

A Facile Preparation of (4-Aminophenyl)(3-guaiazulenyl)methylum Hexafluorophosphate: Comparative Studies on Spectroscopic, Chemical, and Electrochemical Properties of Monocarbenium Ion and *p*-Benzoquinodimethane Monoiminium Ion Compounds

Shin-ichi Takekuma,^{*1} Naohiko Ijibata,¹ Toshie Minematsu,² and Hideko Takekuma¹

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

²School of Pharmaceutical Sciences, Kinki University, 3-4-1 Kowakae, Higashi-Osaka 577-8502

Received October 28, 2008; E-mail: takekuma@apch.kindai.ac.jp

Reaction of guaiazulene with 4-aminobenzaldehyde in CH₃OH in the presence of hexafluorophosphoric acid at 25 °C for 2 h gives the title compound, with an equiv of HPF₆, in 56% yield. Interestingly, a solution of the obtained new monocarbenium ion compound, forming a protonated amino group (4-H₃N⁺PF₆⁻), in CH₃CN is allowed to stand at room temperature for 48 h, gradually converting to a new 4-(3-guaiazulenyl)methylene-2,5-cyclohexadiene-1-iminium hexafluorophosphate, completely. Furthermore, reductions of the above two products with NaBH₄ in a mixed solvent of EtOH and CH₃CN afford 4-amino-1-(3-guaiazulenylmethyl)benzene, selectively. Comparative studies on spectroscopic, chemical, and electrochemical properties of the monocarbenium ion compound with those of the 4-methylene-2,5-cyclohexadiene-1-iminium ion compound, are reported.

Azulene and its derivatives have been studied to a considerable extent over the past 50 y and an extremely large number of the studies have been well documented and further, naturally occurring guaiazulene (=7-isopropyl-1,4-dimethylazulene, **1**)¹ has been widely used clinically as an antiinflammatory and antiulcer agent; however, nothing has really been used as other industrial materials. As a series of our basic studies on creation of novel functional materials with a 3-guaiazulenyl (=7-isopropyl-1,4-dimethylazulene-3-yl) (or another azulene-1-yl) group possessing a large dipole moment and on their potential utility, we have been working on facile preparation and crystal structures as well as spectroscopic, chemical, and electrochemical properties of delocalized mono- and dicarbenium ion compounds stabilized by expanded π -electron systems possessing a 3-guaiazulenyl [or an azulene-1-yl or a 3-(methoxycarbonyl)azulene-1-yl] group.^{2–18} During the course of our basic and systematic investigations, we found the following interesting results, namely, the reaction of **1** with 4-(dimethylamino)benzaldehyde, (or 4-hydroxybenzaldehyde or 4-methoxybenzaldehyde) in methanol in the presence of tetrafluoroboric acid (or hexafluorophosphoric acid) at 25 °C for 2 h gave the corresponding monocarbenium ion compound **A**, quantitatively, possessing interesting resonance structures of the 3-guaiazulenyl cation structure **C** and the *p*-benzoquinoid structure **B** in acetonitrile (Figure 1)^{6,10,17} and further, the X-ray crystallographic analyses of **10** and **12** could be achieved, apparently indicating the crystal structures with the resonance structures **A–C** in their single crystals.^{6,17} In relation to the above results, we quite recently isolated the title compound (4-aminophenyl)(3-guaiazulenyl)methylum hexafluorophosphate

(**3a**), with an equiv of HPF₆, and **3b** possessing a *p*-benzoquinodimethane monoiminium ion (=4-methylene-2,5-cyclohexadiene-1-iminium ion) structure, the products of which enabled us to compare their properties as the first example. On the other hand, in 2003 Cho et al. reported that the ¹H and ¹³C NMR spectral data of ¹³C α -labeled Malachite Green indicated the existence of a resonance structure with a cationic charge located in the central C α carbon atom, forming a triphenylmethyl cation structure (Chart 1),¹⁹ and further, the synthesis, chemical properties, material chemistry, and crystal structure of Crystal Violet have been studied (Chart 1);^{20–24} however, none have really been documented for comparative studies on the properties of the isolated triphenylmethyl cation and *p*-benzoquinodimethane monoiminium ion compounds (Chart 1). We now wish to report detailed studies on the title chemistry, namely, a facile preparation as well as the spectroscopic, chemical, and electrochemical properties of the target monocarbenium ion compound **3a**, with the resonance structure **3c** possessing a 3-guaiazulenyl cation, and the isolated **3b** possessing a *p*-benzoquinodimethane monoiminium ion structure with a view to comparative study.

Experimental

General. Thermal (TGA and DTA) and elemental analyses were taken on a Shimadzu DTG-50H thermal analyzer and a Yanaco MT-3 CHN coder. 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-ECA600 (600 MHz for ¹H and 150 MHz for

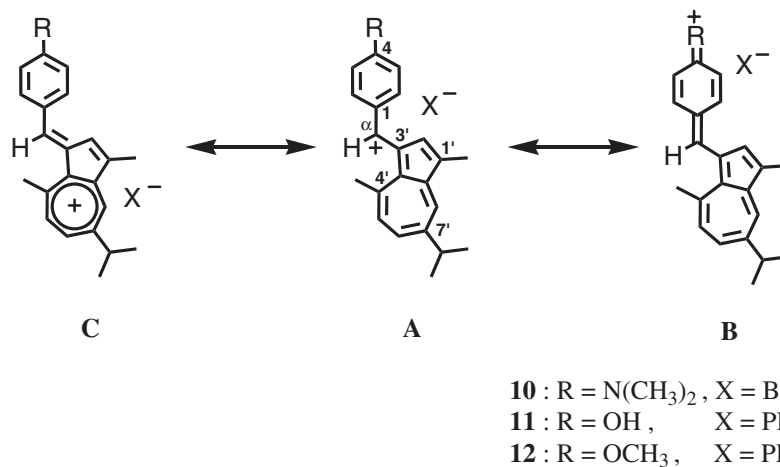
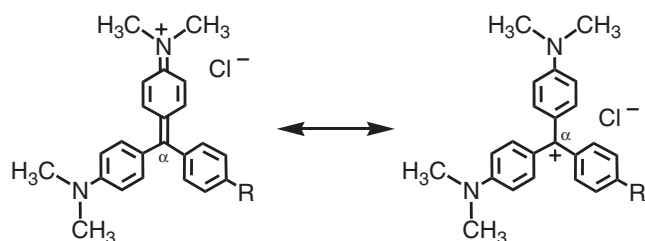


Figure 1. The monocarbenium ion structure **A** of **10–12**, possessing the corresponding resonance structures of the 3-guaiazulenylmethylum ion structure **C** and the *p*-benzoquinoid structure **B** in CH₃CN.



Malachite Green : R = H
 Crystal Violet : R = N(CH₃)₂

Chart 1.

¹³C) cryospectrometer and a JNM-ECA500 (470 MHz for ¹⁹F and 202 MHz for ³¹P) cryospectrometer at 25 °C. ¹H NMR spectra were assigned using computer-assisted simulation (software: gNMR developed by Adept Scientific plc) on a DELL Dimension XPS T500 personal computer with a Pentium III processor. Cyclic and differential pulse voltammograms were measured with an ALS Model 600 electrochemical analyzer.

Preparation of (4-Aminophenyl)(3-guaiazulenyl)methylum Hexafluorophosphate (3a). To a solution of commercially available guaiazulene (**1**) (158 mg, 0.80 mmol) in methanol (2.0 mL) was added a solution of commercially available 4-aminobenzaldehyde (**2**) (91 mg, 0.75 mmol) in methanol (2.0 mL) containing hexafluorophosphoric acid (60% aqueous solution, 70 μL). The mixture was stirred at 25 °C for 2 h, precipitating a reddish-brown powder and then was centrifuged at 2.6 krpm for 2 min. The crude product thus obtained was carefully washed with diethyl ether, giving pure **3a** (252 mg, 0.42 mmol, 56% yield) with an equiv of HPF₆.

