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Reaction of guaiazulene with *o*-formylbenzoic acid in diethyl ether (or methanol) in the presence of hexafluorophosphoric acid: comparative studies on ^{1}H and ^{13}C NMR spectral properties of 3-guaiazulenylmethylium- and 3-guaiazulenium-ion structures

Shin-ichi Takekuma,[a,*] Kazutaka Sonoda,[a] Chika Fukuhara[a] and Toshie Minematsu[b]

[a]*Department of Applied Chemistry, Faculty of Science and Engineering, Kinki University, 3-4-1 Kowakae, Higashi-Osaka-shi, Osaka 577-8502, Japan*
[b]*School of Pharmaceutical Sciences, Kinki University, 3-4-1 Kowakae, Higashi-Osaka-shi, Osaka 577-8502, Japan*

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Abstract—Reaction of guaiazulene (**1**) with *o*-formylbenzoic acid (**2**) in diethyl ether in the presence of hexafluorophosphoric acid at 25 °C for 90 min gives the corresponding monocarbenium-ion compound, [2-(carboxy)phenyl](3-guaiazulenyl)methylium hexafluorophosphate (**3**), quantitatively, which upon treatment with aq $NaHCO_3$ leads to 3-(3-guaiazulenyl)-2-benzofuran-1(3*H*)-one (**5**) in 96% isolated yield. Similarly, reaction of **1** with **2** in methanol under the same conditions as the above reaction affords two kinds of inseparable monocarbenium-ion compounds, **3** and (3-guaiazulenyl)[2-(methoxycarbonyl)phenyl]methylium hexafluorophosphate (**4**) with an equilibrium between them, which upon reaction with a solution of $NaBH_4$ in ethanol at 25 °C for 30 min leads to **5** in 46% isolated yield and (3-guaiazulenyl)-[2-(methoxycarbonyl)phenyl]methane (**6**) in 37% isolated yield. Along with the ^{1}H and ^{13}C NMR spectral properties of a solution of **5** in trifluoroacetic acid-d_1 at 25 °C, whose molecular structure is converted to a ca. 1:1 equilibrium mixture of **7** possessing a partial structure of the 3-guaiazulenylmethylium-ion and **8** possessing a partial structure of the 3-guaiazulenium-ion, comparative studies on the ^{1}H and ^{13}C NMR spectral properties of **7** and **8** with those of the monocarbenium-ion compound, (3-guaiazulenyl)[4-(methoxycarbonyl)phenyl]methylium hexafluorophosphate (**A**), **5**, and **6** are reported. From these NMR studies, it can be inferred that the positive charge of the 3-guaiazulenylmethylium-ion part of **7** apparently is transferred to the seven-membered ring, generating a resonance form of the 3-guaiazulenylium-ion structure η′, and the same result can be inferred for the previously documented monocarbenium-ion compounds **A**–**I**. Moreover, referring to a comparative study on the C–C bond lengths of **A** observed by the X-ray crystallographic analysis with those of the optimized (3-guaiazulenyl)[4-(methoxycarbonyl)phenyl]methylium-ion structure for **A** calculated by a WinMOPAC (Ver. 3.0) program using PM3, AM1, or MNDOD as a semiempirical Hamiltonian, the optimized [2-(carboxy)phenyl](3-guaiazulenyl)methylium-ion structure for **3** calculated using PM3 is described.

1. Introduction

The synthesis, stability, spectroscopic and chemical properties, crystal structures, electrochemical behavior, and theoretical study (e.g., ab initio calculations, DFT, GIAO-NMR, and NICS) of the azulenium-,[1–3] azulenylium-, and azulenylmethylium-ion structures[4–14] have been studied to a considerable extent, and a large number of the results and discussion regarding those delocalized carbocation compounds have been well documented. In relation to those basic studies, we previously reported a facile preparation and the crystal structures as well as the spectroscopic, chemical, and electrochemical properties of the delocalized mono- and dicarbenium-ion compounds stabilized by the expanded π-electron systems with a 3-guaiazulenyl group.[15–28] During the course of our systematic investigations on the delocalized 3-guaiazulenyl-substituted carbenium-ion compounds derived from naturally occurring guaiazulene[29] (**1**), we have recently found (i) that the reaction of **1** with methyl terephthalaldehydate in methanol in the presence of hexafluorophosphoric acid at 25 °C for 2 h gave the corresponding monocarbenium-ion compound, (3-guaiazulenyl)[4-(methoxycarbonyl)phenyl]methylium hexafluorophosphate (**A**), in 94% isolated yield; (ii) that the spectroscopic data of **A** led to the molecular structure with a resonance form of the 3-guaiazulenylium-ion structure **A′** in acetonitrile (see Chart 1);[23] and (iii) that along with the spectroscopic data for **A** in acetonitrile, the X-ray crystallographic analysis for **A** (see Fig. 1a,b) also led to the crystal structure with a resonance

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* Corresponding author. Tel.: +81 6 6730 5880x4020; fax: +81 6 6727 4301; e-mail: takekuma@apch.kindai.ac.jp

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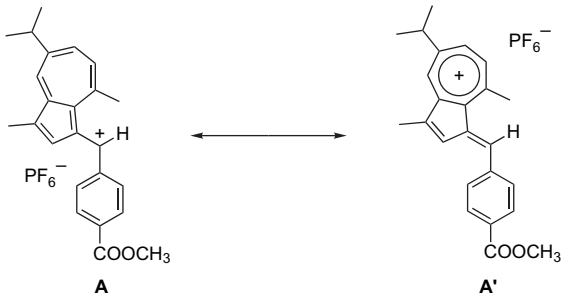

Chart 1.

form of **A′**. As a systematic investigation on the above chemistry, our interest has quite recently been focused on a facile preparation, the molecular structure, and properties of the delocalized monocarbenium-ion compound, [2-(carboxy)-phenyl](3-guaiazulenyl)methylium hexafluorophosphate (**3**), which upon treatment with aq $NaHCO_3$ leads to the formation of 3-(3-guaiazulenyl)-2-benzofuran-1(3*H*)-one (**5**). We now wish to report the detailed studies on the reaction of **1** with *o*-formylbenzoic acid (**2**) in diethyl ether (or methanol) in the presence of hexafluorophosphoric acid affording **3** and (3-guaiazulenyl)[2-(methoxycarbonyl)phenyl]methylium hexafluorophosphate (**4**), whose compounds can be led to **5** and (3-guaiazulenyl)[2-(methoxycarbonyl)phenyl]methane (**6**), respectively, and comparative studies on the ^{1}H and ^{13}C NMR spectral properties of **7** possessing a partial structure of the 3-guaiazulenylmethylium-ion and **8** possessing a partial structure of the 3-guaiazulenium-ion, with an equilibrium between them, yielded from **5** dissolved in trifluoroacetic acid-d_1 at 25 °C (see Fig. 2) with those of **A**, **5**, **6**, and the previously documented monocarbenium-ion

