UNIVERSITAT DE BARCELONA

FACULTAT DE FARMÀCIA

DEPARTAMENT DE FARMACOLOGIA I QUÍMICA TERAPÈUTICA

SISTEMES MOLECULARS CATIÒNICS I DICATIÒNICS: ESTRUCTURES BASADES EN SALS D'IMIDAZOLI

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6. EXPERIMENTAL SECTION

6.1. GENERAL CONSIDERATIONS

Melting point: CTP-MP 300 hot-plate apparatus with ASTM 2C thermometer. IR (NaCl or KBr disks): Nicolet 205 FT spectrophotometer. Optical rotations $[\alpha]^{25}_{D}$ were measured on a Perkin-Elmer 241 polarmeter using a 589 nm sodium light.

^{1}H NMR: Varian Gemini 200 (200 MHz), Varian Gemini 300 (300 MHz) and Mercury 400 (400 MHz) spectrometers at 298 K. Chemical shifts were referenced and expressed in ppm (δ) relative to the central peak of deuterium oxide (4.63 ppm), methanol-d_4 (3.40 ppm), DMSO-d_6 (2.49 ppm) and TMS for chloroform-d_3. ^{13}C NMR: Varian Gemini 200 (50.3 MHz), Varian Gemini 300 (75.4 MHz) and Mercury 400 (100.6 MHz) spectrometers at 298 K. Chemical shifts were referenced and expressed in ppm (δ) relative to the central peak of methanol-d_4 (49.0 ppm), DMSO-d_6 (39.7 ppm) and chloroform-d_3 (77.0 ppm). HMBC, HSQC and NOESY experiments: Mercury 400 spectrometer (400 MHz).

Mass spectra were obtained using chemical ionisation or electronic impact at 70 eV in a Hewlett-Packard spectrometer (HP-5989A model). Positive-ion ESI mass spectrometric analyses were performed on a Waters ZQ mass spectrometer from Micromass Instruments (Manchester, UK) at Serveis Científico-Tècnics of Universitat de Barcelona under the following experimental conditions: • Solvent: H_2O:CH_3CN (1:1, v/v) • Source temperature: 100 ºC • Focus voltage: 0-40 V • Flow rate: 1-10 $\mu L \cdot min^{-1}$ • Nebulizer gas: N_2 (60 $L \cdot h^{-1}$) • Drying gas: N_2 (416 $L \cdot h^{-1}$) • Capillary voltage: 3.5 KV. Spectra were scanned at a rate of 2 s over the mass range *m/z* 100-1500 and were recorded and processed using the MassLynx software, version 4.0 (Micromass). Mass calibration was performed with a 2 $mg \cdot mL^{-1}$ standard solution of NaI in 2-propanol/H_2O (1:1, v/v).

TLC: Merck precoated silica gel 60 F_{254} plates or Merck neutral aluminium oxide 60 F_{254} plates using UV light (254 nm) as visualizing agent

and/or H_2PtCl_2 3% aq./KI 10% aq. (1:1) or $KMnO_4$ ethanolic solution. Flash column chromatography was performed on silica gel 60 A C.C 35-70 μm Chromagel (SDS) or neutral aluminium oxide 90 activity II-III (Merck).

Elemental analysis were performed in a Eager 200 analyser at Serveis Científico-Tècnics of Universitat de Barcelona and in a Thermo Finnigan Flash EA 1112 SERIES or Carlo Erba Instruments EA 1108 at Servei de Microanàlisi of Consell Superior d'Investigacions Científiques (CSIC).

The electronic absorption spectra were obtained by using a Varian Cary 1E U.V-Visible spectrophotometer and a 1 cm path-lenght quartz cuvette. The concentrations of solution samples for electronic absortion measurements were typically in the range of $1.25 \cdot 10^{-5}$ M to $2.5 \cdot 10^{-3}$ M.

To transform the Ion exchange resin Amberlite® IRA-400 (Aldrich) chloride form (commercially available) to hydroxide form, a column packed with resin (50 or 75 g) was washed with aqueous 10 % NaOH (ca. 4 L) until it was free of halide ion ($AgNO_3$-HNO_3 test), and with water until the eluent was no longer alkaline (pH=7) and then stored in water. For using, a column (1.2 cm of diameter) with Ion exchange resin Amberlite® IRA-400 (OH^- form) until 12 cm of height, was packed and washed with following eluents: H_2O (50 mL), ethanol 20 % (50 mL), ethanol 50% (50 mL), ethanol 70% (50 mL) and ethanol 96% (50 mL) <91JOC4223, 92JOC4834>. When necessary, pH was measured with *Crison micropH 2001*, using pH electrode for hydroalcoholic solutions.

Materials used are specified in each section.

6.2. *N*-ARYLAZOLES AND *N*-ARYLBENZIMIDAZOLES

Materials

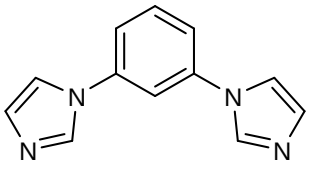
Solvents: Dichloromethane, 1,4-Dioxane, DME, DMF (dry with molecular sieves), IPA, methanol, THF and toluene were distilled prior to use and dried.

Commercially available products: *N,N'*-dimethylethylenediamine, racemic *trans*-1,2-cyclohexanediamine, pyridine, imidazole **18**, 1,3-diiodobenzene **19a**, 1,3-dibromobenzene **20a**, 2,4-dibromomesitylene **20b**, 2-iodo-1,3,5-trimethylbenzene **26a**, 2-bromonaphthalene **26c**, 1-bromonaphthalene **26d**, 2,4,6-trimethylphenylboronic acid **27a**, 1-naphthylboronic acid **27d**, phenylboronic acid **27e**, 4-methylphenylboronic acid **27f**, 5,6-dimethyl-1*H*-benzimidazole **30**, 1,2,4,5-tetrabromobenzene **34**, *t*-BuLi 1.5 M in pentane, Cs_2CO_3, CsOAc, CuCl, CuI, anhydrous $Cu(OAc)_2$, K_2CO_3, KHF_2 and triisopropyl borate.

The following products were prepared according to the literature: 1-iodo-2,6-diisopropylbenzene **26b** <00PCT1> and $[Cu(OH)\cdot TMEDA]_2Cl_2$ <99JOC2264>.

Compounds described in the literature were characterized by comparing their ^1H NMR spectra to the previously reported data.

6.2.1. SYNTHESIS OF 1,3-BIS(1-IMIDAZOLYL)BENZENE 5a



An oven-dried resealeable tube was back-filled with argon and charged with imidazole **18** (0.16 g, 2.40 mmol), CuI (0.019 g, 0.10 mmol), Cs_2CO_3 (1.37 g, 4.20 mmol), 1,3-diiodobenzene **19a** (0.33 g, 1 mmol), racemic *trans*-1,2-cyclohexanediamine (0.048 mL, d=0.951 g/mL, 0.40 mmol) and dry 1,4-dioxane (2 mL) under a stream of argon. The reaction tube was quickly sealed and the contents were stirred while heating at 95 ºC for 24 h. The cooled reaction mixture was diluted with EtOAc and filtered through a plug of silica gel eluting with additional EtOAc saturated with NH_3. The filtrate was concentrated and the resulting residue was purified by column chromatography on silica gel [hexane/EtOAc (1:1); EtOAc-NH_3;

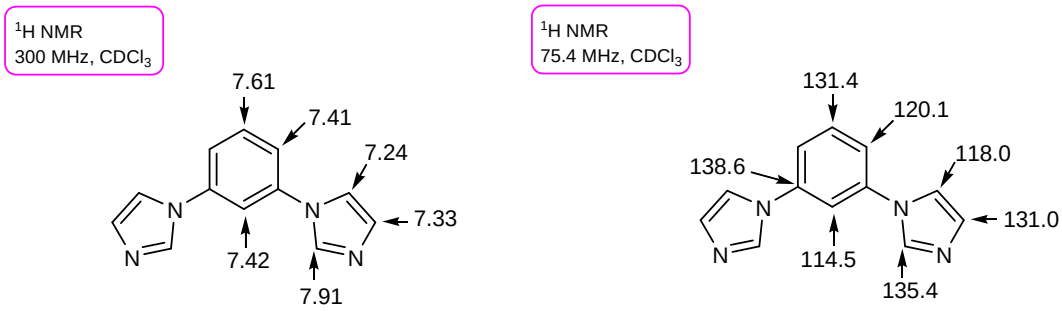
EtOAc/MeOH (9:1)] to provide 0.014 g (5% yield) of 1-(3-iodophenyl)-1*H*-imidazole **21a** and 0.20 g (95% yield) of 1,3-bis(1-imidazolyl)benzene **5a** (see, Table 6.1)

1,3-Bis(1-imidazolyl)benzene 5a: The product was obtained as an off-white solid. Mp 136-137 ºC.

