyl group of **7**. The C4–O bond length (1.354 Å) of **15** coincided with those of **7** (1.351 Å) and **19** (1.361 Å), while the bond length of which was shorter than the C3–O bond length of **15** (1.375 Å).

Furthermore, the C4–O bond length of **14** was longer than the corresponding C–O bond lengths of **2** (1.318 Å) and **20** (1.243 Å). Similar to **14**, the C3–OH···O–C4 distance of **15** (2.14 Å) and the space-filling structure of **15** shown in Fig. 2d were suggested to form a C3–OH···O–C4 hydrogen bond between them. In conclusion, it can be inferred that the total structural parameters based on the X-ray crystallographic analysis of **15**, compared with those of the related compounds **2**, **7**, **19**, and **20**, apparently led to the crystal structure (3-guaiazulenyl)(3,4-dihydroxyphenyl)methylium hexafluorophosphate together with two representative resonance structures, i.e., the protonated quinonemethide form **15a** and the 3-guaiazulenylium ion form **15b**, illustrated in Chart 3. Along with the experimental results, the accurate parameters for the crystal structures of **14**, with an equivalent of a recrystallization solvent molecule CH_3CN, and **15** were transferred to a WinMOPAC (Ver. 3.0) program[44] and their atomic charges were calculated. Although the atomic charges of **14** could not be calculated, those of **15** could be calculated as follows. The order of larger positive charge for **15** was C-4 (0.223)>C-3 (0.117)>C-6 (0.089)>C-7′ (0.082)>C-α and C-8a′ (0.064 each)>C-4′ (0.035)>C-5′ (0.024)>C-1 (0.008)>C-3a′ (−0.004)>C-8′ (−0.007)>C-3′ (−0.016)>C-6′ (−0.024)>C-1′ (−0.031)>C-2′ (−0.037)>C-2 (−0.068)>C-5 (−0.134), the calculation of which suggested the formation of the resonance structures **15a** and **15b** illustrated in Chart 3.

Along with the ORTEP drawings and the space-filling structures of **14** and **15**, the top and side views for the packing structures of **14**, with an equivalent of a recrystallization solvent molecule CH_3CN, and **15** revealed that these compounds formed π-stacking structures in their single crystals, respectively, and showed that each average inter-plane distance between over-lapping structures [i.e., the 3-guaiazulenylmethylium plane of a compound and the 2-hydroxy-3-methoxyphenyl (or 3,4-dihydroxyphenyl) plane of another compound], which were overlapped so that those dipole moments might be negated mutually, was 3.46 Å for **14** or 3.18 Å for **15** (see Fig. 3).


14 : Top View

14 : Side View

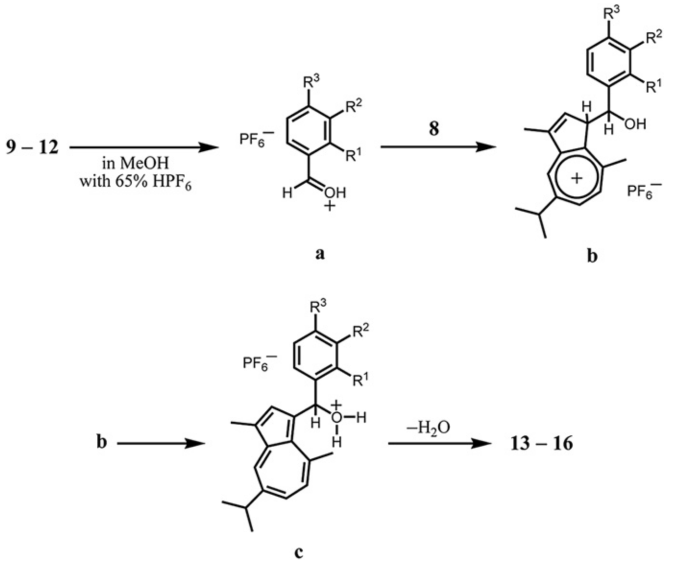
15 : Top View

15 : Side View

Fig. 3. Top and side views for the packing structures of **14**, with an equivalent of CH_3CN, and **15**, the hydrogen atoms of which are omitted for reasons of clarity.

2.5. A plausible reaction pathway for the formation of 13–16

From the structures of the resulting products **13**–**16**, a plausible reaction pathway for the formation of **13**–**16** can be inferred as illustrated in Scheme 3: namely, the generated oxonium ion forms **a** are gradually converted into the target monocarbenium ion compounds **13**–**16**, presumably via the azulenium ion forms **b** and the alkyl oxonium ion forms **c**, whose structures are yielded by a proton transfer from **b** to **c**. The basic studies of our structural analyses for **13**–**16** support the existence of the oxonium ion forms **a** under the reaction conditions illustrated in Scheme 3.



Scheme 3. A plausible reaction pathway for the formation of **13**–**16** yielded by the reactions of **8** with **9**–**12** in methanol in the presence of hexafluorophosphoric acid (i.e., 65% aqueous solution) at 25 °C for 2 h.

