Synthesis of Tripodal and Hexapodal Pyrazole- and Benzimidazole-Bearing Compounds

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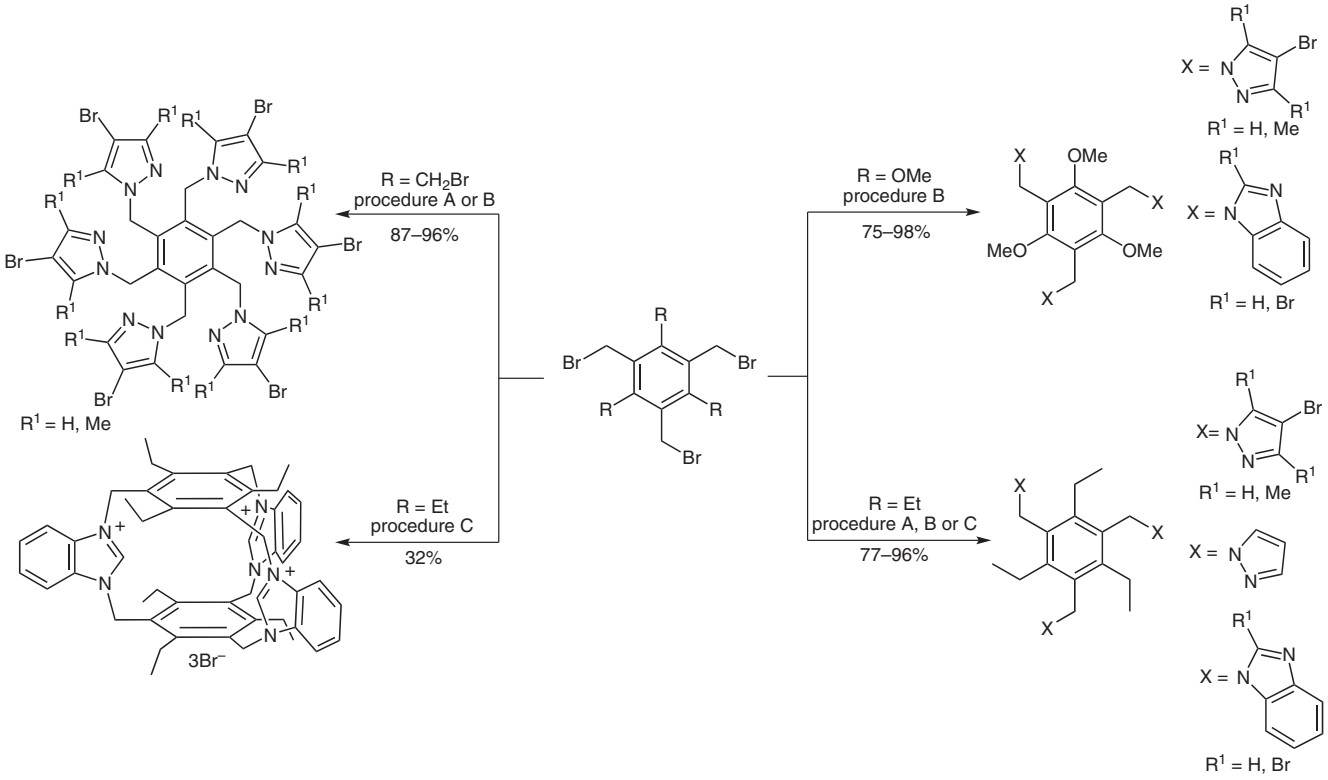
Received: 30.04.2013; Accepted after revision: 11.07.2013

PSP No 261

Abstract: The syntheses of eight new tripodal and hexapodal benzimidazole- and pyrazole-bearing compounds, which are all potentially applicable for use as artificial receptors, are described. The prepared compounds contain either bromo-substituted heteroaromatic rings, able to participate in halogen-bonding interactions, or their analogues lacking the bromo substituents. Furthermore, the preparation of a new tris-benzimidazolium cage is included in this work. All used practical synthetic procedures are facilely accomplishable and provide the products in good to excellent yields. In addition, slightly modified, simplified synthetic procedures for five known tripodal compounds, which lead to better yields than those previously reported, are also detailed.

Key words: triethylbenzene scaffold, trimethoxybenzene scaffold, tripodal receptors, hexapodal receptors, cyclophanes



Scheme 1 Procedures for the practical preparation of tripodal and hexapodal pyrazole- and benzimidazole-bearing compounds

Introduction

The design and development of artificial tripodal receptors for the selective recognition of cations, anions[1a,b] and neutral molecules[1c,d] represents an active area in supramolecular chemistry. Compounds bearing heterocyclic recognition sites such as benzimidazole and pyrazole units are reported to be effective in the molecular recognition of ions.[1a,2–4] Moreover, our group has shown that pyrazole- and benzimidazole-based receptors are also useful in carbohydrate recognition for both neutral[5a] and anionic substrates.[5b] It should also be noted that a hexapodal receptor bearing pyrazole units is reported to be effective in the recognition of ion pairs.[6]

SYNTHESIS 2013, 45, 3341–3348
Advanced online publication: 29.08.2013
DOI: 10.1055/s-0033-1338518; Art ID: SS-2013-Z0324-PSP

In this paper, we describe the syntheses of eight new benzimidazole- and pyrazole-based compounds that enforce tripodal or hexapodal topologies (compounds **1**–**4**, **6**, **8**, **12** and **13**; see Figure 1 and Scheme 1) and which are all potentially applicable for use as artificial receptors. The prepared compounds contain either bromo-substituted heteroaromatic rings, able to participate in halogen-bonding interactions, or their analogues lacking the bromo substituents. The tripodal compounds are based on the trimethoxybenzene or triethylbenzene scaffold, both of which are widely used as building blocks for supramolecular systems. To provide a complete description of the preparation of the tripodal bromo-substituted derivatives and their non-brominated analogues, slightly modified synthetic procedures for the known compounds **5**, **7**, **9**–**11** are also included. In the case of the synthesis of compound **7**, we observed the formation of the previously unreported trisbenzimidazolium cage **14** [prepared as the tribromide salt **14a** and the tris(hexafluorophosphate) salt **14b**], which is also part of this work.