^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.24 (br s, 2H, Imi), 7.33 (br s, 2H, Imi), 7.41 (d, *J*=8.0 Hz, 2H, Aryl), 7.42 (s, 1H, Aryl), 7.61 (t, *J*=8.0 Hz, 1H, Aryl), 7.91 (br s, 2H, Imi).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 114.5 (*C*H_3), 118.0 (Imi), 120.1 (Aryl), 131.0 (Imi), 131.4 (Aryl), 135.4 (Imi), 138.6 (*C*q).

EI-MS *m/z* (%): 210 (100) [$M^{+\cdot}$]. The NMR spectroscopic data and elemental analysis are in accordance with those reported <03OL4847>.



1-(3-Iodophenyl)-1*H*-imidazole 21a: The product was obtained as a colorless foam.

^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.17-7.23 (m, 2H, Aryl), 7.26 (br s, 1H, Imi), 7.36 (d, *J*=8.0 Hz, 1H, Aryl), 7.70 (d, *J*=8.0 Hz, 1H, Aryl), 7.75 (br s, 1H, Imi), 7.84 (br s, 1H, Imi).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ (ppm) 94.6 (*C*q), 117.9 (Imi), 120.5 (Aryl), 130.2 (Aryl), 130.6 (Imi), 131.1 (Aryl), 135.3 (Imi), 136.3 (Aryl), 138.1 (*C*q).

EI-MS *m/z* (%): 270 (100) [$M^{+\cdot}$].

Anal. Calcd for $C_9H_7IN_2 \cdot 0.5\ C_3H_6O$: C, 42.16; H, 3.37; N, 9.36. Found: C, 42.43; H, 3.16; N, 9.08.

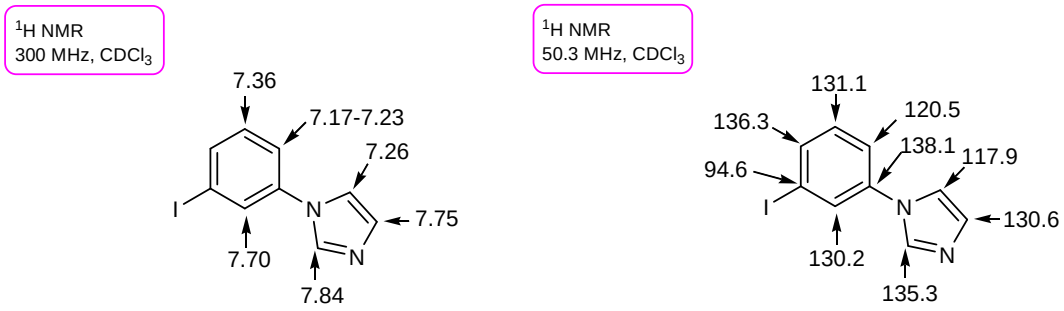
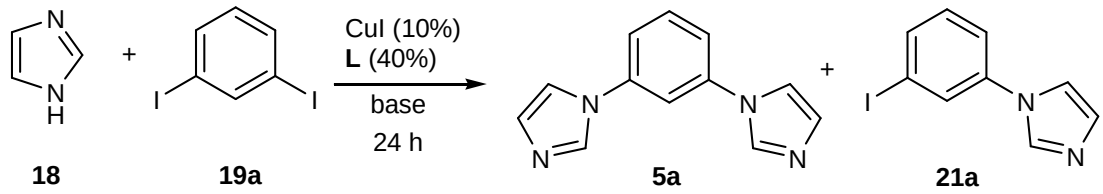
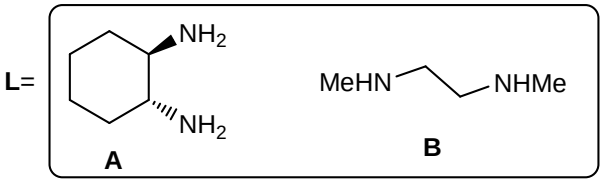


Table 6.1. Results of the reaction between imidazole **18** and 1,3-diiodobenzene **19a**[a]





Entry[a]	L	Base	T(ºC)	Yield (%)[b]	
				5a	**21a**
1	A	K_2CO_3	110	5[c]	34
2	A	Cs_2CO_3	110	80	15
3	A	Cs_2CO_3	110[d]	79	15
4	A	Cs_2CO_3	95[e]	95	5
5	B	Cs_2CO_3	95[e]	—	10[c]
6[f]	A	Cs_2CO_3	95[e]	89[g]	8

[a]All reactions 0.5 M in 1,4-dioxane with respect to 1,3-diiodobenzene **21a** unless otherwise noted. [b]Isolated yield after chromatographic purification. [c]Calculated by ^{1}H RMN from treated reaction mixture. [d]48 h. [e]Sealed tube. [f]Scale up to 5 mmol. [g]76% yield from first crystallization of reaction mixture in hexanes/Me_2CO.

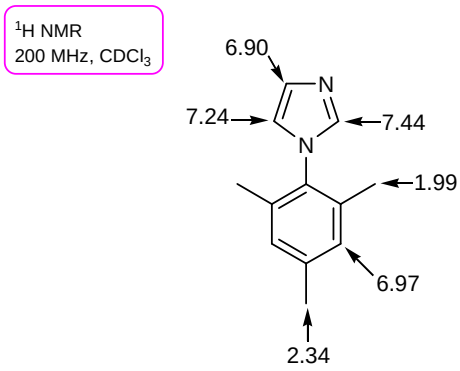
6.2.2. SYNTHESIS OF *N*-ARYLIMIDAZOLES 6a-f

⇒ **From Aryl Halides 26a-d**

General procedure: An oven-dried resealeable tube was back-filled with argon and charged with arylhalide **26a-d** (1 mmol), imidazole **18** (0.082 g, 1.20 mmol), CuI (0.019 g, 0.10 mmol), dry DMF (1 mL), *N,N'*-dimethylethylenediamine (0.041 mL, d=0.819 g/mL, 0.40 mmol) and Cs_2CO_3 (0.68 g, 2.10 mmol) under a stream of argon. The tube was sealed with a Teflon valve and the reaction mixture was stirred magnetically at 170 ℃ for 48 h. The resulting suspension was cooled to room temperature, and CH_2Cl_2 (20 mL) and NH_4OH (20 mL) were added. The separate layers were washed, and combined organic layers were dried and solvent removed. The residue was purified by flash chromatography on silica gel (EtOAc) to afford pure product.