2.6. Electrochemical behavior of 14 and 15

We have been interested further in the electrochemical properties of **14** and **15**, the crystal structures of which could be determined, with a view to comparative study. The electrochemical behavior of **14** and **15** was, therefore, measured by means of CV (=Cyclic Voltammogram) and DPV (=Differential Pulse Voltammogram) [Potential (in volts) vs SCE] in CH_3CN containing 0.1 M [n-Bu_4N]PF_6 as a supporting electrolyte. As the results, it was found that **14** and **15** underwent one-electron reduction, respectively, at the potentials of −0.33 V (E_{pc}, irreversible) by CV [−0.26 V (E_p) by DPV] for **14** and −0.36 V (E_{pc}, irreversible) by CV [−0.31 V (E_p) by DPV] for **15**, as shown in Fig. 4, generating the corresponding radical-species[45] [i.e.,

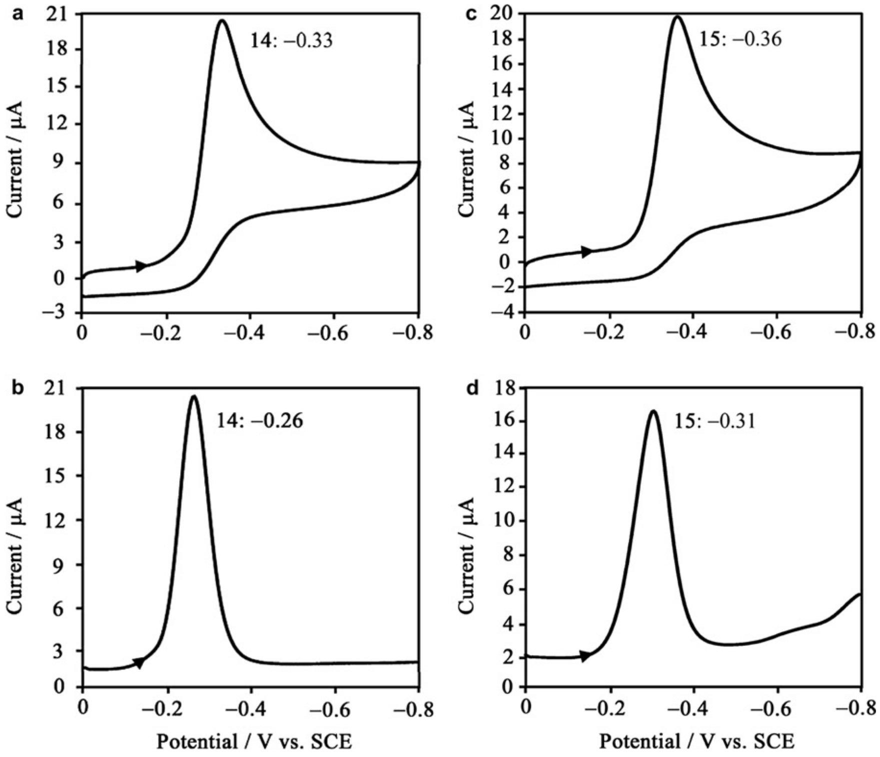
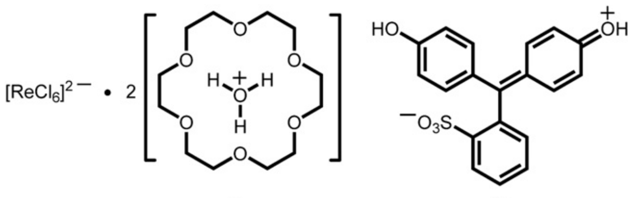


Fig. 4. Cyclic [(a), (c)] and differential pulse [(b), (d)] voltammograms of **14** (3.0 mg, 5.6 μmol) and **15** (3.0 mg, 6.2 μmol) in 0.1 M [n-$Bu_4N]PF_6$, CH_3CN (10 mL) at a glassy carbon (ID: 3 mm) and a platinum wire served as working and auxiliary electrodes; scan rates 100 mV s^{-1} at 25 °C under argon. For comparative purposes, the oxidation potential using ferrocene as a standard material showed +0.42 V (E_p) by DPV and +0.40 V ($E_{1/2}$) by CV under the same electrochemical measurement conditions as for **14** and **15**.



1

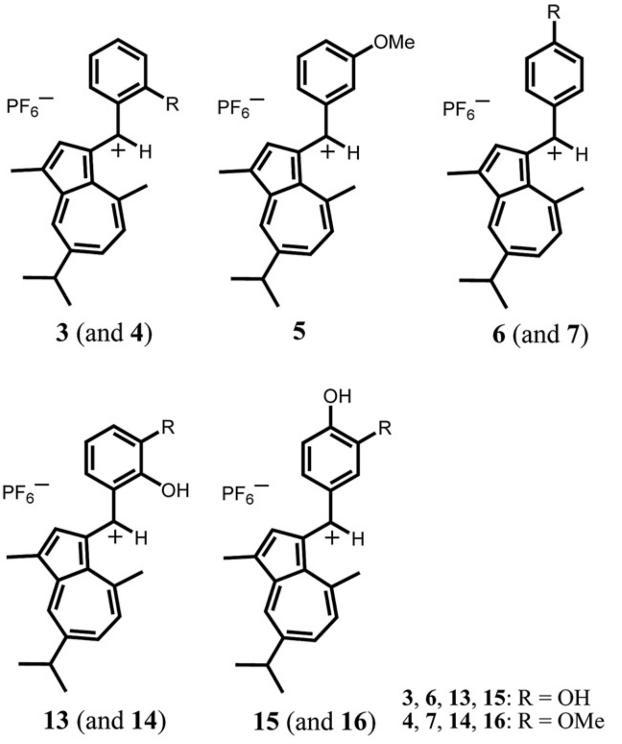
2

Chart 1.

