

Synthesis of *ortho*-Phenylenebis(guanidine) Derivatives with Potential Chirality

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We report the synthesis and potential chirality of *ortho*-phenylenebisguanidines (BGs) with substituents at C(3) and C(6). Guanidinylation of 3,6-disubstituted benzene-1,2-diamines with 2-chloro-4,5-dihydro-1,3-dimethyl-1*H*-imidazolium chloride gave the corresponding BGs. X-Ray crystallography showed that the two guanidine moieties occupy different faces of the benzene ring, creating potential chirality, although optical resolution of 'Bu-substituted BG by chiral HPLC failed. However, a methylated acyclic bisguanidinium salt (BGms) was obtained as a chiral crystal with a space group of $P2_12_12_1$.

Introduction. – Optical resolution is a conventional method for preparing chiral materials from racemic mixtures. However, this method requires a diastereoisomeric environment; for example, in salt formation with optically active acids or bases, attachment of chiral auxiliaries, chiral HPLC, and kinetic resolution [1]. Some achiral compounds form chiral crystals [2], and this property has been exploited in chiral auxiliaries for asymmetric synthesis [3].

We have focused on the chemistry of guanidines [4], particularly on their synthesis [5], on their application as chiral organocatalysts [6], and as nitrogen sources for aziridine formation [7]. In our previous work on proton acceptors and metal-ion scavengers, we observed that *ortho*-phenylenebisguanidine (BG) **1** forms isolable crystalline complexes with proton donors and metal ions [8]. X-Ray crystallography revealed that these complexes adopted a characteristic conformation, where the two guanidine moieties preferentially occupy different faces of the benzene ring (*s-trans*) rather than the same face (*s-cis*)²⁾. The restriction of rotation around the Ar–N and C=N bonds, and the steric interaction between the H-atoms on the benzene ring and the guanidinium moiety in the *s-trans* conformation of these complexes suggested that these BGs may exhibit potential chirality (Fig. 1, a). Conformational analyses of BG **1**, phenanthroline derivative **2** (Fig. 1, b), and their corresponding protonated species by temperature-dependent ¹H-NMR experiments showed that the rotation of Ar–N bonds in protonated **2** was restricted [9]. This led to the design and synthesis of mono-*N*-alkylated and monoprotonated phenylenebis(guanidinium) salts (BGmss). Methylated and ethylated BGmss **3** with a hexafluorophosphate ion (PF₆[–]) as the counter-anion spontaneously crystallized with a chiral space group of $P2_12_12_1$ (Fig. 1, c) [10].

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²⁾ Structures of the free amine form are shown in Fig. 1, a, for clarity.

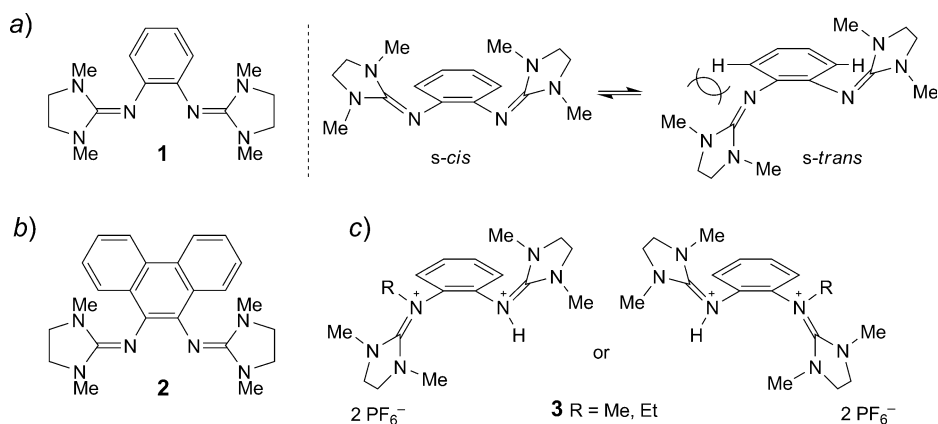


Fig. 1. a) Structures of BG **1** and possible conformational isomers. b) Structure of BG **2**. c) Structures of BGmss **3** with potential chirality.

We herein report our investigation of various BGs and BGmss with more stable potential chirality. We achieved this by synthesizing BGs **4** with increased steric repulsion between guanidines and substituents R at C(3) and C(6), thus suppressing racemization to *ent-4* (Fig. 2), and by modifying the guanidinium moiety of BGmss **3** and monoguanidinium salts (MGmss) to enable spontaneous chiral crystallization.

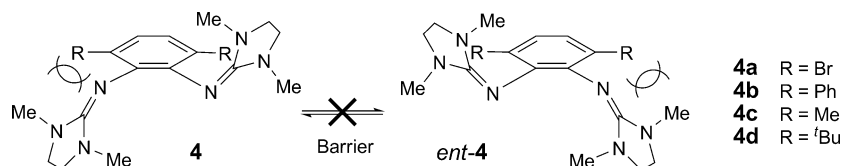
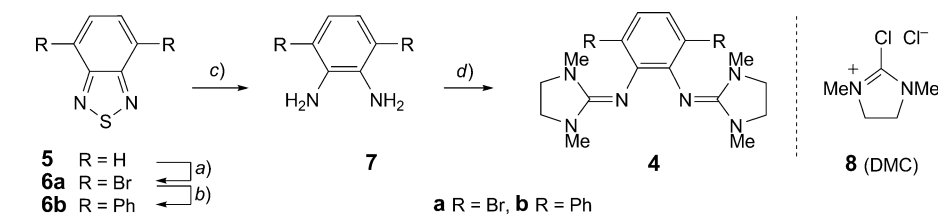


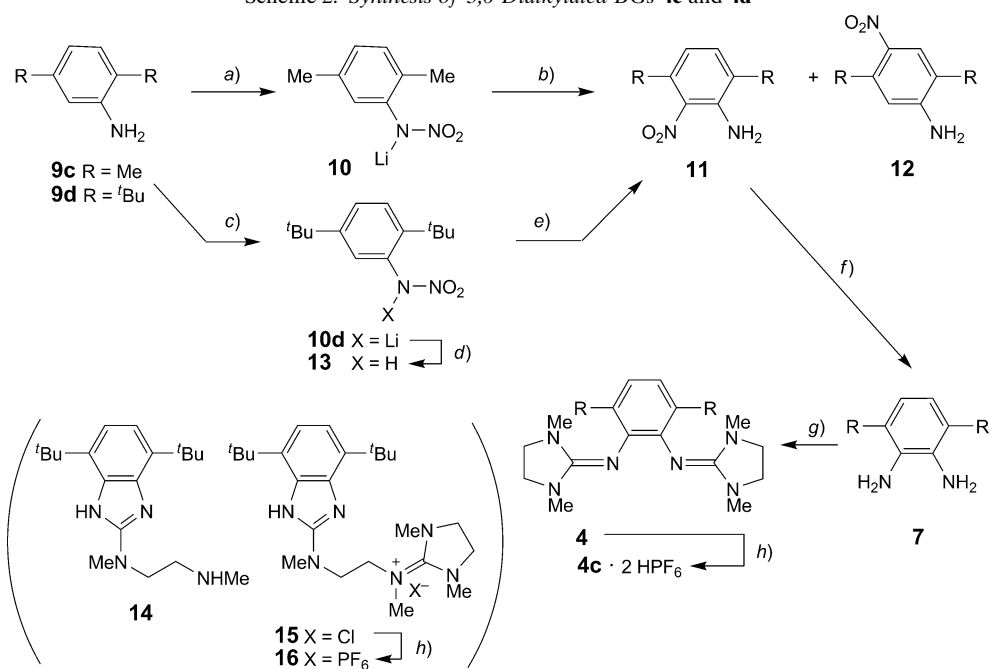
Fig. 2. Assumed steric hindrance between guanidine moieties and substituents (R) at C(3) and C(6) of BGs **4**.

Results and Discussions. – First, we synthesized 3,6-disubstituted BGs **4**. 2,1,3-Benzothiadiazole (**5**) was brominated [11], and dibromo derivative **6a** underwent *Suzuki–Miyaura* coupling with PhB(OH)₂ to give diphenylbenzothiadiazole **6b** [12]. LiAlH₄ Reduction of **6a** and **6b**, and guanidinylation of the resulting benzene-1,2-diamines **7a** and **7b** with 2-chloro-4,5-dihydro-1,3-dimethyl-1*H*-imidazolium chloride (**8**) gave dibromo-BG **4a** and diphenyl-BG **4b**, respectively (Scheme 1).

