 

# Approaches to the Potential Chirality of Bisguanidinobenzenes by Dynamic NMR Analysis

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The isomerization process, which is related to racemization of symmetrical 1,2-bis(diaminomethyleneamino)benzenes (=bisguanidinobenzenes) with potential chirality, is caused by bond rotation of aryl–(diaminomethyleneamino) (=aryl–guanidinyl) bond and/or diaminomethylene–imino (=guanidinyl imine) bond. This process was evaluated by temperature-dependent $^1$H NMR experiments. The guanidinyl imine bond rotation, which is important for the early stage of the inhibition of racemization process, was not restricted by substitution at the *ortho*-position of the benzene core or alkylation of guanidine function, while protonation of *ortho*-substituted bisguanidinobenzenes increased the rotation barrier. Changing the guanidine function from cyclic to acyclic caused the rotation about both bonds to become restricted, which could be observed by temperature-dependent $^1$H NMR experiments.

Axial, helical, and planar are important types of chirality sources in the fields of chemical, pharmaceutical, and material sciences; however, they are often hidden within molecular structures.[1] It is known that guanidines are superbases,[2] which can also act as key units in the formation of supermolecules.[3] Recently, we have developed guanidine chemistry focusing on uncovering the potential abilities of the diaminomethyleneamino (=guanidinyl) functions, such as acting as chiral auxiliaries.[4] In the course of these studies, we designed a new bisguanidinobenzene derivative, *N*,*N*′-bis(1,3-dimethyl-2-imidazolidinylidene)-*o*-benzenediamine (**1**, Fig. 1), as a potential hydrogen acceptor.[5] Trial experiments for complexation of **1** with a variety of hydrogen-donor aromatics carrying OH groups, such as benzoic acid, phenol, and benzyl alcohol, led to isolation of the expected 1 + 1 crystalline complexes, regardless of the acidity of the hydrogen donors. In the case of benzoic acid, additional crystalline complexes of **1** and benzoic acid were formed under rigorous conditions of stoichiometry-controlled complexation. It has been suggested that **1** has potential helical chirality[6] in the *s-trans* isomer, as shown in Fig. 1. But the chirality disappears in solution by rapid racemization through *s-trans* and *s-cis* isomerization.[7] If **1** can be made to remain chiral in solution, a new type of chiral bisguanidinobenzenes can be prepared. In this molecular system, the chirality originates from the separation of the symmetrical guanidinyl substituents by the benzene plane, and this property should be useable in asymmetric synthesis and chiral recognition. Thus, we decided to investigate the potential chirality of bisguanidinobenzenes using dynamic NMR analysis. In this paper, we discuss the changes in the bond rotation barrier associated with the racemization of bisguanidinobenzenes in solution caused by the modification of either the benzene ring or the guanidine moiety.

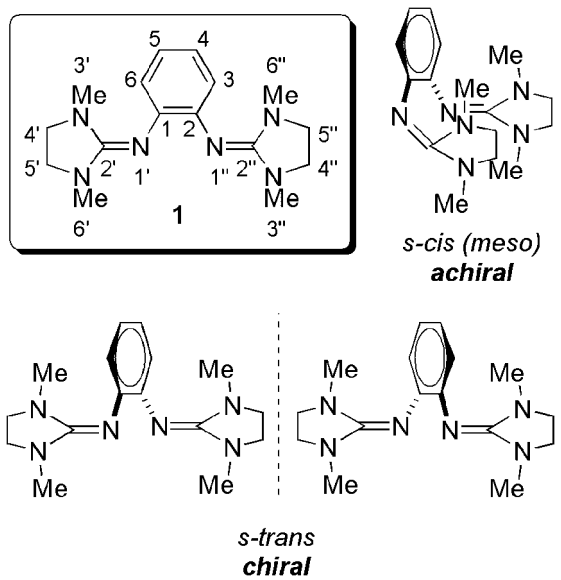


Fig. 1. Potential chirality of bisguanidinobenzene **1**.

## Results and Discussion

In bisguanidinobenzene **1**, restriction of free rotation of aryl–guanidinyl ($C^1$–$N^{1'}$ or $C^2$–$N^{1''}$) bond could induce chirality (Fig. 1). It was assumed that introduction of bulky substituents at the *ortho* positions of the benzene ring (Fig. 2a) and/or structural modification of the guanidine moieties, such as quaternization (Fig. 2b) or alteration of the cyclic form to an acyclic one (Fig. 2c), could give valuable information for the creation of new types of benzene derivatives with helical chirality. Thus, in order to increase bond rotation barrier around guanidinyl functions, 9,10-bis(diaminomethyleneamino)phenanthrene (=bisguanidinophenanthrene, **2**) (Fig. 3) was prepared from 9,10-diaminophenanthrene by treatment with 2-

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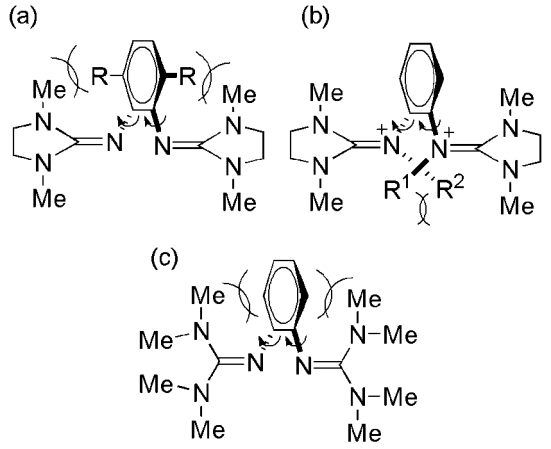


Fig. 2. Schematic restriction of free rotation of aryl–guanidinyl [$C^1$–$N^{1'}$ (or $C^2$–$N^{1''}$)] bond induced by (a) substitution at *ortho* position of benzene ring, (b) quaternization of guanidine unit, and (c) conversion of cyclic to acyclic guanidine.