the (3-guaiazulenyl)(2-hydroxy-3-methoxyphenyl)methyl and (3-guaiazulenyl)(3,4-dihydroxyphenyl)methyl radical-species]. Thus, **14** is slightly susceptible to reduction as compared with **15**, owing to a difference in electron affinity based on each delocalized π-electron system and further, **14** is slightly less susceptible to reduction than **4** [−0.28 V (E_{pc}, irreversible) by CV (−0.25 V by DPV)],[32] while the reduction potential of **15** coincided with that of **7** [−0.35 V (E_{pc}, irreversible) by CV (−0.29 V by DPV)].[32] In conclusion, the facility of one-electron reduction is in the order of **14**>**15**, the result of which coincided with those of **3**>**6**[25] and of **4**>**7**.[32]

3. Conclusion

We have reported the following six interesting points (i)–(vi) in this paper: namely, (i) the reaction of guaiazulene (**8**) with 2,3-dihydroxybenzaldehyde (**9**) in methanol in the presence of hexafluorophosphoric acid (i.e., 65% aqueous solution) at 25 °C for 2 h gave (3-guaiazulenyl)(2,3-dihydroxyphenyl)methylium hexafluorophosphate (**13**) in 86% yield. Similarly, the reaction of **8** with 2-hydroxy-3-methoxybenzaldehyde (**10**) [or 3,4-dihydroxybenzaldehyde (**11**) or 4-hydroxy-3-methoxybenzaldehyde (**12**)] under the same reaction conditions as for **9** afforded (3-guaiazulenyl)(2-hydroxy-3-methoxyphenyl)methylium hexafluorophosphate (**14**) (63% yield) [or (3-guaiazulenyl)(3,4-dihydroxyphenyl)methylium hexafluorophosphate (**15**) (43% yield) or (3-guaiazulenyl)(4-hydroxy-3-methoxyphenyl)methylium hexafluorophosphate (**16**) (77% yield)], the products of which are stabilized by 3-guaiazulenyl and dihydroxyphenyl (or hydroxymethoxyphenyl) groups; (ii) although the hydride-reductions of the 1,2-dihydroxybenzene derivatives **13** and **15** with $NaBH_4$ in a mixed solvent of ethanol and acetonitrile at 25 °C for 1 h gave several products simultaneously, the hydride-reductions of the 1-hydroxy-2-methoxybenzene derivatives **14** and **16** with $NaBH_4$ under the same reaction conditions as for **13** and **15** afforded (3-guaiazulenyl)(2-hydroxy-3-methoxyphenyl)methane (**17**) and (3-guaiazulenyl)(4-hydroxy-3-methoxyphenyl)methane (**18**) quantitatively (94% yield each). Thus, a hydride-ion attached to each HC^+-α position of **14** and **16** selectively; (iii) the chemical shifts (δ) for the ^1H and ^{13}C NMR signals of **13**–**16** compared with those of **17** and **18** were shown in Tables 2–5, apparently leading to the formation of **13**–**16** with two representative resonance structures, respectively, i.e., a protonated *o*- (or *p*-) benzoquinonemethide form and a 3-guaiazulenylium ion form, illustrated in Chart 3; (iv) although it was very difficult to obtain a single crystal of **13** (and **16**) suitable for X-ray crystallographic analysis, the recrystallization of **14** (and **15**) from a mixed solvent of acetonitrile and diethyl ether provided a stable single crystal, respectively, suitable for that purpose; (v) similar to the above NMR spectral results (iii), the structural parameters based on the X-ray crystallographic analyses of **14** and **15**, compared with those of the related compounds **2**, **4BF₄**, **7**, **19**, and **20**, led to the crystal structures with two representative resonance structures, respectively, i.e., a protonated *o*- (or *p*-) benzoquinonemethide form and a 3-guaiazulenylium ion form, illustrated in Chart 3, and further, it could be inferred that **14** possessed a unique C–H⋯O–H⋯O–CH_3 intramolecular hydrogen bond; and (vi) the reduction potentials of **14** and **15** based on CV and DPV data indicated that the facility of one-electron reduction was in the order of **14**>**15**, the result of which coincided with those of **3**>**6** and of **4**>**7**.