Next, we synthesized 3,6-dialkylated BGs **4c** and **4d** (Scheme 2). 3,6-Dialkylated benzene-1,2-diamines **7c** and **7d** were synthesized by the rearrangement of *N*-nitroanilines as reported by *Olah et al.* [13]. Commercially available 2,5-dimethylaniline (**9c**) was treated with BuLi and ^tBuONO₂ to give *N*-lithio-*N*-nitroaniline **10c**. Rearrangement of the NO₂ group of **10c** under acidic conditions gave 3,6-dimethyl-2-nitroaniline (**11c**) in 18% yield. However, the 2,5-dimethyl-4-nitroaniline (**12c**) by-product was obtained from **9c** in 16% yield. The yields and regioselectivity were lower than those previously reported [13]. Attempts to improve the yield and selectivity by

Scheme 1. Synthesis of 3,6-Disubstituted BGs **4a** and **4b**

a) Br₂, 48% aq. HBr, reflux, 5 h; 86%. b) PhB(OH)₂, Pd(PPh₃)₄, Na₂CO₃, DMF, 130°, 13 h; 91%. c) LiAlH₄, THF (for **7a**: 40°, 22 h; 87%; for **7b**: reflux, 8 h; 88%). d) 2-chloro-4,5-dihydro-1,3-dimethyl-1H-imidazolium chloride (**8**); Et₃N, CH₂Cl₂, r.t. (for **4a**: 44 h, 78%; for **4b**: 6 h, 79%).

Scheme 2. Synthesis of 3,6-Dialkylated BGs **4c** and **4d**

a) From **9c**: BuLi, *i*BuONO₂, Et₂O, r.t., 20 h. b) Conc. HCl, AcOH, r.t., 20 h; 18% for **11c** and 16% for **12c**. c) For **9d**: BuLi, *i*BuONO₂, Et₂O, r.t., 20 h. d) Sat. aq. NH₄Cl; 49% (35% recovery of **9d**). e) Conc. HCl, AcOH, r.t., 20 min; 57% for **11d** and 34% for **12d**. f) Na₂S₂O₄, EtOH/ H₂O (for **7c**: 90°, 30 min; 99%; for **7d**: 75°, 1.5 h; 98%). g) Compound **8**, Et₃N, CH₂Cl₂ (from **7d**: 15% for **4d**, 23% for **14**, and 14% for **15**). h) NH₄PF₆, acetone (from **7c** via **4c**: 54%; for **16**: 66%).

altering the reaction conditions (acid, temperature, *etc.*) to promote the rearrangement were unsuccessful. The 2-nitro isomer **11c** was reduced with sodium dithionite (Na₂S₂O₄) to furnish 3,6-dimethylbenzene-1,2-diamine (**7c**), which was guanidinylation with **8** to give 3,6-dimethyl-BG **4c** as an oil. After treating **4c** with NH₄PF₆, the

corresponding HPF_6 salt **4c**·2 HPF_6 was obtained as a crystalline solid. 3,6-Di(*tert*-butyl)-BG **4d** was synthesized from 2,5-di(*tert*-butyl)aniline (**9d**) *via* a similar route. After nitration of **9d** with BuLi and $t\text{BuONO}_2$, *N*-lithio-*N*-nitroaniline **10d** was converted to the free *N*-nitroaniline **13** with saturated aqueous NH_4Cl in 49% yield (from **9d**), because **10d** was difficult to handle. Starting material **9d** was recovered in 35% yield from this process. Nitroaniline **13** was subjected to the acidic rearrangement conditions to give 3,6-di(*tert*-butyl)-2-nitroaniline (**11d**) and the by-product 2,5-di(*tert*-butyl)-4-nitroaniline (**12d**) in 28 and 17% yields, respectively, from **9d**. The 2-nitro isomer **11d** was converted to 3,6-di(*tert*-butyl)benzene-1,2-diamine (**7d**) by reduction with $\text{Na}_2\text{S}_2\text{O}_4$. Guanidinylation of **7d** with **8** afforded BG **4d**; however, benzimidazole by-products **14** and **15** were also formed. The structures of **14** and **16**, which is the corresponding PF_6^- salt of chloride **15**, were determined by X-ray crystallography (Fig. 3). These side-products were probably generated *via* the following mechanism

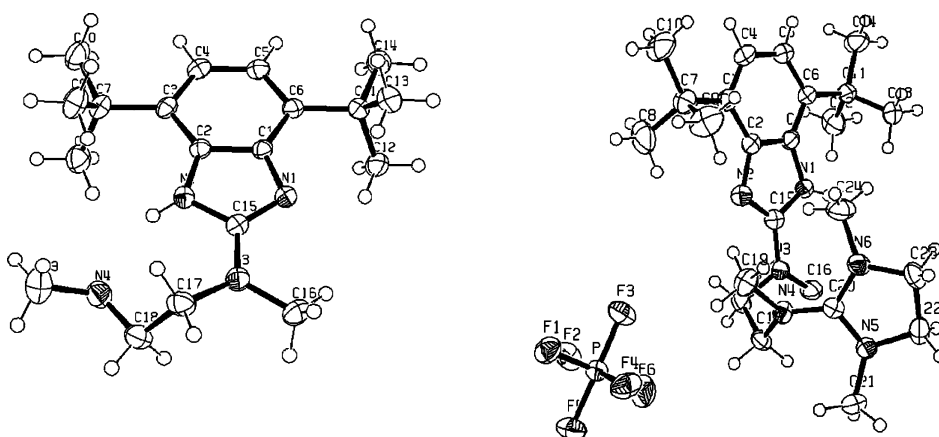
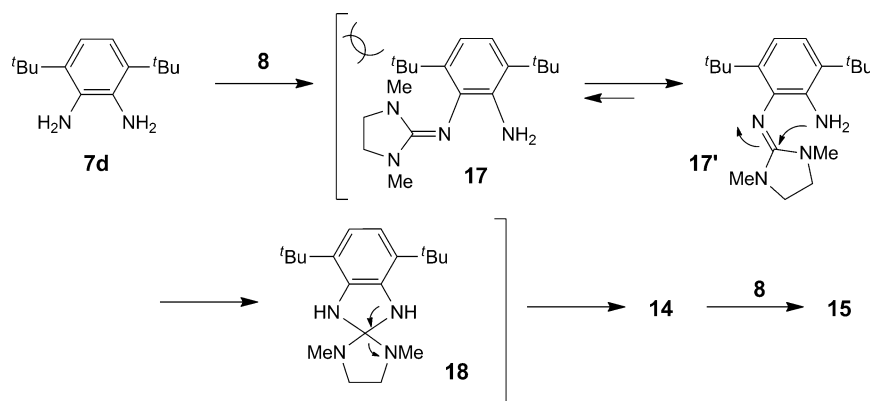


Fig. 3. ORTEP Plots of **14** (left) and **16** (right)

Scheme 3. Proposed Mechanism of the Generation of **14** and **15** from **7d**



(Scheme 3): the initial reaction of **7d** and **8** gives MG **17**, which can be partially converted to the conformational isomer **17'**, because of steric repulsion between the bulky 'Bu group and the guanidine moiety. Cyclization of **17'** through intramolecular addition of the aniline N-atom to the guanidine C-atom and the ring opening of aminal **18** gives **14**. A proportion of **14** is further guanidinylated with **8** to afford **15**.

X-Ray crystal structures of 3,6-disubstituted BGs **4a**, **4b**, **4c**·2 HPF₆, and **4d** are shown in Figs. 4–7, respectively. All the BG crystals had achiral space groups (*P*2₁/*c* for **4a** and **4b**, *P*2₁/*m* for **4c**·2 HPF₆, *P*1̄ for **4d**). The two guanidine moieties in **4** occupy different faces of the aromatic ring as expected. The crystal lattice (Fig. 5, *a*) contains the two conformational isomers of diphenyl-BG **4b**, in which the two benzene rings at C(3) and C(6) are either in the same plane or perpendicular to each other (Fig. 5, *b* and *c*)³. The distance between the two guanidine C-atoms of each BG was estimated as 4.41 Å for **4a**, 3.23 and 3.15 Å for **4b**, 3.35 Å for **4c**·2 HPF₆, and 3.13 Å for **4d**, implying that the distances for these BG substituents were in the order 'Bu < Ph < Me < Br. However, the steric effects of the substituents at C(3) and C(6) are indicated by the A values ('Bu (19.7) > Ph (11.7) > Me (7.3) > Br (2.8); in kJ mol^{−1}) [1]. These results reveal that BGs with bulkier substituents at C(3) and C(6) had two guanidines that were closer together. Although di(*tert*-butyl)-BG **4d** was expected to have sufficiently stable chirality to be separated into enantiomers, optical resolution by chiral HPLC failed.