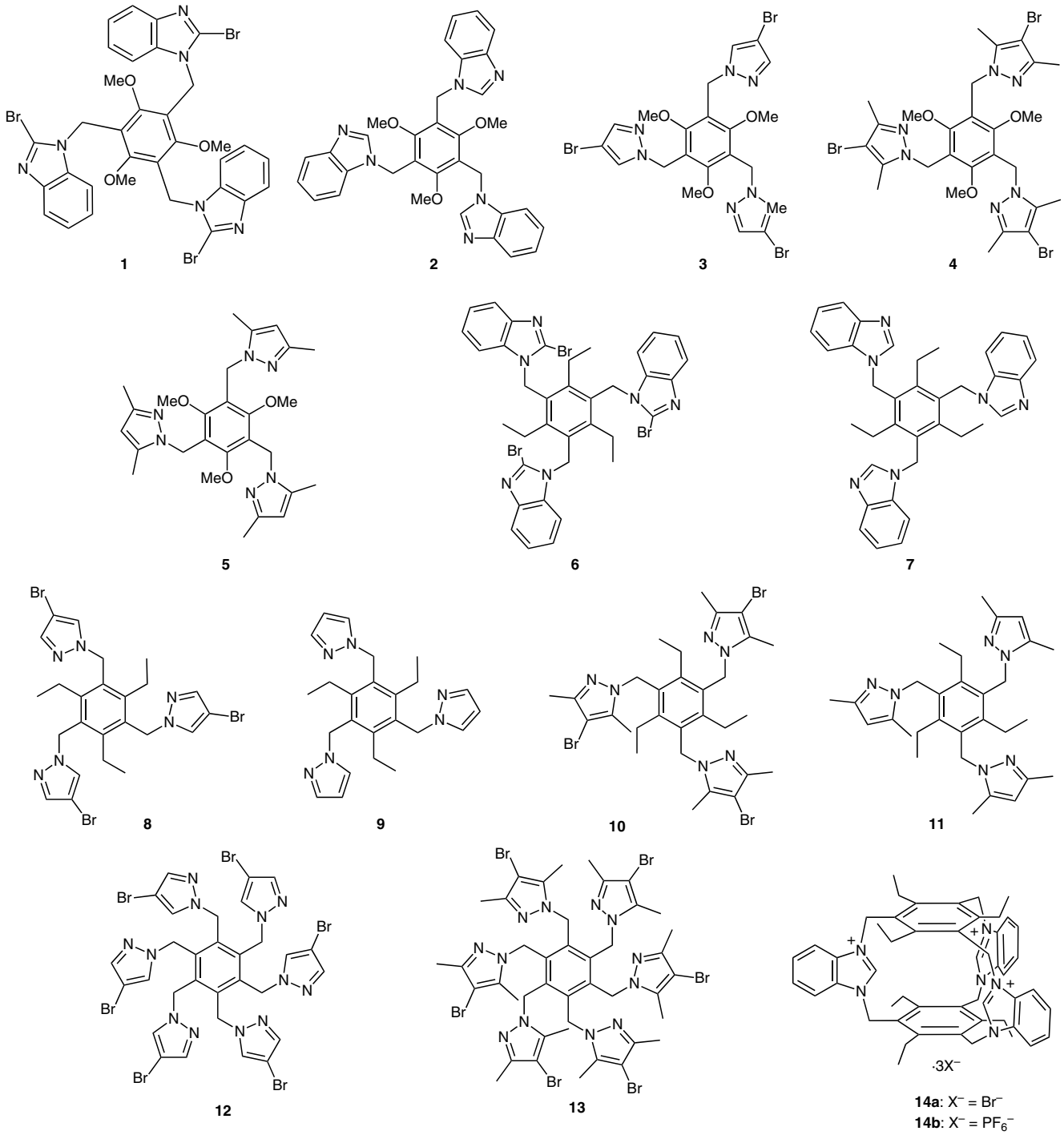


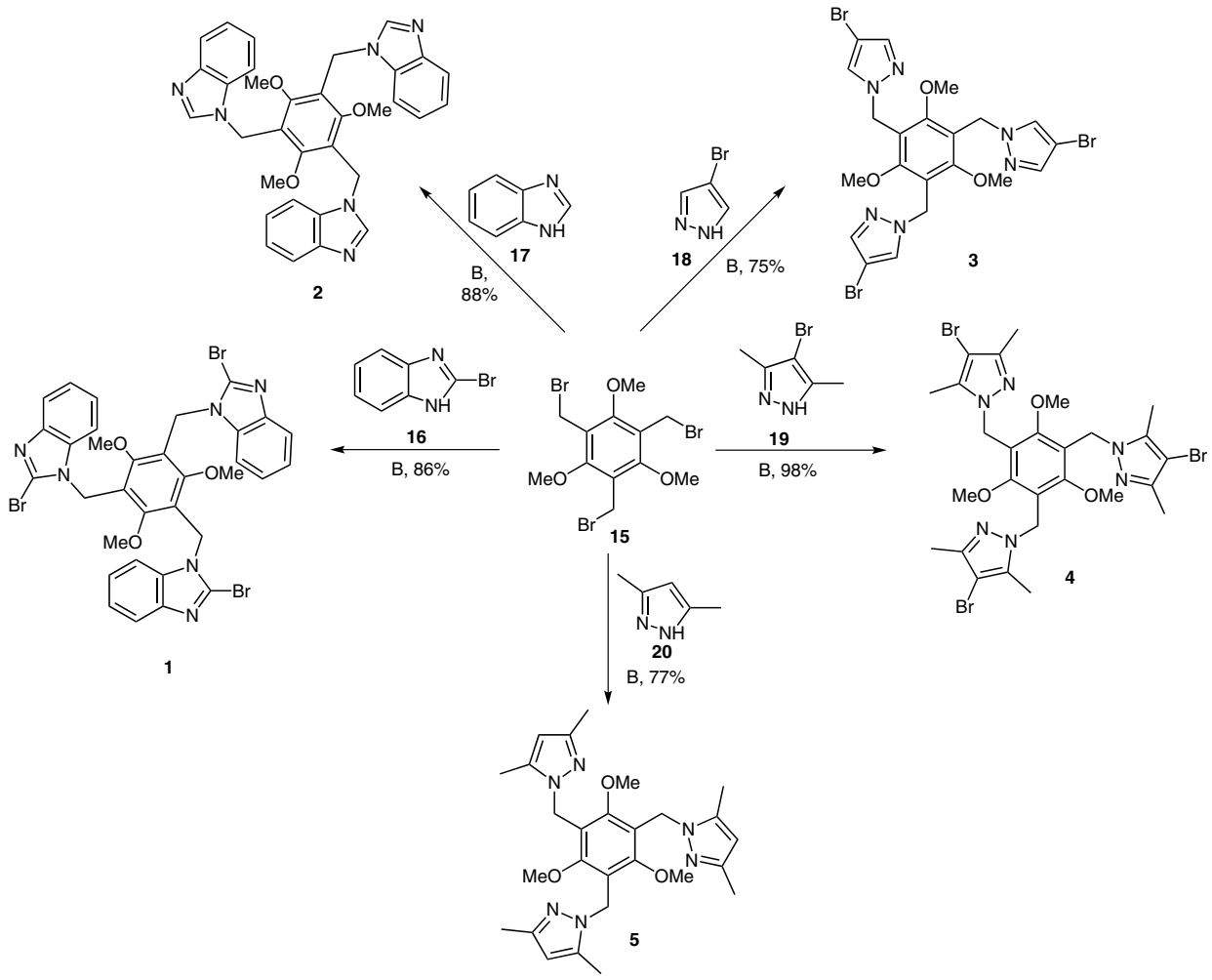
Figure 1 Structures of the benzimidazole- and pyrazole-bearing compounds described in this work

The pyrazole-containing compounds **9**–**11** are reported to be selective receptors for ammonium ions[2a,b] and have been used as building blocks in the self-assembly of a three-dimensional cage,[7] whereas compound **5** was described as an intermediate in the synthesis of a phloroglucinol model compound.[8] The benzimidazole-bearing compound **7** has been described as an anion receptor with perchlorate binding preference.[2c] These previously reported, interesting applications show the potential of these structurally rather simple molecules and clarifies the need for facile syntheses of related compounds.