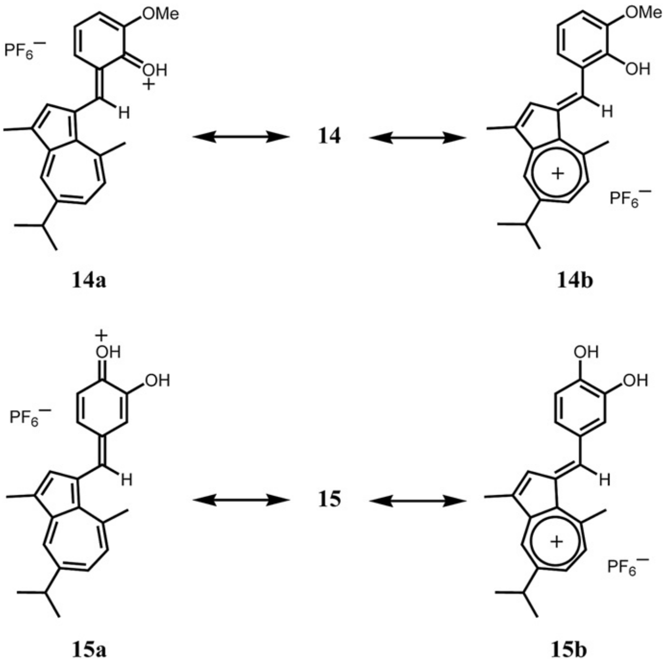


3 (and **4**) **5** **6** (and **7**)

13 (and **14**) **15** (and **16**)

3, **6**, **13**, **15**: R = OH
4, **7**, **14**, **16**: R = OMe

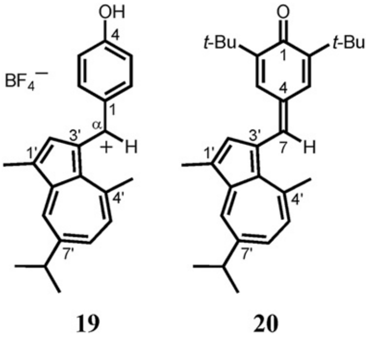
Chart 2.



14a **14b**

15a **15b**

Chart 3.



19 **20**

Chart 4.

4. Experimental

4.1. General

Melting points were taken on a Yanagimoto MP-S3 instrument. MS spectra were taken on a JEOL The Tandem Mstation JMS-700 TKM data system. UV–vis and IR spectra were taken on a Beckman DU640 spectrophotometer and a Shimadzu FTIR-4200 Grating spectrometer. NMR spectra were recorded with a JNM-ECA500 (500 MHz for ^{1}H and 125 MHz for ^{13}C) or JNM-ECA700 (700 MHz for ^{1}H and 176 MHz for ^{13}C) cryospectrometer at 25 °C. ^{1}H NMR spectra were assigned using computer-assisted simulation (software: *g*NMR developed by Adept Scientific plc) on a DELL Dimension 9150 personal-computer with a Pentium IV processor. Cyclic and differential pulse voltammograms were measured by an ALS Model 600 electrochemical analyzer.

4.1.1. *Preparation of (3-guaiazulenyl)(2,3-dihydroxyphenyl)methylium hexafluorophosphate (**13**).*

To a solution of commercially available guaiazulene (**8**) (70 mg, 0.35 mmol) in methanol (1.0 mL) was added a solution of commercially available 2,3-dihydroxybenzaldehyde (**9**) (55 mg, 0.40 mmol) in methanol (1.0 mL) containing hexafluorophosphoric acid (65% aqueous solution, 0.2 mL). The mixture was stirred at 25 °C for 2 h, and then evaporated in vacuo. The obtained residue was recrystallized from acetonitrile/diethyl ether (1:5, vol/vol) (several times) to provide pure **13** (150 mg, 0.30 mmol, 86% yield).

Compound **13**: Dark-red powder, mp >149 °C (decomp.); Found: C, 52.75; H, 4.68%. Calcd for $C_{22}H_{23}O_4F_6P$ (i.e., $C_{22}H_{23}O_2+PF_6+O_2$): C, 53.23; H, 4.67%; IR ν_{max} (KBr) cm^{-1}, 3452 (O–H) and 841, 559 (PF_6^-); exact FABMS (3-nitrobenzyl alcohol matrix), found: *m*/*z* 319.1693; calcd for $C_{22}H_{23}O_2$: $[M-PF_6]^+$, *m*/*z* 319.1693; 700 MHz ^{1}H NMR (CD_3CN), signals based on a (3-guaiazulenyl)methylium ion structure: 1.45 (6H, d, *J*=6.8 Hz, $(CH_3)_2$CH-7′), 2.50 (3H, d, *J*=0.8 Hz, Me-1′), 3.33 (3H, s, Me-4′), 3.48 (1H, sept, *J*=6.8 Hz, $(CH_3)_2CH$-7′), 7.99 (1H, br s, H-2′), 8.38 (1H, dd, *J*=11.3, 2.0 Hz, H-6′), 8.48 (1H, d, *J*=11.3 Hz, H-5′), 8.57 (1H, d, *J*=2.0 Hz, H-8′), and 9.00 (1H, br s, HC^+-α); signals based on a 2,3-dihydroxyphenyl group: 6.93 (1H, t, *J*=7.8 Hz, H-5), 7.07 (1H, br d, *J*=7.8 Hz, H-4), and 7.22 (1H, br d, *J*=7.8 Hz, H-6). The two OH signals at the C-2 and C-3 positions were included in a signal of slightly existing water molecule in CD_3CN; 176 MHz ^{13}C NMR (CD_3CN), 171.0 (C-7′), 161.2 (C-8a′), 157.6 (C-4′), 153.6 (C-3a′), 150.3 (C-5′), 148.2 (C-2) 146.0 (HC^+-α), 145.7 (C-1′), 145.4 (C-1), 144.8 (C-6′), 142.1 (C-2′), 139.8 (C-8′), 139.4 (C-3′), 125.5 (C-6), 124.2 (C-3), 121.8 (C-5), 120.3 (C-4), 40.2 ($(CH_3)_2CH$-7′), 29.8 (Me-4′), 23.8 ($(CH_3)_2$CH-7′), and 13.8 (Me-1′).