Next, we investigated the synthesis of *N*-methylated quaternary guanidinium salts MGmss **19**, permethylated BGmss **20** (cf. Scheme 4), acyclic BGms **21** (cf. Scheme 5), and 3,6-diphenyl-BGms **22** (cf. Scheme 6), and their potential chirality. Cyclic MGM

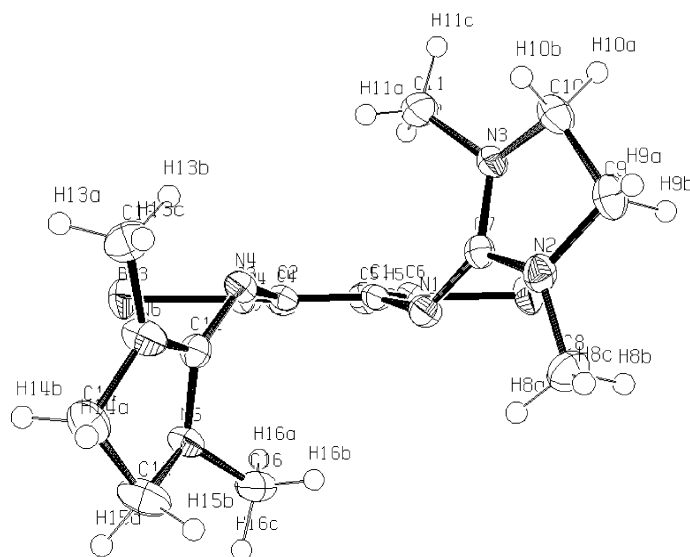


Fig. 4. ORTEP Plot of BG **4a**

³) Side views of each conformer created in Chem3D are shown in Fig. 5, *b* and *c* for clarity.

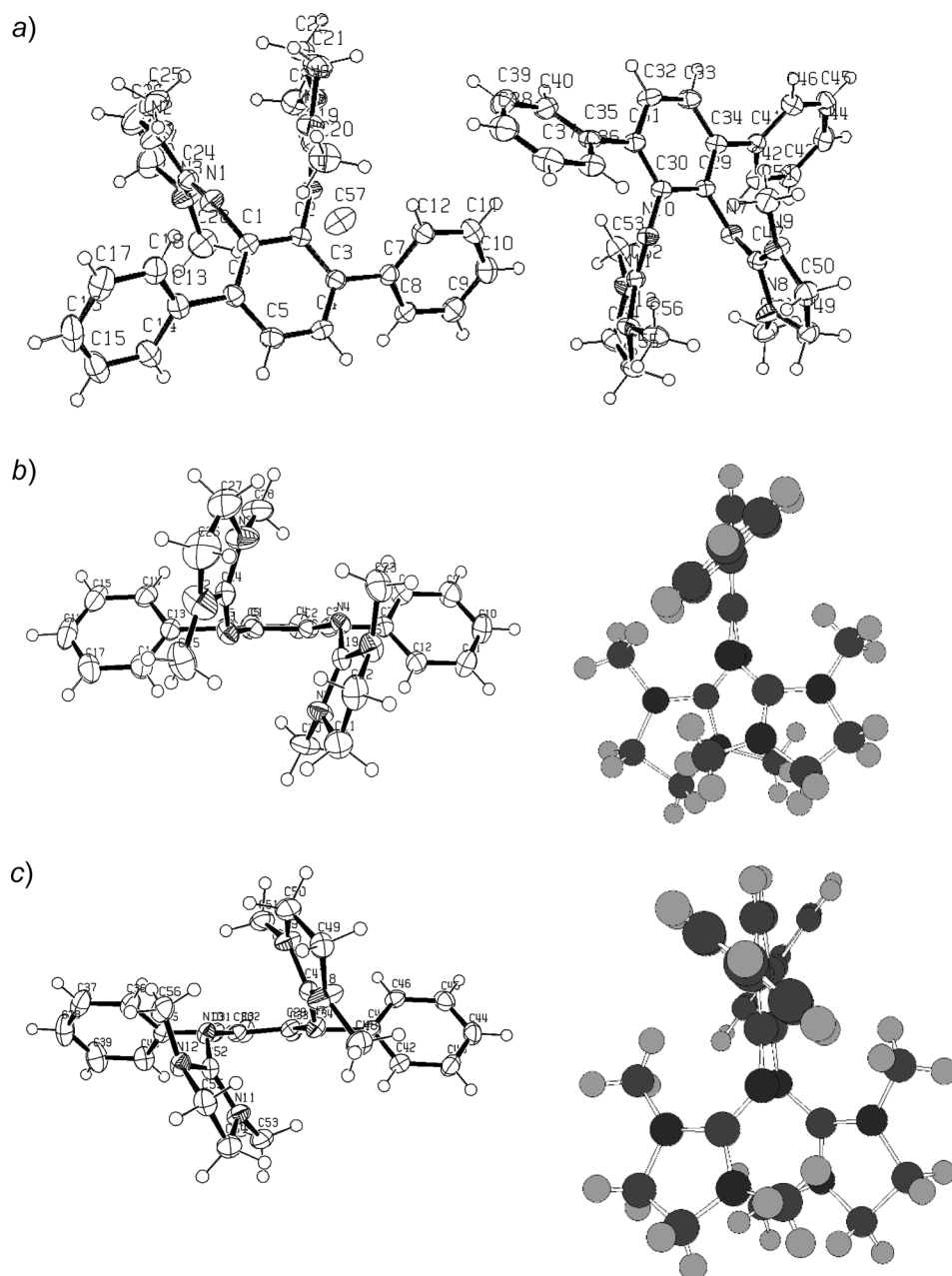


Fig. 5. ORTEP Plots and Chem3D views of BG a) **4b** (included two conformational isomers in one crystal lattice), b) **4b** with two benzene rings at C(3) and C(6) in plane, and c) **4b** with two Ph groups perpendicular to each other (left: front views, right: side view)

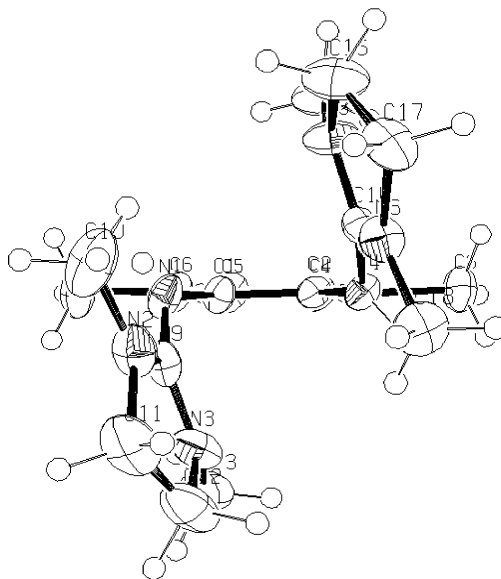


Fig. 6. ORTEP Plot of BG **4c** (two PF_6^- anions were omitted for clarity)

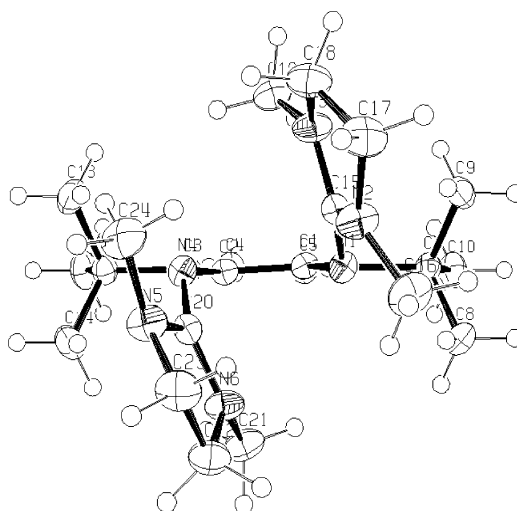
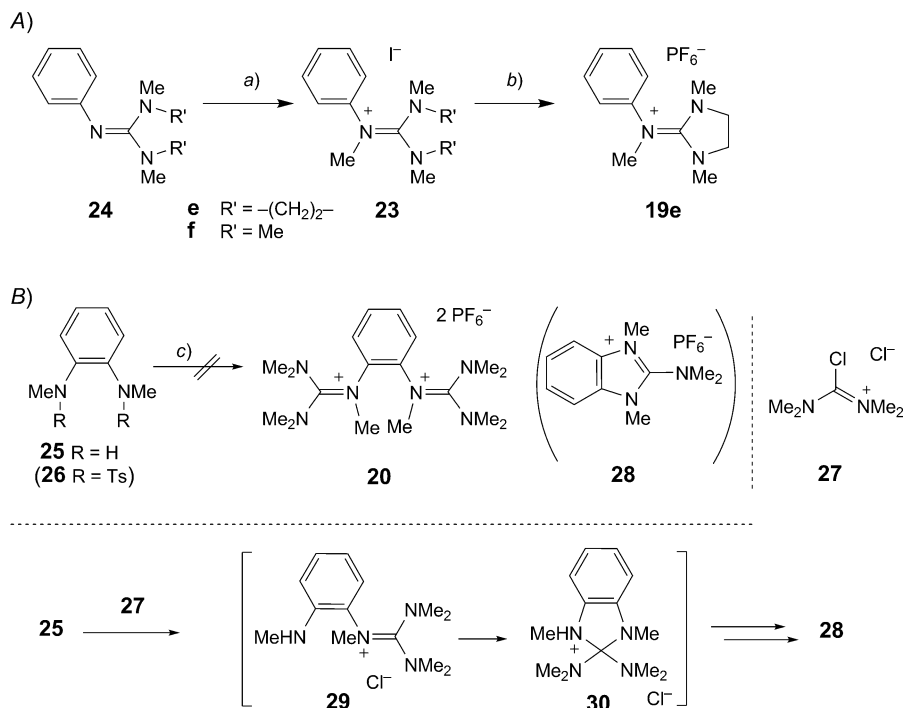