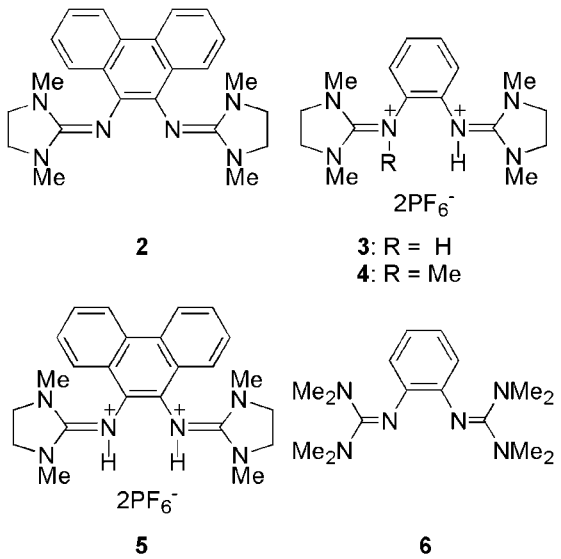


Fig. 3. The structures of bisguanidinobenzenes.

chloro-1,3-dimethylimidazolium chloride (DMC)[8] as a model of bisguanidinobenzene with bulky substituent on the benzene ring. Guanidinium salts were derived from bisguanidinobenzene **1** or bisguanidinophenanthrene **2** by either protonation or methylation, and an acyclic-type guanidine, like **6** (Fig. 3), was prepared using 2-chloro-1,1,3,3-tetramethylformamidinium chloride.

**Effect of the *ortho*-Substitution.** Temperature-dependent $^1$H NMR analysis was used to study rotational behavior of guanidines. For this purpose, signals due to the *N*-methyl substituent of bis(dimethylamino)methyleneamino group (=guanidinyl methyl), as the most indicative, were followed. In addition to aryl–guanidinyl ($C^1$–$N^{1'}$ or $C^2$–$N^{1''}$) rotation, the ability of the guanidinyl imine ($N^{1'}$=$C^{2'}$ or $N^{1''}$=$C^{2''}$) bond to rotate should be also considered.[9] Thus, three different possibilities were deduced: the presence of completely equivalent methyl groups due to free rotation on each bond, as shown in Fig. 4(I), the presence of two non-equivalent methyl groups caused by partial restriction of the imine bond rotation (Fig. 4(II)), and the presence of four kinds of methyl groups due to full rotational restriction of the both bonds (Fig. 4(III)). Note that pyramidal inversion of $N^{3'}$, $N^{6'}$, $N^{3''}$, and/or $N^{6''}$ center (Fig. 1) is not shown in Fig. 4, which was not observed in this case.[10]

Bisguanidinobenzene **1** and bisguanidinophenanthrene **2** were subjected to temperature-dependent $^1$H NMR measurements and, their spectra in acetone-$d_6$ solution recorded at different temperatures are given in Figs. 5(I) and 5(II). In these spectra, signals corresponding to acetone are marked by one (*) and $H_2O$ signals by two asterisks (**). Both compounds exhibited sharp signals at 20 °C and single methyl resonance [each (a) in (I) and (II) of Fig. 5], indicating free rotation. Peak broadening started at around −80 °C [(c) in (I) and (II) of Fig. 5]. Coalescence temperatures[11] were −88 °C for **1** [(d) in (I) of Fig. 5] and −84 °C for **2** [(d) in (II) of Fig. 5], and separation into two peaks occurred at −94 °C for both compounds [each (e) in (I) and (II) of Fig. 5]. There were no changes in the aromatic regions of both spectra. From these experiments, the free energy of bond rotation ($\Delta G^{\neq}$) was estimated to be 8.6 and 8.5 kcal mol$^{-1}$ for **1** and **2**, respectively.

Appearance of only one methyl peak in both compounds at 20 °C suggests that rapid rotation of the both bonds takes place. Observation of only two methyl peaks even in spectra recorded at the lowest temperature (−94 °C) indicates that the introduction of bulky substituent at the *ortho* position could not completely restrict the bond rotation even at low temperature. On the basis of these results, we turned our attention to the modification of the guanidine moiety.

**Effect of Modification of Guanidine Moiety. Quaternization:** It is thought that quaternization of guanidine moiety lowers the potential energy level by effective resonance stabilization of the resulted guanidinium salts. In other words, equivalent ring-methyl signals of the cyclic guanidinium system should be observed in $^1$H NMR spectra even at lower temperature. This prediction is in a good agreement with the temperature-dependent $^1$H NMR spectra of diprotonated **3** (Fig. 6) and methylated/protonated bisguanidinobenzene **4** (Fig. 7), because their guanidine methyl peaks did not separate upon cooling the sample even down to −94 °C.