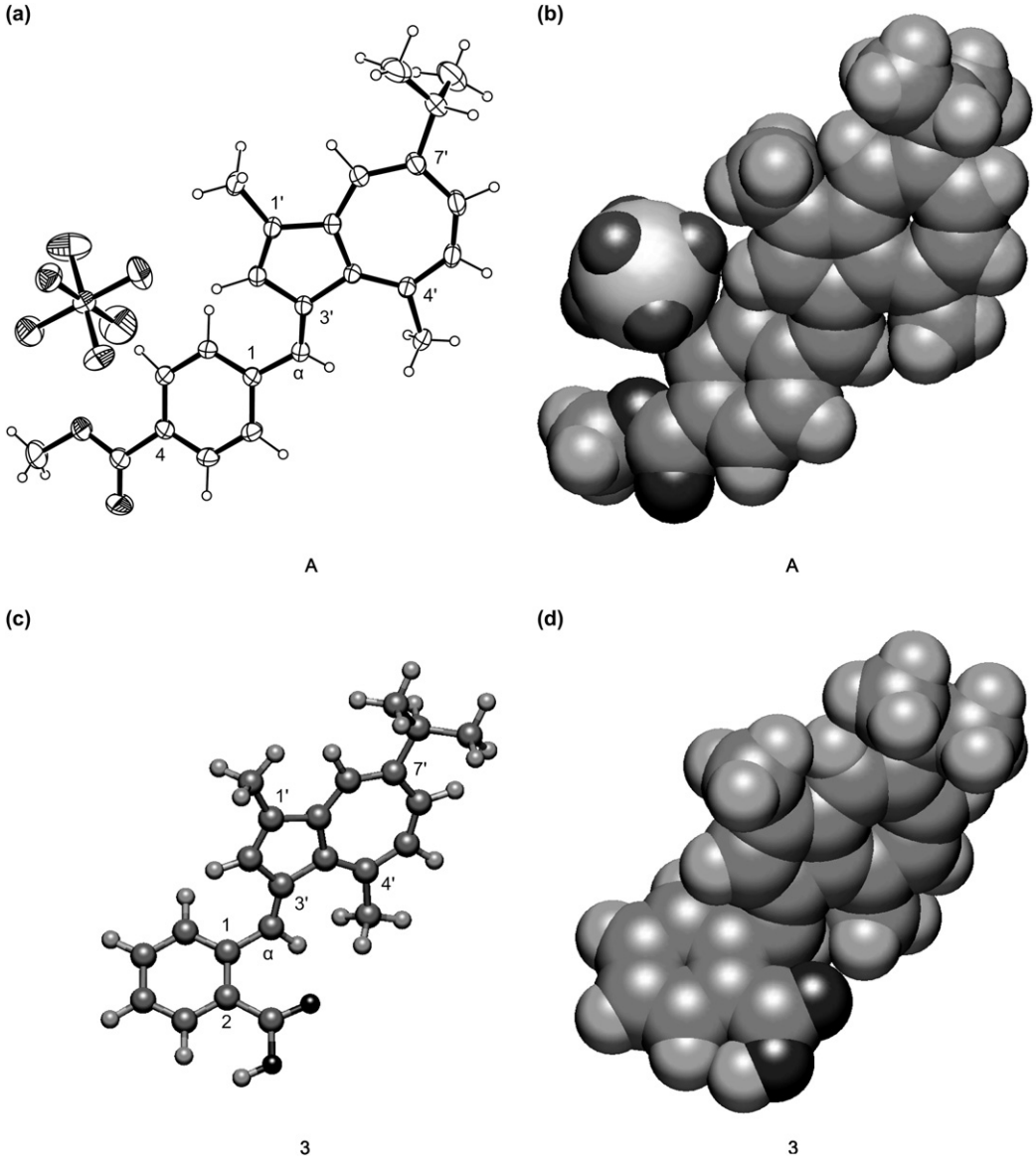

Figure 1. (a) The ORTEP drawing of **A** (30% probability thermal ellipsoids).[23] (b) The crystal structure of **A** shown using a space-filling mode. (c) The optimized [2-(carboxy)phenyl](3-guaiazulenyl)methylium-ion structure for **3**[33] shown using a ball-and-stick mode. The selected bond lengths (Å): C1–C2: 1.405, C2–C3: 1.398, C3–C4: 1.389, C4–C5: 1.391, C5–C6: 1.390, C6–C1: 1.398, C1–Cα: 1.462, C1′–C2′: 1.361, C2′–C3′: 1.465, C3′–C3a′: 1.479, C3a′–C4′: 1.390, C4′–C5′: 1.408, C5′–C6′: 1.373, C6′–C7′: 1.405, C7′–C8′: 1.387, C8′–C8a′: 1.389, C8a′–C1′: 1.466, C8a′–C3a′: 1.434, C3′–Cα: 1.349. (d) The optimized [2-(carboxy)phenyl](3-guaiazulenyl)methylium-ion structure for **3**[33] shown using a space-filling mode.

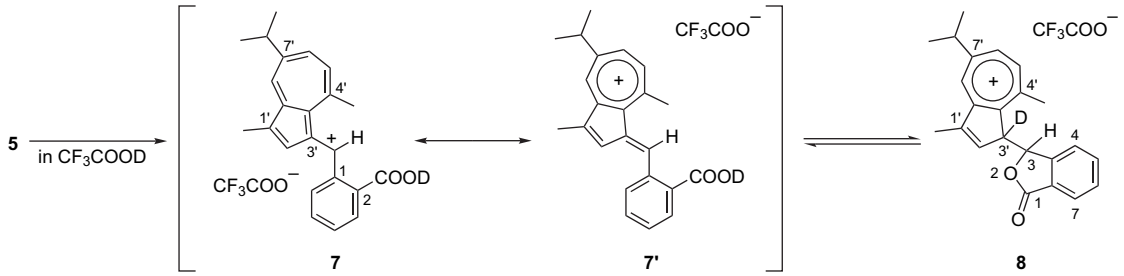

Figure 2. The formation of a ca. 1:1 equilibrium mixture of **7** (with a resonance form **7′**) and **8** from **5** dissolved in CF_3COOD at 25 °C.

compounds **B**–**I**[17,19,23,24] (see Chart 2). Moreover, referring to a comparative study on the C–C bond lengths of **A** observed by the X-ray crystallographic analysis with those of the optimized (3-guaiazulenyl)[4-(methoxycarbonyl)-phenyl]methylium-ion structure for **A** calculated by a WinMOPAC (Ver. 3.0) program using PM3, AM1, or MNDOD as a semiempirical Hamiltonian, the optimized [2-(carboxy)phenyl](3-guaiazulenyl)methylium-ion structure for **3** calculated using PM3 is described.

2. Results and discussion

2.1. Reaction of guaiazulene (1) with *o*-formylbenzoic acid (2) in diethyl ether (or methanol) in the presence of hexafluorophosphoric acid; preparation and properties of 3-(3-guaiazulenyl)-2-benzofuran-1(3*H*)-one (5) and (3-guaiazulenyl)[2-(methoxycarbonyl)phenyl]methane (6)

The reaction of **1** with **2** in diethyl ether in the presence of hexafluorophosphoric acid at 25 °C for 90 min gave the corresponding monocarbenium-ion compound, [2-(carboxy)-phenyl](3-guaiazulenyl)methylium hexafluorophosphate[30,31] (**3**) (yellow powder; $C_{23}H_{23}O_2$: $[M-PF_6]^+$, determined by the exact FABMS spectrum using 3-nitrobenzyl alcohol as a matrix reagent), quantitatively, which upon treatment with aq $NaHCO_3$ led to 3-(3-guaiazulenyl)-2-benzofuran-1(3*H*)-one (**5**) in 96% isolated yield (see Fig. 3 and Section 4.1.1), whose molecular structure was established on the basis of spectroscopic data [UV–vis, IR, exact FABMS, ^1H, and ^{13}C NMR including 2D NMR (i.e., H–H COSY, HMQC—^1H detected hetero nuclear multiple quantum coherence, and HMBC—^1H detected hetero nuclear multiple bond connectivity)].

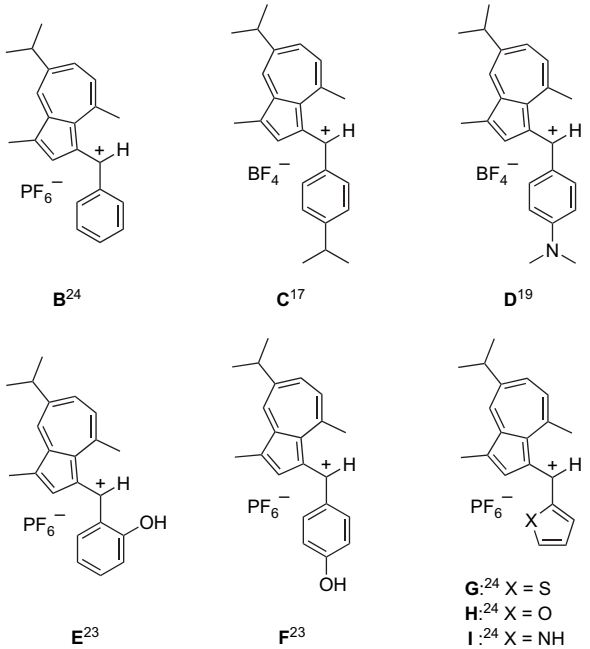

Chart 2.