Fig. 7. ORTEP View of BG **4d**

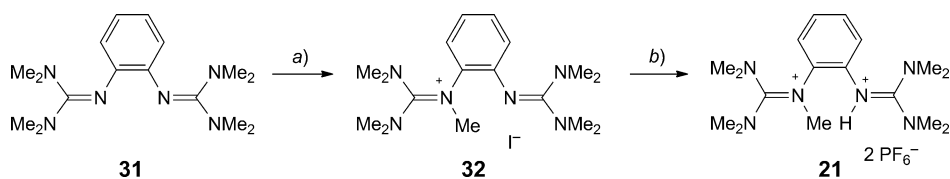
iodo derivative **23e** was prepared by methylating guanidine **24e** with MeI [9], and the acyclic MGms **23f** was prepared by a similar method from guanidine **24f** [14]. Cyclic MGms **23e** underwent anionic exchange of I^- by PF_6^- to give the crystalline MGms **19e** as colorless prisms after recrystallization from AcOEt/MeOH [9]. In contrast, no crystals of the corresponding acyclic PF_6^- salt **19f** were obtained after a similar anion exchange of **23f** (Scheme 4, A).

Scheme 4. A) Synthesis of MGms **19e** and **23f**; B) Trials for the Synthesis of Permethylated BGms **20f**

a) MeI, MeCN, r.t., 1.5–2 h; 88% for **23e**; 98% for **23f**. b) From **23e**: NH_4PF_6 , H_2O , r.t.; 27%.
 c) 1) **26** \rightarrow **27**, Et_3N , CH_2Cl_2 , r.t., 5 h, 2) NH_4PF_6 , H_2O , r.t.; 38%.

The synthesis of permethylated BGms **20** was attempted by first hydrolyzing *N,N'*-ditosylbenzene-1,2-diamine **26** to *N,N'*-dimethylbenzene-1,2-diamine (**25**), which was then reacted with [(chloro)(dimethylamino)methylidene]dimethylaminonium chloride (**27**) [15][16], but this procedure did not afford the desired hexamethylated BGms **20**. Instead, the by-product, benzimidazole **28**, was obtained upon anion exchange, which was intended to generate **20f**, by cyclizing MGms **29** to amina **30** (Scheme 4, B).

We next synthesized acyclic protonated monomethylated BGms **21**. Monomethylation of acyclic BG **31** [17], followed by anion exchange and protonation of BGms **32**,

Scheme 5. Synthesis of BGms **21**

a) MeI, MeCN, r.t., 2 h; 74%. b) NH_4PF_6 , H_2O , acetone, r.t.; 64%.

gave dihexafluorophosphate **21** in crystalline form. Recrystallization from acetone/AcOEt furnished colorless prisms (*Scheme 5*).

The methylation of diphenyl-BG **4b** did not afford monomethylated BGms **22**, and benzimidazole **33** was obtained instead (*Scheme 6*). The structure of **33** was determined by X-ray crystallography (*Fig. 8*). We propose that **33** was formed through

Scheme 6. Trial for the Synthesis of BGms 22

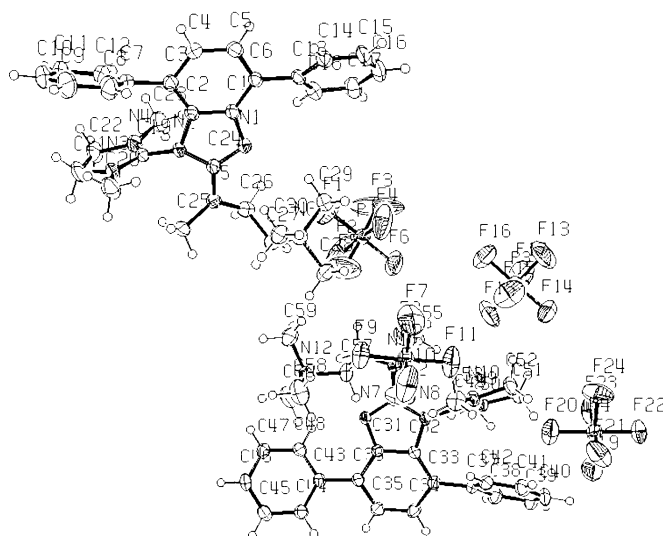
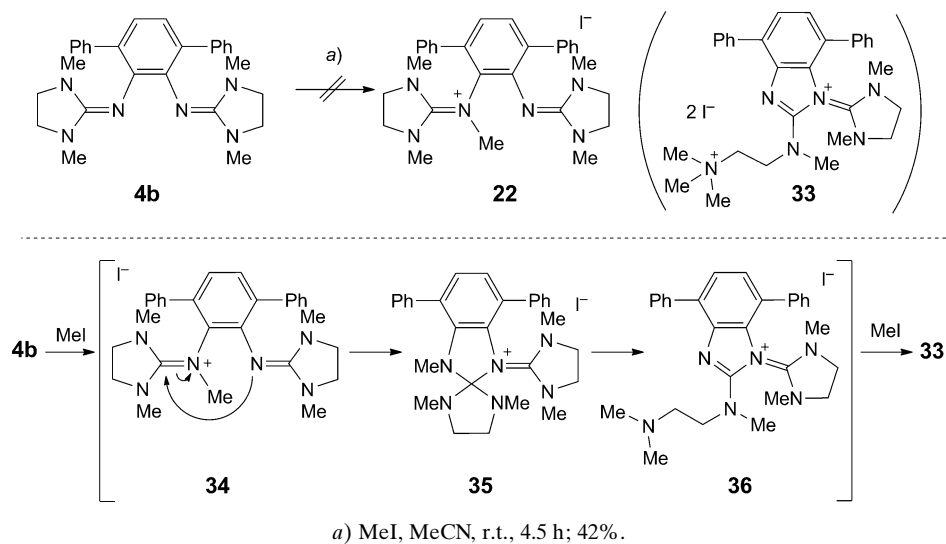


Fig. 8. ORTEP Plot of 33

the methylation of **4b** to **34**, cyclization to aiminal **35**, Me migration and ring opening to **36**, and further methylation.

Single-crystal X-ray analysis of *N*-methylated MGms **19e** and acyclic BGms **21** revealed that **19e** formed an achiral crystal with a space group of $P2_1/m$. However, BGms **21** formed a chiral crystal with a space group of $P2_12_12_1$, and the two guanidinium moieties adopted the *s-trans* conformation (Fig. 9).

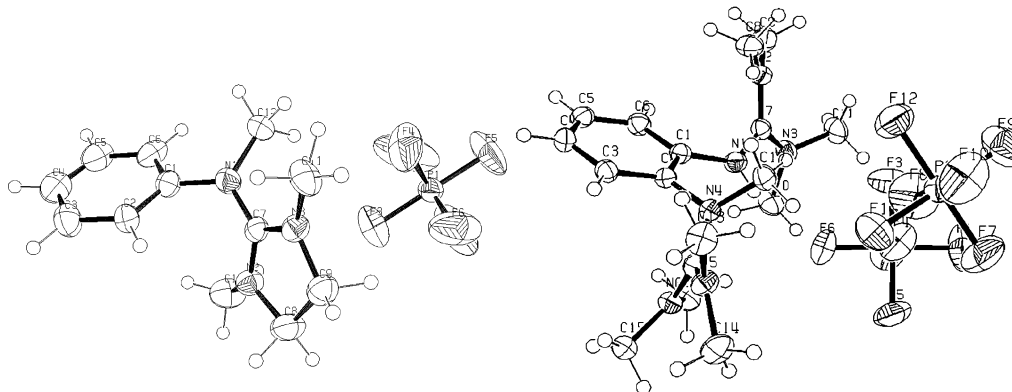


Fig. 9. ORTEP Plots of **19e** (left) and **21** (right)

Conclusions. – We have synthesized *ortho*-phenylenebis(guanidines) (BGs) with substituents at adjacent positions in the guanidine moieties. X-Ray crystallography showed an *s-trans* conformation, indicating potential chirality. However, optical resolution of di(*tert*-butyl)-BG **4d** by chiral HPLC failed. Monoguanidinium salts (MGms) and modified bisguanidinium salts (BGmss) were synthesized to achieve spontaneous chiral crystallization. Cyclic MGms **19e** formed an achiral crystal, whereas pentamethylated BGms **21** with acyclic guanidines formed a chiral crystal with a space group of $P2_12_12_1$. The synthesis of more sophisticated BGs and BGmss would produce a wider variety of chiral crystals.