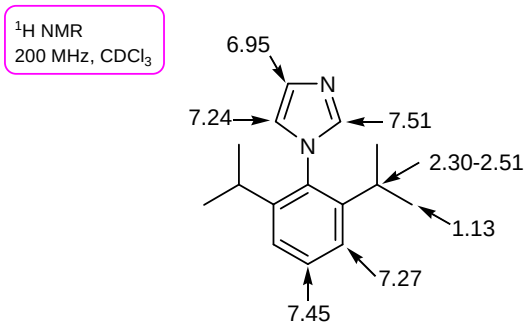
1-(2,4,6-Trimethylphenyl)-1*H*-imidazole 6a: The product was obtained as a colorless crystalline solid (0.095 g, 50% yield). Mp 116-117 ºC.

^{1}H NMR (200 MHz, $CDCl_3$): δ (ppm) 1.99 (s, 6H, C*H*$_3$), 2.34 (s, 3H, C*H*$_3$), 6.90 (s, 1H, Imi), 6.97 (s, 2H, Aryl), 7.24 (s, 1H, Imi), 7.44 (s, 1H, Imi). The NMR data are in accordance with those reported <03JA113>.



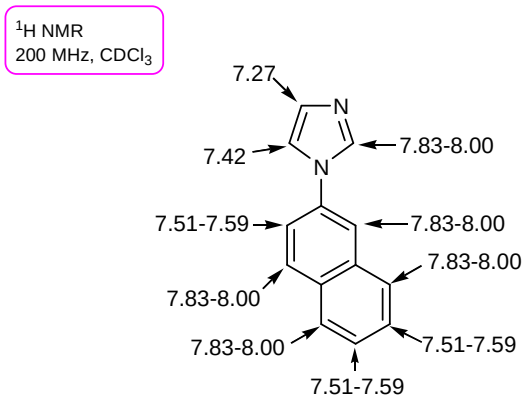
1-(2,6-Diisopropylphenyl)-1*H*-imidazole 6b: The product was obtained as a colorless needles solid (0.044 g, 19% yield). Mp 122-123 ºC.

^{1}H NMR (200 MHz, $CDCl_3$): δ (ppm) 1.13 (d, *J*=6.9 Hz, 12H, C*H*$_3$), 2.30-2.51 (m, 1H, C*H*$(CH_3)_2$), 6.95 (br s, 1H, Imi), 7.24 (s, 1H, Imi), 7.27 (d, *J*=7.8 Hz, 2H, Aryl), 7.45 (t, *J*=8.0 Hz, 1H, Aryl), 7.51 (br s, 1H, Imi). The NMR <03JA113> data and Mp <03S2661> are in accordance with those reported.



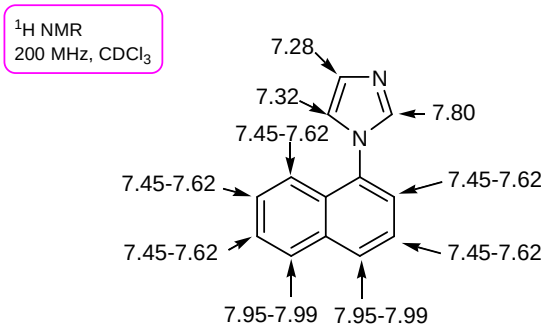
1-(2-Naphthyl)-1*H*-imidazole 6c: The product was obtained as a white solid (0.156 g, 80% yield). Mp 122-123 ºC.

^{1}H NMR (200 MHz, $CDCl_3$): δ (ppm) 7.27 (s, 1H, Imi), 7.42 (br s, 1H, Imi), 7.51-7.59 (m, 3H, Aryl), 7.83-8.00 (m, 5H, Aryl, Imi). The NMR data and Mp are in accordance with those reported <03JA113>.



1-(1-Naphthyl)-1*H*-imidazole 6d: The product was obtained as a white solid (0.112 g, 57% yield). Mp 72-73 ºC.

^{1}H NMR (200 MHz, $CDCl_3$): δ (ppm) 7.28 (s, 1H, Imi), 7.32 (s, 1H, Imi), 7.45-7.62 (m, 5H, Aryl), 7.80 (s, 1H, Imi), 7.95-7.99 (m, 2H, Aryl). The NMR data are in accordance with those reported <03JA113>.



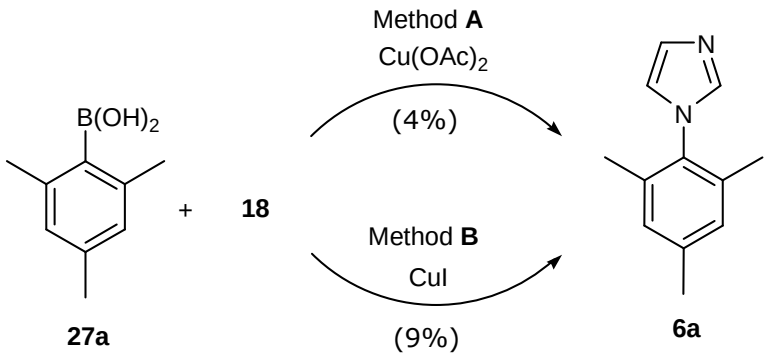
⇒ **From Arylboronic acids 27a-f**

- **1-(2,4,6-Trimethylphenyl)imidazole 6a** (Scheme 6.1)

Method A: An oven-dried two-necked round-bottom 50 mL flask was charged with a magnetic stirrer bar, 2,4,6-trimethylphenylboronic acid **27a** (0.70 g, 4.24 mmol), anhydrous $Cu(OAc)_2$ (0.42 g, 2.33 mmol), pyridine (0.38 mL, d=0.978 g/mL, 4.66 mmol) and CH_2Cl_2 (10 mL). After five minutes, imidazole **18** (0.14 g, 2.12 mmol) was added and the reaction mixture was stirred under air at room temperature for 48 h. MeOH/NH_3 (6 mL) was added, the solution was evaporated and the residue was filtered through a 1 × 1 cm pad of silica gel and eluted with EtOAc. Purification performed by flash chromatography on alumina (3 × 15 cm; CH_2Cl_2) provided 0.016 g (4% yield) of 1-(2,4,6-trimethylphenyl)imidazole **6a**.

Method B: An oven-dried round-bottom 50 mL flask was charged with a magnetic stirrer bar, 2,4,6-trimethylphenylboronic acid **27a** (0.16 g, 1 mmol), CuI (0.009 g, 0.05 mmol), and dry MeOH (5 mL). After five minutes, imidazole **18** (0.082 g, 1.20 mmol) was added and the reaction mixture was stirred under air at reflux for 6 h. The solvent was evaporated, and NH_4OH solution (10%, 5 mL) and EtOAc (5 mL) was added. The organic layer was washed with water, dried and the solvent removed. Purification performed by flash chromatography on silica gel (1 × 15 cm; EtOAc) provided 0.017 g (9% yield) of 1-(2,4,6-trimethylphenyl)imidazole **6a**.

Scheme 6.1.[a] 1-(2,4,6-Trimethylphenyl)imidazole **6a** from boronic acid **27a**



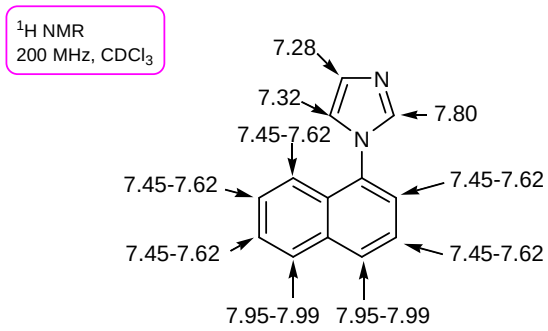
[a]Reagents and conditions: Method **A**=Ar-$B(OH)_2$ (2 mmol), $Cu(OAc)_2$ (1.1 mmol), py (2.2 mmol), **18** (1 mmol), dry CH_2Cl_2, air, 25 ºC, 48 h. Method **B**=Ar-$B(OH)_2$ (1 mmol), CuI (0.05 mmol), **18** (1.2 mmol), dry MeOH, air, reflux, 6 h.