4.1.2. *Preparation of (3-guaiazulenyl)(2-hydroxy-3-methoxyphenyl)methylium hexafluorophosphate (**14**).*

To a solution of commercially available guaiazulene (**8**) (70 mg, 0.35 mmol) in methanol (1.0 mL) was added a solution of commercially available 2-hydroxy-3-methoxybenzaldehyde (**10**) (61 mg, 0.40 mmol) in methanol (1.0 mL) containing hexafluorophosphoric acid (65% aqueous solution, 0.2 mL). The mixture was stirred at 25 °C for 2 h, precipitating the dark-red product **14**, and then was centrifuged at 2.5 krpm for 1 min. The crude product thus obtained was carefully washed with diethyl ether, and was recrystallized from acetonitrile/diethyl ether (1:5, vol/vol) (several times) to provide pure **14** (118 mg, 0.22 mmol, 63% yield).

Compound **14**: Dark-red needles, mp >155 °C (decomp.); Found: C, 56.23; H, 4.91; N, 2.64%. Calcd for $C_{25}H_{28}O_3NF_6P$ (i.e.,

$C_{23}H_{25}O_2$+PF$_6$+CH$_3$CN+1/2O$_2$): C, 56.08; H, 5.27; N, 2.62%; UV–vis λ_{max} (CH$_3$CN) nm (log ε), 201 (4.47), 216 (4.43), 289 (4.27), 333 (3.98), 362 (4.09), 389 (4.01), and 486 (4.12); IR ν_{max} (KBr) cm^{-1}, 3452 (O–H) and 841, 559 (PF$_6^-$); exact FABMS (3-nitrobenzyl alcohol matrix), found: *m*/*z* 333.1834; calcd for $C_{23}H_{25}O_2$: [M−PF$_6$]$^+$, *m*/*z* 333.1855; 700 MHz ^{1}H NMR (CD$_3$CN), signals based on a (3-guaiazulenyl)methylium ion structure: 1.45 (6H, d, *J*=6.9 Hz, (C*H*$_3$)$_2$CH-7′), 2.50 (3H, d, *J*=0.9 Hz, Me-1′), 3.33 (3H, s, Me-4′), 3.48 (1H, sept, *J*=6.9 Hz, (CH$_3$)$_2$C*H*-7′), 8.00 (1H, br s, H-2′), 8.38 (1H, dd, *J*=11.2, 2.0 Hz, H-6′), 8.47 (1H, d, *J*=11.2 Hz, H-5′), 8.57 (1H, d, *J*=2.0 Hz, H-8′), and 9.02 (1H, br s, HC$^+$-α); signals based on a 2-hydroxy-3-methoxyphenyl group: 3.93 (3H, s, MeO-3), 7.03 (1H, t, *J*=8.1 Hz, H-5), 7.16 (1H, br d, *J*=8.1 Hz, H-4), 7.30 (1H, br d, *J*=8.1 Hz, H-6), and 7.58 (1H, br s, HO-2); 176 MHz ^{13}C NMR (CD$_3$CN), 171.0 (C-7′), 161.2 (C-8a′), 157.5 (C-4′), 153.6 (C-3a′), 150.3 (C-5′), 149.2 (C-1), 148.6 (C-2), 145.6 (HC$^+$-α), 145.4 (C-1′), 144.7 (C-6′), 141.9 (C-2′), 139.8 (C-8′), 139.4 (C-3′), 125.5 (C-6), 123.3 (C-3), 121.6 (C-5), 116.3 (C-4), 57.0 (MeO-3), 40.2 ((CH$_3$)$_2$*C*H-7′), 29.7 (Me-4′), 23.7 ((*C*H$_3$)$_2$CH-7′), and 13.8 (Me-1′).

*4.1.3. Preparation of (3-guaiazulenyl)(3,4-dihydroxyphenyl)methylium hexafluorophosphate (**15**).* To a solution of commercially available guaiazulene (**8**) (70 mg, 0.35 mmol) in methanol (1.0 mL) was added a solution of commercially available 3,4-dihydroxybenzaldehyde (**11**) (55 mg, 0.40 mmol) in methanol (1.0 mL) containing hexafluorophosphoric acid (65% aqueous solution, 0.2 mL). The mixture was stirred at 25 °C for 2 h, precipitating the dark-red product **15**, and then was centrifuged at 2.5 krpm for 1 min. The crude product thus obtained was carefully washed with diethyl ether, and was recrystallized from acetonitrile/diethyl ether (1:5, vol/vol) (several times) to provide pure **15** (73 mg, 0.15 mmol, 43% yield).