Compound **3a**: Reddish-brown powder, mp >200 °C (decomp.) [determined by thermal analysis (TGA and DTA)]. Found: C, 44.62; H, 4.35; N, 2.48%. Calcd for C₂₂H₂₄NF₆P + HPF₆: C, 44.53; H, 4.25; N, 2.36%; UV-vis λ_{max} (CH₃CN)/nm (log ε): 234 (4.46), 293 (4.18), 342 (4.16), 424 (4.28), and 522 (4.67); UV-vis λ_{max} (CF₃COOH)/nm (log ε): 276 (4.28), 325 (4.14), 364 (4.35), 443 (4.31), 525sh (3.74), and 650 (2.54); FT-IR (KBr) ν_{max} (cm⁻¹): see Figure 6a; exact FAB-MS (matrix: 3-nitrobenzyl alcohol), found: *m/z* 302.1879; calcd for C₂₂H₂₄N: [M - PF₆]⁺, *m/z* 302.1909; ¹H NMR (600 MHz, CD₃CN), signals based on a 3-

guaiazulenylmethylum substituent: δ 1.46 (6H, d, *J* = 6.8 Hz, (CH₃)₂CH-7'), 2.53 (3H, br s, Me-1'), 3.37 (3H, s, Me-4'), 3.51 (1H, sept, *J* = 6.8 Hz, Me₂CH-7'), 7.98 (1H, br s, H-2'), 8.45 (1H, dd, *J* = 11.5, 2.3 Hz, H-6'), 8.55 (1H, d, *J* = 11.5 Hz, H-5'), 8.60 (1H, d, *J* = 2.3 Hz, H-8'), and 8.73 (1H, br s, HC-α); signals based on a protonated 4-aminophenyl group: δ 6.90 (2H, br s, 4-H₃N⁺PF₆⁻), 7.76 (2H, ddd, *J* = 8.8, 2.5, 1.0 Hz, H-3,5), and 7.98 (2H, ddd, *J* = 8.8, 2.5, 1.0 Hz, H-2,6). A signal based on three protons of the 4-H₃N⁺ group was not observed; ¹H NMR (600 MHz, CD₂Cl₂), signals based on a 3-guaiazulenylmethylum substituent: δ 1.47 (6H, d, *J* = 6.9 Hz, (CH₃)₂CH-7'), 2.59 (3H, br d, *J* = 1.0 Hz, Me-1'), 3.33 (3H, s, Me-4'), 3.37 (1H, sept, *J* = 6.9 Hz, Me₂CH-7'), 8.11 (1H, br s, H-2'), 8.11 (1H, dd, *J* = 11.2, 2.0 Hz, H-6'), 8.16 (1H, d, *J* = 11.2 Hz, H-5'), 8.44 (1H, d, *J* = 2.0 Hz, H-8'), and 8.65 (1H, br s, HC-α); signals based on a 4-aminophenyl group: δ 6.89 (2H, ddd, *J* = 8.8, 2.5, 1.0 Hz, H-3,5) and 7.80 (2H, ddd, *J* = 8.8, 2.5, 1.0 Hz, H-2,6). The H₂N-4 signal was not observed; ¹H NMR (600 MHz, CF₃COOD), signals based on a 3-guaiazulenylmethylum substituent: δ 1.52 (6H, d, *J* = 6.9 Hz, (CH₃)₂CH-7'), 2.51 (3H, br s, Me-1'), 3.40 (3H, s, Me-4'), 3.48 (1H, sept, *J* = 6.9 Hz, Me₂CH-7'), 7.81 (1H, br s, H-2'), 8.43 (1H, dd, *J* = 11.2, 2.0 Hz, H-6'), 8.57 (1H, d, *J* = 11.2 Hz, H-5'), 8.65 (1H, d, *J* = 2.0 Hz, H-8'), and 8.74 (1H, br s, HC-α); signals based on a deuterated 4-aminophenyl group: δ 7.74 (2H, br d, *J* = 8.0 Hz, H-3,5) and 7.84 (2H, br d, *J* = 8.0 Hz, H-2,6). The signal of the deuterated amino group was not observed; ¹³C NMR (150 MHz, CD₃CN): δ 172.5 (C-7'), 161.7 (C-8a'), 161.1 (C-4), 158.3 (C-4'), 153.7 (C-3a'), 151.2 (C-5'), 148.1 (HC-α), 146.9 (C-1'), 145.3 (C-6'), 140.8 (C-2'), 140.1 (C-8'), 136.1 (C-1), 135.5 (C-2,6), 121.0 (C-3,5), 40.4 (Me₂CH-7'), 29.8 (Me-4'), 23.8 ((CH₃)₂CH-7'), and 13.9 (Me-1'). The C-3' signal was included in the other signals; ¹³C NMR (150 MHz, CF₃COOD): δ 176.3 (C-7'), 159.5 (C-4'), 155.2 (C-3a'), 152.6 (C-5'), 148.2 (HC-α), 146.5 (C-6'), 143.8 (C-1'), 141.9 (C-2'), 140.3 (C-8'), 137.4 (C-1), 135.4 (C-2,6), 133.0 (C-3'), 126.3 (C-3,5), 42.3 (Me₂CH-7'), 30.0 (Me-4'), 24.4 ((CH₃)₂CH-7'), and 14.0 (Me-1'). The C-4 and C-8a' signals were included in the solvent signals; ¹⁹F NMR (470 MHz, CD₃CN), a signal based on a hexafluorophosphate: δ -72.7 (d, *J*_{F,P} = 707.0 Hz, PF₆⁻); ³¹P NMR (202 MHz, CD₃CN), a signal based on a hexafluorophosphate: δ -143.4 (sept, *J*_{F,P} = 707.0 Hz, PF₆⁻).

Preparation of 4-(3-Guaiazulenyl)methylene-2,5-cyclohexadiene-1-iminium Hexafluorophosphate (3b). A solution of **3a**

(25 mg, 42 μmol), with an equiv of HPF_6 , in CH_3CN (2.0 mL) was allowed to stand at 25 $^\circ\text{C}$ for 48 h, turning the red solution into a blue solution, gradually. The blue solution thus obtained was evaporated in vacuo, giving pure **3b** (23 mg, 42 μmol , 100% yield) with 1/2 equiv of HPF_6 and 1/2 equiv of CH_3CN .

Compound 3b: Dark-green solid, mp >130 $^\circ\text{C}$ (decomp.) [determined by thermal analysis (TGA and DTA)]. Found: C, 51.21; H, 4.57; N, 3.67%. Calcd for $\text{C}_{22}\text{H}_{24}\text{NF}_6\text{P} + 1/2\text{HPF}_6 + 1/2\text{CH}_3\text{CN}$: C, 51.07; H, 4.85; N, 3.88%; UV-vis λ_{max} (CH_3CN)/nm (log ϵ): 235 (4.53), 293 (4.19), 352 (4.17), 423 (4.17), and 593 (4.71); UV-vis λ_{max} (CF_3COOH)/nm: the spectrum coincided with that of **3a** in CF_3COOH ; FT-IR (KBr) ν_{max} (cm^{-1}): see Figure 6b; exact FAB-MS (matrix: 3-nitrobenzyl alcohol), found: m/z 303.1970; calcd for $\text{C}_{22}\text{H}_{25}\text{N}$: $[\text{M} - \text{PF}_6 + \text{H}]^+$, m/z 303.1987; ^1H NMR (600 MHz, CD_3CN): signals based on a 3-guaiazulenyl group: δ 1.42 (6H, d, $J = 7.0$ Hz, $(\text{CH}_3)_2\text{CH}-7'$), 2.56 (3H, d, $J = 1.0$ Hz, Me-1'), 3.28 (3H, s, Me-4'), 3.38 (1H, sept, $J = 7.0$ Hz, $\text{Me}_2\text{CH}-7'$), 8.17 (3H, br s, H-2',5',6'), and 8.51 (1H, br s, H-8'); signals based on a *p*-benzoquinodimethane moniminium ion part: δ 6.55 (2H, br s, H_2N^+-1), 6.85 (2H, ddd, $J = 8.8, 2.5, 1.0$ Hz, H-2,6), 7.85 (2H, ddd, $J = 8.8, 2.5, 1.0$ Hz, H-3,5), and 8.70 (1H, s, HC-4); ^1H NMR (600 MHz, CD_2Cl_2 or CF_3COOD): the signals coincided with those of **3a** in CD_2Cl_2 or CF_3COOD ; ^{13}C NMR (150 MHz, CD_3CN): δ 163.5 (C-7'), 157.2 (C-1), 155.4 (C-8a'), 155.1 (C-4'), 153.6 (HC-4), 151.0 (C-3a'), 145.1 (C-5'), 142.7 (C-6'), 142.1 (C-2'), 140.8 (C-1'), 140.1 (C-3,5), 138.8 (C-8'), 132.8 (C-3'), 125.6 (C-4), 116.5 (C-2,6), 39.6 ($\text{Me}_2\text{CH}-7'$), 30.1 (Me-4'), 24.0 ($(\text{CH}_3)_2\text{CH}-7'$), and 13.5 (Me-1'); ^{13}C NMR (150 MHz, CF_3COOD): the signals coincided with those of **3a** in CF_3COOD .