- ***N*-Arylimidazoles 6d-f**

General procedure: An oven-dried round-bottom 50 mL flask was charged with a magnetic stirrer bar, arylboronic acid **27d-f** (1 mmol), CuI (0.009 g, 0.05 mmol), and dry MeOH (5 mL). After five minutes, imidazole **18** (0.082 g, 1.20 mmol) was added and the reaction mixture was stirred under air at reflux for 3-6 h. The solvent was evaporated, and NH_4OH solution (10%, 5 mL) and EtOAc (5 mL) was added. The organic layer was washed with water, dried and the solvent removed. Purification performed by flash chromatography on silica gel (1 × 15 cm; EtOAc) provided the corresponding *N*-arylimidazole **6d-f**.

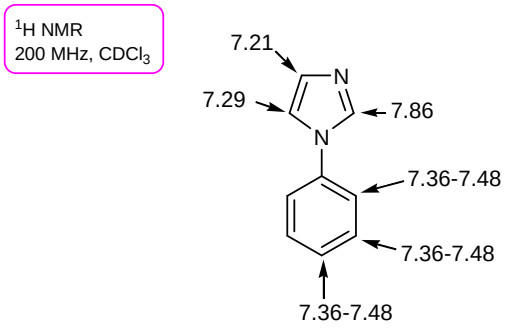
1-(1-Naphthyl)-1*H*-imidazole 6d: The product was obtained as a white solid (0.084 g, 43% yield) (see, Scheme 6.2). Mp 72-73 ºC.

^{1}H NMR (200 MHz, $CDCl_3$): δ (ppm) 7.28 (s, 1H, Imi), 7.32 (s, 1H, Imi), 7.45-7.62 (m, 5H, Aryl), 7.80 (s, 1H, Imi), 7.95-7.99 (m, 2H, Aryl). The NMR data are in accordance with those reported <03JA113>.



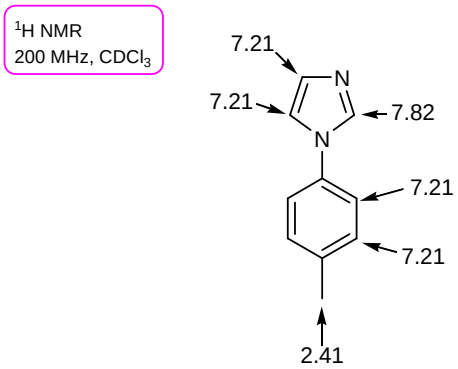
1-Phenyl-1*H*-imidazole 6e: The product was obtained as an oil at room temperature (0.110 g, 76% yield) (see, Scheme 6.3).

^{1}H NMR (200 MHz, $CDCl_3$): δ (ppm) 7.21 (s, 1H, Imi), 7.29 (s, 1H, Imi), 7.36-7.48 (m, 5H, Aryl), 7.86 (s, 1H, Imi). The NMR data are in accordance with those reported <00OL1233>.



1-(4-Methylphenyl)-1*H*-imidazole 6f. The product was obtained as an oil at room temperature (0.028 g, 18% yield).

^{1}H NMR (200 MHz, $CDCl_3$): δ (ppm) 2.41 (s, 3H, C*H*$_3$), 7.21 (br s, 6H, AA'BB' syst. Aryl, Imi), 7.82 (s, 1H, Imi). The NMR data are in accordance with those reported <00OL1233>.

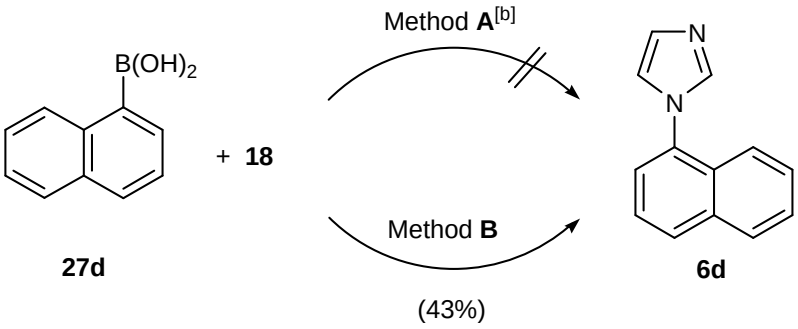


Attempt to prepare 1-Naphthyl-1*H*-imidazole 6d from boronic acid 27d (Scheme 6.2)

Method A: An oven-dried two-necked round-bottom 50 mL flask was charged with a magnetic stirrer bar, 1-naphthylboronic acid **27d** (0.69 g, 4.40 mmol), anhydrous $Cu(OAc)_2$ (0.40 g, 2.20 mmol), pyridine (0.35 mL, d=0.978 g/mL, 4.40 mmol), and dry CH_2Cl_2 (8 mL). After five minutes, imidazole **18** (0.14 g, 2 mmol) was added and the reaction mixture was stirred under air at room temperature for 48 h. MeOH/NH_3 (6 mL) was added, the solution was evaporated and the residue was filtered through a 1 × 1 cm pad of silica gel and eluted with EtOAc. TLC and ^{1}H NMR do not show the presence of 1-naphthylimidazole **6d** and only naphthalene was identified.

Method B: see, *N*-Arylimidazoles **6d-f** (General procedure).

Scheme 6.2.[a]1-Naphthyl-1*H*-imidazole **6d** from boronic acid **27d**



[a]Reagents and conditions: Method **A**=Ar-B(OH)$_2$ (2 mmol), Cu(OAc)$_2$ (1.1 mmol), py (2.2 mmol), **18** (1 mmol), dry CH_2Cl_2, air, 25 ºC, 48 h. Method **B**=Ar-B(OH)$_2$ (1 mmol), CuI (0.05 mmol), **18** (1.2 mmol), dry MeOH, air, reflux, 6 h. [b]Only naphtalene was identified.

Selected experiments to prepare 6e from Phenylboronic acid 27e

(Scheme 6.3)

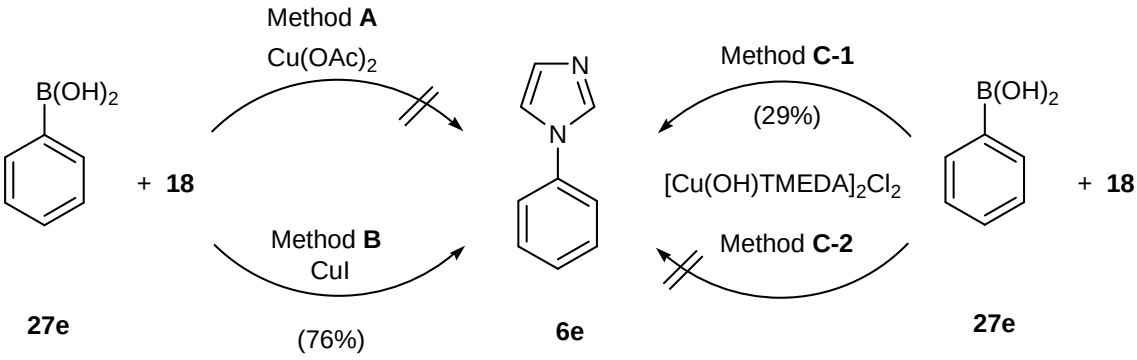
Method A: An oven-dried two-necked round-bottom 50 mL flask was charged with a magnetic stirrer bar, phenylboronic acid **27e** (0.24 g, 2 mmol), anhydrous Cu(OAc)$_2$ (0.27 g, 1.15 mmol), pyridine (0.16 mL, d=0.978 g/mL, 2 mmol), 4Å MS (0.75 g) and CH_2Cl_2 (10 mL). After five minutes, imidazole **18** (0.068 g, 1 mmol) was added and the reaction mixture was stirred under air at room temperature for 48h. MeOH/NH_3 (3 mL) was added, the solution was evaporated and the residue was filtered through a 1 × 1 cm pad of silica gel and eluted with EtOAc. TLC and ^{1}H NMR do not show the presence of 1-phenylimidazole **6e**.