On the other hand, the methyl signals of diprotonated bisguanidinophenanthrene **5** split at −60 °C (Fig. 8c). The coalescence temperature (−36 °C) was surprisingly high for the methyl peak (Fig. 8b). From these results, the free energy of bond rotation ($\Delta G^{\ddagger}$) was estimated to be 10.5 kcal mol$^{-1}$, which is 2.0 kcal mol$^{-1}$ higher than the corresponding free base **2**. These facts show that quaternization of guanidine function by protonation of bisguanidinobenzene can result in the restriction of the rotation about the guanidinyl imine ($C^{2'}$=$N^{1'}$ or $C^{2''}$=$N^{1''}$) bond in more sterically crowded cases, as depicted in Fig. 4(II). Taking only the electronic effect into account, the order of guanidinyl imine ($C^{2'}$=$N^{1'}$ or $C^{2''}$=$N^{1''}$) bond becomes lower, and the rotation barrier decreases, as supported by theoretical calculations.[12] The increase in the rotation barrier of **5** can be explained as steric effect resulted from protonation, which is influenced greatly in sterically more crowded cases. Since quaternization did not lead to sufficient restriction of the guanidinyl imine ($C^{2'}$=$N^{1'}$ or $C^{2''}$=$N^{1''}$) bond rotation,

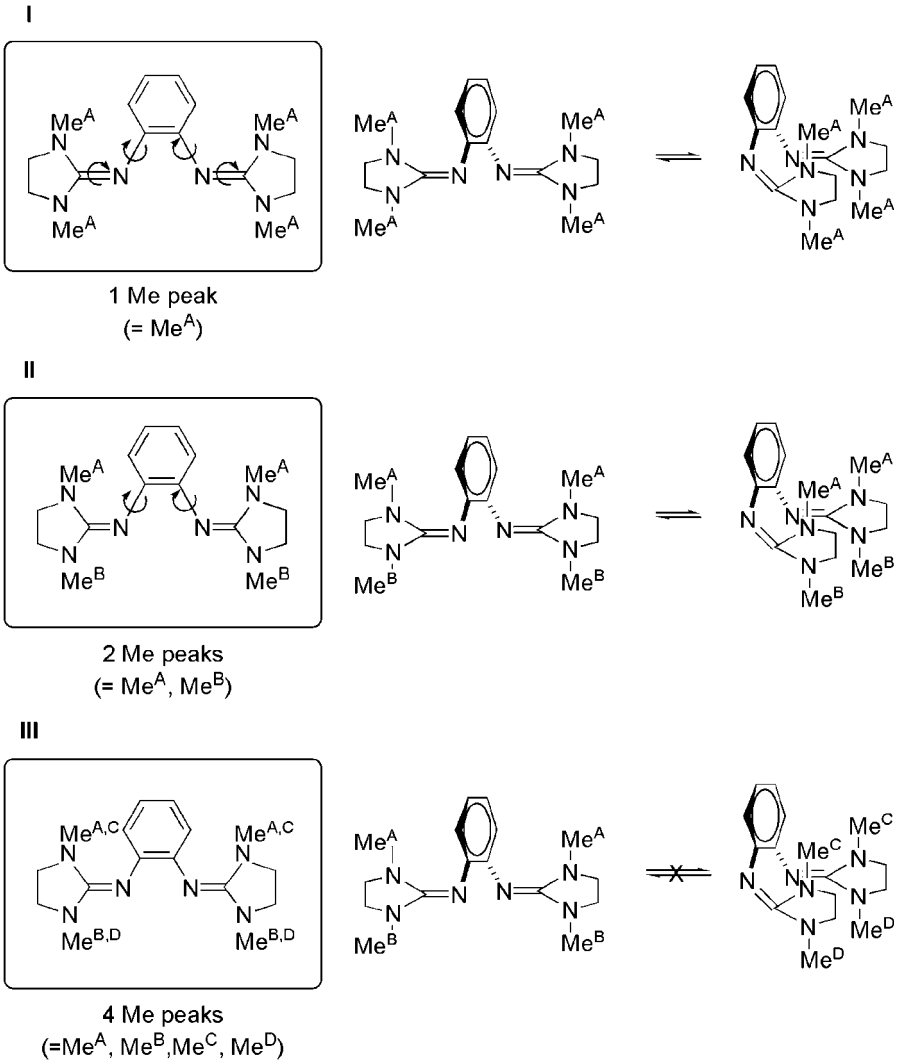


Fig. 4. Models for restriction of rotation and expected number of methyl peaks.