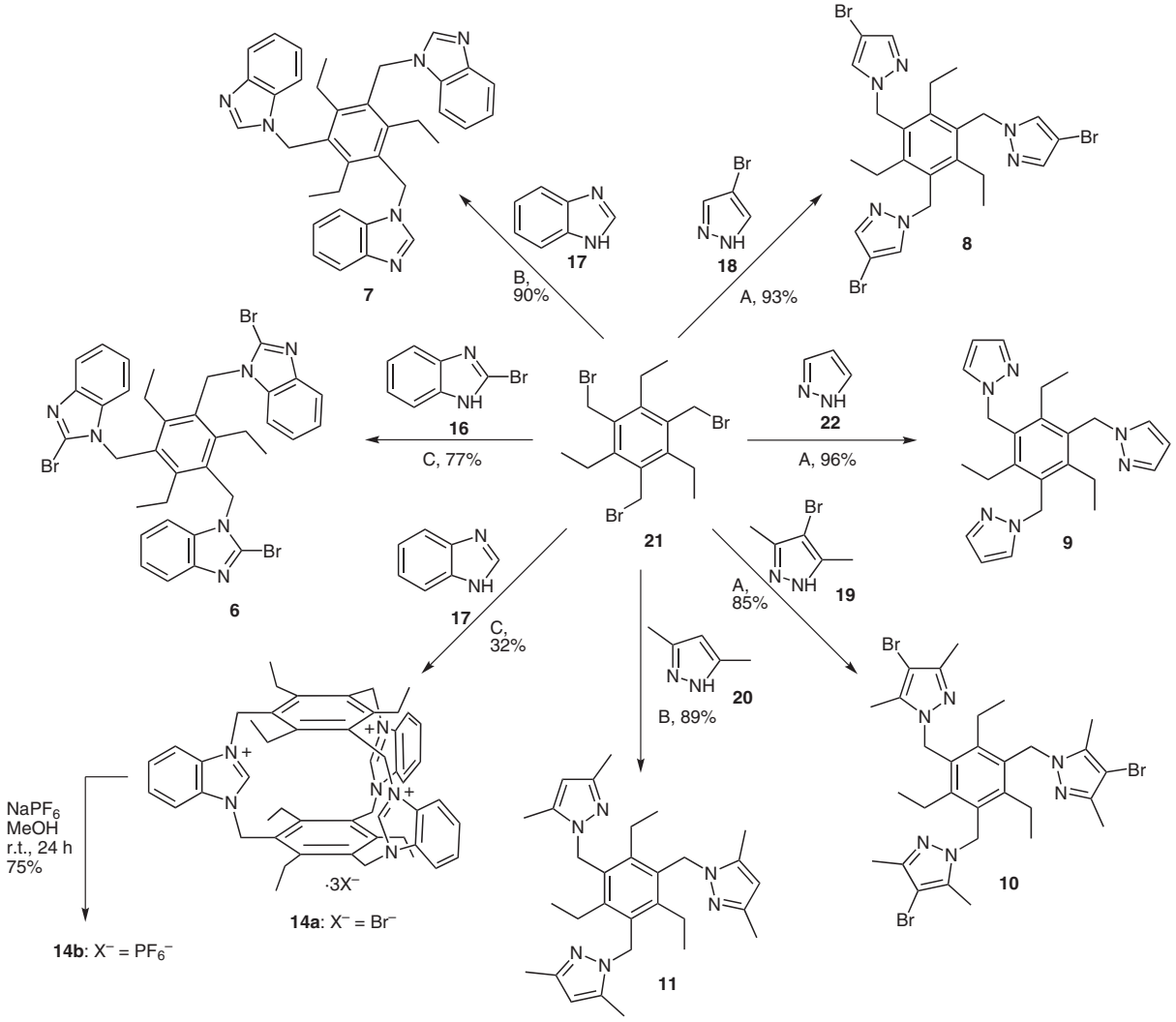
Scope and Limitations

The tripodal compounds **1**–**11**, containing a trimethoxybenzene- or triethylbenzene-derived core, were prepared via reactions of 1,3,5-tris(bromomethyl)-2,4,6-trimethoxybenzene (**15**)[9] or 1,3,5-tris(bromomethyl)-2,4,6-triethylbenzene (**21**)[10] with commercially available benzimidazole and pyrazole derivatives, such as 2-bromo-1*H*-benzimidazole (**16**), 1*H*-benzimidazole (**17**), 4-bromo-1*H*-pyrazole (**18**), 4-bromo-3,5-dimethyl-1*H*-pyrazole (**19**), 3,5-dimethyl-1*H*-pyrazole (**20**) and 1*H*-pyrazole (**22**) (see Scheme 2 and Scheme 3). The reaction of hexakis(bromomethyl)benzene (**23**)[11] with the bromo-substituted pyrazoles **18** and **19** gave the hexapodal compounds **12** and **13**, respectively (see Scheme 4).

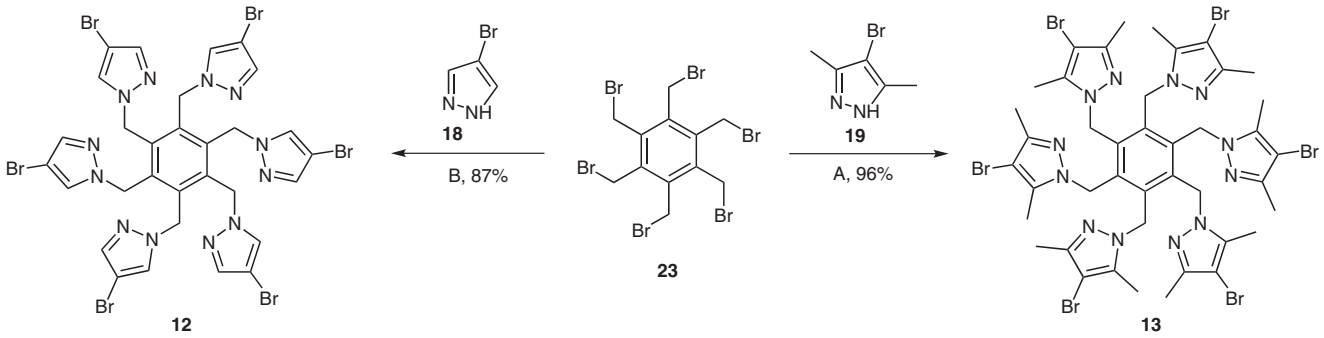
For the syntheses of compounds **1**–**13**, we tested three methods. In procedure A, adopted from a previously described synthesis of hexakis[(1*H*-pyrazol-1-yl)methyl]benzene,[6] the employed benzimidazole or pyrazole was deprotonated with finely ground sodium hydroxide in *N*,*N*-dimethylformamide (DMF) before reaction with the corresponding bromomethyl-substituted benzene compound (**15**, **21** or **23**). The reaction mixture was stirred under mild heating, then poured into ice water. While unreacted starting materials remain in the water/DMF mixture, the