Compound **5** was blue prisms [R_f=0.25 on silica gel TLC (hexane–AcOEt=8:2, v/v)], mp 113 °C and decomp. >200 °C [determined by the thermal analysis (TGA and DTA)]. The characteristic UV–vis (CH_3CN) absorption bands based on guaiazulene[32] (**1**) were observed and the longest visible absorption wavelength appeared at λ_{max} 590 nm ($\log\varepsilon$=2.71), indicating a hypsochromic shift in comparison with that of **1** (λ_{max} 600 nm; $\log\varepsilon$=2.68). The IR (KBr) spectrum showed a specific band based on the C=O group of lactone at 1755 cm^{-1}. The protonated molecular formula $C_{23}H_{23}O_2$ ($[M+H]^+$) was determined by the exact FABMS spectrum using 3-nitrobenzyl alcohol as a matrix reagent. The 500 MHz ^1H NMR (CD_3CN) spectrum showed signals based on the structure of 2-benzofuran-1(3*H*)-one possessing a 3-guaiazulenyl group at the C-3 position, whose signals (δ and J values) were carefully assigned using the H–H COSY technique and the computer-assisted simulation analysis (see Section 4.1.1). The 125 MHz ^{13}C NMR (CD_3CN) spectrum exhibited 22 carbon signals (δ, ppm) assigned by the HMQC and HMBC techniques (see Section 4.1.1). Thus, these spectroscopic data for **5** led to the molecular structure, 3-(3-guaiazulenyl)-2-benzofuran-1(3*H*)-one (see Fig. 3). Furthermore, the reaction of **5** with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) in CH_2Cl_2 at 25 °C for 10 min gave numerous products, simultaneously, whose compounds were observed by the silica gel TLC (hexane–AcOEt=8:2, v/v). Thus, 3-(3-guaiazulenyl)-2-benzofuranium-1-one could not be obtained by this reaction.

Similarly, the reaction of **1** with **2** in methanol under the same conditions as the above reaction afforded two kinds of inseparable monocarbenium-ion compounds, **3** and (3-guaiazulenyl)[2-(methoxycarbonyl)phenyl]methylium hexafluorophosphate (**4**) with an equilibrium between them (yellow powder; $C_{24}H_{25}O_2$: $[M-PF_6]^+$, determined by the exact FABMS spectrum using 3-nitrobenzyl alcohol as a matrix reagent), which upon reaction with a solution of $NaBH_4$ in ethanol at 25 °C for 30 min led to **5** in 46% isolated yield

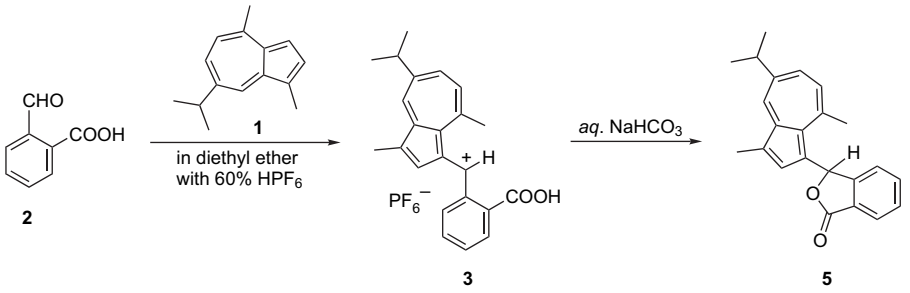

Figure 3. Reaction of **1** with **2** in diethyl ether in the presence of hexafluorophosphoric acid at 25 °C for 90 min gives **3**, quantitatively, which upon treatment with aq $NaHCO_3$ leads to **5** in 96% isolated yield.

and (3-guaiazulenyl)[2-(methoxycarbonyl)phenyl]methane (**6**) in 37% isolated yield (see Fig. 4 and Section 4.1.2), whose molecular structures were established on the basis of similar spectroscopic analyses as for **5**.

Compound **6** was a blue powder [R_f=0.50 on silica gel TLC (hexane–AcOEt=8:2, v/v)], mp 87 °C and decomp. >200 °C [determined by the thermal analysis (TGA and DTA)]. The characteristic UV–vis (CH_3CN) absorption bands based on guaiazulene[32] (**1**), which spectral pattern resembled those of **1** and **5**, were observed and the longest visible absorption wavelength appeared at λ_{max} 622 nm (log ε=2.69), indicating a bathochromic shift in comparison with those of **1** (λ_{max} 600 nm; log ε=2.68) and **5** (λ_{max} 590 nm; log ε=2.71). The IR (KBr) spectrum showed a specific band based on the C=O group of ester at 1713 cm^{-1}, which revealed lower wavenumber shift as compared with that of **5** (1755 cm^{-1}). The molecular formula $C_{24}H_{26}O_2$ (M^+) was determined by the exact FABMS spectrum using 3-nitrobenzyl alcohol as a matrix reagent. The 500 MHz ^1H NMR (CD_3CN) spectrum showed signals based on the structure of 2-(methoxycarbonyl)benzene possessing a 3-guaiazulenylmethyl group at the C-1 position, which signals (δ and J values) were carefully assigned using the H–H COSY technique and the computer-assisted simulation analysis (see Section 4.1.2). The 125 MHz ^{13}C NMR (CD_3CN) spectrum exhibited 23 carbon signals (δ, ppm) assigned by the HMQC and HMBC techniques (see Section 4.1.2). Thus, these spectroscopic data for **6** led to the molecular structure, (3-guaiazulenyl)[2-(methoxycarbonyl)phenyl]-methane (see Fig. 4). Similarly, as in the case of **5**, the reaction of **6** with DDQ in CH_2Cl_2 at 25 °C for 10 min afforded many products, simultaneously, whose compounds were observed by the silica gel TLC (hexane–AcOEt=8:2, v/v). Thus, (3-guaiazulenyl)[2-(methoxycarbonyl)phenyl]methylium-ion compound could not be obtained by this reaction.

2.2. ^1H and ^{13}C NMR spectral properties of 5 in trifluoroacetic acid-d_1 and comparative studies on ^1H and ^{13}C NMR spectral properties of 5–8 with those of A–I

The ^1H and ^{13}C NMR spectra including 2D NMR (i.e., H–H COSY, HMQC, and HMBC) of a solution of **5** in trifluoroacetic acid-d_1, whose molecular structure was converted to