Compound **15**: Dark-red blocks, mp >160 °C (decomp.); Found: C, 54.99; H, 4.57%. Calcd for $C_{22}H_{23}O_3F_6P$ (i.e., $C_{22}H_{23}O_2$+PF$_6$+1/2O$_2$): C, 55.01; H, 4.83%; UV–vis λ_{max} (CH$_3$CN) nm (log ε) 233 (4.35), 306 (3.97), 336 (3.97), and 530 (4.54); IR ν_{max} (KBr) cm^{-1}, 3444, 3274 (O–H) and 844, 559 (PF$_6^-$); exact FABMS (3-nitrobenzyl alcohol matrix), found: *m*/*z* 319.1724; calcd for $C_{22}H_{23}O_2$: [M−PF$_6$]$^+$, *m*/*z* 319.1693; 700 MHz ^{1}H NMR (CD$_3$CN), signals based on a (3-guaiazulenyl)methylium ion structure:™ δ 1.46 (6H, d, *J*=6.8 Hz, (C*H*$_3$)$_2$CH-7′), 2.53 (3H, d, *J*=0.8 Hz, Me-1′), 3.32 (3H, s, Me-4′), 3.46 (1H, sept, *J*=6.8 Hz, (CH$_3$)$_2$C*H*-7′), 8.09 (1H, s, H-2′), 8.35 (1H, dd, *J*=11.3, 2.2 Hz, H-6′), 8.42 (1H, dd, *J*=11.3 Hz, H-5′), 8.56 (1H, d, *J*=2.2 Hz, H-8′), and 8.65 (1H, br s, HC$^+$-α); signals based on a 3,4-dihydroxyphenyl group:™ 7.04 (1H, d, *J*=8.7 Hz, H-5), 7.25 (1H, br s, HO-3), 7.38 (1H, dd, *J*=8.7, 2.2 Hz, H-6), 7.41 (1H, d, *J*=2.2 Hz, H-2), and 7.87 (1H, br s, HO-4); 176 MHz ^{13}C NMR (CD$_3$CN):™ δ 169.2 (C-7′), 159.6 (C-8a′), 157.1 (C-4′), 153.3 (C-3a′), 151.8 (HC$^+$-α), 151.8 (C-4), 149.0 (C-5′), 146.6 (C-3), 146.6 (C-1′), 144.3 (C-6′), 141.8 (C-2′), 139.6 (C-8′), 137.5 (C-3′), 130.3 (C-6), 129.2 (C-1), 120.1 (C-2), 117.4 (C-5), 40.1 ((CH$_3$)$_2$*C*H-7), 30.0 (Me-4), 23.9 ((*C*H$_3$)$_2$CH-7), and 13.8 (Me-1).

*4.1.4. Preparation of (3-guaiazulenyl)(4-hydroxy-3-methoxyphenyl)methylium hexafluorophosphate (**16**).* To a solution of commercially available guaiazulene (**8**) (70 mg, 0.35 mmol) in methanol (1.0 mL) was added a solution of commercially available 4-hydroxy-3-methoxybenzaldehyde (**12**) (61 mg, 0.40 mmol) in methanol (1.0 mL) containing hexafluorophosphoric acid (65% aqueous solution, 0.2 mL). The mixture was stirred at 25 °C for 2 h, precipitating the dark-red product **16**, and then was centrifuged at 2.5 krpm for 1 min. The crude product thus obtained was carefully washed with diethyl ether, and was recrystallized from acetonitrile/diethyl ether (1:5, vol/vol) (several times) to provide pure **16** (150 mg, 0.27 mmol, 77% yield).

Compound **16**: Dark-red blocks, mp >108 °C (decomp.); Found: C, 54.60; H, 4.83; N 2.53%. Calcd for $C_{25}H_{28}O_4NF_6P$ (i.e., $C_{23}H_{25}O_2$+PF$_6$+CH$_3$CN+O$_2$): C, 54.45; H, 5.11; N, 2.53%; UV–vis λ_{max} (CH$_3$CN) nm (log ε), 233 (4.42), 307 (4.03), 338 (4.06), and 527 (4.59); IR ν_{max} (KBr) cm^{-1}, 3468 (O–H) and 841, 559 (PF$_6^-$); exact FABMS (3-nitrobenzyl alcohol matrix), found: *m*/*z* 333.1861; calcd for $C_{23}H_{25}O_2$: [M−PF$_6$]$^+$, *m*/*z* 333.1855; 700 MHz ^{1}H NMR (CD$_3$CN), signals based on a (3-guaiazulenyl)methylium ion structure: δ 1.44 (6H, d, *J*=6.8 Hz, (C*H*$_3$)$_2$CH-7′), 2.54 (3H, d, *J*=1.0 Hz, Me-1′), 3.34 (3H, s, Me-4′), 3.46 (1H, sept, *J*=6.8 Hz, (CH$_3$)$_2$C*H*-7′), 8.12 (1H, br s, H-2′), 8.35 (1H, dd, *J*=11.3, 2.2 Hz, H-6′), 8.42 (1H, dd, *J*=11.3 Hz, H-5′), 8.57 (1H, d, *J*=2.2 Hz, H-8′), and 8.72 (1H, br s, HC$^+$-α); signals based on a 4-hydroxy-3-methoxyphenyl group: δ 3.98 (3H, s, MeO-3), 7.01 (1H, d, *J*=8.4 Hz, H-5), 7.45 (1H, br d, *J*=1.8 Hz, H-2), 7.50 (1H, dd, *J*=8.4, 1.8 Hz, H-6), and 7.69 (1H, br s, HO-4); 176 MHz ^{13}C NMR (CD$_3$CN): ™δ 169.2 (C-7′), 159.6 (C-8a′), 157.1 (C-4′), 153.3 (C-3a′), 153.2 (C-4), 151.8 (HC$^+$-α), 149.2 (C-3), 149.0 (C-5′), 144.6 (C-1′), 144.3 (C-6′), 141.8 (C-2′), 139.6 (C-8′), 137.5 (C-3′), 130.9 (C-6), 129.0 (C-1), 117.2 (C-5), 117.1 (C-2), 57.0 (MeO-3), 40.1 ((CH$_3$)$_2$*C*H-7′), 30.0 (Me-4′), 23.9 ((*C*H$_3$)$_2$CH-7′), and 13.8 (C-1′).