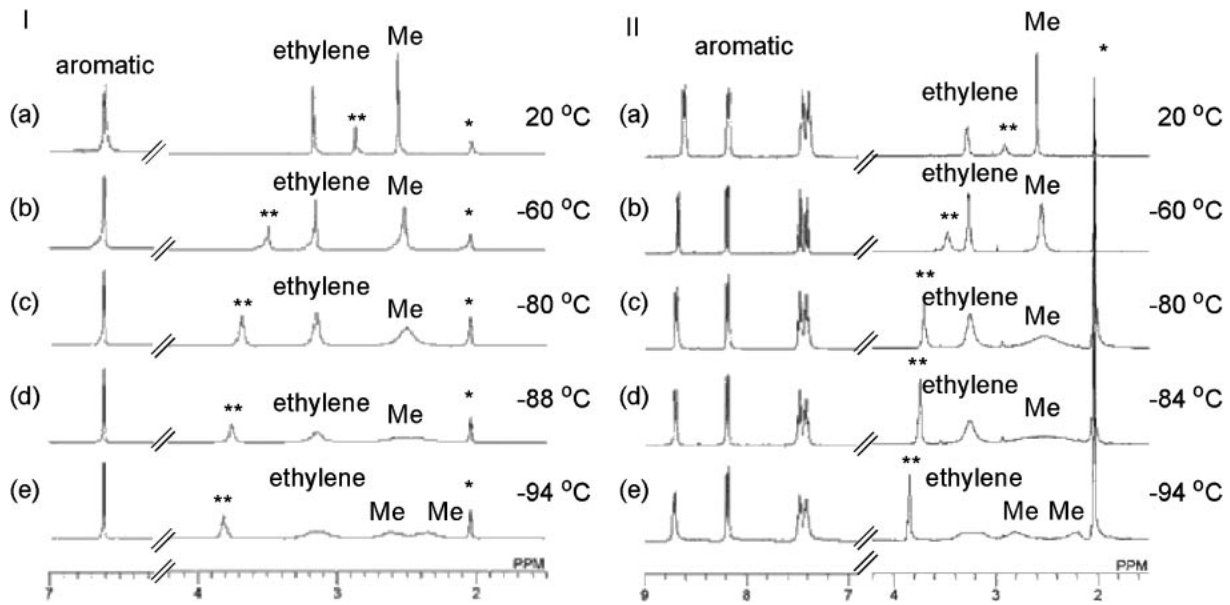


Fig. 5. Temperature-dependent $^1$H NMR spectra (in acetone-$d_6$): (I) bisguanidinobenzene **1**; (II) bisguanidinophenanthrene **2** (* and ** denote acetone and $H_2O$ signals).

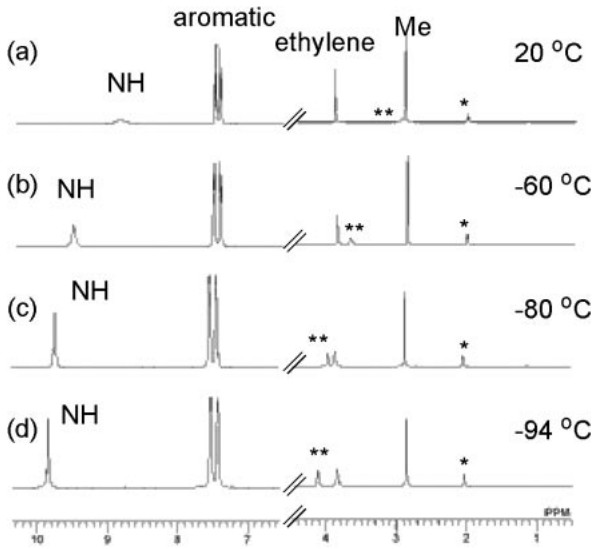


Fig. 6. Temperature-dependent $^1$H NMR spectra of diprotonated bisguanidinobenzene **3** (in acetone-$d_6$) (* and ** denote acetone and $H_2O$ signals).

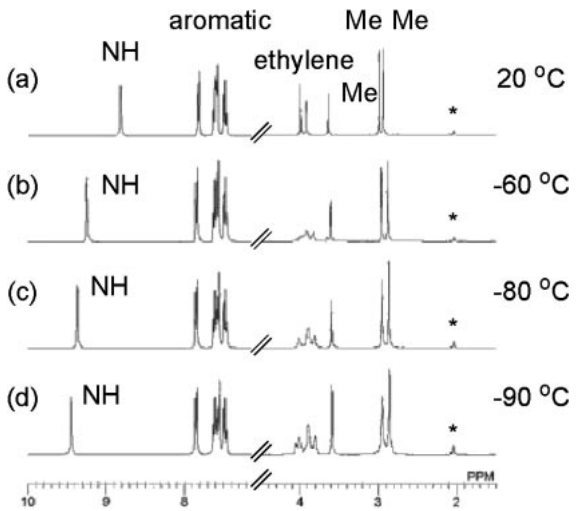


Fig. 7. Temperature-dependent $^1$H NMR spectra of methylated/protonated bisguanidinobenzene **4** (in acetone-$d_6$) (* and ** denote acetone and $H_2O$ signals).

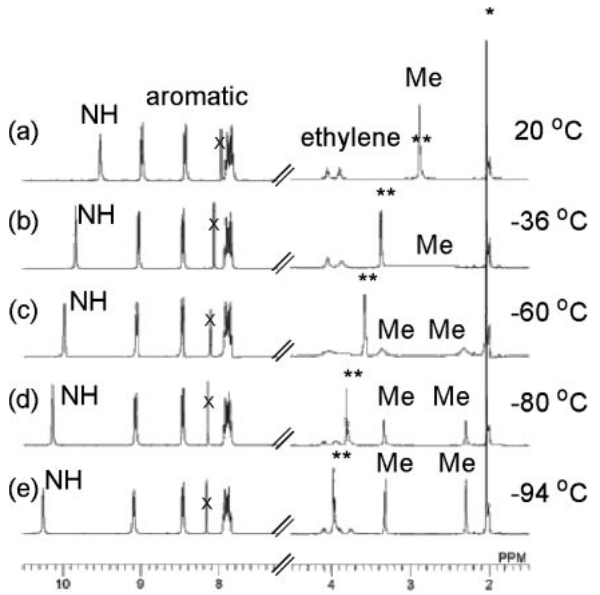


Fig. 8. Temperature-dependent $^1$H NMR spectra of protonated bisguanidinophenanthrene **5** (in acetone-$d_6$) (* and ** denote acetone and $H_2O$ signals; × denotes impurity from solvent).