Method B: see, *N*-Arylimidazoles **6d-f** (General procedure).

Method C-1: An oven-dried two-necked round-bottom 50 mL flask was charged with a magnetic stirrer bar, phenylboronic acid **27e** (0.24 g, 2 mmol), [Cu(OH)·TMEDA]$_2Cl_2$ (0.044 g, 0.10 mmol), imidazole **18** (0.068 g, 1 mmol) and dry CH_2Cl_2 (4 mL). The reaction mixture was stirred at room temperature for 16 h under an atmosphere of O_2. The suspension was filtered, and evaporated. Purification performed by flash chromatography on silica gel (1 × 15 cm; EtOAc) provided 0.042 g (29% yield) of 1-phenylimidazole **6e**.

Method C-2: A two-necked round-bottom 50 mL flask was charged with a magnetic stirrer bar, phenylboronic acid **27e** (0.24 g, 2 mmol), $[Cu(OH)\cdot TMEDA]_2Cl_2$ (0.044 g, 0.10 mmol), imidazole **18** (0.068 g, 1 mmol) and water (10 mL). The reaction mixture was stirred at room temperature for 16 h under an atmosphere of O_2. The suspension was filtered, and evaporated. TLC and ^1H NMR do not show the presence of 1-phenylimidazole **6e**.

Scheme 6.3. [a] 1-Phenyl-1*H*-imidazole **6e** from Phenylboronic acid **27e**



[a]Reagents and conditions: Method **A**=Ph-$B(OH)_2$ **27e** (2 mmol), $Cu(OAc)_2$ (1.5 mmol), py (2 mmol), **18** (1 mmol), 4Å MS, dry CH_2Cl_2, air, 25 ºC, 48 h. Method **B**=Ph-$B(OH)_2$ **27e** (1 mmol), CuI (0.05 mmol), **18** (1.2 mmol), dry MeOH, air, reflux, 3 h; Method **C**=Ph-$B(OH)_2$ (2 mmol), $[Cu(OH)\cdot TMEDA]_2Cl_2$ (0.1 mmol), **18** (1 mmol), O_2, 25 ºC, 16 h: **C-1**=dry CH_2Cl_2, **C-2**=H_2O

⇒ **From Potassium Aryltrifluoroborates 28e-f**

- **1-Phenyl-1*H*-imidazole 6e** (Scheme 6.4)

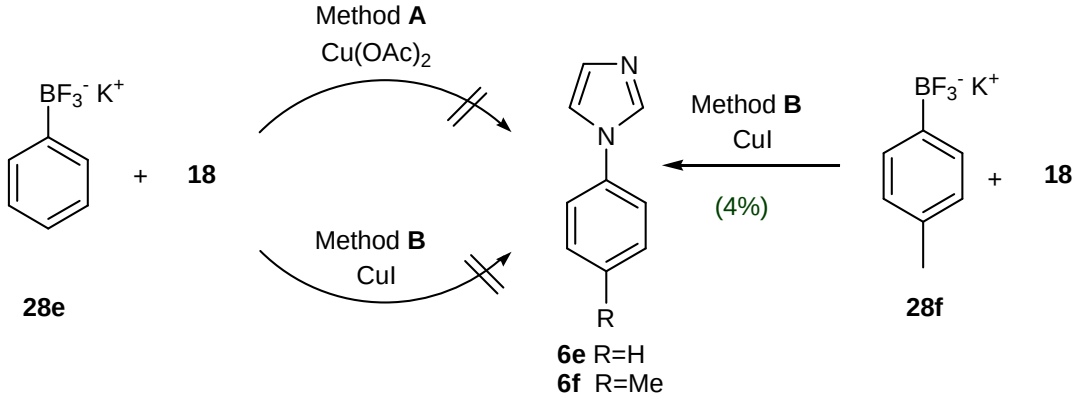
Method A: An oven-dried two-necked round-bottom 50 mL flask was charged with a magnetic stirrer bar, potassium phenyltrifluoroborate **28e** (0.37 g, 2 mmol), anhydrous $Cu(OAc)_2$ (0.27 g, 1.50 mmol), pyridine (0.16 mL, d=0.978 g/mL, 2 mmol), dry CH_2Cl_2 (10 mL) and 4Å MS (0.75 g). After five minutes, imidazole **18** (0.14 g, 2 mmol) was added and the reaction mixture was stirred under air at room temperature for 48 h. The solution was evaporated and the residue was filtered through a 1 × 1 cm pad of silica gel and eluted with EtOAc. Purification performed by flash chromatography on alumina (3 × 15 cm; EtOAc) provided 0.030 g (21% yield) of 1-phenylimidazole **6e**. Only one time this result was obtained, but four attempts to repeat the experiment were unsuccessful and do not observed the formation of **6e**.

Method B: An oven-dried round-bottom 50 mL flask was charged with a magnetic stirrer bar, potassium phenyltrifluoroborate **28e** (0.18 g, 1 mmol), CuI (0.009 g, 0.05 mmol), and dry MeOH (4 mL). After five minutes, imidazole **18** (0.082 g, 1.20 mmol) was added and the reaction mixture was stirred under air at reflux for 3 h. The solvent was evaporated and NH_4OH solution (10%, 5 mL) and EtOAc (5 mL) were added. The organic layer was washed with water, dried and the solvent removed. By TLC, no traces of 1-phenylimidazole **6e** were observed.

- **1-(4-Methylphenyl)-1*H*-imidazole 6f** (Scheme 6.4)

Method B: An oven-dried round-bottom 50 mL flask was charged with a magnetic stirrer bar, potassium 4-methylphenyltrifluoroborate **28f** (0.20 g, 1 mmol), CuI (0.009 g, 0.05 mmol), and dry MeOH (4 mL). After five minutes, imidazole **18** (0.082 g, 1.20 mmol) was added and the reaction mixture was stirred under air at reflux for 3 h. The solvent was evaporated, and NH_4OH solution (10%, 5 mL) and EtOAc (5 mL) were added. The organic layer was washed with water, dried and the solvent removed. Purification performed by flash chromatography on silica gel (1 × 15 cm; EtOAc) provided 0.060 g (4% yield) of 1-(4-methylphenyl)imidazole **6f**.

Scheme 6.4.[a] 1-Phenyl-1*H*-imidazole **6e** from Phenylboronic acid **27e**



[a]Reagents and conditions: Method **A**=Ph-$BF_3^-K^+$ **28e** (2 mmol), $Cu(OAc)_2$ (1.1 mmol), py (2.2 mmol), **18** (1 mmol), dry CH_2Cl_2, air, 25 ºC, 48 h. Method **B**=Ar-$BF_3^-K^+$ **28e-f** (2 mmol), CuI (0.05 mmol), **18** (1.2 mmol), dry MeOH, air, reflux, 3 h.

6.2.3. SYNTHESIS OF 5,6-DIMETHYL-1-(4-METHYLPHENYL)-1*H*-BENZIMIDAZOLE 7f (Scheme 6.5)

Method A: An oven-dried two-necked round-bottom 50 mL flask was charged with a magnetic stirrer bar, 4-methylphenylboronic acid **27f** (0.27 g, 2 mmol), anhydrous $Cu(OAc)_2$ (0.20 g, 1.10 mmol), pyridine (0.18 mL, d=0.978 g/mL, 2.20 mmol) and CH_2Cl_2 (4 mL). After five minutes, 5,6-dimethylbenzimidazole **30** (0.15 g, 1 mmol) was added and the reaction mixture was stirred under air at room temperature for 48 h. MeOH/NH_3 (3 mL) was added, the solution was evaporated and the residue was filtered through a 1 × 1 cm pad of silica gel and eluted with EtOAc. Purification performed by flash chromatography on silica gel (2 × 15 cm; EtOAc) provided 0.15 g (64% yield) of 5,6-dimethyl-1-(4-methylphenyl)-1*H*-benzimidazole **7f**.