Experimental Part

General. Anh. CH_2Cl_2 and DMF were purchased from *Kanto Chemical*, and anh. THF and Et_2O were purchased from *Wako Chemical*. Anh. MeCN was used after distillation from CaH_2 . TLC: *Fuji Silysia NH-TLC* plate. Column chromatography (CC): *Kanto Chemical* silica gel 60, spherical, and *Fuji Silysia NH* silica gel (100–200 mesh). M.p.: *Yanagimoto MPSI* melting-point apparatus; uncorrected. IR Spectra: Attenuated Total Reflectance (ATR) system on a *JASCO FT/IR-300E* spectrophotometer, $\tilde{\nu}$ in cm^{-1} . ^1H - and ^{13}C -NMR (400 and 100 MHz, resp.) spectra: *JEOL JNM-ECP-400* instrument; δ in ppm rel. to Me_4Si as internal standard, J in Hz. MS: *JEOL JNM MS-GCMATE* for EI-MS and *JEOL JNM HX-110* for FAB-MS, resp., in m/z (rel. %). X-Ray structures: suitable single crystals were analyzed on *Bruker Smart APEX II* CCD area detector with MoK_α radiation (λ 0.71073 Å; graphite monochromator); structures were solved by direct methods with SHELXL97 [18] and refined by full-matrix least-squares on F^2 (SHELXL97) [18]. If possible, the H-atoms were located from a difference electron-density map, and refined isotropically or constrained at ideal positions and included in the structure factor calculation.

4,7-Dibromo-2,1,3-benzothiadiazole (6a) [11]. To a mixture of **5** (5.05 g, 36.4 mmol) in 48% aq. HBr (75 ml, 0.45 mol), Br₂ (6.20 ml, 121 mmol) in 48% aq. HBr (50 ml, 0.30 mol) was added at r.t. for 30 min. The mixture was refluxed for 5 h. After cooling, 10% aq. NaHSO₃ was added until the color of the mixture turned from yellow to reddish brown. The precipitates were collected by filtration, washed with H₂O, and dried. The resulting yellowish brown solid was recrystallized from hexane/AcOEt 3 : 1 to give **6a** (9.40 g, 86%). Yellow needles. M.p. 195–196.5° ([11]: 187–188°). IR: No characteristic absorption. ¹H-NMR (CDCl₃): 7.73 (s, 2 H).

4,7-Diphenyl-2,1,3-benzothiadiazole (6b) [12]. A mixture of **6a** (1.13 g, 3.85 mmol), PhB(OH)₂ (1.61 g, 12.8 mmol), Pd(PPh₃)₄ (73 mg, 0.063 mmol), and Na₂CO₃ (3.27 g, 30.9 mmol) in DMF (4.5 ml) was stirred at 130° (bath temp.) for 13 h in a sealed tube. After cooling, H₂O (100 ml) was added, and the mixture was extracted with CHCl₃ (1 × 100 ml, 2 × 50 ml). The combined org. layers were washed with H₂O (1 × 50 ml) and brine (1 × 50 ml), and dried (Na₂SO₄). The solvent was evaporated *in vacuo*, and the residue was purified by CC (hexane CHCl₃ 3 : 1) to give **6b** (1.01 g, 91%). Green-yellow needles. M.p. 142–143° ([12]: 127°). IR: No characteristic absorption. ¹H-NMR (CDCl₃): 7.45–7.49 (diffused *t*, *J* = 7.3, 2 H); 7.54–7.58 (diffused *t*, *J* = 7.4, 4 H); 7.80 (s, 2 H); 7.96–7.98 (diffused *d*, *J* = 7.1, 4 H).

3,6-Dibromobenzene-1,2-diamine (7a) [19]. To a suspension of LiAlH₄ (826 mg, 21.8 mmol) in THF (50 ml), a soln. of **6a** (2.00 g, 6.81 mmol) in THF (50 ml) was added, and the mixture was stirred at 40° for 22 h. After cooling to r.t., H₂O (15 ml), 20% aq. NaOH (15 ml), and CH₂Cl₂/MeOH (8 : 1, 100 ml) were added successively, and the mixture was stirred for 1 h. The precipitates were filtered through a pad of Celite® and washed with CH₂Cl₂ (100 ml). The filtrate and the washing were combined, washed with H₂O (1 × 50 ml) and brine (1 × 50 ml), dried (MgSO₄), and evaporated *in vacuo* to give **7a** (1.57 g, 87%). Brown solids. M.p. 96–98° ([19]: 92–94°). IR: 3366, 3325. ¹H-NMR (CDCl₃): 3.90 (br. s, 4 H); 6.85 (s, 2 H). FAB-MS: 268 ([M(2 × ⁸¹Br)]⁺), 267 ([M(⁸¹Br + ⁷⁹Br) + H]⁺), 266 ([M(⁸¹Br + ⁷⁹Br)]⁺), 265 ([M(2 × ⁷⁹Br) + H]⁺), 264 ([M(2 × ⁷⁹Br)]⁺).

1,1':4,1''-Terphenyl-2',3'-diamine (7b). To a suspension of LiAlH₄ (424 mg, 11.2 mmol) in THF (10 ml), a soln. of **6b** (604 mg, 2.09 mmol) in THF (20 ml) was added, and the mixture was refluxed for 8 h. After cooling to r.t., H₂O (18 ml) and 20% aq. NaOH (8 ml) were added successively. The mixture was diluted with CH₂Cl₂/MeOH 8 : 1 (50 ml) and stirred for 1 h. The precipitates were filtered off and washed with CH₂Cl₂ (50 ml). The filtrate and the washing were combined, washed with brine, and dried (Na₂SO₄). The solvent was evaporated *in vacuo* and the residue was recrystallized from CHCl₃/MeOH 1 : 2 to give **7b** (476 mg, 88%). Pale-yellow plates. M.p. 207–208.5°. IR: 3413, 3328. ¹H-NMR (CDCl₃): 3.32 (br. s, 4 H); 6.74 (s, 2 H); 7.34–7.40 (*m*, 2 H); 7.45–7.51 (*m*, 8 H). ¹³C-NMR (CDCl₃): 120.9; 127.2; 128.4; 128.8; 129.2; 132.1; 139.6. EI-MS: 260 (*M*⁺, 100), 242 (34). Anal. calc. for C₁₈H₁₆N₂ (260.34): C 83.04, H 6.19, N 10.76; found: C 82.69, H 6.07, N 10.69.

N,N'-(3,6-Dibromobenzene-1,2-diyl)bis(1,3-dimethylimidazolidin-2-imine) (4a). To a soln. of **7a** (1.95 g, 7.33 mmol) and Et₃N (4.5 ml, 32.2 mmol) in CH₂Cl₂ (35 ml), a soln. of 2-chloro-4,5-dihydro-1,3-dimethyl-1H-imidazolium chloride (**8**; 2.88 g, 16.8 mmol) in CH₂Cl₂ (35 ml) was added at 0° within 10 min. The mixture was stirred at r.t. for 21 h. Further Et₃N (4.5 ml, 32.2 mmol) and a soln. of **8** (2.76 g, 16.0 mmol) in CH₂Cl₂ (35 ml) were added at 0° during 10 min. The mixture was stirred at r.t. for further 23 h and extracted with 10% HCl (1 × 100 ml, 3 × 50 ml). The combined aq. layers were basified with 6N aq. NaOH to pH 11 at 0° and extracted with toluene (3 × 100 ml). The combined org. layers were washed with H₂O (3 × 30 ml) and brine (1 × 30 ml), dried (Na₂SO₄), and evaporated *in vacuo* to give a brown oil, which was triturated with MeOH/H₂O 100 : 1 and recrystallized from AcOEt to give **4a** (2.60 g, 78%). Brown prisms. M.p. 124–125°. IR: 1635. ¹H-NMR (400 MHz): 2.64 (s, 12 H); 3.19–3.24 (*m*, 4 H); 3.25–3.30 (*m*, 4 H); 6.89 (s, 2 H). ¹³C-NMR (100 MHz): 33.6; 47.9; 116.1; 123.6; 142.6; 153.2. FAB-MS: 461 ([M(2 × ⁸¹Br) + H]⁺), 460 ([M(2 × ⁸¹Br)]⁺), 459 ([M(⁸¹Br + ⁷⁹Br) + H]⁺), 458 ([M(⁸¹Br + ⁷⁹Br)]⁺), 457 ([M(2 × ⁷⁹Br) + H]⁺), 456 ([M(2 × ⁷⁹Br)]⁺). Crystal structure of **4a**: CCDC No. 929040.