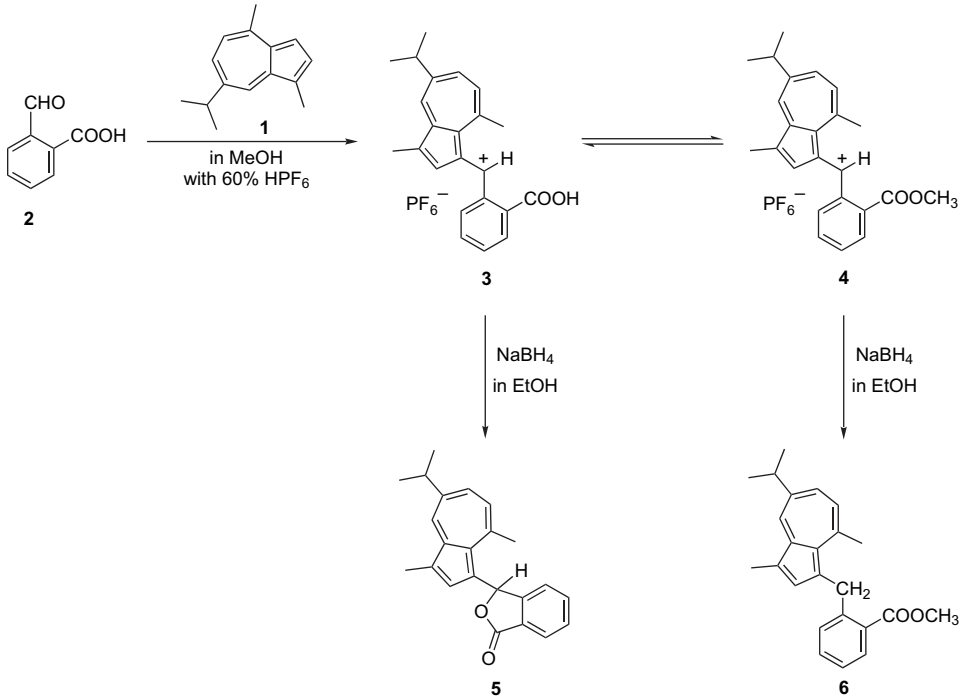

Figure 4. Reaction of **1** with **2** in methanol in the presence of hexafluorophosphoric acid at 25 °C for 90 min affords **3** and **4**, with an equilibrium between them, which upon reaction with a solution of $NaBH_4$ in ethanol at 25 °C for 30 min leads to **5** in 46% isolated yield and **6** in 37% isolated yield.

two kinds of carbocation compounds, i.e., the deuteronated **5** at the carbonyl group, which rapidly led to the formation of [2-(carboxy-d_1)phenyl](3-guaiazulenyl)methylium-ion structure **7**, and the deuteronated 3-(3-guaiazulenyl)-2-benzofuran-1(3*H*)-one **8** at the C-3′ position (see Fig. 2), simultaneously, were measured. A careful study of the 600 MHz ^{1}H NMR signals for this measured solution at 25 °C led us to a ca. 1:1 equilibrium mixture of **7** and **8**, whose compounds were extremely stable in trifluoroacetic acid-d_1 without decomposition. It is noteworthy that, although **8** possesses two diastereomers, a kind of NMR signals based on **8** was observed.

Comparative studies on the chemical shifts (δ, ppm) for the ^{1}H and ^{13}C NMR signals of the 3-guaiazulenylium-ion part of **7** with those of the 3-guaiazulenium-ion part of **8** are shown in Tables 1 and 2. As a result, it was found (i) that, although the H-8′ (8.63) proton signal of **8** coincided with that of **7** (8.66), the H-2′ (6.50) proton signal of **8** showed larger up-field shift in comparison with that of **7** (H-2′: 7.61), and the H-5′ (8.65) and H-6′ (8.58) proton signals of **8** revealed slight down-field shifts in comparison with those of **7** (H-5′: 8.57 and H-6′: 8.43) (see Table 1); and (ii) that, although the deuteronated C-3′ (57.4, J_{C-D}=19.4 Hz) carbon signal of **8** showed larger up-field shift in comparison with that of **7** (C-3′: 141.1), the other carbon signals of **8** revealed down-field shifts in comparison with those of **7** (see Table 2); namely, the order of the larger down-field shift was C-3a′ ($\Delta\delta$ 12.1 ppm)>C-8a′ (6.0)>C-7′ (5.2)>C-1′ (3.6)>C-2′ (3.4)>C-6′ (2.0)>C-4′ (1.4)>C-8′ (1.3)>C-5′ (0.8). Thus, an apparent difference between the chemical shifts for the ^{1}H and ^{13}C NMR signals of the 3-guaiazulenylium-ion part of **7** and those of the 3-guaiazulenium-ion part of **8** was observed. Furthermore, comparative studies on the chemical shifts for the ^{1}H and ^{13}C NMR signals of the 3-guaiazulenylium-ion part of **7** with those of (3-guaiazulenyl)[4-(methoxycarbonyl)phenyl]methylium hexafluorophosphate[23] (**A**) under the same measurement conditions are shown in Tables 1 and 2. As a result, it was found (i) that, although the H-2′ (7.61) proton signal of **7** showed larger up-field shift in comparison with that of **A** (H-2′: 7.89), owing to the influence of the ring current of the benzene ring, whose influence was supported by the optimized [2-(carboxy)phenyl](3-guaiazulenyl)methylium-ion structure of **3** (see Fig. 1c,d),[33] the other proton signals of **7** coincided with those of **A** (see Table 1); and (ii) that the chemical shifts for all the carbon signals of **7** resembled those of **A** (see Table 2).

Table 1. The ^{1}H NMR chemical shifts (δ, ppm) for the 3-guaiazulenylium-ion parts of **A** and **7**, and the 3-guaiazulenium-ion part of **8** in CF_3COOD

Compound	**A**	**7**	**8**	Difference[a]
H-2′	7.89	7.61	6.50	+1.11
H-5′	8.58	8.57	8.65	−0.08
H-6′	8.44	8.43	8.58	−0.15
H-8′	8.65	8.66	8.63	+0.03

[a] Differential of the chemical shifts for **7** and **8**.

Table 2. The ^{13}C NMR chemical shifts (δ, ppm) for the 3-guaiazulenylium-ion parts of **A** and **7**, and the 3-guaiazulenium-ion part of **8** in CF_3COOD

Compound	**A**	**7**	**8**	Difference[a]
C-1′	148.7	146.3	149.9	−3.6
C-2′	142.6	142.1	145.5	−3.4
C-3′	143.8	141.1	57.4	+83.7
C-3a′	155.4	154.1	166.2	−12.1
C-4′	159.4	158.4	159.8	−1.4
C-5′	152.5	151.4	152.2	−0.8
C-6′	146.5	145.4	147.4	−2.0
C-7′	176.1	174.5	179.7	−5.2
C-8′	140.4	139.4	140.7	−1.3
C-8a′	164.6	164.1	170.1	−6.0

[a] Differential of the chemical shifts for **7** and **8**.

Comparative studies on the chemical shifts for the ^{1}H and ^{13}C NMR signals of **5** with those of **8** are shown in Tables 3 and 4. As a result, it was found (i) that, although the H-2′ (6.50) and H-3 (6.58) proton signals of **8** showed larger up-field shifts in comparison with those of **5** (H-2′: 6.99; H-3: 7.56), the other proton signals of **8** revealed down-field shifts in comparison with those of **5** (see Table 3); namely, the order of the larger down-field shift was H-5′ ($\Delta\delta$ 1.43 ppm)>H-6′ (1.02)>H-4 (0.53)>H-8′ (0.37)>H-5 (0.25)>H-6 (0.13)>H-7 (0.08); (ii) that, although the deuteronated C-3′ (57.4, J_{C-D}=19.4 Hz) carbon signal of the 3-guaiazulenium-ion part of **8** showed larger up-field shift in comparison with that of the 3-guaiazulenyl group of **5** (C-3′: 121.5), the other carbon signals of **8** revealed down-field shifts in comparison with those of **5** (see Table 4); namely, the order of the larger down-field shift was C-7′ ($\Delta\delta$ 36.6 ppm)>C-3a′ (30.6)>C-8a′ (30.0)>C-1′ (24.1)>C-5′ (22.4)>C-4′ (13.3)>C-6′ (10.8)>C-2′ (7.5)>C-8′ (5.0); and (iii) that, although the C-3 (79.5), C-3a (149.1), C-4 (123.2), and C-7a (125.2) carbon signals for the 2-benzofuran-1(3*H*)-one part of **8** showed up-field shifts in comparison with those of **5** (C-3: 80.2, C-3a: 152.0, C-4: 124.8, and C-7a: 127.6), the other carbon signals of **8** revealed down-field shifts in comparison with those of **5** (see Table 4); namely, the order of the larger down-field shift was C-1 ($\Delta\delta$ 4.3 ppm)>C-5 (2.8)>C-6 (2.3)>C-7 (2.2). Thus, an apparent difference between the chemical shifts for the ^{1}H and ^{13}C NMR signals of **5** and those of **8** was observed.