Method B: An oven-dried round-bottom 50 mL flask was charged with a magnetic stirrer bar, 4-methylphenylboronic acid **27f** (0.14 g, 1 mmol) or potassium 4-methylphenyltrifluoroborate **28f** (0.20 g, 1 mmol), CuI (0.009 g, 0.05 mmol) and dry MeOH (4 mL). After five minutes, 5,6-dimethylbenzimidazole **30** (0.18 g, 1.20 mmol) was added and the reaction mixture was stirred under air at reflux for 3 h. The solvent was evaporated, and NH_4OH solution (10%, 5 mL) and EtOAc (5 mL) were added. The organic layer was washed with water, dried and the solvent removed. Purification performed by flash chromatography on silica gel (1 × 15 cm; EtOAc) provided 5,6-dimethyl-1-(4-methylphenyl)-1*H*-benzimidazole **7f**.

Method C: An oven-dried two-necked round-bottom 50 mL flask was charged with a magnetic stirrer bar, potassium 4-methylphenyltrifluoroborate **28f** (0.22 g, 1.10 mmol), anhydrous $Cu(OAc)_2$ (0.20 g, 1.10 mmol), pyridine (0.18 mL, d=0.978 g/mL, 2.20 mmol) and dry 1,4-dioxane (4 mL). After five minutes, 5,6-dimethylbenzimidazole **30** (0.15 g, 1 mmol) was added and the reaction mixture was stirred under air at room temperature for 24 h. MeOH/NH_3 (6 mL) was added, the solution was evaporated, and the residue was filtered through a 1 × 1 cm pad of silica gel and eluted with EtOAc. Purification performed by preparative chromatography on a silica gel plate using

EtOAc/$CHCl_3$ (75:25) as eluent, provided 0.013 g (6% yield) of 5,6-dimethyl-1-(4-methylphenyl)-1*H*-benzimidazole **7f**.

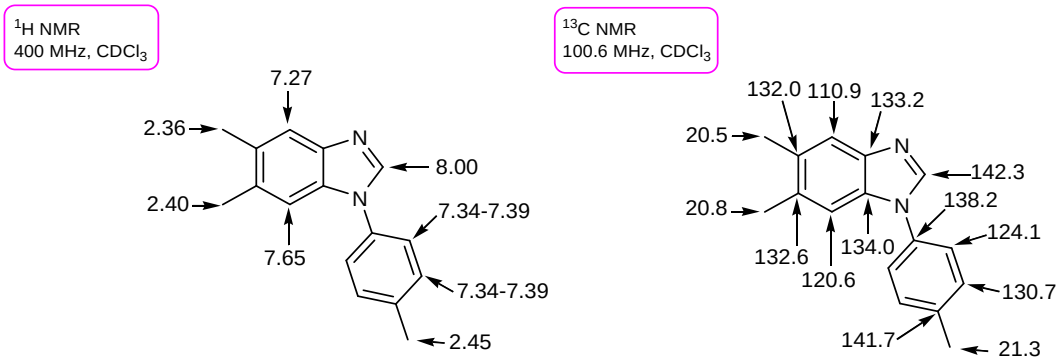
5,6-Dimethyl-1-(4-methylphenyl)-1*H*-benzimidazole 7f: The product was obtained as a white solid. Mp 96-97 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.36 (s, 3H, C*H*$_3$), 2.40 (s, 3H, C*H*$_3$), 2.45 (s, 3H, C*H*$_3$), 7.27 (s, 1H, Aryl), 7.34-7.39 (s, 4H, AA'BB' syst. Aryl), 7.65 (s, 1H, Aryl), 8.00 (s,1H, Imi).

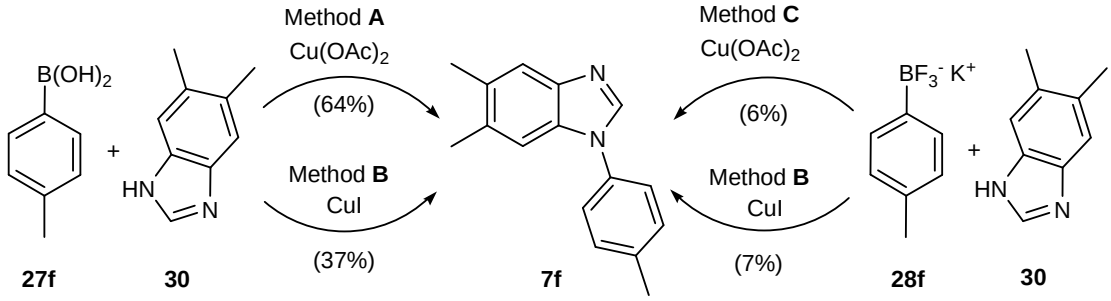
^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 20.5 (*C*H$_3$), 20.8 (*C*H$_3$), 21.3 (*C*H$_3$), 110.9 (Aryl), 120.6 (Aryl), 124.1 (Aryl), 130.7 (Aryl), 132.0 (*C*q), 132.6 (*C*q), 133.2 (*C*q), 134.0 (*C*q), 138.2 (*C*q), 141.7 (*C*q), 142.3 (BzIm).

EI-MS *m/z* (%): 236 (100) [$M^{+\cdot}$].

Anal. Calcd for $C_{16}H_{16}N_2$: C, 81.32; H, 6.82; N, 11.85. Found: C, 81.16; H, 6.98; N, 11.67.



Scheme 6.5.[a] Synthesis of *N*-arylbenzimidazole **7f** from acid **27f** or salt **28f**.



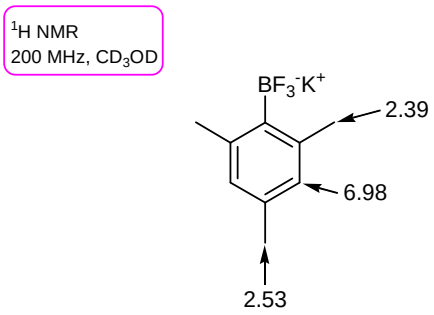
[a]Reagents and conditions: Method **A**=Ar-B(OH)$_2$ (2 mmol), $Cu(OAc)_2$ (1.1 mmol), py (2.2 mmol), **30** (1 mmol), dry CH_2Cl_2, air, 25 ºC, 48 h; Method **B**=Ar-BX$_n$ **27f** or **28f** (1 mmol), CuI (0.05 mmol), **30** (1.2 mmol), dry MeOH, air, reflux, 3 h; Method **C**=Ar-$BF_3^-K^+$ **28f** (1.1 mmol), $Cu(OAc)_2$ (1.1 mmol), py (2.2 mmol), **30** (1 mmol), dry 1,4-dioxane, air, 25 ºC, 48 h.

6.2.4. SYNTHESIS OF POTASSIUM ARYLTRIFLUOROBORATES 28a,d-f

General Procedure: An oven-dried 100 mL Schlenk flask was charged with a magnetic stirrer bar, arylboronic acid **27a,d-f** (10 mmol) and anhydrous THF (20 mL). After cooling to –20 ºC in a dry ice/acetone bath, a solution of potassium hydrogenfluoride (4.70 g, 60 mmol) in desgased water (10 mL) was added slowly. The reaction mixture was stirred at –20 ºC for 1 h. The solution was then allowed to slowly warm to room temperature and was stirred for 1h. Two layers were separated. The aqueous layer was extracted with THF (3 × 20 mL) and the combined organic phase was dried and concentrated providing the corresponding potassium aryltrifluoroborate **28a,d-f** (Scheme 6.6).