N,N'-1,1':4,1''-Terphenyl-2',3'-diylbis(1,3-dimethylimidazolidin-2-imine) (4b). To a soln. of **7b** (513 mg, 1.97 mmol) and Et₃N (1.50 ml, 10.76 mmol) in CH₂Cl₂ (10 ml), a soln. of **8** (903 mg, 5.18 mmol) in CH₂Cl₂ (6 ml) was added at 0° within 10 min. The mixture was stirred at r.t. for 6 h and extracted with 10% HCl (1 × 100 ml, 3 × 30 ml). The aq. layers were combined, basified with 6N aq. NaOH to pH 11, and extracted with toluene (2 × 100 ml, 2 × 50 ml). The combined org. layers were washed with H₂O (2 × 30 ml) and brine (1 × 30 ml), dried (Na₂SO₄), and evaporated *in vacuo* to give yellow solids, which were

recrystallized from hexane AcOEt (5 : 1) to give **4b** (700 mg, 79%). Pale-yellow prisms. M.p. 133–135°. IR: 1646. ¹H-NMR (CDCl₃): 2.62 (s, 12 H); 2.93 (diffused t, *J* = 7.3, 4 H); 3.07 (diffused t, *J* = 7.3, 4 H); 6.91 (s, 2 H); 7.20 (t, *J* = 7.3, 2 H); 7.31 (t, *J* = 7.3, 4 H); 7.57 (d, *J* = 7.3, 4 H). ¹³C-NMR (CDCl₃): 34.2; 48.1; 122.0; 125.5; 127.2; 129.3; 132.0; 140.5; 142.3; 152.6. EI-MS: 452 (*M*⁺, 100), 375 (55), 340 (36), 226 (35). Anal. calc. for C₂₈H₃₂N₆ · 1/2 H₂O (419.58): C 72.85, H 7.21, N 18.21; found: C 73.05, H 7.10, N 18.21. Crystal structure of **4b**: CCDC No. 929035.

3,6-Dimethyl-2-nitroaniline (11c) [13] and **2,5-Dimethyl-4-nitroaniline (12c)** [20]. To a soln. of **9c** (3.0 ml, 24.1 mmol) in Et₂O (30 ml), BuLi in hexane (1.38N, 20.0 ml, 27.6 mmol) was added at 0° within 10 min. Then, ^tBuONO₂ (7.5 ml, 64.2 mmol) was added at the same temp., and the mixture was stirred at r.t. for 27 h. The precipitates were collected by filtration, washed with hexane, and dissolved in AcOH (35 ml) and conc. HCl (35 ml). The soln. was stirred at r.t. for 20 h. After cooling in ice-bath, 20% aq. NaOH was added to pH > 10, and the mixture was extracted with Et₂O (1 × 100 ml, 2 × 50 ml). The combined org. layers were washed with H₂O (2 × 50 ml) and brine (1 × 50 ml), dried (MgSO₄), and evaporated *in vacuo* to give a reddish-brown oil, which was purified by CC (hexane/AcOEt 5 : 1) to give **11c** as a reddish-brown oil (M.p. [13]: 32–33°; 700 mg, 18%) and **12c** as brown prisms (640 mg, 16%).

Data of 11c. IR: 3498, 3394, 1515, 1334. ¹H-NMR (CDCl₃): 2.19 (s, 3 H); 2.42 (s, 3 H); 5.10 (br. s, 2 H); 6.52 (d, *J* = 7.4, 1 H); 7.07 (d, *J* = 7.4, 1 H). EI-MS: 166 (*M*⁺, 23), 149 (29), 84 (100).

Data of 12c. M.p. 148–150° ([20]: 144–146°). IR: 3468, 3374, 1518. ¹H-NMR (CDCl₃): 2.17 (s, 3 H); 2.57 (s, 3 H); 4.16 (br. s, 2 H); 6.46 (s, 1 H); 7.94 (s, 1 H).

3,6-Dimethylbenzene-1,2-diamine (7c) [21]. To a soln. of **11c** (611 mg, 3.50 mmol) in EtOH (13 ml), a suspension of Na₂S₂O₄ (5.94 g, 34.1 mmol) in H₂O (11 ml) was added, and the mixture was heated at 90° for 30 min. After cooling, the mixture was extracted with CHCl₃ (3 × 30 ml). The combined org. layers were washed with H₂O (1 × 20 ml) and brine (1 × 20 ml), dried (MgSO₄), and evaporated *in vacuo* to give **7c** (470 mg, 99%). Brown powder. M.p. 68–70° ([21]: 75°). IR: 3627, 3398. ¹H-NMR (CDCl₃): 2.17 (s, 6 H); 3.24 (br. s, 4 H); 6.53 (s, 2 H).

Hydrogen Hexafluorophosphate–N,N'-(3,6-Dimethylbenzene-1,2-diyl)bis(1,3-dimethylimidazolidin-2-imine) (2 : 2 : 1) (4c · 2 HPF₆). To a soln. of **7c** (301 mg, 2.10 mmol) in CH₂Cl₂ (10 ml), Et₃N (2.50 ml, 17.9 mmol) was added at 0°. A soln. of **8** (1.01 g, 5.75 mmol) in CH₂Cl₂ (10 ml) was added within 10 min, and the mixture was stirred at r.t. for 6 h, and extracted with 10% HCl (3 × 20 ml). The combined aq. layers were basified with 6N aq. NaOH to pH 11 and extracted with toluene (4 × 30 ml). The combined org. layers were washed with H₂O (5 × 20 ml) and brine (1 × 20 ml), and dried (Na₂SO₄). The solvent was evaporated *in vacuo*, and the residue was dissolved in acetone (5 ml). NH₄PF₆ (794 mg, 4.63 mmol) was added to the soln., and the solvent was evaporated *in vacuo*. The residue was washed with AcOEt and recrystallized from acetone AcOEt 2 : 1 to give **4c · 2 HPF₆** (697 mg, 54%). Colorless prisms. M.p. 264–266°. IR: 3346, 1609. ¹H-NMR ((D₆)acetone): 2.42 (s, 6 H); 2.90 (s, 12 H); 3.89–3.98 (*m*, 8 H); 7.43 (s, 2 H); 8.82 (br. s, 2 H). ¹³C-NMR ((D₆)acetone): 18.3; 33.9; 49.9; 132.1; 132.5; 136.2; 157.2. FAB-MS: 475 ([*M* – PF₆]⁺). Anal. calc. for C₁₈H₃₀F₁₂N₆P₂ (620.40): C 34.85, H 4.87, N 13.55; found: C 34.78, H 4.71, N 13.51. Crystal structure of **4c · 2 HPF₆**: CCDC No. 929041.

2,5-Di(tert-butyl)-N-nitroaniline (13). To a mixture of **9d** (12.1 g, 58.9 mmol) in Et₂O (180 ml), BuLi in hexane (1.60 N, 81.0 ml, 130 mmol) was added at –20° within 30 min. The mixture turned to red, and colorless precipitates formed. After the completion of addition, the mixture was warmed to r.t., and ^tBuONO₂ (18.0 ml, 153.3 mmol) was added within 2 h. The mixture turned to orange. The precipitates were once dissolved, and finally colorless precipitates were regenerated. After stirring at r.t. for 48 h, the mixture was cooled to 0°, and sat. aq. NH₄Cl (100 ml) was added. After stirring at r.t. for 15 min, H₂O (100 ml) was added, and the mixture was extracted with Et₂O (3 × 100 ml). The combined org. layers were washed with H₂O (1 × 50 ml) and brine (1 × 50 ml), and dried (MgSO₄). The solvent was evaporated *in vacuo* to give a reddish-brown oil (19.0 g, 129%), which was purified by CC (hexane) to give **13** (7.34 g) and recovered **9d** (4.18 g, 35%). The former was recrystallized from hexane to give **13** (7.20 g, 49%). Colorless prisms. M.p. 92–93°. IR: 3258, 1576, 1330. ¹H-NMR (CDCl₃): 1.31 (s, 9 H); 1.38 (s, 9 H); 7.23–7.24 (*m*, 1 H); 7.39–7.44 (*m*, 2 H); 9.81 (s, 1 H). ¹³C-NMR (CDCl₃): 30.9; 31.1; 34.3; 34.7; 127.1; 127.2; 127.5; 132.4; 144.5; 150.5. EI-MS: 250 (*M*⁺, 22), 205 (81), 204 (100), 189 (68), 174 (71), 148 (100). Anal. calc. for C₁₄H₂₂N₂O₂ (250.30): C 67.17, H 8.86, N 11.19; found: C 67.30, H 8.99, N 11.21.