Comparative studies on the chemical shifts for the ^{1}H and ^{13}C NMR signals of **6** with those of **7** are shown in Tables 5 and 6. As a result, it was found (i) that all the proton signals of **7** showed larger down-field shifts in comparison with those of **6** (see Table 5); namely, the order of the larger down-field shift was HC-α ($\Delta\delta$ 4.56 ppm)>H-5′ (1.75)>H-6′ (1.12)>H-6 (0.74)>H-8′ (0.55)>H-3 (0.53)>H-5 (0.50)>H-4 (0.46)>H-2′ (0.39); (ii) that all the carbon signals for the 3-guaiazulenylmethylium-ion part of **7** showed down-field shifts in comparison with those for the

Table 3. The selected ^{1}H NMR chemical shifts (δ, ppm) for **5** in CD_3CN and **8** in CF_3COOD

Compound	**5**	**8**	Difference	Compound	**5**	**8**	Difference
H-2′	6.99	6.50	+0.49	H-3	7.56	6.58	+0.98
H-5′	7.22	8.65	−1.43	H-4	7.42	7.95	−0.53
H-6′	7.56	8.58	−1.02	H-5	7.74	7.99	−0.25
H-8′	8.26	8.63	−0.37	H-6	7.63	7.76	−0.13
				H-7	7.92	8.00	−0.08

Table 4. The selected ^{13}C NMR chemical shifts (δ, ppm) for **5** in CD_3CN and **8** in CF_3COOD

Compound	5	8	Difference	Compound	5	8	Difference
C-1′	125.8	149.9	−24.1	C-1	171.2	175.5	−4.3
C-2′	138.0	145.5	−7.5	C-3	80.2	79.5	+0.7
C-3′	121.5	57.4	+64.1	C-3a	152.0	149.1	+2.9
C-3a′	135.6	166.2	−30.6	C-4	124.8	123.2	+1.6
C-4′	146.5	159.8	−13.3	C-5	135.1	137.9	−2.8
C-5′	129.8	152.2	−22.4	C-6	130.1	132.4	−2.3
C-6′	136.6	147.4	−10.8	C-7	125.8	128.0	−2.2
C-7′	143.1	179.7	−36.6	C-7a	127.6	125.2	+2.4
C-8′	135.7	140.7	−5.0				
C-8a′	140.1	170.1	−30.0				

Table 5. The selected ^{1}H NMR chemical shifts (δ, ppm) for **6** in CD_3CN and **7** in CF_3COOD

Compound	6	7	Difference	Compound	6	7	Difference
H-2′	7.22	7.61	−0.39	H-3	7.87	8.40	−0.53
H-5′	6.82	8.57	−1.75	H-4	7.27	7.73	−0.46
H-6′	7.31	8.43	−1.12	H-5	7.35	7.85	−0.50
H-8′	8.11	8.66	−0.55	H-6	6.80	7.54	−0.74
				HC-α	4.91[a]	9.47[b]	−4.56

[a] 1-CH_2-3′.
[b] HC^+-α.

Table 6. The selected ^{13}C NMR chemical shifts (δ, ppm) for **6** in CD_3CN and **7** in CF_3COOD

Compound	6	7	Difference	Compound	6	7	Difference
C-1′	125.5	146.3	−20.8	C-1	145.3	138.8	+6.5
C-2′	141.5	142.1	−0.6	C-2	130.6	128.9	+1.7
C-3′	126.6	141.1	−14.5	C-3	131.1	133.9	−2.8
C-3a′	134.0	154.1	−20.1	C-4	126.8	132.3	−5.5
C-4′	146.4	158.4	−12.0	C-5	132.9	135.5	−2.6
C-5′	127.1	151.4	−24.3	C-6	131.5	134.2	−2.7
C-6′	135.9	145.4	−9.5	C-α	35.9[a]	151.8[b]	−115.9
C-7′	140.1	174.5	−34.4				
C-8′	134.4	139.4	−5.0				
C-8a′	138.8	164.1	−25.3				

[a] 1-CH_2-3′.
[b] HC^+-α.

3-guaiazulenylmethyl group of **6** (see Table 6); namely, the order of the larger down-field shift was C-α ($\Delta\delta$ 115.9 ppm)>C-7′ (34.4)>C-8a′ (25.3)>C-5′ (24.3)>C-1′ (20.8)>C-3a′ (20.1)>C-3′ (14.5)>C-4′ (12.0)>C-6′ (9.5)>C-8′ (5.0)>C-2′ (0.6); and (iii) that, although the C-1 (138.8) and C-2 (128.9) carbon signals for the 2-(carboxy)phenyl group of **7** showed up-field shifts in comparison with those of the 2-(methoxycarbonyl)phenyl group of **6** (C-1: 145.3; C-2: 130.6), the other carbon signals of **7** revealed down-field shifts in comparison with those of **6** (see Table 6); namely, the order of the larger down-field shift was C-4 ($\Delta\delta$ 5.5 ppm)>C-3 (2.8)>C-6 (2.7)>C-5 (2.6). Thus, an apparent difference between the chemical shifts for the ^{1}H and ^{13}C NMR signals of **6** and those of **7** was observed.

From comparative studies on the ^{1}H and ^{13}C NMR spectral properties of **7** possessing a partial structure of the 3-guaiazulenylmethylium-ion and **8** possessing a partial structure of the 3-guaiazulenium-ion with those of **A**, **5**, and **6**, it could be inferred that the positive charge of the 3-guaiazulenylmethylium-ion part of **7** apparently was transferred to the seven-membered ring or the benzene ring, generating a resonance form of the 3-guaiazulenylium- or phenylium-ion structure and, further, the same result could be inferred for **A**. Moreover, comparative studies on the chemical shifts for the ^{1}H and ^{13}C NMR signals of the 3-guaiazulenylmethylium-ion part for **7** with those of the 3-guaiazulenylmethylium-ion parts for the previously documented monocarbenium-ion compounds **B**–**I**[17,19,23,24] (see Chart 2) are shown in Tables 7 and 8. The chemical shifts for all the proton and carbon signals of **B**–**I** resembled those of **7** and **A**. Thus, the same results as for **7** and **A** could be inferred for **B**–**I**.

2.3. The optimized [2-(carboxy)phenyl](3-guaiazulenyl)methylium-ion structure for 3

In the previous paper,[23] we reported the crystal structure of (3-guaiazulenyl)[4-(methoxycarbonyl)phenyl]methylium hexafluorophosphate (**A**) (see Fig. 1a,b). The structural parameters of **A** revealed (i) that, from the dihedral angles between the least-squares planes, it was found that the plane of the 4-(methoxycarbonyl)phenyl group twisted by 33.4° from the plane of the 3-guaiazulenyl group owing to the influence of a slight steric hindrance between the H-2 and H-6 atoms of the 4-(methoxycarbonyl)phenyl group and

Table 7. The ^{1}H NMR chemical shifts (δ, ppm) for the 3-guaiazulenylmethylium-ion parts of **7** and **B–I**

Compound	**7**[a]	**B**[b]	**C**[b]	**D**[a]	**E**[b]	**F**[b]	**G**[a]	**H**[a]	**I**[a]
H-2′	7.61	7.99	8.06	7.81	7.98	8.08	8.40	8.68	8.37
H-5′	8.57	8.55	8.53	8.60	8.48	8.43	8.40	8.36	8.29
H-6′	8.43	8.44	8.44	8.45	8.39	8.37	8.30	8.28	8.30
H-8′	8.66	8.59	8.61	8.66	8.57	8.56	8.63	8.62	8.73
HC^{+}-α	9.47	8.78	8.79	8.74	9.01	8.72	8.91	8.34	8.81

[a] In CF_3COOD.
[b] In CD_3CN.