Reduction of 3a (or 3b) with NaBH_4 . To a solution of NaBH_4 (54 mg, 1.42 mmol) in ethanol (5.0 mL) was added a solution of **3a** (150 mg, 0.25 mmol), with an equiv of HPF_6 , in acetonitrile (4.0 mL). The mixture was stirred at 25 $^\circ\text{C}$ for 1 h and then evaporated in vacuo. The residue thus obtained was dissolved in dichloromethane and filtered. The reaction solution was evaporated in vacuo, giving a greenish-blue pasty residue, which was carefully separated by silica gel column chromatography with hexane–ethyl acetate (4:1, vol/vol) as an eluant, giving pure 4-amino-1-(3-guaiazulenylmethyl)benzene (**4**) (76 mg, 0.25 mmol, 100% yield). Similarly, as in the case of **3a**, to a solution of NaBH_4 (9 mg, 0.24 mmol) in ethanol (5.0 mL) was added a solution of **3b** (25 mg, 46 μmol), with 1/2 equiv of HPF_6 molecule and 1/2 equiv of CH_3CN molecule, dissolved in acetonitrile (4.0 mL). The mixture was stirred at 25 $^\circ\text{C}$ for 1 h and then evaporated in vacuo. The residue thus obtained was dissolved in dichloromethane and filtered. The reaction solution was evaporated in vacuo, giving a greenish-blue pasty residue, which was carefully separated by silica gel column chromatography with hexane–ethyl acetate (4:1, vol/vol) as an eluant, giving pure **4** (11 mg, 36 μmol , 78% yield) and several chromatographically inseparable products.

Compound 4: Greenish-blue paste [$R_f = 0.06$ on silica gel TLC (hexane/EtOAc = 4:1, vol/vol)]; UV-vis λ_{max} (CH_3CN)/nm (log ϵ): 202 (4.61), 249 (4.42), 290 (4.46), 354 (3.65), 370 (3.56), 392 (2.79), and 626 (2.41); FT-IR (KBr) ν_{max} (cm^{-1}): see Figure 9; exact EI-MS (70 eV), found: m/z 303.2013; calcd for $\text{C}_{22}\text{H}_{25}\text{N}$: M^+ , m/z 303.1987; ^1H NMR (600 MHz, CD_3CN), signals based on a 3-guaiazulenylmethyl group: δ 1.31 (6H, d, $J = 6.8$ Hz, $(\text{CH}_3)_2\text{CH}-7'$), 2.56 (3H, s, Me-1'), 2.80 (3H, s, Me-4'), 3.01 (1H, sept, $J = 6.8$ Hz, $\text{Me}_2\text{CH}-7'$), 4.40 (2H, s, 1- CH_2-3'), 6.78 (1H, d, $J = 10.7$ Hz, H-5'), 7.28 (1H, dd, $J = 10.7, 2.0$ Hz, H-6'), 7.35 (1H, br s, H-2'), and 8.08 (1H, d, $J = 2.0$ Hz, H-8'); signals based

on a 4-aminophenyl group: δ 3.94 (2H, br s, $\text{H}_2\text{N}-4$), 6.49 (2H, ddd, $J = 8.6, 2.5, 1.0$ Hz, H-3,5), and 6.71 (2H, ddd, $J = 8.6, 2.5, 1.0$ Hz, H-2,6); ^{13}C NMR (150 MHz, CD_3CN): δ 148.4 (C-4), 147.0 (C-4'), 142.7 (C-2'), 140.4 (C-7'), 139.4 (C-8a'), 136.2 (C-6'), 134.8 (C-8'), 134.2 (C-3a'), 133.1 (C-1), 130.4 (C-2,6), 128.6 (C-3'), 127.4 (C-5'), 125.7 (C-1'), 114.4 (C-3,5), 38.9 ($\text{Me}_2\text{CH}-7'$), 37.2 (1- CH_2-3'), 27.5 (Me-4'), 25.4 ($(\text{CH}_3)_2\text{CH}-7'$), and 13.5 (Me-1').

Results and Discussion

Preparation and Spectroscopic Properties of 3a. The target monocarbenium ion compound **3a** was prepared in methanol according to the procedures shown in Figure 2 and Experimental section. The structure of the product **3a** was established on the basis of elemental analysis and spectroscopic data [UV-vis, IR, exact FAB-MS, ^1H and ^{13}C NMR including 2D NMR (i.e., H–H COSY, HMQC, and HMBC), and ^{19}F and ^{31}P NMR].

Compound **3a**· HPF_6 (56% yield) was obtained as a reddish-brown powder (decomp. >200 $^\circ\text{C}$), while a solution of **3a** in acetonitrile was red. The UV-vis (CH_3CN) spectrum showed that the spectral pattern of **3a** was close to those of structurally related compounds **11**¹⁰ and **12**¹⁷ (Figure 3), while the longest absorption wavelength of **3a** (λ_{max} 522 nm, log $\epsilon = 4.67$) revealed a bathochromic shift in comparison with those of **11** (λ_{max} 510 nm, log $\epsilon = 4.67$) and **12** (λ_{max} 507 nm, log $\epsilon =$

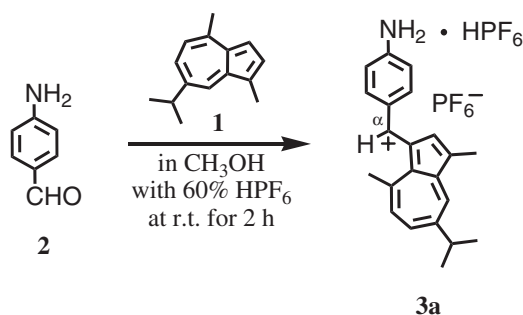


Figure 2. The reaction of **1** with **2** in methanol in the presence of hexafluorophosphoric acid (60% aqueous solution) at 25 $^\circ\text{C}$ for 2 h, giving **3a**, with an equiv of HPF_6 , as a reddish-brown powder.

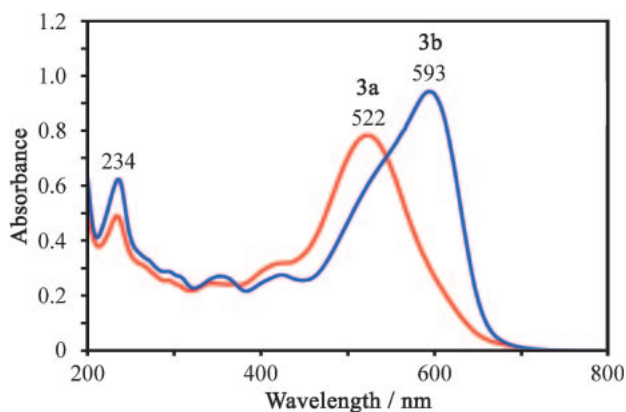


Figure 3. The UV-vis spectra of **3a** and **3b** in CH_3CN . Concentrations, **3a**: 169 $\mu\text{mol L}^{-1}$ and **3b**: 185 $\mu\text{mol L}^{-1}$. Length of the cell, 0.1 cm each. **3a**: λ_{max} 522 nm (log $\epsilon = 4.67$). **3b**: λ_{max} 593 nm (log $\epsilon = 4.71$).

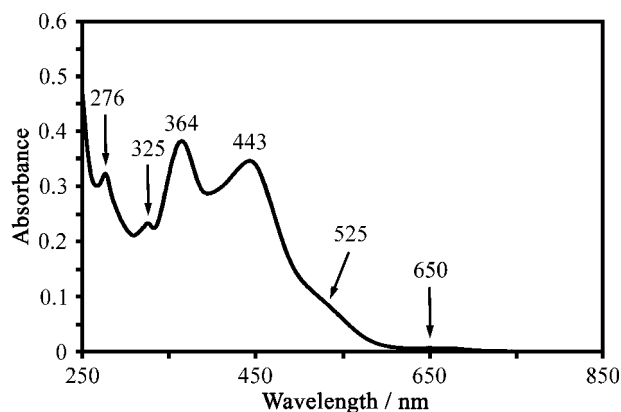


Figure 4. The UV-vis spectrum of **3a** in CF_3COOH . Concentration, **3a**: $169 \mu\text{mol L}^{-1}$. Length of the cell, 0.1 cm. **3a**: λ_{max} 443 nm ($\log \epsilon = 4.31$).