desired products precipitate as fluffy solids and can be easily collected by filtration with a Büchner funnel (to complete the precipitation, the mixtures can be kept in a fridge overnight). To free the product from DMF, the filter cake has to be washed thoroughly with water and then dried in a desiccator. With this procedure, the triethylbenzene-based compounds **8**–**10** and the hexapodal derivative **13** were synthesized in very good to excellent



Scheme 2 Synthesis of the trimethoxybenzene-based compounds. *Reagents and conditions*: (B) NaH (4.5 equiv), MeCN, r.t.



Scheme 3 Syntheses of the triethylbenzene-based compounds. *Reagents and conditions*: (A) NaOH (4 equiv), DMF, 70 °C; (B) NaH (4.5 equiv), MeCN, r.t.; (C) DIPEA (3.3 equiv), THF, MeCN, r.t.



Scheme 4 Syntheses of the pyrazole-bearing hexapodal compounds **12** and **13**. *Reagents and conditions*: (A) NaOH (7 equiv), DMF, 70 °C; (B) NaH (6.6 equiv), MeCN, r.t.

yields. The yield of **9** was 96%, raised from the literature yields of 60%[7] and 65%,[2a,b] while **10** was obtained in 85% yield in a single step, using the commercially available 4-bromo-3,5-dimethyl-1*H*-pyrazole (**19**), compared to the earlier 71% yield in two steps.[2a,b] Compounds **8** and **13** have not been previously reported. It is notable that none of the trimethoxybenzene-containing compounds could be synthesized in satisfactory yields with this method.