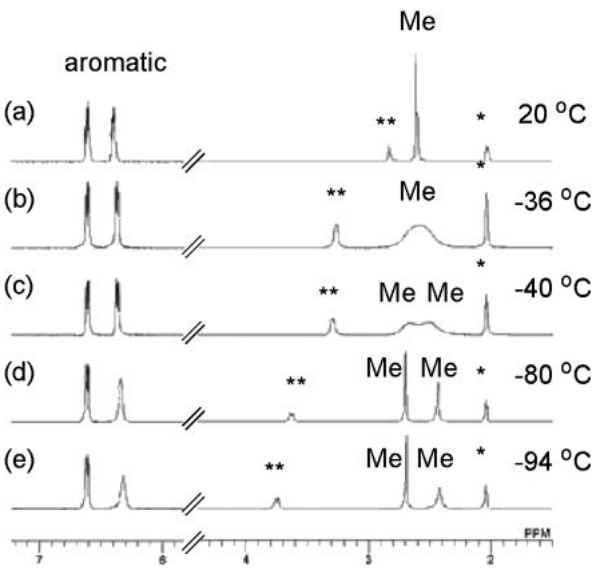


Fig. 9. Temperature-dependent $^1$H NMR spectra of acyclic bisguanidinobenzene **6** (* and ** denote acetone and $H_2O$ signals).

in the continuation of our study, the effects of the change of cyclic guanidine moiety to acyclic were examined.

**Acyclic Guanidine:** Temperature-dependent $^1$H NMR spectra of acyclic bisguanidinobenzene **6** showed peak separation (Fig. 9) starting at around −40 °C, and the coalescence temperature was −36 °C. From this information, the free energy of bond rotation ($\Delta G^{\ddagger}$) was estimated to be 11.2 kcal mol$^{-1}$. Furthermore, additional peak broadenings were observed at −94 °C, and these peaks were assigned to be aromatic proton ($H^a$) at the *ortho*-position and the methyl group ($Me^b$) close to the benzene ring (Fig. 10). These facts indicate slow rotation of aryl–guanidinyl bond within the NMR time scale,[13] resulting from the inhibition of *s-cis* and *s-trans* isomerization between the two guanidinyl moieties, as depicted in Fig. 4(III). On the basis of these results, it is suggested that suitable modification of this acyclic system should lead to optical resolution of bisguanidinobenzenes.

In order to further study the aryl–guanidinyl bond rotation, dynamic properties of several model (diaminomethyleneamino)benzenes (=monoguanidinobenzenes) were investigated in detail (Fig. 11). Cyclic monoguanidinobenzene **7**, its protonated form **8**, and methylated form **9** were prepared by the reaction of aniline and DMC[8] and subjected to temperature-dependent $^1$H NMR measurements. Their spectra recorded at different temperatures are shown in Fig. 12(I–III), respectively. In the case of free base **7**, methyl peak became broad at

−80 °C, while in the cases of **8** and **9**, the methyl peak remained sharp, even at −94 °C. These results differ from the reported ones on acyclic systems **10**–**13**,[9] in which the rotation barrier of the guanidinyl imine bond remains essentially unchanged after protonation (**11**) and becomes higher after methylation (**12**). Furthermore, introduction of methyl group at the *ortho*-position of the benzene core in the protonated guanidine **13** resulted in restriction of the aryl–guanidinyl bond rotation at low temperature.

Observed differences between acyclic and cyclic guanidines may be the result of structural planarity. Acyclic guanidines and guanidiniums are known to have twisted structures,[14,15] whereas cyclic guanidines form rather planar structures.[5] As a result, the planar structure can contribute to the higher degree of delocalization of electrons, resulting in single bond-like character around which guanidinyl imine bond rotation could occur easier. Therefore, substitution with bulky group at the *ortho*-position of acyclic bisguanidinobenzene system could effectively inhibit aryl–guanidinyl bond rotation, leading to the generation of novel helical chiral bisguanidinobenzenes.

## Conclusion

The isomerization process related to the racemization of potentially chiral bisguanidinobenzenes was observed by temperature-dependent $^1$H NMR experiments. The guanidinyl imine bond rotation, which is important for the early stage of the inhibition of racemization process, was not effectively restricted by substitution at the *ortho*-position of the benzene core or alkylation of the guanidine function. Only protonation of *ortho*-substituted bisguanidinobenzenes increased the rota-

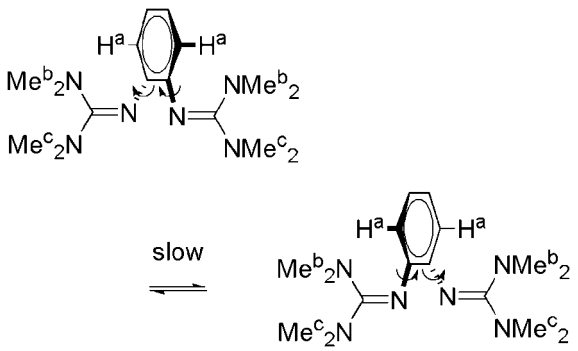


Fig. 10. Restriction of rotation between aryl–guanidinyl bonds.

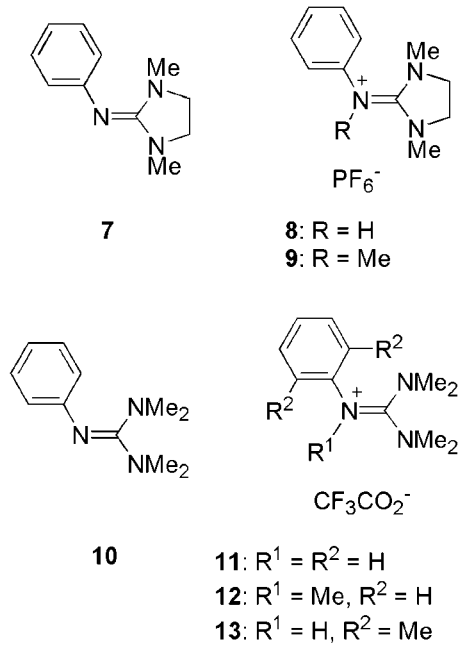


Fig. 11. The structures of monoguanidinobenzenes.