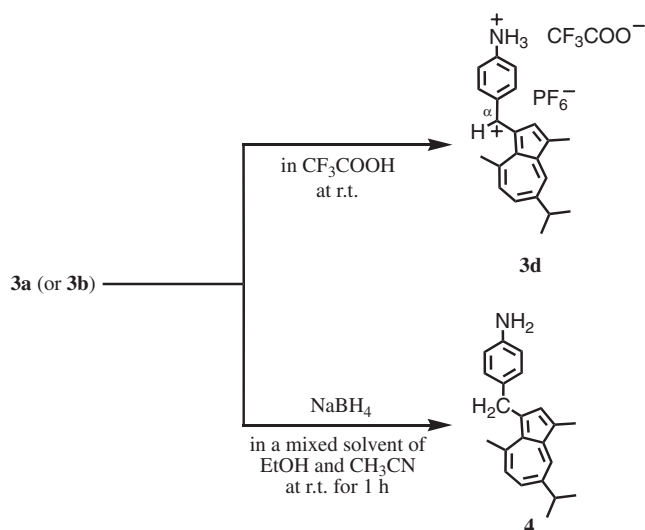


Figure 5. The protonation of **3a** (or **3b**) in CF_3COOH at 25°C and the reduction of **3a** (or **3b**) with NaBH_4 in a mixed solvent of EtOH and CH_3CN at 25°C for 1 h.

4.58). Although a solution of **3a** in acetonitrile was red, a solution of **3a** in trifluoroacetic acid was reddish-orange. The UV-vis (CF_3COOH) spectral pattern of **3a** (Figure 4), forming a protonated amino group (see **3d** in Figure 5), changed in comparison with that of **3a** in acetonitrile. The IR (KBr) spectrum showed specific bands based on the N-H bond (ν_{max} 3476 and 3382 cm^{-1}) and the C-N bond (ν_{max} 1338 cm^{-1}) of a 4-aminophenylmethylum ion structure. The specific bands based on the counter anion (PF_6^- : ν_{max} 844 and 559 cm^{-1}) coincided with those of **11**¹⁰ and **12**¹⁷ (Figure 6a). The formula $\text{C}_{22}\text{H}_{24}\text{N}$ for the monocarbenium ion structure $[\text{M} - \text{PF}_6]^+$ was determined by exact FAB-MS spectrum. An elemental analysis confirmed the formula $\text{C}_{22}\text{H}_{25}\text{NF}_6\text{P}_2$ (i.e., $\text{C}_{22}\text{H}_{24}\text{NF}_6\text{P} + \text{HPF}_6$). The ^1H NMR (CD_3CN) spectrum showed signals based on a 3-guaiazulenylmethylum ion structure with a resonance structure of a 3-guaiazulenylum ion, and revealed signals based on a protonated 4-aminophenylmethylum ion structure, the signals (δ and J values) of which were carefully assigned using H-H COSY technique and computer-assisted simulation based on first-order analysis (Table 1). The protonated $\text{H}_2\text{N}-4$

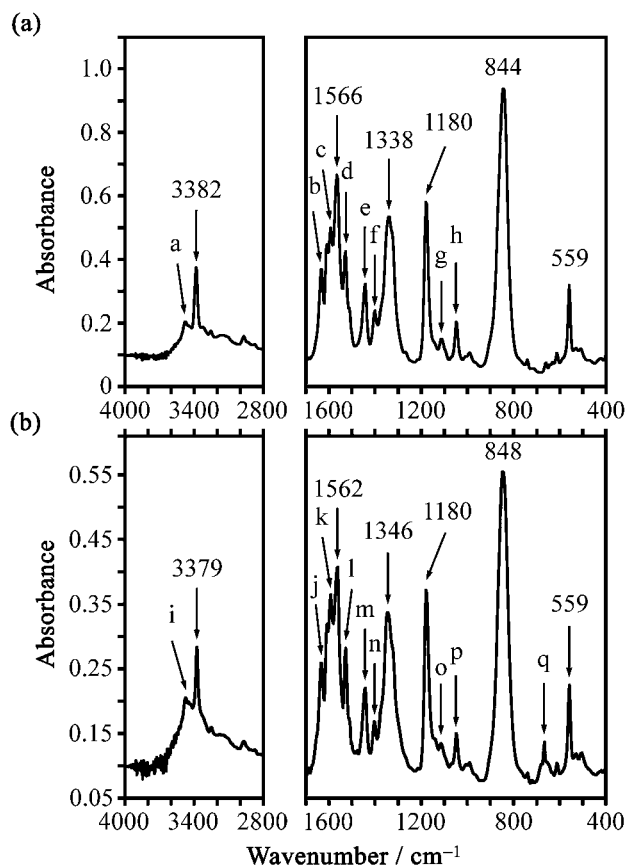


Figure 6. The IR spectra of **3a** (a) and **3b** (b). **3a**: ν_{max} (KBr) (cm^{-1}): a, 3476; b, 1632; c, 1609; d, 1528; e, 1443; f, 1400; g, 1111; h, 1049. **3b**: ν_{max} (KBr) (cm^{-1}): i, 3476; j, 1666; k, 1593; l, 1528; m, 1443; n, 1404; o, 1115; p, 1049; q, 667.

signal appeared at δ 6.90 (br s). The ^{19}F and ^{31}P NMR (CD_3CN) spectra showed a signal based on a hexafluorophosphate, indicating the existence of two equivalent PF_6^- . Therefore, the elemental analysis and the IR spectrum suggested the formation of **3a**, with an equiv of HPF_6 , forming a non-protonated $\text{H}_2\text{N}-4$ group at the solid state,²⁵ while the ^1H , ^{19}F , and ^{31}P NMR spectra indicated the formation of the protonated **3a** (i.e., $4\text{-H}_3\text{N}^+\text{PF}_6^-$) in the solvent. Although the H-2' and H-5',6' proton signals of the 3-guaiazulenylmethylum ion structure showed slight up- and down-field shifts in comparison with those of **11** and **12**, the other signals [i.e., HC- α , Me-1',4', $(\text{CH}_3)_2\text{CH}-7'$, and H-8'] coincided with those of **11** and **12** (Table 1). The ^{13}C NMR (CD_3CN) spectrum exhibited 18 carbon signals assigned by HMQC and HMBC techniques (Table 2). The carbon signals (C-3a',8') of the 3-guaiazulenylmethylum ion structure coincided with those of **11** and **12**; however, the signals (C-1',4',5',6',7',8a') showed down-field shifts and the signals (HC- α and C-2') revealed up-field shifts in comparison with those of **11** and **12** (Table 2). Furthermore, the ^1H and ^{13}C NMR signals of **3a** in trifluoroacetic acid- d_1 , forming a deuterated $\text{H}_2\text{N}-4$ group, are shown in Tables 1 and 2 (see **3a**^c for ^1H and **3a**^b for ^{13}C). The ^1H and ^{13}C NMR (CF_3COOD) chemical shifts for the $\text{HC}^+-\alpha$ carbenium ion center of **3a** coincided with those signals in acetonitrile- d_3 and further, those of the other proton and carbon signals in

Table 1. Selected ^1H NMR Chemical Shifts (δ) for **3a**, **3b**,^{a)} **4**, and **10–12** in CD_3CN (or CD_2Cl_2 or CF_3COOD)

Compound	HC- α	Me-1'	H-2'	Me-4'	H-5'	H-6'	$(\text{CH}_3)_2\text{CH}-7'$	$\text{Me}_2\text{CH}-7'$	H-8'	H-2,6	H-3,5
3a	8.73	2.53	7.98	3.37	8.55	8.45	1.46	3.51	8.60	7.98	7.76
3b	8.70	2.56	8.17	3.28	8.17	8.17	1.42	3.38	8.51	7.85	6.85
3a ^{b)} (or 3b ^{b)})	8.65	2.59	8.11	3.33	8.16	8.11	1.47	3.37	8.44	7.80	6.89
3a ^{c)} (or 3b ^{c)})	8.74	2.51	7.81	3.40	8.57	8.43	1.52	3.48	8.65	7.84	7.74
4	4.40 ^{d)}	2.56	7.35	2.80	6.78	7.28	1.31	3.01	8.08	6.71	6.49
10	8.70	2.59	8.18	3.27	8.07	8.11	1.43	3.37	8.49	7.94	6.97
10 ^{c)}	8.74	2.53	7.81	3.42	8.60	8.45	1.53	3.47	8.66	7.94	7.84
11	8.72	2.53	8.08	3.33	8.43	8.37	1.44	3.46	8.56	7.83	7.04
12	8.74	2.53	8.09	3.34	8.45	8.36	1.45	3.47	8.57	7.90	7.16

a) For comparative purposes, the numbering scheme of the 4-(3-guaiazulenyl)methylene-2,5-cyclohexadiene-1-iminium ion structure **3b** was changed to that of the 1-(3-guaiazulenyl)methylene-2,5-cyclohexadiene-4-iminium ion structure as shown in Table 1. b) In CD_2Cl_2 . c) In CF_3COOD . d) 1- CH_2 -3'.