3,6-Di(tert-butyl)-2-nitroaniline (11d) and 2,5-Di(tert-butyl)-4-nitroaniline (12d). To a soln. of **13** (6.60 g, 26.3 mmol) in AcOH (80 ml), conc. HCl (8.0 ml, 81.2 mmol) was added within 20 min at r.t. The mixture turned from a colorless soln. to a blue-green suspension. After stirring at r.t. for 10 min, 20% aq. NaOH (300 ml) was added at 0° within 30 min (pH > 10). The mixture was extracted with Et₂O (1 × 200 ml, 2 × 100 ml). The combined org. layers were washed with H₂O (2 × 50 ml) and brine (1 × 50 ml), and dried (MgSO₄). The solvent was evaporated *in vacuo*, and the residue was purified by CC (hexane) to give **11d** (3.77 g, 57%) and **12d** (2.44 g, 34%).

Data of 11d. Reddish-brown prisms. M.p. 93–94°. IR: 3497, 3382, 1517, 1365. ¹H-NMR (CDCl₃): 1.35 (s, 9 H); 1.41 (s, 9 H); 4.06 (br. s, 2 H); 6.85 (d, *J* = 8.6, 1 H); 7.22 (d, *J* = 8.6, 1 H). ¹³C-NMR (CDCl₃): 29.6; 30.8; 34.3; 35.2; 117.0; 127.4; 133.7; 136.4; 139.4; 141.8. EI-MS: 250 (*M*⁺, 76), 235 (100). Anal. calc. for C₁₄H₂₂N₂O₂ (250.30): C 67.17, H 8.86, N 11.19; found: C 67.23, H 9.17, N 11.15.

Data of 12d. Yellow prisms. M.p. 133–135°. IR: 3516, 3410, 1364. ¹H-NMR (CDCl₃): 1.38 (s, 18 H); 4.26 (br. s, 2 H); 6.67 (s, 1 H); 7.37 (s, 1 H). ¹³C-NMR (CDCl₃): 29.0; 30.5; 33.7; 35.0; 116.0; 124.5; 130.5; 141.8; 142.6; 147.3. FAB-MS: 251 ([*M* + *H*]⁺). Anal. calc. for C₁₄H₂₂N₂O₂ (250.30): C 67.17, H 8.86, N 11.19; found: C 67.27, H 9.16, N 11.15.

3,6-Di(tert-butyl)benzene-1,2-diamine (7d). To a suspension of Na₂S₂O₄ (13.9 g, 79.9 mmol) in H₂O (40 ml), a soln. of **11d** (2.00 g, 7.99 mmol) in EtOH (40 ml) was added at r.t., and the mixture was stirred at 75° for 1.5 h. The mixture turned from a yellow suspension to a colorless soln. After cooling to r.t., the soln. was concentrated *in vacuo* to ca. 40 ml and extracted with Et₂O (1 × 100 ml, 2 × 50 ml). The combined org. layers were washed with H₂O (2 × 30 ml) and brine (1 × 30 ml), and dried (MgSO₄). The solvent was evaporated *in vacuo* to give pale-yellow solid (1.78 g), which was purified by CC (hexane AcOEt 50:1) to give **7d** (1.72 g, 98%). Colorless prisms. M.p. 97–99°. IR: 3469, 3306. ¹H-NMR (CDCl₃): 1.43 (s, 18 H); 3.66 (br. s, 4 H); 6.77 (s, 2 H). ¹³C-NMR (CDCl₃): 30.1; 33.8; 116.8; 133.0; 134.1. HR-FAB-MS: 220.1940 ([*M* + *H*]⁺, C₁₄H₂₅N₂⁺; calc. 220.1939).

N,N'-(3,6-Di(tert-butyl)benzene-1,2-diyl)bis(1,3-dimethylimidazolidin-2-imine) (4d), N-[4,7-Di(tert-butyl)-1H-benzimidazol-2-yl]-N'-dimethylethane-1,2-diamine (14), and N-(2-{[4,7-Di(tert-butyl)-1H-benzimidazol-2-yl](methyl)amino}ethyl)-N,1,3-trimethylimidazolidin-2-iminium Chloride (15). To a soln. of **8** (9.01 g, 52.3 mmol) in CH₂Cl₂ (40 ml), Et₃N (17.0 ml, 122 mmol) was added at 0°. A soln. of **7d** (1.78 g, 8.08 mmol) in CH₂Cl₂ (40 ml) was added at r.t. within 2 h. The mixture was stirred at r.t. for 2 d. The solvent was evaporated *in vacuo*, and the residue was suspended in THF (100 ml). The mixture was filtered, and the precipitates were washed with THF (2 × 200 ml). The filtrate and the washings were combined, and the solvent was evaporated *in vacuo*. The residue was purified by CC (NH silica gel, hexane only → Et₂O only → CHCl₃/MeOH 20:1) to give **4d** (494 mg, 15%), **14** (596 mg, 23%), and **15** (523 mg, 14%).

Data of 4d. Colorless prisms. M.p. 210–211°. IR: 1739. ¹H-NMR (CDCl₃): 1.37 (s, 18 H); 2.61 (br. s, 12 H); 3.17 (br. s, 8 H); 6.77 (s, 2 H). ¹³C-NMR (CDCl₃): 29.7; 33.5; 34.9; 48.1; 116.1; 137.3; 140.8; 148.4. EI-MS: 412 (*M*⁺, 100), 355 (63). Anal. calc. for C₂₄H₄₀N₆ (412.60): C 69.86, H 9.77, N 20.37; found: C 69.76, H 10.13, N 20.35. Crystal structure of **4d**: CCDC No. 929039.

Data of 14. Colorless prisms. M.p. 183–185°. IR: 3312, 1698. ¹H-NMR (CDCl₃): 1.41 (s, 9 H); 1.57 (s, 9 H); 2.50 (s, 3 H); 2.91 (*t*, *J* = 4.4, 2 H); 3.24 (s, 3 H); 3.39 (*t*, *J* = 4.4, 2 H); 6.83 (*d*, *J* = 7.9, 1 H); 6.92 (*d*, *J* = 7.9, 1 H); 11.57 (s, 1 H). ¹³C-NMR (CDCl₃): 29.7; 29.9; 33.6; 34.7; 36.6; 38.7; 52.4; 52.9; 115.0; 116.3; 130.0; 131.7; 136.3; 142.6; 155.8. EI-MS: 316 (*M*⁺, 16), 272 (12), 259 (100), 244 (36). Anal. calc. for C₁₉H₃₂N₄ · 1/4 H₂O (327.50): C 71.09, H 10.21, N 17.45; found: C 71.11, H 10.43, N 17.50. Crystal structure of **14**: CCDC No. 929038.

Data of 15. Colorless plates. M.p. 133–135°. IR: 1733. ¹H-NMR (CDCl₃): 1.52 (s, 9 H); 1.55 (s, 9 H); 2.86 (s, 6 H); 3.16 (s, 3 H); 3.42 (s, 3 H); 3.73 (*t*, *J* = 4.4, 2 H); 3.89 (s, 4 H); 3.92 (*t*, *J* = 4.4, 2 H); 6.90 (*d*, *J* = 7.9, 1 H); 6.95 (*d*, *J* = 7.9, 1 H); 10.40 (s, 1 H). ¹³C-NMR (CDCl₃): 30.1; 30.3; 33.9; 34.7; 36.4; 38.4; 38.7; 48.4; 49.7; 50.4; 116.0; 117.1; 131.4; 131.5; 136.2; 141.4; 154.4; 163.8. FAB-MS: 413 ([*M* – Cl]⁺). Anal. calc. for C₂₄H₄₁ClN₆ · 2 H₂O (485.11): C 59.42, H 9.35, N 17.32; found: C 59.08, H 9.71, N 17.19. Crystal structure of **15**: CCDC No. 929037.

N,1,3-Trimethyl-N-phenylimidazolidin-2-iminium Iodide (23e). To a soln. of **24e** [9] (321 mg, 1.70 mmol) in MeCN (2.0 ml), MeI (0.24 ml, 3.70 mmol) was added at r.t., and the mixture was stirred at r.t., for 2 h. The solvent was evaporated *in vacuo* to give **23e** (496 mg, 88%). Pale-yellow oil. IR:

1579. $^1\text{H-NMR}$ (CDCl_3): 2.96 (s, 6 H); 3.60 (s, 3 H); 4.11 (s, 4 H); 7.20 (d, $J = 7.5$, 1 H); 7.24 (d, $J = 7.6$, 2 H); 7.43 (dd, $J = 7.6$, 7.5, 2 H).