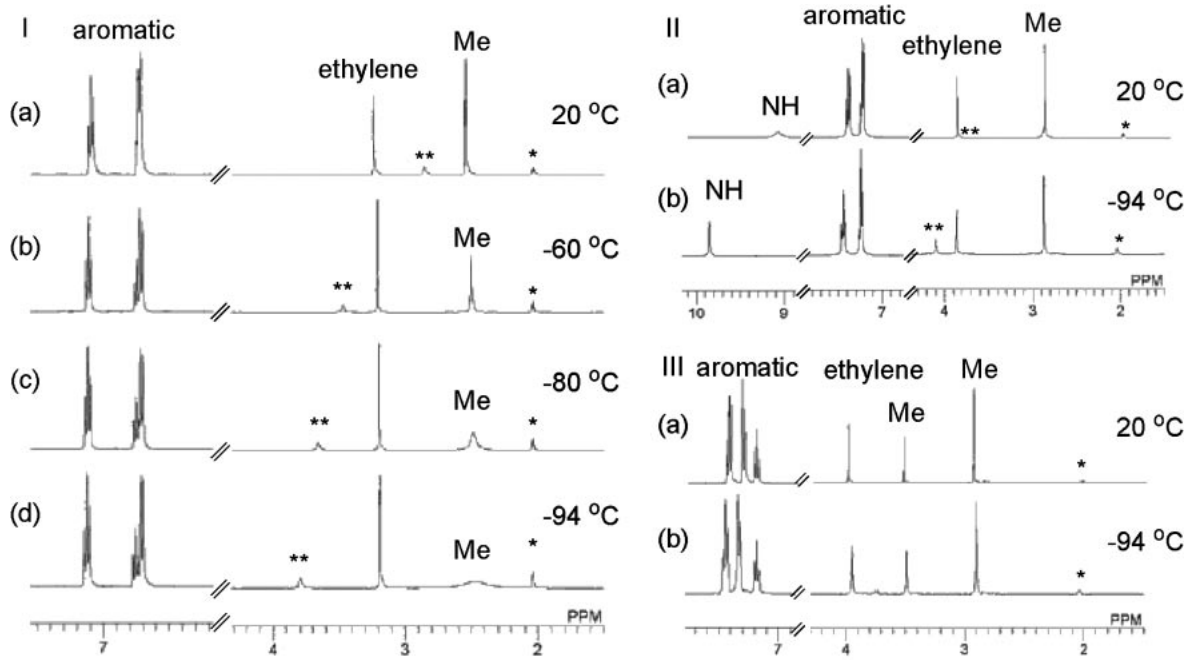


Fig. 12. Temperature-dependent $^1$H NMR spectra: (I) monoguanidinobenzene **7**; (II) protonated monoguanidinobenzene **8**; (III) methylated monoguanidinobenzene **9** (in acetone-$d_6$) (* and ** denote acetone and $H_2O$ signals).

tion barrier. However, aryl–guanidinyl bond rotation, which is associated directly to racemization process, was not restricted by these derivatizations. By changing the guanidine function from cyclic to acyclic, both the bond rotations were restricted and observed by NMR. Theoretical studies of the effect of substitution on rotation barriers are currently in progress, and these results will be published in due course.

## Experimental

**General.** Reagents and solvents were purchased from Aldrich, TCI, or Kanto Chemicals. IR spectra were recorded on a JASCO FT/IR-300E equipped with an attenuated total reflection (ATR) instrument and are reported as wavenumber ($\nu$) in $cm^{-1}$. NMR spectra were obtained in acetone-$d_6$ by either JEOL JNM-ECP 600, JEOL JNM-ALPHA 500, or JEOL JNM-ECP 400 spectrometers and are reported as chemical shift ($\delta$) in ppm relative to tetramethylsilane ($\delta = 0$). Spin multiplicities are reported as s (singlet), d (doublet), t (triplet), with coupling constant given in Hz, or m (multiplet). Low- (FAB-MS) and high-resolution FAB-MS (HR-FAB-MS) were performed on JEOL JMS-HX 110A and JMS-700-T spectrometers. Elemental analyses were obtained using Perkin-Elmer 2400 apparatus.

**Synthesis of Materials. *N*,*N*′-Bis(1,3-dimethyl-2-imidazolidinylidene)-*o*-benzenediamine (1):** Compound **1** was synthesized by the method previously described by us.[5]