Table 2. Selected ^{13}C NMR Chemical Shifts (δ) for **3a**, **3b**,^{a)} **4**, and **10–12** in CD_3CN (or CF_3COOD)

Compound	HC- α	C-1'	C-2'	C-3'	C-3a'	C-4'	C-5'	C-6'	C-7'	C-8'	C-8a'	C-1	C-2,6	C-3,5	C-4
3a	148.1	146.9	140.8	— ^{d)}	153.7	158.3	151.2	145.3	172.5	140.1	161.7	136.1	135.5	121.0	161.1
3b	153.6	140.8	142.1	132.8	151.0	155.1	145.1	142.7	163.5	138.8	155.4	125.6	140.1	116.5	157.2
3a ^{b)} (or 3b ^{b)})	148.2	143.8	141.9	133.0	155.2	159.5	152.6	146.5	176.3	140.3	— ^{d)}	137.4	135.4	126.3	— ^{d)}
4	37.2 ^{c)}	125.7	142.7	128.6	134.2	147.0	127.4	136.2	140.4	134.8	139.4	133.1	130.4	114.4	148.4
10	153.0	139.5	142.0	131.8	149.8	154.3	143.6	142.1	161.4	138.5	153.8	124.9	140.0	115.0	156.8
11	151.7	144.6	141.8	137.3	153.3	157.1	149.1	144.3	169.3	139.6	159.6	128.6	137.6	118.3	163.3
12	151.3	144.9	141.7	137.8	153.4	157.3	149.4	144.5	169.7	139.7	159.9	129.2	137.1	116.4	165.1

a) For comparative purposes, the numbering scheme of the 4-(3-guaiazulenyl)methylene-2,5-cyclohexadiene-1-iminium ion structure **3b** was changed to that of the 1-(3-guaiazulenyl)methylene-2,5-cyclohexadiene-4-iminium ion structure as shown in Table 2. b) In CF_3COOD . c) 1- CH_2 -3'. d) The signal was included in the other (or solvent) signals.

trifluoroacetic acid- d_1 more resembled those of **3a** in acetonitrile- d_3 in comparison with those of **3b** in acetonitrile- d_3 . Moreover, the ^1H NMR (CF_3COOD) chemical shifts of **3a** coincided with those of **10**, forming a deuterated $(\text{CH}_3)_2\text{N}-4$ group, in trifluoroacetic acid- d_1 (see **10**^{c)} in Table 1). Along with the ^{19}F and ^{31}P NMR spectral data, comparative studies on the above ^1H and ^{13}C NMR spectral data led to the structure (4-aminophenyl)(3-guaiazulenyl)methylum hexafluorophosphate for **3a**, with the resonance structure **3c** possessing a 3-guaiazulenylmethylum ion, forming a protonated amino group (4- $\text{H}_3\text{N}^+\text{PF}_6^-$). A similar reaction pathway to that of the previous monocarbenium ion compound¹⁶ can be inferred for the formation of **3a**.

Preparation and Spectroscopic Properties of 3b. A solution of **3a**, with an equiv of HPF_6 , in CH_3CN was allowed to stand at 25 °C for 48 h, gradually turning the red solution into a blue solution. The blue solution thus obtained was evaporated in vacuo, giving pure **3b** (100% yield), with 1/2 equiv of HPF_6 and 1/2 equiv of CH_3CN , as a solid. The structure of the product **3b** was established on the basis of elemental analysis and similar spectroscopic analyses to those of **3a**. Along with the above results, the time-dependent UV–visible (CH_3CN) spectra of **3a**, forming a protonated amino group (4- $\text{H}_3\text{N}^+\text{PF}_6^-$), apparently indicated that **3a** (the longest specific band: λ_{max} 523 nm) was gradually converted to **3b** (the longest specific band: λ_{max} 596 nm) (Figure 7) as a result of deprotonation (Figure 8). Therefore, the solvent served as a base, the permittivity (ϵ) of which is 38.8 at 20 °C. Moreover, a solution of **3a**· HPF_6 dissolved in an organic solvent [i.e., CH_2Cl_2 ,

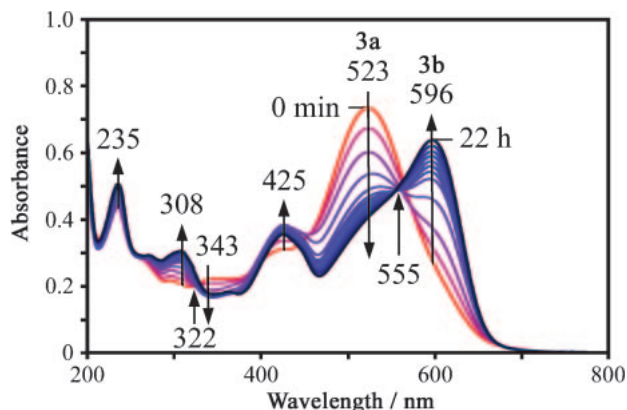


Figure 7. The time-dependent UV–vis spectra; reaction conditions: a solution of **3a** (1.0 mg, 1.69 μmol), with an equiv of HPF_6 , in CH_3CN (10 mL) was allowed to stand at room temperature for 22 h, gradually converting to **3b**; length of the cell: 0.1 cm; interval time: 2 h.

($\text{CH}_3)_2\text{CO}$, or $\text{C}_5\text{H}_5\text{N}$ (pyridine)] was converted to a solution of **3b** in each solvent, rapidly, as a result of dehydrogen hexafluorophosphate. The difference between the two is as follows: the permittivities (ϵ) of CH_2Cl_2 , $(\text{CH}_3)_2\text{CO}$, and $\text{C}_5\text{H}_5\text{N}$ are smaller than that of CH_3CN , and are 7.77 at 10 °C, 20.7 at 25 °C, and 12.3 at 25 °C. The ^1H NMR (CD_2Cl_2) signals of **3a**, converting to **3b** in the solvent, are shown in Table 1 (see **3a**^{b)}).

Compound **3b**·1/2 HPF_6 ·1/2 CH_3CN (100% yield) was obtained as a dark-green solid (decomp. >130 °C), while a

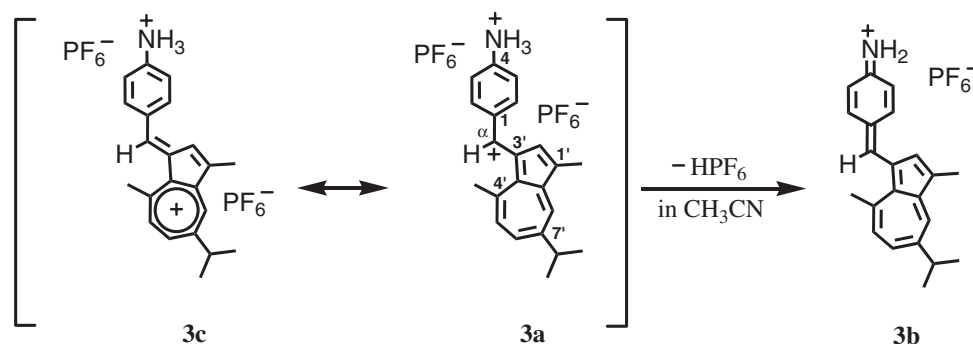


Figure 8. The formation of **3b** via **3a**, with the resonance structure **3c**, forming a 4- $\text{H}_3\text{N}^+\text{PF}_6^-$ in CH_3CN .