Table 8. The ^{13}C NMR chemical shifts (δ, ppm) for the 3-guaiazulenylmethylium-ion parts of **7** and **B–I**

Compound	**7**[a]	**B**[b]	**C**[b]	**D**[a]	**E**[b]	**F**[b]	**G**[a]	**H**[a]	**I**[a]
C-1′	146.3	145.5	153.9	145.8	145.4	144.6	146.1	145.6	142.6
C-2′	142.1	140.6	141.7	141.9	141.8	141.8	141.7	144.4	142.1
C-3′	141.1	139.6	145.9	144.4	139.2	137.3	137.0	136.1	132.4
C-3a′	154.1	152.9	155.6	149.4	153.6	153.3	155.5	155.1	153.1
C-4′	158.4	157.3	157.9	155.5	157.5	157.1	157.3	156.9	155.4
C-5′	151.4	150.1	150.5	147.6	150.3	149.1	150.0	149.7	146.3
C-6′	145.4	144.3	145.0	146.8	144.8	144.3	145.2	144.9	143.7
C-7′	174.5	171.2	171.4	176.8	170.9	169.3	171.6	171.4	165.9
C-8′	139.4	139.1	139.9	140.6	139.8	139.6	140.1	139.7	139.5
C-8a′	164.1	160.9	161.2	159.9	161.1	159.6	161.6	161.7	157.7
C^{+}-α	151.8	149.6	151.0	153.0	146.2	151.7	143.5	133.0	139.7

[a] In CF_3COOD.
[b] In CD_3CN.

the H-2′ atom of the 3-guaiazulenyl group; (ii) that the 3-guaiazulenylmethylium substituent clearly underwent bond alternation between the single and double bonds; (iii) that the 4-(methoxycarbonyl)phenyl group also clearly underwent bond alternation between the single and double bonds; (iv) that the average C–C bond length for the seven-membered ring of the 3-guaiazulenyl group was 1.401 Å; (v) that the bond lengths of the five-membered ring of the 3-guaiazulenyl group appreciably varied between 1.345 and 1.491 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 (1.437 Å); and (vi) that the C3′–Cα bond length (1.352 Å) was also characteristically shorter than the Cα–C1 bond length (1.468 Å). Moreover, it could be inferred (vii) that, from the C–C bond lengths, although the positive charge of **A** in the single crystal was mainly localized at the Cα carbon atom, forming a 3-guaiazulenylmethylium-ion structure, the positive charge apparently was transferred to the seven-membered ring, forming a 3-guaiazulenylium-ion structure; and (viii) that, from the result of the dihedral angle between the least-squares planes of the 3-guaiazulenyl group and the 4-(methoxycarbonyl)phenyl group, formation of a conjugated π-electron system between them, which combined with the Cα carbon atom, was possible. Thus, the X-ray crystallographic analysis of **A** led to the crystal structure, (3-guaiazulenyl)[4-(methoxycarbonyl)phenyl]methylium hexafluorophosphate with a resonance form of the 3-guaiazulenylium-ion structure **A′** (see Chart 1). Along with the crystal structure of **A**, from a comparative study on the C–C bond lengths of the crystal structure of **A** with those of the optimized (3-guaiazulenyl)[4-(methoxycarbonyl)phenyl]-methylium-ion structure calculated by a WinMOPAC (Ver. 3.0) program using PM3, AM1, or MNDOD as a semiempirical Hamiltonian, the C–C bond lengths calculated using PM3 more resembled those of the crystal structure of **A** in comparison with those calculated using AM1 and MNDOD (see Table 9). Thus, referring to the above results, the optimized [2-(carboxy)phenyl](3-guaiazulenyl)methylium-ion structure for **3** has been calculated using PM3 (see Fig. 1c,d),[33] because it was very difficult to obtain a single crystal of **3** suitable for the X-ray crystallographic analysis.

Table 9. The selected bond lengths (Å) of the X-ray crystal structure and the optimized (3-guaiazulenyl)[4-(methoxycarbonyl)phenyl]methylium-ion structure for **A**

Atom	**A** (X-ray)	**A** (PM3)	**A** (AM1)	**A** (MNDOD)
C1′–C2′	1.345	1.362	1.369	1.375
C2′–C3′	1.454	1.464	1.469	1.476
C3′–C3a′	1.491	1.478	1.480	1.494
C3a′–C4′	1.401	1.391	1.389	1.410
C4′–C5′	1.416	1.408	1.408	1.423
C5′–C6′	1.365	1.375	1.377	1.394
C6′–C7′	1.409	1.401	1.402	1.419
C7′–C8′	1.391	1.386	1.390	1.409
C8′–C8a′	1.386	1.389	1.387	1.408
C8a′–C1′	1.459	1.462	1.471	1.482
C3a′–C8a′	1.438	1.438	1.444	1.459
C3′–Cα	1.352	1.353	1.353	1.365
Cα–C1	1.468	1.455	1.450	1.477
C1–C2	1.403	1.401	1.406	1.415
C2–C3	1.373	1.389	1.391	1.405
C3–C4	1.392	1.396	1.402	1.413
C4–C5	1.389	1.395	1.399	1.412
C5–C6	1.385	1.390	1.393	1.406
C6–C1	1.403	1.399	1.403	1.415

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, AM1, or MNDOD; 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 (3-guaiazulenyl)[4-(methoxycarbonyl)phenyl]methylium-ion structure; PM3: 0.017, AM1: 0.013, MNDOD: 0.022.

From the C–C bond lengths (see Fig. 1c caption), it can be inferred that, although the positive charge of **3** is mainly localized at the Cα carbon atom, forming a 3-guaiazulenylmethylium-ion structure, the positive charge apparently is transferred to the seven-membered ring, forming a 3-guaiazulenylium-ion structure.

3. Conclusion

We have reported the following five points in this paper: (i) the reaction of guaiazulene (**1**) with *o*-formylbenzoic acid (**2**) in diethyl ether in the presence of hexafluorophosphoric acid at 25 °C for 90 min gave the corresponding monocarbenium-ion compound, [2-(carboxy)phenyl](3-guaiazulenyl)-methylium hexafluorophosphate (**3**), quantitatively, which upon treatment with aq $NaHCO_3$ led to 3-(3-guaiazulenyl)-2-benzofuran-1(3*H*)-one (**5**) in 96% isolated yield; (ii) similarly, the reaction of **1** with **2** in methanol under the same conditions as the above reaction afforded two kinds of inseparable monocarbenium-ion compounds, **3** and (3-guaiazulenyl)[2-(methoxycarbonyl)phenyl]methylium hexafluorophosphate (**4**) with an equilibrium between them, which upon reaction with a solution of $NaBH_4$ in ethanol at 25 °C for 30 min led to **5** in 46% isolated yield and (3-guaiazulenyl)[2-(methoxycarbonyl)phenyl]methane (**6**) in 37% isolated yield; (iii) along with the ^1H and ^{13}C NMR spectral properties of a solution of **5** in trifluoroacetic acid-d_1 at 25 °C, whose molecular structure was converted to a ca. 1:1 equilibrium mixture of **7** possessing a partial structure of the 3-guaiazulenylmethylium-ion and **8** possessing a partial structure of the 3-guaiazulenium-ion, comparative studies on the ^1H and ^{13}C NMR spectral properties of **7** and **8** with those of the monocarbenium-ion compound, (3-guaiazulenyl)[4-(methoxycarbonyl)phenyl]methylium hexafluorophosphate (**A**), **5**, and **6** were reported; (iv) from these NMR studies, it could be inferred that the positive charge of the 3-guaiazulenylmethylium-ion part of **7** apparently was transferred to the seven-membered ring, generating a resonance form of the 3-guaiazulenylium-ion structure η′, and the same result could be inferred for the previously documented monocarbenium-ion compounds **A**–**I**; and (v) moreover, referring to a comparative study on the C–C bond lengths of **A** observed by the X-ray crystallographic analysis with those of the optimized (3-guaiazulenyl)[4-(methoxycarbonyl)phenyl]methylium-ion structure for **A** calculated by a WinMOPAC (Ver. 3.0) program using PM3, AM1, or MNDOD as a semiempirical Hamiltonian, the optimized [2-(carboxy)phenyl](3-guaiazulenyl)methylium-ion structure for **3** calculated using PM3 was described.