Procedure B revealed the most general application spectrum. It was possible to synthesize the tripodal triethylbenzene- and trimethoxybenzene-based compounds **1**–**5**, **7** and **11**, as well as the hexapodal compound **12**, in good

to excellent yields. With procedure B, the yields of the known compounds **5**, **7** and **11** could be improved from 60% to 77% for **5**,[8] from 85% to 90% for **7**,[2c] and from 73% to 89% for **11**.[2a,b] This procedure is a modified version of the procedure previously described for the synthesis of **5** and **9**–**11**.[2a,b,8] The deprotonation of the heterocyclic unit with sodium hydride was undertaken in anhydrous acetonitrile before the corresponding bromomethyl-substituted benzene derivative was added, and the mixture was stirred at room temperature under nitrogen (in the synthesis reported previously, THF[2a,b] or DMF[8] was used as the solvent). Then, the reaction was quenched by the addition of water, the mixture was extracted with chloroform and the product was purified by flash chromatography on silica gel using a chloroform–methanol mixture as the eluent. In the case of **2**, the addition of hexane to the eluent was necessary for the complete separation from the remaining 1*H*-benzimidazole (**17**).

The last method, procedure C, employs *N*,*N*-diisopropylethylamine (DIPEA) as the base and tetrahydrofuran–acetonitrile as the solvent. This procedure emerged to be the most facile one for the synthesis of compound **6**, because of the very easy workup, resulting from the precipitation of the desired compound from the employed solvent mixture during the reaction. The workup consisted only of collection of the solid by filtration and washing with tetrahydrofuran. Although the yield of 77% is at the lower end of the scale relative to other yields in this work, the quick workup along with no need for further chromatographic purification (such as in procedure B) makes this route to **6** notable.

Interestingly, if procedure C is used for the preparation of **7**, the expected tripodal compound is not recovered as the precipitate; rather, the reaction provided the corresponding trisbenzimidazolium cage as its tribromide salt **14a**, which was converted into the corresponding tris(hexafluorophosphate) salt **14b**. Closely related cage compounds have been reported as selective anion receptors[12] and, as their copper(I) and silver(I) complexes,[13] as N-heterocyclic carbene derivatives.

In summary, we have reported three possible practical synthetic procedures for the preparation of new tripodal trimethoxybenzene-based (**1**–**4**) and triethylbenzene-based (**6**, **8**) compounds, as well as new hexapodal compounds (**12**, **13**), bearing either bromo-substituted benzimidazole/pyrazole units or their analogues lacking the bromo substituents. In addition, the preparation of the new trisbenzimidazolium cage **14** [as the tribromide and the tris(hexafluorophosphate) salts **14a**,**b**] was included in this work. All used procedures are facilely accomplishable and provided the desired products in good to excellent yields. For the known compounds **5**, **7** and **9**–**11**, we have suggested slightly modified syntheses that simplify the reaction procedures and lead to better yields than those previously reported. The scale-up of the presented procedures to a gram scale can be performed with ease. Reactions conducted with a doubled or tripled amount of the starting materials provided the desired compounds in similarly high yields. The prepared compounds are able to participate in multiple noncovalent interactions, including halogen-bonding interactions, and are all potentially applicable for use as artificial receptors.

MeCN and THF were purchased as 'AcroSeal Extra Dry Solvents' from Acros Organics. DMF was dried over CaH_2 and distilled under N_2 atmosphere before use. All other chemicals were commercially available of reagent grade (Acros Organics, Sigma Aldrich or ABCR) and used without further purification, unless otherwise noted. Analytical TLC was performed on commercial Merck plates coated with silica gel (TLC Silica Gel 60 F_{254}) and the silica gel used for flash chromatography was Merck Kieselgel 60. Melting points were measured on a Mettler Toledo MP50 Melting Point System apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were determined for solutions in $CDCl_3$ or DMSO-d_6 with TMS, $\delta = 0.00$ ppm as an internal standard on Bruker DRX-400 ([^{1}H]: 399.97 MHz, [^{13}C]: 100.57; at 25 °C), Bruker AV III-400 ([^{1}H]: 400.40 MHz, [^{13}C]: 100.68 MHz; at 25 °C) and Bruker DRX-500 ([^{1}H]: 500.13 MHz, [^{13}C]: 125.76 MHz; at 22 °C) instruments. HRMS data were measured on Finnigan MAT 95x (EI-MS and EI-HRMS) and Finnigan 95XL Thermo (ESI-HRMS) mass spectrometers. Elemental analyses were determined on an Elementar Analysesysteme Vario Micro Cube.

Compounds 8–10 and 13; General Procedure (Procedure A)

The corresponding pyrazole derivative **18**, **19** or **22** (4 or 7 equiv) was dissolved in alkaline DMF [containing NaOH (4 or 7 equiv)] and the solution was stirred for 30 min at r.t. The bromomethyl-substituted benzene derivative **21** or **23** (1 equiv) was added and the reaction mixture was stirred for 24–48 h at 70 °C. The solution was cooled to r.t., then poured into ice water (50 mL), and the resulting precipitate was collected by filtration, washed thoroughly with H_2O (3 × 15 mL) and dried in a desiccator.

1,3,5-Tris[(4-bromo-1*H*-pyrazol-1-yl)methyl]-2,4,6-triethylbenzene (8)

The reaction of compound **21** (200 mg, 0.45 mmol) with 4-bromo-1*H*-pyrazole (**18**; 267 mg, 1.81 mmol) in DMF [5 mL, containing NaOH (73 mg, 1.81 mmol)] afforded compound **8** as a white solid (reaction time: 24 h); yield: 270 mg (93%); mp 144 °C.

^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.95$ (t, $J = 7.6$ Hz, 9 H), 2.72 (q, $J = 7.6$ Hz, 6 H), 5.40 (s, 6 H), 7.06 (s, 3 H), 7.50 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 15.16$, 23.48, 50.31, 93.27, 128.35, 130.03, 140.12, 146.34.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{24}H_{28}Br_3N_6$: 638.99007; found: 638.99060.

Anal. Calcd for $C_{24}H_{27}Br_3N_6$: C, 45.10; H, 4.26; N, 13.15. Found: C, 45.30; H, 4.13; N, 13.11.