***N*,*N*′-Bis(1,3-dimethyl-2-imidazolidinylidene)-9,10-phenanthrenediamine (2):** To a solution of 9,10-diaminophenanthrene (300 mg, 1.44 mmol) in diethyl ether (200 mL) was added triethylamine (678 mg, 0.934 mL, 6.77 mmol). A solution of DMC (536 mg, 3.17 mmol) in dichloromethane (80 mL) was added to the above solution under ice cooling, and the solution was stirred at room temperature for 25 h. After evaporation of the solvent, the reaction mixture was dissolved in 10% citric acid (100 mL) and washed with chloroform (100 mL × 3). To the aqueous solution, 20% NaOH (75 mL) was added and extracted with chloroform (100 mL × 5). The combined organic solutions were washed with brine and dried ($Na_2SO_4$), and the solvent was evaporated. The resulting crude product was obtained as green-yellow oil (1.73 g) and purified after salt formation of hexafluorophosphate. Pure crystals of **7** (vide infra) (176 mg, 0.254 mmol) were partitioned with toluene (10 mL × 3) and 20% NaOH (1 mL). The organic solution was washed with brine and dried ($Na_2SO_4$), and the solvent was evaporated to produce a pure yellowish green needles (42.2 mg, 12%): mp 250 °C (dec); IR (neat) 3342, 2937, 2856, 1631, 1479, 1411, 1282; $^1$H NMR (400 MHz) $\delta$ 2.61 (s, 12H, Me), 3.29 (s, 8H, $CH_2$), 7.39 (m, 2H, Ar–H), 7.46 (m, 2H, Ar–H), 8.18 (d, $J = 5.2$ Hz, 2H, Ar–H), 8.62 (d, $J = 7.2$ Hz, 2H, Ar–H); $^{13}$C NMR (125 MHz) $\delta$ 33.2, 48.1, 121.8, 123.0, 125.0, 125.4, 127.0, 130.3, 131.1, 152.8; HR-FAB-MS $m/z$ 401.2454, calcd for $C_{24}H_{29}N_6$: 401.2448.

***N*,*N*′-Bis(1,3-dimethyl-2-imidazolidinylidene)-*o*-benzenediammonium Bis(hexafluorophosphate) (3):** A mixture of **1** (410 mg, 1.37 mmol) and $NH_4PF_6$ (451 mg, 2.74 mmol) in acetone (5 mL) was stirred at room temperature for 5 min, and the organic solvent was removed by evaporation. The resulting crude mixture was washed with $H_2O$ (0.5 mL × 2) to produce a crude solid (1.25 g), which was recrystallized from MeOH to produce colorless crystals (354 mg, 44%): mp 255–258 °C; IR (neat) 1591, 1517, 1486, 1417, 1305, 833; $^1$H NMR (400 MHz) $\delta$ 2.93 (s, 12H, Me), 3.93 (s, 8H, $CH_2$), 7.45 (m, 2H, Ar–H), 7.51 (m, 2H, Ar–H), 8.93 (brs, 2H, NH); $^{13}$C NMR (150 MHz) $\delta$ 33.9, 49.1, 126.4, 128.2, 130.6, 157.1; FAB-MS $m/z$: 447 [$(M - PF_6)^+$]; Anal. Found: C, 32.35; H, 4.32; N, 14.12%. Calcd for $C_{16}H_{26}F_{12}N_6P_2$: C, 32.44; H, 4.42; N, 14.19%.

***N*,*N*′-Bis(1,3-dimethyl-2-imidazolidinylidene)-*N*-methyl-*o*-benzenediammonium Bis(hexafluorophosphate) (4):** A mixture of **1** (3.43 g, 9.98 mmol) and methyl iodide (1.38 mL, 22.2 mmol) in acetonitrile (3 mL) was stirred at room temperature for 12 h, and then, the solvent was evaporated to give brown oil (5.03 g). To the oil, $NH_4PF_6$ (3.62 g, 22.2 mmol) and $H_2O$ (3 mL) were added, and the solution was stirred at room temperature for 5 min. The precipitate was collected by centrifuging and washed with $H_2O$ (1 mL × 2) to produce crude product (5.87 g), and then the solid was recrystallized from acetone–ethyl acetate to produce colorless crystals (5.30 g, 89%): mp 245–248 °C; IR (neat) 3348, 1612, 1502, 1417, 1385, 1303, 831; $^1$H NMR (400 MHz) $\delta$ 2.94 (s, 6H, Me), 3.00 (s, 6H, Me), 3.64 (s, 3H, Me), 3.92 (s, 4H, $CH_2$), 3.99 (s, 4H, $CH_2$), 7.46–7.50 (m, 1H, Ar–H), 7.57–7.63 (m, 2H, Ar–H), 7.81–7.83 (m, 1H, Ar–H), 8.80 (s, 1H, NH); $^{13}$C NMR (125 MHz) $\delta$ 34.4, 35.7, 40.5, 49.8, 50.0, 126.9, 129.1, 129.6, 130.7, 130.9, 131.0, 156.7, 162.2; FAB-MS $m/z$: 461 [$(M - PF_6)^+$]; Anal. Found: C, 33.79; H, 4.80; N, 14.24%. Calcd for $C_{17}H_{28}F_{12}N_6P_2$: C, 33.67; H, 4.65; N, 13.86%.

***N*,*N*′-Bis(1,3-dimethyl-2-imidazolidinylidene)-9,10-phenanthrenediammonium Bis(hexafluorophosphate) (5):** A mixture of crude **2** (1.73 g, calcd as 1.44 mmol) and $NH_4PF_6$ (1.41 g, 8.30 mmol) in $H_2O$ (0.42 mL) was stirred at room temperature for 10 min. The precipitate was collected by centrifuging and washed with $H_2O$ (0.5 mL × 2) to produce crude product (309 mg), which was recrystallized from acetone–ethyl acetate to produce colorless crystals (250 mg, 28%): mp 236–240 °C; IR (neat) 3647, 3575, 3377, 3344, 1603, 1379, 1302, 831; $^1$H NMR (500 MHz) $\delta$ 2.85 (s, 12H, Me), 3.89–3.96 (m, 4H, $CH_2$), 4.01–4.08 (m, 4H, $CH_2$), 7.84 (dd, $J = 8.5$, 8.5 Hz, 2H, Ar–H), 7.90 (dd, $J = 8.5$, 8.5 Hz, 2H, Ar–H), 8.43 (d, $J = 8.5$ Hz, 2H, Ar–H), 8.98 (d, $J = 8.5$ Hz, 2H, Ar–H), 9.50 (brs, 2H, NH); $^{13}$C NMR (125 MHz) $\delta$ 34.0, 50.0, 124.5, 125.8, 128.7, 129.3, 129.5, 130.2, 131.5, 157.7; FAB-MS $m/z$: 547 [$(M - PF_6)^+$]; Anal. Found: C, 41.76; H, 4.47; N, 11.96%. Calcd for $C_{24}H_{30}F_{12}N_6P_2$: C, 41.63; H, 4.37; N, 12.14%.