solution of **3b** in CH_3CN was blue. The UV-vis (CH_3CN) spectrum showed that the longest absorption wavelength of **3b** (λ_{max} 593 nm, $\log \epsilon = 4.71$) revealed a bathochromic shift ($\Delta 71$ nm) and a slight hyperchromic effect ($\Delta \log \epsilon = 0.04$) in comparison with that of **3a** (Figure 3), and showed that the spectral pattern of **3b** was close to that of **10**,⁶ while the longest absorption wavelength of **3b** revealed a hypsochromic shift ($\Delta 45$ nm) and a hypochromic effect ($\Delta \log \epsilon = 0.17$) in comparison with that of **10** (λ_{max} 638 nm, $\log \epsilon = 4.88$). The UV-vis (CF_3COOH) spectrum coincided with that of **3a**, forming a protonated amino group, in the solvent (Figure 4). The IR (KBr) spectrum showed specific bands based on the N-H bond (ν_{max} 3476 and 3379 cm^{-1}) and the C-N bond (ν_{max} 1346 cm^{-1}) of a *p*-benzoquinodimethane monoiminium ion structure and the counter anion (PF_6^- : ν_{max} 848 and 559 cm^{-1}) and further, the IR spectral pattern was almost the same as that of **3a** (Figure 6b). The formula $\text{C}_{22}\text{H}_{25}\text{N}$ for the protonated monocation part $[\text{M} - \text{PF}_6 + \text{H}]^+$ was determined by exact FAB-MS spectrum. An elemental analysis confirmed the formula $\text{C}_{22}\text{H}_{24}\text{NF}_6\text{P}$ with 1/2 equiv of HPF_6 and 1/2 equiv of CH_3CN . The ^1H NMR (CD_3CN) spectrum showed signals based on a 3-guaiazulenyl group and a *p*-benzoquinodimethane monoiminium ion framework, the signals of which were carefully assigned using similar techniques to those of **3a** (Table 1). The iminium ion ($\text{H}_2\text{N}^+=$) signal appeared at δ 6.55 (br s). Therefore, the elemental analysis and the IR and ^1H NMR spectra suggested the formation of a *p*-benzoquinodimethane monoiminium ion structure. Although the proton signals (Me-4', H-5',6',8', Me_2CH -7', and H-2,3,5,6) and the H-2' signal of **3b** showed up- and down-field shifts in comparison with those of **3a**, the other signals [i.e., HC- α , Me-1', and (CH_3) $_2\text{CH}$ -7'] of **3b** coincided with those of **3a** (Table 1). Furthermore, the ^1H NMR (CD_3CN) chemical shifts of **3b** were almost the same as those of **10** (Table 1), suggesting the formation of a *p*-benzoquinodimethane monoiminium ion structure. The ^{13}C NMR (CD_3CN) spectrum exhibited 19 carbon signals assigned by HMQC and HMBC techniques (Table 2). The signals (C-1',3a',4',5',6',7',8',8a' and C-1,3,4,5) of **3b** showed up-field shifts; however, the signals (HC- α , C-2', and C-2,6) revealed down-field shifts in comparison with those of **3a** (Table 2). Furthermore, the ^1H NMR (CD_2Cl_2) and ^1H and ^{13}C NMR (CF_3COOD) spectra of **3b** coincided with those of **3a** in CD_2Cl_2 and CF_3COOD (see **3b**^b) and **3b**^c) in Table 1 and **3b**^b) in Table 2). Moreover, the ^{13}C NMR (CD_3CN) chemical shifts of **3b** were almost the same as those of **10** (Table 2).

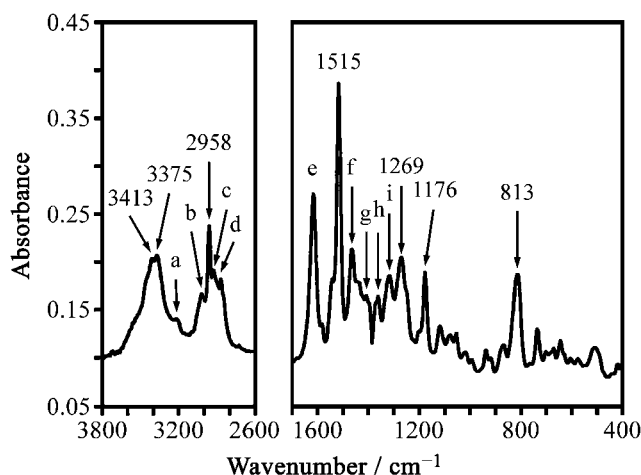


Figure 9. The IR spectrum of **4**: ν_{max} (KBr) (cm^{-1}): a, 3221; b, 3020; c, 2924; d, 2866; e, 1616; f, 1466; g, 1408; h, 1362; i, 1315.

Thus, the elemental analysis and the spectroscopic data for **3b** led to the structure 4-(3-guaiazulenyl)methylene-2,5-cyclohexadiene-1-iminium hexafluorophosphate illustrated in Figure 8. From the structures of the resulting products **3a** and **3b**, it can be inferred that the obtained **3a**, forming a 4- $\text{H}_3\text{N}^+\text{PF}_6^-$ in CH_3CN , owing to the kinetic control is converted to the stabilized **3b** owing to the thermodynamic control (i.e., stability of conjugated π -electron system) in the solvent (Figure 8).

Reductions of **3a and **3b** with NaBH_4 .** The reduction of **3a** with NaBH_4 in a mixed solvent of ethanol and acetonitrile at 25 $^\circ\text{C}$ for 1 h gave **4** in 100% yield (Figure 5). Similarly, as in the case of **3a**, the NaBH_4 -reduction of **3b** under the same reaction conditions as for **3a** gave **4** in 78% yield (Figure 5), along with several chromatographically inseparable products, the molecular structure of which was established on the basis of exact EI-MS spectrum and similar spectroscopic analyses to those of **3a**. The UV-vis spectrum showed specific bands based on a 3-guaiazulenyl group.²⁶ The IR (KBr) spectrum showed specific bands based on the N-H bond (ν_{max} 3413 and 3375 cm^{-1}), the aromatic C-C bond (ν_{max} 1616, 1515, and 1466 cm^{-1}), and the C-N bond (ν_{max} 1269 cm^{-1}) of a 4-aminobenzene part (Figure 9). The molecular formula $\text{C}_{22}\text{H}_{25}\text{N}$ was determined by exact EI-MS spectrum. The ^1H NMR spectrum revealed signals based on a 3-guaiazulenylmethyl-substituted 4-aminobenzene at the C-1 position, the signals of

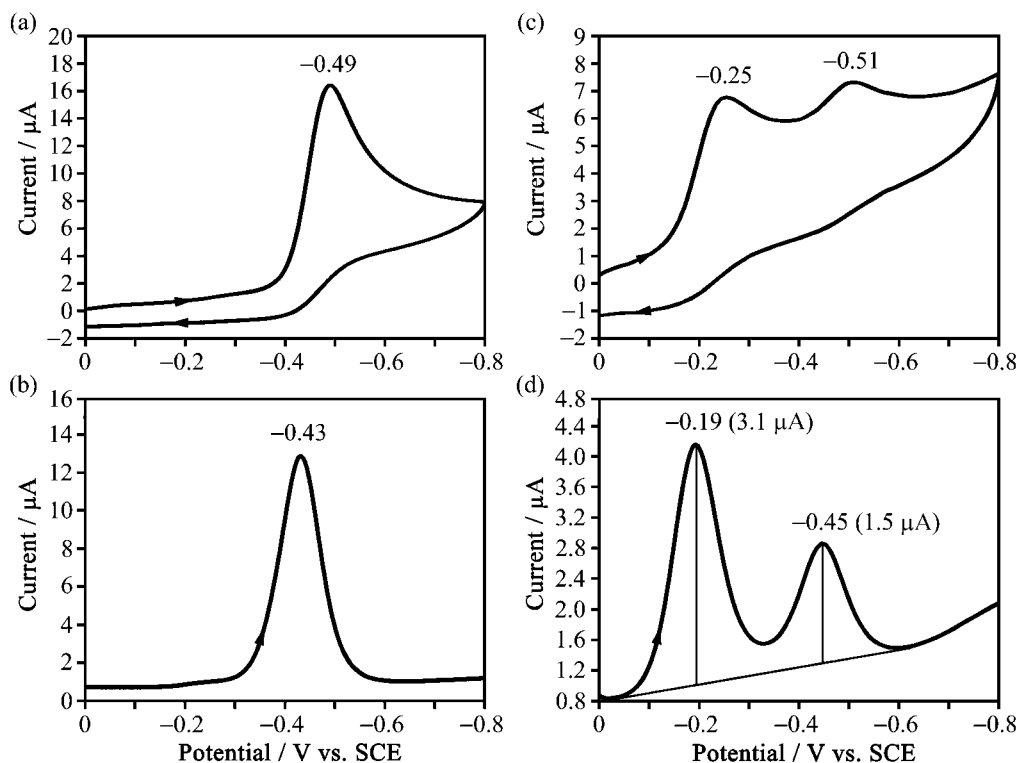


Figure 10. Cyclic and differential pulse voltammograms of **3b** (3.0 mg, 5.55 μmol), with 1/2 equiv of HPF_6 and 1/2 equiv of CH_3CN , [see (a), (b)] and **3a** (3.0 mg, 5.06 μmol), with an equiv of HPF_6 , [see (c), (d)] in 0.1 M $[n\text{-Bu}_4\text{N}]\text{PF}_6$, CH_3CN (10 mL) at a glassy carbon (ID: 3 mm) and a platinum wire served as the working and auxiliary electrodes; scan rates 100 mV s^{-1} at 25 $^\circ\text{C}$ 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 **3a** and **3b**.