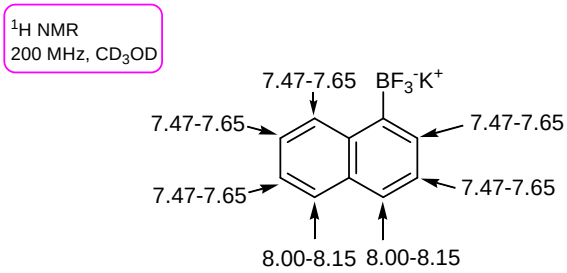
Potassium 2,4,6-Trimethylphenyltrifluoroborate 28a: The product was obtained as a white solid in 27% yield.

^{1}H NMR (200 MHz, CD_3OD): δ (ppm) 2.39 (s, 6H, C*H*$_3$), 2.53 (s, 3H, C*H*$_3$), 6.98 (s, 2H, Aryl).



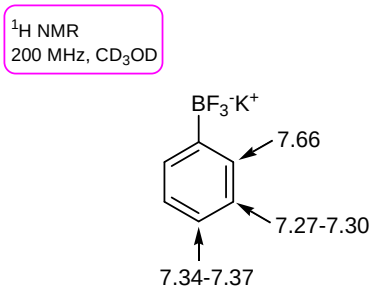
Potassium 1-Naphthyltrifluoroborate 28d: The product was obtained as a white solid in 95% yield.

^{1}H NMR (200 MHz, CD_3OD): δ (ppm) 7.47-7.65 (m, 5H, Aryl), 8.00-8.15 (m, 2H, Aryl).



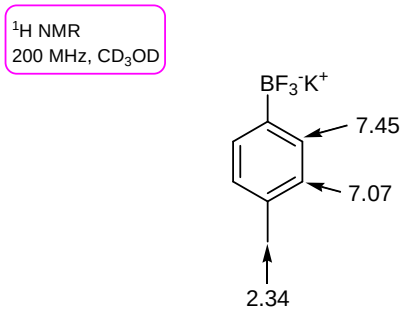
Potassium Phenyltrifluoroborate 28e: The product was obtained as a white solid in 97% yield. Mp 296-297 ºC.

^{1}H NMR (200 MHz, CD_3OD): δ (ppm) 7.27-7.30 (m, 2H, Aryl), 7.34-7.37 (m, 1H, Aryl), 7.66 (d, *J*=8.0 Hz, 2H, Aryl). This product is also commercially available.

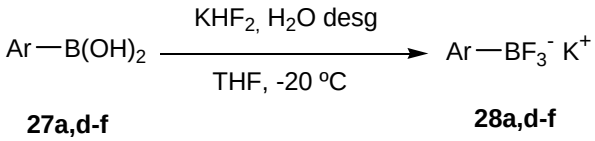


Potassium 4-Methylphenyltrifluoroborate 28f: The product was obtained as a white solid in 99% yield. Mp > 300 ºC.

^{1}H NMR (200 MHz, CD_3OD): δ (ppm) 2.34 (s, 3H, C*H*$_3$), 7.07 (d, *J*=8.0 Hz, 2H, Aryl), 7.45 (d, *J*=8.0 Hz, 2H, Aryl). This product is also commercially available.

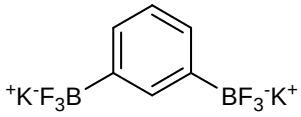


Scheme 6.6. Synthesis of Potassium aryltrifluoroborates **28a,d-f** from Arylboronic acids **27a,d-f**



27a,d-f **28a,d-f**

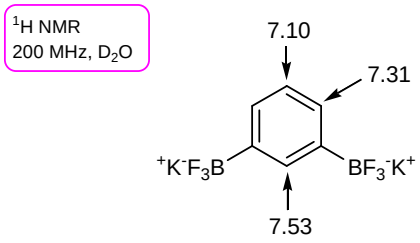
6.2.5. SYNTHESIS OF 1,3-BIS(POTASSIUM TRIFLUOROBORATE) BENZENE 32



An oven-dried 25 mL Schlenk flask was charged with a magnetic stirrer bar, 1,3-dibromobenzene **20a** (0.61 mL, d=1.952 g/mL, 5 mmol) and anhydrous THF (20 mL). The resulting solution was cooled to –78 ºC in a dry ice/acetone bath, and *t*-BuLi in pentane (6.67 mL, 1.5 M, 10 mmol) was added under argon. After 1 h of stirring triisopropyl borate (3.46 mL, d=0.815 g/mL, 15 mmol) was added dropwise. The reaction mixture was stirred at –78 ºC for 1 h. The solution was then allowed to slowly warm to –20 ºC and was stirred for 1h. After, a solution of potassium hydrogenfluoride (4.70 g, 60 mmol) in 10 mL of desgased water was added slowly. The reaction mixture was stirred at –20 ºC for 1 h. The solution was then allowed to slowly warm to room temperature and was stirred for 1h. Two layers were separated. The aqueous layer was extracted with THF (3 × 20 mL) and the combined organic phase was dried and concentrated to provide 0.41 g (31% yield) of potassium 3-bromophenyltrifluoroborate **31** and 0.15 g (10% yield) of dipotassium dipotassium 1,3-bis(potassium trifluoroborate)benzene **32**.

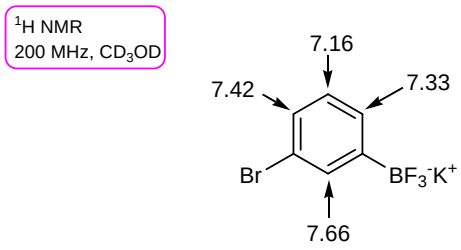
1,3-Bis(potassium trifluoroborate)benzene 32: The product was obtained as a white solid.

^{1}H NMR (200 MHz, D_2O): δ (ppm) 7.10 (t, *J*=8.0 Hz, 1H, Aryl), 7.31 (d, *J*=8.0 Hz, 2H, Aryl), 7.53 (s,1H, Aryl).



Potassium 3-bromophenyltrifluoroborate 31: The product was obtained as a white solid.

^{1}H NMR (200 MHz, CD_3OD): δ (ppm) 7.16 (t, *J*=8.0 Hz, 1H, Aryl), 7.33 (d, *J*=8.0 Hz, 1H, Aryl), 7.42 (d, *J*=8.0 Hz ,1H, Aryl), 7.66 (s,1H, Aryl).

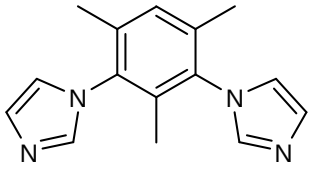


Attempted preparation of 1,3-Bis(potassium trifluoroborate)benzene 32 from Potassium 3-bromophenyltrifluoroborate 31 (Scheme 6.2)

An oven-dried 25 mL Schlenk flask was charged with a magnetic stirrer bar, 3-bromophenyltrifluoroborate **31** (0.41 g, 1.54 mmol) and anhydrous THF (6 mL). The resulting solution was cooled to –78 ºC in a dry ice/acetone bath, and *t*-BuLi in pentane (1.03 mL, 1.5 M, 1.54 mmol) was added under argon. After 1 h of stirring triisopropyl borate (0.53 mL, d=0.815 g/mL, 2.31 mmol) was added dropwise. The reaction mixture was stirred at –78 ºC for 1 h. The solution was then allowed to slowly warm to –20 ºC and was stirred for 1h. After, a solution of potassium hydrogenfluoride (0.72 g, 9.24 mmol) in 2 mL of desgased water was added slowly. The reaction mixture was stirred at –20 ºC for 1 h. The solution was then allowed to slowly warm to room temperature and was stirred for 1h. Two layers were separated. The aqueous layer was extracted with THF (3 × 20 mL) and the combined organic phase was dried and concentrated. TLC and ^{1}H NMR do not show the presence of 1,3-bis(potassium trifluoroborate)benzene **32**.