***N*,*N*′-Bis(*N*,*N*,*N*′,*N*′-tetramethyldiaminomethylidene)-*o*-benzenediamine (6):** Compound **6** was synthesized by the method previously described by us.[15]

***N*-(1,3-Dimethyl-2-imidazolidinylidene)benzeneamine (7):** Compound **7** was synthesized by the method previously described by us.[16]

***N*-(1,3-Dimethyl-2-imidazolidinylidene)benzeneammonium Hexafluorophosphate (8):** A mixture of **7** (1.05 g, 5.55 mmol) and $NH_4PF_6$ (1.15 g, 7.06 mmol) in $H_2O$ (10 mL) was stirred at room temperature for 5 min. The precipitate was collected by centrifuging and washed with $H_2O$ (3 mL × 2) to produce crude product (2.71 g), which was recrystallized from EtOH to produce colorless crystals (1.92 g, quant.): mp 122–123 °C; IR (neat) 3377, 1629, 1502, 1442, 1373, 1300, 833; $^1$H NMR (400 MHz) $\delta$ 2.94 (s, 6H, Me), 3.92 (s, 4H, $CH_2$), 7.28–7.34 (m, 3H, Ar–H), 7.43–7.47 (m, 2H, Ar–H), 9.11 (brs, 1H, NH); $^{13}$C NMR (125 MHz) $\delta$ 34.84, 49.83, 124.3, 127.2, 130.5, 137.2, 157.9; FAB-MS $m/z$ 190 [$(M - PF_6)^+$], 525 [$(2M - PF_6)^+$]; Anal. Found: C, 39.42; H, 4.85; N, 12.50%. Calcd for $C_{11}H_{16}F_6N_3P$: C, 39.41; H, 4.81; N, 12.53%.

***N*-(1,3-Dimethyl-2-imidazolidinylidene)-*N*-methylbenzeneammonium Hexafluorophosphate (9):** A mixture of **7** (272 mg, 0.143 mmol) and methyl iodide (107 μL, 1.72 mmol) in acetonitrile (1 mL) was stirred at room temperature for 16 h and then

evaporated to give pale yellow oil (439 mg). To a part of the oil (240 mg), $NH_4PF_6$ (147 mg, 0.868 mmol), and $H_2O$ (1 mL) was added and the whole was stirred for 5 min. The precipitates were collected by centrifuging and washed with $H_2O$ (0.5 mL × 2) to produce crude product (318 mg), which was recrystallized from EtOH to produce colorless crystals (245 mg, 91%): mp 103–104 °C; IR (neat) 1591, 1500, 1412, 1389, 1304, 835; $^1$H NMR (500 MHz) $\delta$ 2.95 (s, 6H, Me), 3.54 (s, 3H, Me), 4.00 (s, 4H, $CH_2$), 7.21 (dd, $J$ = 8.5, 7.5 Hz, 1H, Ar–H), 7.32 (d, $J$ = 7.5 Hz, 2H, Ar–H), 7.44 (dd, $J$ = 8.5, 8.5 Hz, 2H, Ar–H); $^{13}$C NMR (125 MHz) $\delta$ 35.4, 38.9, 49.8, 120.9, 125.7, 130.7, 143.1, 162.4; FAB-MS $m/z$ 204 [$(M - PF_6)^+$], 553 [$(2M - PF_6)^+$]; Anal. Found: C, 41.18; H, 5.11; N, 11.94%. Calcd for $C_{12}H_{18}F_6N_3P$: C, 41.27; H, 5.19; N, 12.03%.

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6 The chiral crystals were obtained by complexation of bisguanidinobenzene **1** and (2*S*,3*S*)-(+)-*O*,*O*′-dibenzoyltartaric acid. In these crystals, only one enantiomer of the *s-trans* form of **1** exists. Chirality disappeared when the crystal was dissolved in solvent. Surprisingly, a chiral crystal was also obtained from the complex of **1** and achiral benzoic acid. In this crystal, the complex formed a helical supermolecule with only the *s-trans* enantiomer of **1**. These results will be reported elsewhere in the near future.

7 Calculations using RHF/6-31G* show that *s-trans* conformation of **1** is 3.5 kcal mol$^{-1}$ more stable than *s-cis* one, which means there is no considerable difference in stability between the two isomers (Ref. 12). This is supported by X-ray crystallographic analysis of **1** and its derivatives, in which both isomers were obtained (unpublished data).

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10 Pyramidal inversion should cause differences in the ratio of separated methyl peaks or the methyl peak shift due to the rather stable conformation of methyl groups to be in the opposite side (=*anti* forms), which was not observed in this case. The *anti* forms of methyl groups of **1** in crystal structures support that they are more stable than *syn* form (Ref. 5).

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