4. Experimental

4.1. General

Thermal (TGA/DTA) analysis was carried out on a Shimadzu DTG-50H thermal analyzer. FABMS 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, respectively. NMR spectra were recorded with a JEOL GX-500 (500 MHz for ^1H and 125 MHz for ^{13}C) or JNM-ECA600 (600 MHz for ^1H and 150 MHz for ^{13}C) cryospectrometer at 25 °C. The ^1H NMR spectra were assigned using the computer-assisted simulation analysis (the software: *g*NMR developed by Adept Scientific plc) on Dell Dimension 8300 personal computer with a Pentium (R) 4 processor.

4.1.1. Preparation of 3-(3-guaiazulenyl)-2-benzofuran-1(3*H*)-one (5). To a solution of commercially available guaiazulene (**1**) (50 mg, 0.25 mmol) in diethyl ether (1.0 mL) was added a solution of commercially available *o*-formylbenzoic acid (**2**) (58 mg, 0.39 mmol) in diethyl ether (1.0 mL) containing hexafluorophosphoric acid (60% aqueous solution, 150 μL), turning the dark-blue solution into a yellow solution, rapidly. The mixture was stirred at 25 °C for 90 min, giving a monocarbenium-ion compound, [2-(carboxy)phenyl](3-guaiazulenyl)methylium hexafluorophosphate[30,31] (**3**), quantitatively. After the reaction, the reactant was carefully neutralized with aq $NaHCO_3$ and extracted with diethyl ether (3×10 mL). The extract was washed with water, dried (Na_2SO_4), and evaporated in vacuo. The residue thus obtained was purified by silica gel column chromatography with hexane–ethyl acetate (8:2, v/v) as an eluant. The obtained crude product **5** was recrystallized from hexane–benzene (5:1, v/v) (several times) to provide pure **5** as stable crystals (80 mg, 0.24 mmol, 96% yield).

Compound **3**:[30,31] yellow powder; mp >100 °C (decomp.) [determined by thermal analysis (TGA and DTA)]; UV–vis λ_{max} (CF_3COOH) nm 277, 358, and 437; IR ν_{max} (KBr) cm^{-1} 1701 (C=O), 1277, 1053 (C–O), and 856, 559 (PF_6^-); FABMS (3-nitrobenzyl alcohol matrix), *m*/*z* 331 ($[M-PF_6]^+$, 100%); exact FABMS (3-nitrobenzyl alcohol matrix) found: *m*/*z* 331.1678, calcd for $C_{23}H_{23}O_2$: $[M-PF_6]^+$, *m*/*z* 331.1698.

Compound **5**: blue prisms [R_f=0.25 on silica gel TLC (hexane–AcOEt=8:2, v/v)], mp 113 and >200 °C (decomp.) [determined by thermal analysis (TGA and DTA)]; UV–vis λ_{max} (CH_3CN) nm (log ε) 245 (4.48), 292 (4.68), 305sh (4.38), 338sh (3.67), 352 (3.81), 368 (3.82), 590 (2.71), 636sh (2.62), and 704sh (2.18); IR ν_{max} (KBr) cm^{-1} 1755 (C=O); FABMS (3-nitrobenzyl alcohol matrix) *m*/*z* 331 ($[M+H]^+$, 100%) and 330 (M^+, 72%); exact FABMS (3-nitrobenzyl alcohol matrix) found: *m*/*z* 331.1697, calcd for $C_{23}H_{23}O_2$: $[M+H]^+$, 331.1698; 500 MHz ^1H NMR (CD_3CN), signals based on the 3-guaiazulenyl group: δ 1.35 (6H, d, *J*=6.9 Hz, $(CH_3)_2$CH-7′), 2.46 (3H, s, Me-1′), 3.12 (1H, sept, *J*=6.9 Hz, Me_2CH-7′), 3.20 (3H, s, Me-4′), 6.99 (1H, s, H-2′), 7.22 (1H, d, *J*=10.5 Hz, H-5′), 7.56 (1H, dd, *J*=10.5, 2.0 Hz, H-6′), and 8.26 (1H, d, *J*=2.0 Hz, H-8′); signals based on the 2-benzofuran-1(3*H*)-one part: δ 7.42 (1H, ddd, *J*=7.7, 1.2, 0.9 Hz, H-4), 7.56 (1H, s, H-3), 7.63 (1H, br ddd, *J*=7.8, 7.6, 1.2 Hz, H-6), 7.74 (1H, ddd, *J*=7.7, 7.6, 1.2 Hz, H-5), and 7.92 (1H, ddd, *J*=7.8, 1.2, 0.9 Hz, H-7); 125 MHz ^{13}C NMR (CD_3CN) δ 171.2 (C-1), 152.0 (C-3a), 146.5 (C-4′), 143.1 (C-7′), 140.1 (C-8a′), 138.0 (C-2′), 136.6 (C-6′), 135.7 (C-8′), 135.6 (C-3a′), 135.1 (C-5), 130.1 (C-6), 129.8 (C-5′), 127.6 (C-7a), 125.8 (C-7), 125.8 (C-1′), 124.8 (C-4), 121.5 (C-3′), 80.2 (C-3), 38.4 (Me_2CH-7′), 27.8 (Me-4′), 24.7 ($(CH_3)_2$CH-7′), and 12.8 (Me-1′).

4.1.2. Preparation of 3-(3-guaiazulenyl)-2-benzofuran-1(3*H*)-one (5) and (3-guaiazulenyl)[2-(methoxycarbonyl)phenyl]methane (6). To a solution of guaiazulene (**1**) (22 mg, 0.11 mmol) in methanol (1.0 mL) was added a solution of *o*-formylbenzoic acid (**2**) (26 mg, 0.17 mmol) in methanol (1.0 mL) containing hexafluorophosphoric acid (60% aqueous solution, 50 μL), turning the dark-blue solution into a yellow solution, rapidly. The mixture was stirred at 25 °C for 90 min, giving two kinds of inseparable monocarbenium-ion compounds, [2-(carboxy)phenyl]-(3-guaiazulenyl)methylium hexafluorophosphate (**3**) and (3-guaiazulenyl)[2-(methoxycarbonyl)phenyl]methylium hexafluorophosphate (**4**), efficiently, and then a solution of $NaBH_4$ (100 mg, 2.64 mmol) in ethanol (5.0 mL) was added and further stirred at 25 °C for 30 min. After the reaction, the reaction solution was evaporated in vacuo. The reactant thus obtained was dissolved in diethyl ether (30 mL), washed with water, dried (Na_2SO_4), and evaporated in vacuo. The obtained residue was purified by silica gel column chromatography with benzene–hexane (1:1, v/v) as an eluant (several times), giving pure products **5** (17 mg, 52 μmol, 46% yield) and **6** (14 mg, 40 μmol, 37% yield), respectively.

Compound **3**: see Section 4.1.1.

Compound **4**: yellow powder; FABMS (3-nitrobenzyl alcohol matrix), *m/z* 345 ($[M-PF_6]^+$, 100%); exact FABMS (3-nitrobenzyl alcohol matrix) found: *m/z* 345.1869, calcd for $C_{24}H_{25}O_2$: $[M-PF_6]^+$, *m/z* 345.1855.

Compound **5**: see Section 4.1.1.