*4.1.5. Reduction of (3-guaiazulenyl)(2-hydroxy-3-methoxyphenyl)methylium hexafluorophosphate (**14**) with NaBH$_4$.* To a solution of NaBH$_4$ (20 mg, 0.52 mmol) in ethanol (1.5 mL) was added a solution of **14** (96 mg, 0.18 mmol) in acetonitrile (2.0 mL). The mixture was stirred at 25 °C for 1 h, and then was evaporated in vacuo. The obtained residue was carefully separated by silica gel column chromatography with hexane/ethyl acetate (9:1, vol/vol) as an eluant, and was recrystallized from acetone/distilled water (1:5, vol/vol) (several times) to provide pure (3-guaiazulenyl)(2-hydroxy-3-methoxyphenyl)methane (**17**) (57 mg, 0.17 mmol, 94% yield).

Compound **17**: Blue needles [R_f=0.45 on silica gel TLC (hexane:AcOEt=9:1, vol/vol)], mp 118 °C; IR ν_{max} (KBr) cm^{-1}, 3436 (O–H); exact FABMS (3-nitrobenzyl alcohol matrix), found: *m*/*z* 334.1939; calcd for $C_{23}H_{26}O_2$: M$^+$, *m*/*z* 334.1933; 700 MHz ^{1}H NMR (CD$_3$CN), signals based on a (3-guaiazulenyl)methyl group: 1.31 (6H, d, *J*=6.8 Hz, (C*H*$_3$)$_2$CH-7′), 2.56 (3H, s, Me-1′), 2.77 (3H, s, Me-4′), 3.03 (1H, sept, *J*=6.8 Hz, (CH$_3$)$_2$C*H*-7′), 4.49 (1H, s, CH$_2$-3′), 6.80 (1H, d, *J*=10.8 Hz, H-5′), 7.28 (1H, dd, *J*=10.8, 2.2 Hz, H-6′), 7.32 (1H, br s, H-2′), and 8.09 (1H, d, *J*=2.2 Hz, H-8′); 2-hydroxy-3-methoxyphenyl group:™ δ 3.85 (3H, s, MeO-3), 6.13 (1H, dd, *J*=7.8, 1.0 Hz, H-6), 6.57 (1H, br s, HO-2), 6.63 (1H, t, *J*=7.8 Hz, H-5), and 6.78 (1H, dd, *J*=7.8, 1.0 Hz, H-4); 176 MHz ^{13}C NMR (CD$_3$CN), 147.6 (C-3), 146.4 (C-4′), 143.9 (C-2), 141.7 (C-2′), 139.8 (C-7′), 138.7 (C-8a′), 135.7 (C-6′), 134.2 (C-8′), 133.9 (C-3a′), 130.3 (C-1), 126.8 (C-5′), 126.4 (C-3′) 125.0 (C-1′), 122.8 (C-6), 120.1 (C-5), 109.9 (C-4), 56.7 (MeO-3), 38.2 ((CH$_3$)$_2$*C*H-7′), 31.4 (CH$_2$-3′), 26.4 (Me-4′), 24.7 ((*C*H$_3$)$_2$CH-7′), and 12.8 (Me-1′).

*4.1.6. Reduction of (3-guaiazulenyl)(4-hydroxy-3-methoxyphenyl)methylium hexafluorophosphate (**16**) with NaBH$_4$.* To a solution of NaBH$_4$ (20 mg, 0.52 mmol) in ethanol (1.5 mL) was added a solution of **16** (96 mg, 0.17 mmol) in acetonitrile (2.0 mL). The mixture was stirred at 25 °C for 1 h, and then was evaporated in vacuo. The residue thus obtained was dissolved in hexane and filtered. The hexane filtrate was evaporated in vacuo, giving a blue paste residue, which was carefully separated by silica gel column chromatography with hexane/ethyl acetate (9:1, vol/vol) as an eluant, and was recrystallized from hexane to provide pure (3-guaiazulenyl)(4-hydroxy-3-methoxyphenyl)methane (**18**) (55 mg, 0.16 mmol, 94% yield).