1,3,5-Tris[(1*H*-pyrazol-1-yl)methyl]-2,4,6-triethylbenzene (9)

The reaction of compound **21** (810 mg, 1.84 mmol) with 1*H*-pyrazole (**22**; 500 mg, 7.34 mmol) in DMF [10 mL, containing NaOH (294 mg, 7.34 mmol)] afforded compound **9** as a white solid (reaction time: 24 h); yield: 710 mg (96%); mp 125 °C.

^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.96$ (t, $J = 7.6$ Hz, 9 H), 2.72 (q, $J = 7.6$ Hz, 6 H), 5.45 (s, 6 H), 6.20 (t, $J = 2.0$ Hz, 3 H), 6.98 (d, $J = 2.2$ Hz, 3 H), 7.55 (d, $J = 1.6$ Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 15.18$, 23.31, 49.59, 105.57, 127.81, 130.44, 139.48, 146.05.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{24}H_{31}N_6$: 403.26047; found: 403.26069.

Anal. Calcd for $C_{24}H_{30}N_6$: C, 71.61; H, 7.51; N, 20.88. Found: C, 71.36; H, 7.59; N, 20.92.

1,3,5-Tris[(4-bromo-3,5-dimethyl-1*H*-pyrazol-1-yl)methyl]-2,4,6-triethylbenzene (10)

The reaction of compound **21** (500 mg, 1.13 mmol) with 4-bromo-3,5-dimethyl-1*H*-pyrazole (**19**; 794 mg, 4.53 mmol) in DMF [10 mL, containing NaOH (181 mg, 4.53 mmol)] afforded compound **10** as a white solid (reaction time: 24 h); yield: 697 mg (85%); mp 156 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 7.5 Hz, 9 H), 2.12 (s, 9 H), 2.15 (s, 9 H), 2.71 (q, *J* = 7.5 Hz, 6 H), 5.19 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.46, 12.27, 14.63, 23.72, 48.07, 94.46, 130.00, 137.06, 145.38, 145.79.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{30}H_{40}Br_3N_6$: 723.08402; found: 723.08420.

Anal. Calcd for $C_{30}H_{39}Br_3N_6$: C, 49.81; H, 5.43; N, 11.62. Found: C, 49.45; H, 5.39; N, 11.94.

Hexakis[(4-bromo-3,5-dimethyl-1*H*-pyrazol-1-yl)methyl]benzene (13)

The reaction of compound **23** (200 mg, 0.31 mmol) with 4-bromo-3,5-dimethyl-1*H*-pyrazole (**19**; 386 mg, 2.20 mmol) in DMF [5 mL, containing NaOH (88 mg, 2.20 mmol)] afforded compound **13** as a white solid (reaction time: 48 h); yield: 365 mg (96%); mp 289 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.98 (s, 18 H), 2.04 (s, 18 H), 5.24 (s, 12 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.21, 12.26, 49.23, 94.52, 136.42, 137.13, 145.75.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{42}H_{49}Br_6N_{12}$: 1200.92434; found: 1200.92419.

Anal. Calcd for $C_{42}H_{48}Br_6N_{12}$: C, 42.03; H, 4.03; N, 14.00. Found: C, 42.16; H, 4.13; N, 13.89.

Compounds 1–5, 7, 11 and 12; General Procedure (Procedure B)

To the corresponding benzimidazole or pyrazole **16**–**20** (4.5 or 6.6 equiv), dissolved under N_2 atmosphere in anhyd MeCN, NaH (60% dispersion in mineral oil, 4.5 or 6.6 equiv) was added and the mixture was stirred for 30 min at r.t. Then, the bromomethyl-substituted benzene derivative **15**, **21** or **23** (1 equiv) was added and the reaction mixture was stirred for up to 5 d at r.t. under N_2 atmosphere. The reaction was quenched with H_2O (10 mL) and extracted with $CHCl_3$ (3 × 10 mL). The organic layers were combined, dried over $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography using $CHCl_3$–MeOH or $CHCl_3$–MeOH–hexane as the eluent.

1,3,5-Tris[(2-bromo-1*H*-benzimidazol-1-yl)methyl]-2,4,6-trimethoxybenzene (1)

The reaction of compound **15** (200 mg, 0.45 mmol) with 2-bromo-1*H*-benzimidazole (**16**; 397 mg, 2.01 mmol) and NaH (60% dispersion in mineral oil; 80 mg, 2.01 mmol) in MeCN (5 mL) afforded compound **1** as a white solid (reaction time: 3 d; column chromatography: $CHCl_3$–MeOH, 15:1 v/v, R_f = 0.53); yield: 306 mg (86%); mp >160 °C (dec).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.61 (s, 9 H), 5.35 (s, 6 H), 6.44 (d, *J* = 8.1 Hz, 3 H), 6.50 (ddd, *J* = 1.2, 7.2, 8.2 Hz, 3 H), 7.09 (ddd, *J* = 1.2, 7.2, 8.1 Hz, 3 H), 7.62 (d, *J* = 8.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 39.93, 63.97, 109.80, 119.15, 119.42, 122.46, 123.33, 130.47, 134.70, 142.81, 160.35.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{33}H_{28}Br_3N_6O_3$: 796.97352; found: 796.97364.

Anal. Calcd for $C_{33}H_{27}Br_3N_6O_3$: C, 49.84; H, 3.42; N, 10.57. Found: C, 49.90; H, 3.34; N, 10.30.

1,3,5-Tris[(1*H*-benzimidazol-1-yl)methyl]-2,4,6-trimethoxybenzene (2)

The reaction of compound **15** (200 mg, 0.45 mmol) with 1*H*-benzimidazole (**17**; 238 mg, 2.01 mmol) and NaH (60% dispersion in mineral oil; 80 mg, 2.01 mmol) in MeCN (5 mL) afforded compound **2** as a white solid (reaction time: 3 d; column chromatography: $CHCl_3$–MeOH–hexane, 1:1:1 v/v/v, R_f = 0.47); yield: 220 mg (88%); mp >194 °C (dec).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.51 (s, 9 H), 5.31 (s, 6 H), 7.25–7.30 (m, 6 H), 7.45–7.51 (m, 3 H), 7.76–7.82 (m, 3 H), 7.93 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 38.43, 63.40, 109.85, 120.41, 120.46, 122.39, 123.29, 133.63, 143.08, 143.64, 160.36.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{33}H_{31}N_6O_3$: 559.24522; found: 559.24518.