Bis(dimethylamino)-N-methyl-N-phenylmethaniminium Iodide (23f). To a soln. of **24f** (1.01 g, 5.27 mmol) in MeCN (5 ml), MeI (0.75 ml, 11.8 mmol) was added at r.t., and the mixture was stirred at r.t. for 1.5 h. The solvent was evaporated *in vacuo* to give pale-yellow solid, which was dissolved in acetone. By addition of AcOEt, colorless solids precipitated were collected by filtration to give **23f** (1.70 g, 98%). Colorless prisms. M.p. 214–216° ([14]: 133°⁴). IR: 1618. $^1\text{H-NMR}$ (CDCl_3): 2.92 (s, 6 H); 3.23 (s, 6 H); 3.55 (s, 3 H); 7.10 (d, $J = 7.9$, 2 H); 7.29 (d, $J = 7.6$, 1 H); 7.46 (dd, $J = 7.9$, 7.6, 2 H).

N,1,3-Trimethyl-N-phenylimidazolidin-2-iminium Hexafluorophosphate (19e). To a soln. of **23e** (1.71 g, 4.52 mmol) in MeOH (1.0 ml), a soln. of NH_4PF_6 (2.21 g, 12.9 mmol) in H_2O (1.5 ml) was added at r.t. Colorless precipitates formed. After addition of MeOH (3 ml), the precipitates were collected by filtration and recrystallized from AcOEt/MeOH 1:5 to give **19e** (427 mg, 27%). Colorless prisms. M.p. 112–113°. IR: 1589. $^1\text{H-NMR}$ ($(\text{D}_6)\text{acetone}$): 3.01 (s, 6 H); 3.59 (s, 3 H); 4.07 (s, 4 H); 7.24 (dd, $J = 7.3$, 7.3, 1 H); 7.34 (d, $J = 8.3$, 2 H); 7.46 (dd, $J = 8.3$, 7.3, 2 H). $^{13}\text{C-NMR}$ ($(\text{D}_6)\text{acetone}$): 34.0; 49.0; 123.5; 126.4; 129.7; 136.4; 157.0. FAB-MS: 204 ($[M - \text{PF}_6]^+$). Anal. calc. for $\text{C}_{12}\text{H}_{18}\text{F}_6\text{N}_3\text{P}$ (349.26): C 41.27, H 5.19, N 12.03; found: C 41.18, H 5.11, N 11.94. Crystal structure of **19e**: CCDC No. 929032.

2-(Dimethylamino)-1,3-dimethyl-1H-3,1-benzimidazol-3-ium Hexafluorophosphate (28). To a soln. of **27** (496 mg, 3.64 mmol) and Et_3N (2.20 ml, 15.8 mmol) in MeCN (1.7 ml), a soln. of **25** (1.23 g, 7.21 mmol) in MeCN (8.5 ml) was added at 0°, and the mixture was stirred at r.t. for 5 h. The solvent was evaporated *in vacuo* to give a purple oil (1.48 g, 99%). An aliquot (523 mg, 1.29 mmol) was treated with NH_4PF_6 (666 mg, 4.09 mmol) to give purple solid, which was washed with H_2O (5×2 ml), dried, and recrystallized from acetone/AcOEt 1:1 to give **29** (163 mg, 38%). Purple needles. M.p. 220–222°. IR: 1546. $^1\text{H-NMR}$ ($(\text{D}_6)\text{acetone}$): 3.49 (s, 6 H); 4.00 (s, 6 H); 7.52–7.55 (m, 2 H); 7.70–7.73 (m, 2 H). $^{13}\text{C-NMR}$ ($(\text{D}_6)\text{acetone}$): 33.0; 41.8; 112.2; 126.0; 132.1; 154.4. EI-MS: 190 ($[M - \text{PF}_6]^+$). Anal. calc. for $\text{C}_{11}\text{H}_{16}\text{F}_6\text{N}_3\text{P}$ (335.23): C 39.41, H 4.81, N 12.53; found: C 39.36, H 4.65, N 12.33.

N-(2-[[Bis(dimethylamino)methylidene]amino]phenyl)[bis(dimethylamino)]-N-methylmethaniminium Iodide (32). A mixture of **31** (302 mg, 0.99 mmol) and MeI (0.14 ml, 2.21 mmol) in MeCN (1.5 ml) was stirred at r.t. for 2 h. The solvent was evaporated *in vacuo* to give pale-yellow solid, which was recrystallized from acetone to give **32** (332 mg, 74%). Colorless prisms. M.p. 214–216°. IR: 1543. $^1\text{H-NMR}$ ($(\text{D}_6)\text{acetone}$): 2.71 (s, 12 H); 3.10 (s, 12 H); 3.41 (s, 3 H); 6.56 (d, $J = 8.0$, 1 H); 6.94 (dd, $J = 7.7$, 7.5, 1 H); 7.13 (dd, $J = 8.0$, 7.7, 1 H); 7.52 (br. s, 1 H). $^{13}\text{C-NMR}$ ($(\text{D}_6)\text{acetone}$): 40.1; 41.2; 41.6; 121.4; 122.9; 126.4; 128.0; 135.1; 147.5; 161.2; 164.4. EI-MS: 319 ($[M - \text{I}]^+$). Anal. calc. for $\text{C}_{16}\text{H}_{29}\text{N}_6$ (432.35): C 45.38, H 7.03, N 18.68; found: C 45.32, H 6.92, N 18.53.

N-(2-[[Bis(dimethylamino)methylidene]ammonio]phenyl)[bis(dimethylamino)]-N-methylmethaniminium Dihexafluorophosphate (21). A mixture of **32** (753 mg, 1.69 mmol) and NH_4PF_6 (839 mg, 5.14 mmol) in H_2O (0.5 ml) and a small portion of acetone was stirred at r.t. for 10 min. By the addition of AcOEt, precipitates formed was filtered and repeatedly washed with acetone. After combining the filtrate and washings, the mixture was evaporated *in vacuo*. The residue was recrystallized from acetone to give **21** (658 mg, 64%). Colorless prisms. M.p. 246–247.5°. IR: 1616. $^1\text{H-NMR}$ ($(\text{D}_6)\text{acetone}$): 2.71–3.23 (m, 24 H); 3.50 (s, 3 H); 7.27–7.30 (m, 2 H); 7.35 (dd, $J = 7.9$, 7.9, 1 H); 7.52 (dd, $J = 7.9$, 7.9, 1 H); 8.43 (s, 1 H). $^{13}\text{C-NMR}$ ($(\text{D}_6)\text{acetone}$): 38.8; 41.0; 122.8; 127.5; 128.5; 130.5; 132.7; 133.1; 158.8; 164.5. FAB-MS: 465 ($[M - \text{PF}_6]^+$). Anal. calc. for $\text{C}_{17}\text{H}_{32}\text{F}_{12}\text{N}_6\text{P}_2$ (610.41): C 33.45, H 5.28, N 13.77; found: C 33.45, H 5.24, N 13.77. Crystal structure of **21**: CCDC No. 929033.

1-(1,3-Dimethylimidazolidin-2-ylidene)-2-[(methyl)[2-(trimethylammonio)ethyl]amino]-4,7-diphenyl-1H-3,1-benzimidazol-1-ium Diiodide (33). To a soln. of **4b** (296 mg, 0.66 mmol) in MeCN (2.0 ml), MeI (0.13 ml, 2.05 mmol) was added at r.t., and the mixture was stirred at r.t. for 4.5 h. The solvent was evaporated *in vacuo*, and the residue was recrystallized from AcOEt/MeOH 1:1 to give **33** (200 mg, 42%). Colorless prisms. M.p. 266–268°. IR: 1647, 1601. $^1\text{H-NMR}$ (CD_3OD): 2.91 (s, 6 H); 3.10 (s, 3 H); 3.24 (s, 9 H); 3.28–3.34 (m, 2 H); 3.84 (diffused t, $J = 7.4$, 2 H); 4.05–4.13 (m, 4 H); 7.14 (d, $J = 7.9$, 1 H); 7.38 (diffused t, $J = 7.4$, 1 H); 7.42 (diffused d, $J = 7.0$, 1 H); 7.48 (diffused t, $J = 8.6$, 1 H); 7.53 (d, $J = 7.9$, 1 H); 7.58 (diffused t, $J = 7.4$, 1 H); 7.67 (diffused t, $J = 7.4$, 1 H); 7.94 (diffused d, $J = 7.4$, 1 H). $^{13}\text{C-NMR}$

⁴) The crystals may show dimorphism.

(CD₃OD): 34.5; 39.1; 54.25; 54.29; 54.33; 63.0; 125.3; 126.2; 126.3; 128.8; 129.4; 129.9; 130.2; 130.3; 130.4; 131.6; 131.9; 137.8; 139.1; 141.7; 154.5; 156.0. FAB-MS: 609 ($[M - I]^+$), 241 ($[M - 2I]^{2+}$). Anal. calc. for C₃₀H₃₈I₂N₆ (736.47): C 48.93, H 5.20, N 11.41; found: C 48.72, H 5.05, N 11.29. Crystal structure of **33**: CCDC No. 967507.

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