Compound **18**: Blue paste [R_f=0.45 on silica gel TLC (hexane:AcOEt=9:1, vol/vol)]; exact EIMS (70 eV), found: *m*/*z* 334.1963; calcd for $C_{23}H_{26}O_2$: M$^+$, *m*/*z* 334.1933; 500 MHz ^{1}H NMR (CD$_3$CN), signals based on a (3-guaiazulenyl)methyl group: 1.30 (6H, d, *J*=6.9 Hz, (C*H*$_3$)$_2$CH-7′), 2.56 (3H, s, Me-1′), 2.82 (3H, s, Me-4′), 3.02 (1H, sept, *J*=6.9 Hz, (CH$_3$)$_2$C*H*-7′), 4.48 (1H, s, CH$_2$-3′), 6.80 (1H, d, *J*=10.9 Hz, H-5′), 7.28 (1H, dd, *J*=10.9, 2.3 Hz, H-6′), 7.37 (1H, br s, H-2′), and 8.09 (1H, d, *J*=2.3 Hz, H-8′); signals based on a 4-hydroxy-3-methoxyphenyl group:™ 3.73 (3H, s, MeO-3), 6.28

(1H, br s, HO-4), 6.34 (1H, dd, J=8.0, 2.1 Hz, H-6), 6.66 (1H, d, J=8.0 Hz, H-5), and 6.72 (1H, d, J=2.1 Hz, H-2); 125 MHz ^{13}C NMR (CD_3CN), 148.1 (C-3), 146.4 (C-4′), 144.9 (C-4), 141.9 (C-2′), 139.9 (C-7′), 138.8 (C-8a′), 136.2 (C-1), 135.7 (C-6′), 134.3 (C-8′), 133.7 (C-3a′), 127.3 (C-3′) 127.0 (C-5′), 125.1 (C-1′), 121.7 (C-6), 115.4 (C-5), 112.9 (C-2), 56.6 (MeO-3), 38.3 ((CH_3)$_2$CH-7′), 37.1 (CH_2-3′), 26.9 (Me-4′), 24.7 ((CH_3)$_2$CH-7′), and 12.9 (Me-1′).

*4.1.7. X-ray crystal structure of (3-guaiazulenyl)(2-hydroxy-3-methoxyphenyl)methylium hexafluorophosphate (**14**).* The X-ray measurement of the single crystal **14** was made on a Rigaku Saturn CCD area detector with graphite monochromated Mo Kα radiation (λ=0.71075 Å) at −160±1 °C. The structure was solved by direct methods (SIR92) and expanded using Fourier techniques (DIRDIF99). The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined isotropically. The final cycle of full-matrix least-squares refinement was based on F^2. All calculations were performed using the CrystalStructure crystallographic software package developed by Rigaku corporation, Japan. Crystallographic data have been deposited with Cambridge Crystallographic Data Center: Deposition number CCDC-760635 for compound No. **14**. Copies of the data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Center, 12, Union Road, Cambridge, CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).

Crystallographic data for **14**: $C_{25}H_{29}O_2NF_6P$ (FW=520.47), dark-red needle (crystal size, 0.50×0.24×0.20 mm^3), monoclinic, $P2_1/n$ (#14), a=7.841(2) Å, b=24.749(7) Å, c=13.135(4) Å, β=108.145(5)°, V=2422.3(12) Å^3, Z=4, D_{calcd}=1.427 g/cm^3, μ(Mo Kα)=1.830 cm^{-1}, measured reflections=22,903, observed reflections=10,256, No. of variables=569, $R1$=0.0644, $wR2$=0.1438, and goodness of fit indicator=0.970.

*4.1.8. X-ray crystal structure of (3-guaiazulenyl)(3,4-dihydroxyphenyl)methylium hexafluorophosphate (**15**).* The X-ray measurement of the single crystal **15** was made on a Rigaku Saturn CCD area detector with graphite monochromated Mo Kα radiation (λ=0.71075 Å) at −170±1 °C. The structure was solved by direct methods (SIR92) and expanded using Fourier techniques (DIRDIF99). 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 CrystalStructure crystallographic software package developed by Rigaku corporation, Japan. Crystallographic data have been deposited with Cambridge Crystallographic Data Center: Deposition number CCDC-768569 for compound No. **15**.

Crystallographic data for **15**: $C_{22}H_{23}O_2F_6P$ (FW=464.39), dark-red block (crystal size, 0.58×0.16×0.10 mm^3), monoclinic, $P2_1/n$ (#14), a=7.6506(17) Å, b=27.259(6) Å, c=10.119(2) Å, β=108.565(4)°, V=2000.5(7) Å^3, Z=4, D_{calcd}=1.542 g/cm^3, μ(Mo Kα)=2.100 cm^{-1}, measured reflections=18,948, observed reflections=3466, No. of variables=304, $R1$=0.0465, $wR2$=0.1261, and goodness of fit indicator=1.210.

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41. The crystal structure of **4** (see Chart 2) could not be determined because of difficulty in obtaining a single crystal suitable for X-ray crystallographic analysis, while the crystal structure of **4BF$_4$** could be determined.[32]
42. The van der Waals radii of hydrogen and oxygen atoms are 1.2 and 1.4 Å respectively. Therefore, the Cα–H···O–C2 and C2–OH···O–C3 distances of **14** are shorter than the sum of the above radii (2.6 Å).
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44. The computer program was developed by Fujitsu Ltd., Japan. The keywords (1 SCF, PRECISE, VECTORS, ALLVEC, BONDS, PM3, and CHARGE=1) were used.
45. In the previous paper,[25] we proposed a redox mechanism based on the CV and DPV data of (3-guaiazulenyl)[4-(methoxycarbonyl)phenyl]methylium hexafluorophosphate.