Anal. Calcd for $C_{33}H_{30}N_6O_3$: C, 70.95; H, 5.41; N, 15.04. Found: C, 70.65; H, 5.39; N, 14.93.

1,3,5-Tris[(4-bromo-1*H*-pyrazol-1-yl)methyl]-2,4,6-trimethoxybenzene (3)

The reaction of compound **15** (300 mg, 0.67 mmol) with 4-bromo-1*H*-pyrazole (**18**; 444 mg, 3.02 mmol) and NaH (60% dispersion in mineral oil; 121 mg, 3.02 mmol) in MeCN (10 mL) afforded compound **3** as a white solid (reaction time: 3 d; column chromatography: $CHCl_3$–MeOH, 20:1 v/v, R_f = 0.56); yield: 325 mg (75%); mp 115 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.64 (s, 9 H), 5.31 (s, 6 H), 7.42 (s, 3 H), 7.50 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 46.18, 62.88, 93.27, 120.29, 129.68, 139.59, 160.59.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{22}Br_3N_6O_3$: 644.92785; found: 644.92774.

Anal. Calcd for $C_{21}H_{21}Br_3N_6O_3$: C, 39.10; H, 3.28; N, 13.03. Found: C, 39.16; H, 3.15; N, 12.84.

1,3,5-Tris[(4-bromo-3,5-dimethyl-1*H*-pyrazol-1-yl)methyl]-2,4,6-trimethoxybenzene (4)

The reaction of compound **15** (300 mg, 0.67 mmol) with 4-bromo-3,5-dimethyl-1*H*-pyrazole (**19**; 529 mg, 3.02 mmol) and NaH (60% dispersion in mineral oil; 121 mg, 3.02 mmol) in MeCN (10 mL) afforded compound **4** as a white solid (reaction time: 4 d; column chromatography: $CHCl_3$–MeOH, 10:1 v/v, R_f = 0.76); yield: 480 mg (98%); mp 195 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.14 (s, 9 H), 2.24 (s, 9 H), 3.48 (s, 9 H), 5.13 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.34, 12.34, 43.60, 62.33, 93.92, 119.92, 137.44, 145.54, 160.00.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{27}H_{34}Br_3N_6O_3$: 729.02180; found: 729.02325.

Anal. Calcd for $C_{27}H_{33}Br_3N_6O_3$: C, 44.47; H, 4.56; N, 11.52. Found: C, 44.29; H, 4.54; N, 11.33.

1,3,5-Tris[(3,5-dimethyl-1*H*-pyrazol-1-yl)methyl]-2,4,6-trimethoxybenzene (5)

The reaction of compound **15** (300 mg, 0.67 mmol) with 3,5-dimethyl-1*H*-pyrazole (**20**; 290 mg, 3.02 mmol) and NaH (60% dispersion in mineral oil; 121 mg, 3.02 mmol) in MeCN (10 mL) afforded compound **5** as a white solid (reaction time: 4 d; column chromatography: $CHCl_3$–MeOH, 10:1 v/v, R_f = 0.58); yield: 254 mg (77%); mp 167 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.14 (s, 9 H), 2.23 (s, 9 H), 3.46 (s, 9 H), 5.11 (s, 6 H), 5.75 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.16, 13.54, 42.46, 62.14, 104.89, 120.48, 139.32, 146.86, 159.72.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{37}N_6O_3$: 493.29217; found: 493.29249.

Anal. Calcd for $C_{27}H_{36}N_6O_3$: C, 65.83; H, 7.37; N, 17.06. Found: C, 65.94; H, 7.48; N, 17.11.

1,3,5-Tris[(1*H*-benzimidazol-1-yl)methyl]-2,4,6-triethylbenzene (7)

The reaction of compound **21** (500 mg, 1.13 mmol) with 1*H*-benzimidazole (**17**; 603 mg, 5.10 mmol) and NaH (60% dispersion in mineral oil; 204 mg, 5.10 mmol) in MeCN (10 mL) afforded compound **7** as a white solid (reaction time: 5 d; column chromatography: $CHCl_3$–MeOH, 15:1 v/v, R_f = 0.44; yield: 564 mg (90%); mp 173 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.97 (t, *J* = 7.6 Hz, 9 H), 2.69 (q, *J* = 7.6 Hz, 6 H), 5.41 (s, 6 H), 7.31–7.40 (m, 6 H), 7.44–7.47 (m, 6 H), 7.84 (dd, *J* = 1.7, 6.9 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.38, 23.70, 42.94, 109.24, 120.82, 122.72, 123.33, 130.11, 133.96, 141.07, 144.06, 146.41.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{36}H_{37}N_6$: 553.30742; found: 553.30771.

Anal. Calcd for $C_{36}H_{36}N_6$: C, 78.23; H, 6.57; N, 15.21. Found: C, 77.85; H, 6.51; N, 15.04.

1,3,5-Tris[(3,5-dimethyl-1*H*-pyrazol-1-yl)methyl]-2,4,6-triethylbenzene (11)

The reaction of compound **21** (500 mg, 1.13 mmol) with 3,5-dimethyl-1*H*-pyrazole (**20**; 490 mg, 5.10 mmol) and NaH (60% dispersion in mineral oil; 204 mg, 5.10 mmol) in MeCN (10 mL) afforded compound **11** as a white solid (reaction time: 4 d; column chromatography: $CHCl_3$–MeOH, 15:1 v/v, R_f = 0.63); yield: 491 mg (89%); mp 197 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 7.6 Hz, 9 H), 2.13 (s, 9 H), 2.14 (s, 9 H), 2.77 (q, *J* = 7.6 Hz, 6 H), 5.18 (s, 6 H), 5.76 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.34, 13.43, 14.56, 23.69, 46.93, 105.43, 130.62, 138.98, 144.94, 147.20.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{30}H_{43}N_6$: 487.35437; found: 487.35452.