which were carefully assigned using similar techniques to those of **3a** (Table 1). The $\text{H}_2\text{N-4}$ signal appeared at δ 3.94 (br s). The ^{13}C NMR spectrum exhibited 19 carbon signals assigned using similar techniques to those of **3a** (Table 2). Thus, the spectroscopic data for **4** led to the molecular structure 4-amino-1-(3-guaiazulenylmethyl)benzene, in which a hydride ion attached to each HC- α carbon atom of **3a** and **3b**, respectively. The chemical shifts for the ^1H and ^{13}C NMR signals of **3a** and **3b** compared with those of **4** and **10–12** are shown in Tables 1 and 2, leading to the formation of **3a**, possessing a 3-guaiazulenylmethyl cation structure with the resonance structure **3c** of a 3-guaiazulenyl cation, and the formation of **3b**, possessing a *p*-benzoquinodimethane monocation structure, illustrated in Figure 8.

Electrochemical Behavior of 3a and 3b. We have been interested further in the electrochemical properties of **3a** and **3b** with a view to comparative study. The electrochemical behavior of **3a**, with an equiv of HPF_6 , and **3b**, with 1/2 equiv of HPF_6 and 1/2 equiv of CH_3CN , was therefore measured by means of cyclic voltammetry (CV) and differential pulse voltammetry (DPV) [Potential (in volt) vs. SCE] in CH_3CN containing 0.1 M $[n\text{-Bu}_4\text{N}]\text{PF}_6$ as a supporting electrolyte. As a result, it was found that **3b** underwent one-electron reduction at a potential of -0.49 V (E_{pc} , irreversible) by CV [-0.43 V (E_p) by DPV] (Figures 10a and 10b), whose reduction potential coincided with that of **10**,⁶ generating an electrochemically unstable radical-species **3a $\cdot$** (Figure 11), while two reduction potentials observed by DPV were positioned at the E_p values of

-0.19 and -0.45 V for **3a**, whose currents showed 3.1 and 1.5 μA , and further, the corresponding two irreversible reduction potentials determined by CV were located at the values of -0.25 and -0.51 V (E_{pc} each) as shown in Figures 10c and 10d. From the result of the DPV datum [i.e., the ratio of each current (in μA) of the two potentials] for the sample **3a** (Figure 10d), it can be inferred that a solution of ca. 1/3 equiv of **3a**· HPF_6 in CH_3CN in the presence of 0.1 M $[n\text{-Bu}_4\text{N}]\text{PF}_6$ was converted to a solution of **3b** in the solvent as a result of dehydrogen hexafluorophosphate. An electron-transfer mechanism of **3a** with **3b** based on CV datum can be inferred as illustrated in Figure 11: namely, **3a** undergoes one-electron reduction at a potential of -0.25 V, generating the corresponding electrochemically unstable radical-species **3a $\cdot$** and further, the existent **3b** in the solution of **3a** undergoes one-electron reduction at a potential of -0.51 V, whose reduction potential coincided with that of the isolated **3b**, also generating **3a $\cdot$** . Furthermore, the reduction potential of the monocarbonium ion compound **3a** coincided with that of (3-guaiazulenyl)phenylmethyl cation hexafluorophosphate [-0.29 V by CV (-0.20 V by DPV)];¹⁰ however, **3a** was susceptible to reduction as compared with **3b** and **10–12**,^{6,10,17} owing to a difference in electron affinity based on each delocalized π -electron system. Moreover, comparing the ^1H and ^{13}C NMR signals and the reduction potential of **10** to those of **3a** and **3b**, it can be inferred that the positive charge of **10** in CH_3CN is mainly localized at the nitrogen atom of the 4-(dimethylamino)benzene part, forming the *p*-benzoquinodimethane monocation

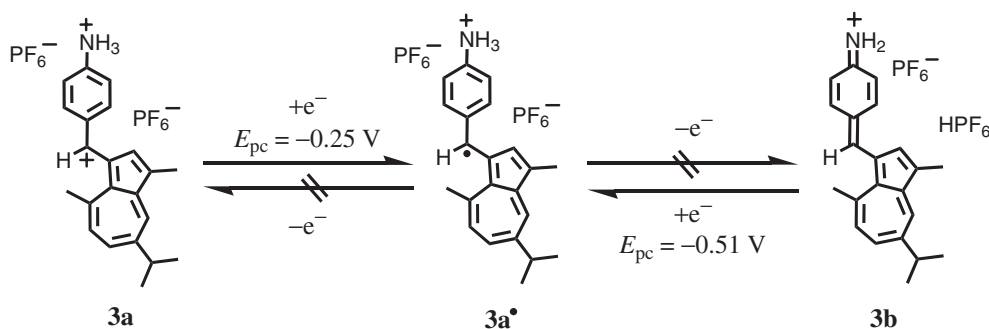


Figure 11. A plausible electron-transfer mechanism based on the CV datum of **3a**, in the presence of **3b**, possessing an equiv of HPF₆.

structure **B**, while the positive charge apparently is transferred to the HC- α carbon atom or the seven-membered ring, forming the 3-guaiazulenylmethylum ion structure **A** or the 3-guaiazulenylum ion structure **C** (Figure 1).

The Optimized (4-Aminophenyl)(3-guaiazulenyl)methylum Ion Structure 3. In a previous paper,⁶ we reported the crystal structure of **10**, leading to the formation of 4-(3-guaiazulenyl)methylene-2,5-cyclohexadiene-1-dimethyliminium tetrafluoroborate (**B**) with the two resonance structures of **A** and **C** (Figure 1). From a comparative study on the C–C and C–N bond lengths of the crystal structure of **10** with those of the optimized 4-(3-guaiazulenyl)methylene-2,5-cyclohexadiene-1-dimethyliminium ion structure calculated by a WinMOPAC (Ver. 3.0) program using PM3 (or AM1) as a semiempirical Hamiltonian, those bond lengths calculated using PM3 more resembled those of the crystal structure of **10** in comparison with those calculated using AM1 (Table 3). Referring to the above results, the optimized (4-aminophenyl)(3-guaiazulenyl)methylum ion structure **3** has been calculated using PM3 (or AM1) (Table 3), because the X-ray crystal structures of **3a** and **3b**²⁷ have not yet been achieved. From the bond lengths of **3** along with the spectroscopic and CV/DPV data and the NaBH₄-reductions of **3a** and **3b**, it can be inferred that similarly as in the case of **10**, the positive charge of **3** is mainly localized at the nitrogen atom of the 4-aminobenzene part, forming a *p*-benzoquinodimethane monoiminium ion structure owing to the thermodynamic control (i.e., stability of conjugated π -electron system), while the positive charge apparently is transferred to the HC- α carbon atom or the seven-membered ring, forming a 3-guaiazulenylmethylum ion or 3-guaiazulenylum ion structure.