Compound **6**: blue powder [R_f=0.50 on silica gel TLC (hexane–AcOEt=8:2, v/v)], mp 87 °C and mp >200 °C (decomp.) [determined by thermal analysis (TGA and DTA)]; UV–vis λ_{max} (CH_3CN) nm (log ε) 219 (4.32), 246 (4.42), 290 (4.67), 306sh (4.29), 338sh (3.62), 353 (3.80), 370 (3.73), 622 (2.69), 675sh (2.60), and 748sh (2.18); IR ν_{max} (KBr) cm^{-1} 1713 (C=O); FABMS (3-nitrobenzyl alcohol matrix) *m/z* 346 (M^+, 100%); exact FABMS (3-nitrobenzyl alcohol matrix) found: *m/z* 346.1930, calcd for $C_{24}H_{26}O_2$: M^+, *m/z* 346.1933; 500 MHz ^1H NMR (CD_3CN), signals based on the 3-guaiazulenylmethyl group: δ 1.32 (6H, d, J=6.9 Hz, $(CH_3)_2CH$-7′), 2.54 (3H, s, Me-1′), 2.75 (3H, s, Me-4′), 3.03 (1H, sept, J=6.9 Hz, Me_2CH-7′), 4.91 (2H, s, 1-CH_2-3′), 6.82 (1H, d, J=10.6 Hz, H-5′), 7.22 (1H, s, H-2′), 7.31 (1H, dd, J=10.6, 2.0 Hz, H-6′), and 8.11 (1H, d, J=2.0 Hz, H-8′); signals based on the 2-(methoxycarbonyl)-benzene part: δ 3.79 (3H, s, 2-$COOCH_3$), 6.80 (1H, dd, J=7.6, 1.4 Hz, H-6), 7.27 (1H, ddd, J=7.7, 7.6, 1.4 Hz, H-4), 7.35 (1H, ddd, J=7.6, 7.6, 1.4 Hz, H-5), and 7.87 (1H, dd, J=7.7, 1.4 Hz, H-3); 125 MHz ^{13}C NMR (CD_3CN) δ 169.0 (2-*C*$OOCH_3$), 146.4 (C-4′), 145.3 (C-1), 141.5 (C-2′), 140.1 (C-7′), 138.8 (C-8a′), 135.9 (C-6′), 134.4 (C-8′), 134.0 (C-3a′), 132.9 (C-5), 131.5 (C-6), 131.1 (C-3), 130.6 (C-2), 127.1 (C-5′), 126.8 (C-4), 126.6 (C-3′), 125.5 (C-1′), 52.5 (2-$COOCH_3$), 38.3 (Me_2CH-7′), 35.9 (1-CH_2-3′), 26.7 (Me-4′), 24.7 ($(CH_3)_2CH$-7′), and 12.9 (Me-1′).

4.1.3. ^1H and ^{13}C NMR spectral data of 3-(3-guaiazulenyl)-2-benzofuran-1(3*H*)-one (5) in trifluoroacetic acid-d_1. The ^1H and ^{13}C NMR spectra including 2D NMR (i.e., H–H COSY, HMQC, and HMBC) of a solution of 3-(3-guaiazulenyl)-2-benzofuran-1(3*H*)-one (**5**) (20 mg, 61 μmol) in trifluoroacetic acid-d_1 (1.0 mL), whose molecular structure was converted to [2-(carboxy-d_1)phenyl](3-guaiazulenyl)-methylium-ion structure **7** via the deuteronated **5** at the carbonyl group and the deuteronated 3-(3-guaiazulenyl)-2-benzofuran-1(3*H*)-one **8** at the C-3′ position (see Fig. 2), quantitatively, were measured. A careful study of the 600 MHz ^1H NMR signals for this measurement solution led to a ca. 1:1 equilibrium mixture of compounds **7** and **8**. Exact FABMS (3-nitrobenzyl alcohol matrix) of this solution, found: *m/z* 332.1729, calcd for $C_{23}H_{22}DO_2$: M^+, *m/z* 332.1761.

Compound **7**: 600 MHz ^1H NMR (CF_3COOD), signals based on the 3-guaiazulenylmethylium-ion part: δ 1.53 (6H, d, J=7.2 Hz, $(CH_3)_2CH$-7′), 2.48 (3H, s, Me-1′), 3.45 (3H, s, Me-4′), 3.49 (1H, sept, J=7.2 Hz, Me_2CH-7′), 7.61 (1H, s, H-2′), 8.43 (1H, dd, J=11.0, 2.0 Hz, H-6′), 8.57 (1H, d, J=11.0 Hz, H-5′), 8.66 (1H, d, J=2.0 Hz, H-8′), and 9.47 (1H, s, HC^+-α); signals based on the benzoic acid part: δ 7.54 (1H, d, J=7.6 Hz, H-6), 7.73 (1H, dd, J=7.8, 7.7 Hz, H-4), 7.85 (1H, dd, J=7.7, 7.6 Hz, H-5), and 8.40 (1H, d, J=7.8 Hz, H-3); 150 MHz ^{13}C NMR (CF_3COOD) δ 174.5 (C-7′), 173.5 (2-COOD), 164.1 (C-8a′), 158.4 (C-4′), 154.1 (C-3a′), 151.8 (HC^+-α), 151.4 (C-5′), 146.3 (C-1′), 145.4 (C-6′), 142.1 (C-2′), 141.1 (C-3′), 139.4 (C-8′), 138.8 (C-1), 135.5 (C-5), 134.2 (C-6), 133.9 (C-3), 132.3 (C-4), 128.9 (C-2), 41.4 (Me_2CH-7′), 28.8 (Me-4′), 23.6 ($(CH_3)_2CH$-7′), and 13.′ (Me-1′).

Compound **8**: 600 MHz ^1H NMR (CF_3COOD), signals based on the 3-guaiazulenylium-ion part: δ 1.54 (6H, d, J=7.2 Hz, $(CH_3)_2CH$-7′), 2.27 (1H, s, Me-1′), 3.30 (3H, s, Me-4′), 3.52 (1H, sept, J=7.2 Hz, Me_2CH-7′), 6.50 (1H, s, H-2′), 8.58 (1H, dd, J=11.0, 2.0 Hz, H-6′), 8.63 (1H, d, J=2.0 Hz, H-8′), and 8.65 (1H, d, J=11.0 Hz, H-5′); signals based on the 2-benzofuran-1(3*H*)-one part: δ 6.58 (1H, s, H-3), 7.76 (1H, dd, J=7.8, 7.7 Hz, H-6), 7.95 (1H, d, J=7.8 Hz, H-4), 7.99 (1H, dd, J=7.8, 7.7 Hz, H-5), and 8.00 (1H, d, J=7.8 Hz, H-7); 150 MHz ^{13}C NMR (CF_3COOD) δ 179.7 (C-7′), 175.5 (C-1), 170.1 (C-8a′), 166.2 (C-3a′), 159.8 (C-4′), 152.2 (C-5′), 149.9 (C-1′), 149.1 (C-3a), 147.4 (C-6′), 145.5 (C-2′), 140.7 (C-8′), 137.9 (C-5), 132.4 (C-6), 128.0 (C-7), 125.2 (C-7a), 123.2 (C-4), 79.5 (C-3), 57.4 (C-3′, J_{C-D}=19.4 Hz), 42.0 (Me_2CH-7′), 26.0 (Me-4′), 23.6 ($(CH_3)_2CH$-7′), and 13.1 (Me-1′).

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30. During the recrystallization of **3**, this compound was gradually converted to **5**.
31. The ^{1}H and ^{13}C NMR spectra including 2D NMR (i.e., H–H COSY, HMQC, and HMBC) of a solution of **3** in trifluoroacetic acid-d_1 at 25 °C showed two kinds of carbocation compounds, i.e., the [2-(carboxy-d_1)phenyl](3-guaiazulenyl)methylium-ion structure **7** and the deuteronated 3-(3-guaiazulenyl)-2-benzofuran-1(3*H*)-one **8** at the C-3′ position of **5** (see Fig. 2). A careful study of the 600 MHz ^{1}H NMR signals for this sample led us to a ca. 1:1 equilibrium mixture of **7** and **8** under this measurement conditions.
32. Guaiazulene **1**: UV–vis λ_{max} (CH_3CN) 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).
33. The following MO calculation program and calculation conditions were used for **3** (i.e., the software: WinMOPAC Ver. 3.0 developed by Fujitsu Ltd., Japan; semiempirical Hamiltonian: PM3; 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 [2-(carboxy)-phenyl](3-guaiazulenyl)methylium-ion structure for **3** showed 0.013.