Anal. Calcd for $C_{30}H_{42}N_6$: C, 74.03; H, 8.70; N, 17.27. Found: C, 74.16; H, 8.68; N, 17.18.

Hexakis[(4-bromo-1*H*-pyrazol-1-yl)methyl]benzene (12)

The reaction of compound **23** (300 mg, 0.47 mmol) with 4-bromo-1*H*-pyrazole (**18**; 458 mg, 3.12 mmol) and NaH (60% dispersion in mineral oil; 125 mg, 3.12 mmol) in MeCN (10 mL) afforded compound **12** as a light-orange solid (reaction time: 4 d; column chromatography: $CHCl_3$–MeOH, 15:1 v/v, R_f = 0.73); yield: 424 mg (87%); mp 224 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.56 (s, 12 H), 7.01 (d, *J* = 0.6 Hz, 6 H), 7.41 (d, *J* = 0.5 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 49.94, 94.08, 129.44, 137.69, 140.71.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{30}H_{25}Br_6N_{12}$: 1032.73621; found: 1032.73657.

Anal. Calcd for $C_{30}H_{24}Br_6N_{12}$: C, 34.91; H, 2.34; N, 16.29. Found: C, 35.04; H, 2.40; N, 16.18.

Compounds 6 and 14a; Procedure C

1,3,5-Tris[(2-bromo-1*H*-benzimidazol-1-yl)methyl]-2,4,6-triethylbenzene (6)

To 2-bromo-1*H*-benzimidazole (**16**; 1.47 g, 7.48 mmol), dissolved in THF–MeCN (4:1, 20 mL), DIPEA (1.27 mL, 7.48 mmol) was added and the mixture was stirred for 1 h at r.t. Then, compound **21** (1 g, 2.27 mmol) was added and the reaction mixture was stirred for 7 d at r.t. The resulting precipitate was collected by filtration, washed thoroughly with THF and dried in vacuo. The desired compound **6** was obtained as a white solid; yield: 1.38 g (77%); mp 252 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.07 (br s, 9 H), 2.83 (q, *J* = 7.5 Hz, 6 H), 5.53 (s, 6 H), 6.31 (br s, 6 H), 7.12 (t, *J* = 7.8 Hz, 3 H), 7.65 (d, *J* = 8.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.05, 23.91, 45.68, 110.67, 119.67, 122.47, 123.31, 129.96, 130.38, 134.98, 143.44, 146.57.

MS (EI, 70 eV): *m*/*z* = 790 [M$^+$], 709, 593, 397, 317.

HRMS (EI): *m*/*z* [M$^+$] calcd for $C_{36}H_{33}Br_3N_6$: 786.03113; found: 786.03085.

Anal. Calcd for $C_{36}H_{33}Br_3N_6$: C, 54.77; H, 4.21; N, 10.65. Found: C, 55.03; H, 4.04; N, 10.58.

Trisbenzimidazolium Tribromide 14a

To 1*H*-benzimidazole (**17**; 442 mg, 3.74 mmol), dissolved in THF–MeCN (4:1, 15 mL), DIPEA (0.64 mL, 3.74 mmol) was added and the mixture was stirred for 1 h at r.t. Then, compound **21** (500 mg, 1.13 mmol) was added and the reaction mixture was stirred for 48 h at r.t. The resulting precipitate was collected by filtration, washed thoroughly with THF and dried in vacuo. Compound **14a** was obtained as a white solid; yield: 180 mg (32%); mp >290 °C (dec).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.07 (t, *J* = 7.4 Hz, 18 H), 2.46 (q, *J* = 7.5 Hz, 12 H), 5.75 (s, 12 H), 6.17 (s, 3 H), 7.94 (dd, *J* = 3.2, 6.4 Hz, 6 H), 8.43 (dd, *J* = 3.2, 6.4 Hz, 6 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 15.87, 22.48, 45.11, 114.64, 127.87, 128.88, 132.51, 133.89, 148.57.

HRMS (ESI): *m*/*z* [M^{3+}] calcd for $C_{51}H_{57}N_6$: 251.15428; found: 251.15435.

Anal. Calcd for $C_{51}H_{57}Br_3N_6$: C, 61.64; H, 5.78; N, 8.46. Found: C, 61.43; H, 5.67; N, 8.54.

Trisbenzimidazolium Tris(hexafluorophosphate) 14b

Trisbenzimidazolium tribromide **14a** (300 mg, 0.30 mmol) was dissolved in hot MeOH (10 mL) and a soln of sodium hexafluorophosphate (458 mg, 2.73 mmol) in MeOH (5 mL) was added. The mixture was stirred for 24 h at r.t., during which time a white precipitate formed. The precipitate was collected by filtration, washed thoroughly with MeOH and dried in vacuo. Product **14b** was obtained as a white solid; yield: 270 mg (75%); mp >300 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.08 (t, *J* = 7.4 Hz, 18 H), 2.43 (q, *J* = 7.1 Hz, 12 H), 5.72 (s, 12 H), 6.15 (s, 3 H), 7.94 (dd, *J* = 3.2, 6.3 Hz, 6 H), 8.38 (dd, *J* = 3.1, 6.4 Hz, 6 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 15.82, 22.47, 45.02, 114.61, 127.95, 128.79, 132.60, 133.74, 148.68.

HRMS (ESI): *m*/*z* [M^{3+}] calcd for $C_{51}H_{57}N_6$: 251.15428; found: 251.15477.

Anal. Calcd for $C_{51}H_{57}F_{18}N_6P_3$: C, 51.52; H, 4.83; N, 7.07. Found: C, 51.56; H, 4.89; N, 6.98.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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