Conclusion

We have reported the following four interesting points in this paper: namely, (i) the reaction of guaiazulene (**1**) with 4-aminobenzaldehyde (**2**) in CH₃OH in the presence of hexafluorophosphoric acid at 25 °C for 2 h gave (4-aminophenyl)(3-guaiazulenyl)methylum hexafluorophosphate (**3a**) possessing the resonance structure **3c** of a 3-guaiazulenylum ion, with an equiv of HPF₆, in 56% yield; (ii) a solution of the obtained new monocarbenium ion compound **3a**, forming a protonated amino group (4-H₃N⁺PF₆[−]), in CH₃CN was allowed to stand at room temperature for 48 h, gradually converting to a new 4-(3-guaiazulenyl)methylene-2,5-cyclohexadiene-1-iminium hexa-

Table 3. Selected Bond Lengths (Å) of the X-ray Crystal and Optimized Structures for **10** and of the Optimized (4-Aminophenyl)(3-guaiazulenyl)methylum Ion Structure **3**^a

Atom	10 (X-ray)	10 (PM3)	10 (AM1)	3 (PM3)	3 (AM1)
C1–C2	1.390	1.415	1.432	1.412	1.429
C2–C3	1.372	1.376	1.375	1.378	1.376
C3–C4	1.405	1.415	1.417	1.414	1.417
C4–C5	1.404	1.408	1.413	1.407	1.412
C5–C6	1.360	1.378	1.377	1.380	1.378
C6–C1	1.403	1.414	1.430	1.411	1.428
C1–N	1.359	1.409	1.372	1.400	1.360
C4–C α	1.414	1.429	1.422	1.432	1.422
C α –C3'	1.396	1.368	1.371	1.366	1.369
C1'–C2'	1.351	1.367	1.376	1.366	1.375
C2'–C3'	1.448	1.453	1.458	1.454	1.459
C3'–C3a'	1.457	1.468	1.467	1.470	1.468
C3a'–C4'	1.385	1.392	1.392	1.392	1.392
C4'–C5'	1.406	1.404	1.403	1.404	1.404
C5'–C6'	1.373	1.376	1.380	1.375	1.380
C6'–C7'	1.386	1.401	1.398	1.401	1.399
C7'–C8'	1.379	1.388	1.391	1.388	1.391
C8'–C8a'	1.392	1.388	1.386	1.388	1.386
C8a'–C1'	1.416	1.455	1.461	1.456	1.462
C8a'–C3a'	1.465	1.444	1.452	1.443	1.451

a) The following MO calculation program and calculation conditions were used (i.e., the software: WinMOPAC Ver. 3.0 developed by Fujitsu Ltd., Japan; semiempirical Hamiltonian: PM3 or AM1; and keywords: CHARGE = 1, PRECISE, VECTORS, ALLVEC, BONDS, GEO-OK, EF, PL, LET, T = 10D, GNORM = 10^{−4}, and SCFCRT = 10^{−10}). The final value of the Gradient Norm of the optimized structure; PM3: 0.011 and AM1: 0.009 for **10**; PM3: 0.010 and AM1: 0.011 for **3**.

fluorophosphate (**3b**), completely, as a result of deprotonation and further, a solution of **3a**·HPF₆ dissolved in an organic solvent [i.e., CH₂Cl₂, (CH₃)₂CO, or C₅H₅N (pyridine)] was converted to a solution of **3b** in each solvent as a result of dehydrogen hexafluorophosphate, rapidly; (iii) the reductions of **3a** (and **3b**) with NaBH₄ in a mixed solvent of EtOH and CH₃CN afforded 4-amino-1-(3-guaiazulenylmethyl)benzene (**4**) (100 and 78% yields from **3a** and **3b**, respectively), in which a hydride ion attached to each HC- α carbon atom of **3a** and **3b**, selectively; and (iv) comparative studies on the spectroscopic, chemical, and electrochemical properties of the

isolated **3a** and **3b** with those of structurally related compounds **10–12** were reported as the first example, whose studies apparently indicated the difference between the formation and properties of **3a** and those of **3b**.

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References

- 1 Y. Matsubara, H. Yamamoto, T. Nozoe, *Studies in Natural Products Chemistry: Stereoselective Synthesis (Part I)*, ed. by Atta-ur-Rahman, Elsevier, Amsterdam, **1994**, Vol. 14, pp. 313–354.
- 2 S. Takekuma, M. Sasaki, H. Takekuma, H. Yamamoto, *Chem. Lett.* **1999**, 999.
- 3 S. Takekuma, S. Takata, M. Sasaki, H. Takekuma, *Tetrahedron Lett.* **2001**, 42, 5921.
- 4 S. Takekuma, M. Tanizawa, M. Sasaki, T. Matsumoto, H. Takekuma, *Tetrahedron Lett.* **2002**, 43, 2073.
- 5 M. Sasaki, M. Nakamura, G. Hannita, H. Takekuma, T. Minematsu, M. Yoshihara, S. Takekuma, *Tetrahedron Lett.* **2003**, 44, 275.
- 6 M. Sasaki, M. Nakamura, T. Uriu, H. Takekuma, T. Minematsu, M. Yoshihara, S. Takekuma, *Tetrahedron* **2003**, 59, 505.
- 7 M. Nakamura, M. Sasaki, H. Takekuma, T. Minematsu, S. Takekuma, *Bull. Chem. Soc. Jpn.* **2003**, 76, 2051.
- 8 S. Takekuma, K. Sasaki, M. Nakatsuji, M. Sasaki, T. Minematsu, H. Takekuma, *Bull. Chem. Soc. Jpn.* **2004**, 77, 379.
- 9 M. Nakatsuji, Y. Hata, T. Fujihara, K. Yamamoto, M. Sasaki, H. Takekuma, M. Yoshihara, T. Minematsu, S. Takekuma, *Tetrahedron* **2004**, 60, 5983.
- 10 S. Takekuma, Y. Hata, T. Nishimoto, E. Nomura, M. Sasaki, T. Minematsu, H. Takekuma, *Tetrahedron* **2005**, 61, 6892.
- 11 S. Takekuma, K. Takahashi, A. Sakaguchi, Y. Shibata, M. Sasaki, T. Minematsu, H. Takekuma, *Tetrahedron* **2005**, 61, 10349.
- 12 S. Takekuma, K. Takahashi, A. Sakaguchi, M. Sasaki, T. Minematsu, H. Takekuma, *Tetrahedron* **2006**, 62, 1520.
- 13 S. Takekuma, M. Hirokawa, S. Morishita, M. Sasaki, T. Minematsu, H. Takekuma, *Tetrahedron* **2006**, 62, 3732.
- 14 S. Takekuma, K. Sonoda, C. Fukuhara, T. Minematsu, *Tetrahedron* **2007**, 63, 2472.
- 15 S. Takekuma, K. Tone, M. Sasaki, T. Minematsu, H. Takekuma, *Tetrahedron* **2007**, 63, 2490.
- 16 S. Takekuma, K. Mizutani, K. Inoue, M. Nakamura, M. Sasaki, T. Minematsu, K. Sugimoto, H. Takekuma, *Tetrahedron* **2007**, 63, 3882.
- 17 S. Takekuma, M. Tamura, T. Minematsu, H. Takekuma, *Tetrahedron* **2007**, 63, 12058.
- 18 S. Takekuma, K. Sonoda, T. Minematsu, H. Takekuma, *Tetrahedron* **2008**, 64, 3802.
- 19 B. P. Cho, T. Yang, L. R. Blankenship, J. D. Moody, M. Churchwell, F. A. Beland, S. J. Culp, *Chem. Res. Toxicol.* **2003**, 16, 285.
- 20 D. Guzmán-Lucero, J. Guzmán, D. Likhatchev, R. Martínez-Palou, *Tetrahedron Lett.* **2005**, 46, 1119.
- 21 T. Tachikawa, C. Handa, S. Tokita, *J. Photopolym. Sci. Technol.* **2003**, 16, 187.
- 22 Y. Soneta, T. Midorikawa, K. Miyamura, *Bull. Chem. Soc. Jpn.* **2006**, 79, 1060.
- 23 S. Lovell, B. J. Marquardt, B. Kahr, *J. Chem. Soc., Perkin Trans. 2* **1999**, 2241.
- 24 J. Lacour, G. Bernardinelli, V. Russell, I. Dance, *CrystEngComm* **2002**, 4, 165.
- 25 In relation to the formation of **3a**, with an equiv of HPF₆, forming a non-protonated H₂N-4 group at the solid state, the crystal structure of {4-[4-(dimethylamino)phenylazo]phenyl}(3-guaiazulenyl)methylum tetrafluoroborate, with an equiv of HBF₄, forming a non-protonated (CH₃)₂N-4 group could be determined by means of X-ray diffraction, recently; details will be reported elsewhere.
- 26 Guaiazulene (**1**): UV-vis λ_{max} (CH₃CN)/nm (log ϵ): 213 (4.10), 244 (4.39), 284 (4.61), 301sh (4.03), 348 (3.65), 365 (3.46), 600 (2.68), 648sh (2.61), and 721sh (2.20).
- 27 The recrystallization of **3a**, providing a stable single crystal suitable for X-ray crystallographic analysis, is very difficult; however, the recrystallization of **3b**, providing a stable single crystal suitable for that purpose, is possible, and is currently under intensive investigation.