6.2.6. *meta*-(*N*-IMIDAZOLYL)-2,4,6-TRIMETHYLBENZENE 5b

- **1,3-Bis(1-imidazolyl)-2,4,6-trimethylbenzene 5b**



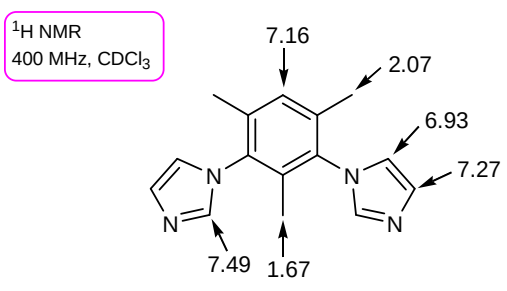
An oven-dried resealeable tube was back-filled with argon and charged with 2,4-dibromomesitylene **20b** (0.28 g, 1 mmol), imidazole **18** (0.16 g, 2.40 mmol), CuI (0.038 g, 0.20 mmol), dry DMF (1 mL), *N,N'*-dimethylethylenediamine (0.082 mL, d=0.819 g/mL, 0.80 mmol) and Cs_2CO_3 (1.37 g, 4.20 mmol) under a stream of argon. The tube was sealed with a Teflon valve and the reaction mixture was stirred magnetically at 170 ℃ for 48 h . The cooled reaction mixture was diluted with EtOAc and filtered through a plug of silica gel eluting with additional EtOAc saturated with NH_3. The filtrate was concentrated and the resulting residue was purified by column chromatography on silica gel [hexane/EtOAc (1:1); EtOAc-NH_3; EtOAc/MeOH (9:1)] to provide 0.026 g (10% yield) of 1,3-bis(*N*-imidazolyl)-2,4,6-trimethylbenzene **5b**. Mp 118-119 ºC.

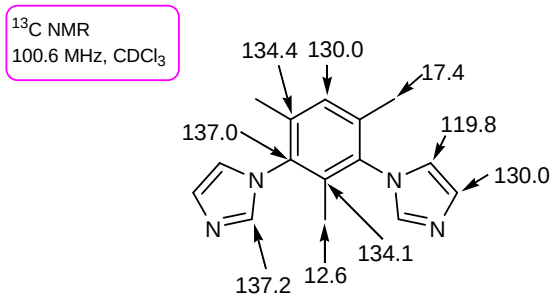
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.67 (s, 3H, C*H*$_3$), 2.07 (s, 6H, C*H*$_3$), 6.93 (s, 2H, Imi), 7.16 (s, 1H, Aryl), 7.27 (s, 2H, Imi), 7.49 (s, 2H, Imi).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 12.6 (*C*H$_3$), 17.4 (*C*H$_3$), 119.8 (Imi), 130.0 (Aryl, Imi), 134.1 (*C*q), 134.4 (*C*q), 137.0 (*C*q), 137.2 (Imi).

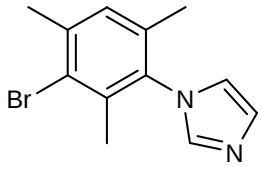
EI-MS *m/z* (%): 252 (100) [$M^{+\cdot}$].

Anal. Calcd for $C_{15}H_{16}N_4 \cdot 0.5\ C_4H_8O$: C, 68.90; H, 6.80; N, 18.90. Found: C, 69.12; H, 6.56; N, 18.94.





- **1-(3-Bromo-2,4,6-trimethylphenyl)-1*H*-imidazole 22b**



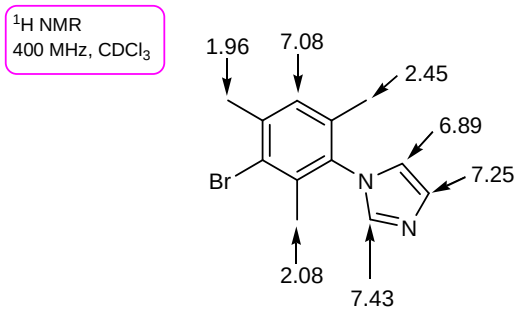
An oven-dried resealeable tube was back-filled with argon and charged with 2,4-dibromomesitylene **20b** (0.28 g, 1 mmol), imidazole **18** (0.082 g, 1.20 mmol), CuI (0.019 g, 0.10 mmol), dry DMF (1 mL), *N,N'*-dimethylethylenediamine (0.041 mL, d=0.819 g/mL, 0.40 mmol) and Cs_2CO_3 (0.69 g, 2.10 mmol) under a stream of argon. The tube was sealed with a Teflon valve and the reaction mixture was stirred magnetically at 170 ℃ for 48 h. The cooled reactio n mixture was diluted with EtOAc and filtered through a plug of silica gel eluting with additional EtOAc saturated with NH_3. The filtrate was concentrated and the resulting residue was purified by column chromatography on silica gel [hexane/EtOAc (1:1); EtOAc-NH_3; EtOAc/MeOH (9:1)] to provide 0.054 g (20% yield) of 1-(3-bromo-2,4,6-trimethylphenyl)-*1H*-imidazole **22b** while 0.14 g of aryldihalide **20b** were recovered (Table 6.7, entry 2). Mp 94-95 ºC.

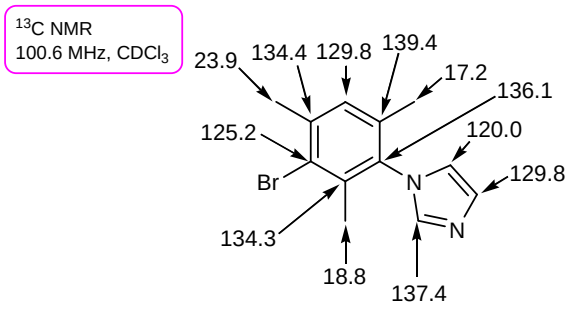
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.96 (s, 3H, C*H*$_3$), 2.08 (s, 3H, C*H*$_3$), 2.45 (s, 3H, C*H*$_3$), 6.89 (s, 1H, Imi), 7.08 (s, 1H, Aryl), 7.25 (s, 1H, Imi), 7.43 (s, 1H, Imi).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 17.2 (*C*H$_3$), 18.8 (*C*H$_3$), 23.9 (*C*H$_3$), 120.0 (Imi), 125.2 (*C*q), 129.8 (Aryl, Imi), 134.3 (*C*q), 134.4 (*C*q), 136.1 (*C*q), 137.4 (Imi), 139.4 (*C*q).

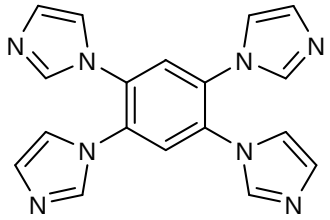
EI-MS *m/z* (%): 158 (100) [$M^{+\cdot}$], 264 (39) [$M^{+\cdot}$-1], 266 (38) [$M^{+\cdot}$+1].

Anal. Calcd for $C_{12}H_{13}BrN_2$: C, 54.36; H, 4.94; N, 10.57. Found: C, 54.05; H, 4.93; N, 10.17.





6.2.7. 1,2,4,5-TETRA(*N*-IMIDAZOLYL)BENZENE 33



An oven-dried resealable tube was back-filled with argon and charged with 1,2,4,5-tetrabromobenzene **34** (0.39 g, 1 mmol), imidazole **18** (0.33 g, 4.80 mmol), CuI (0.038 g, 0.20 mmol), dry DMF (2 mL), *N*,*N'*-dimethylethylenediamine (0.085 mL, d=0.819 g/mL, 0.80 mmol) and Cs_2CO_3 (2.73 g, 8.40 mmol) under stream of argon. The tube was sealed with a Teflon valve and the reaction mixture was stirred magnetically at 170 ºC for 48 h. The resulting suspension was cooled to room temperature, and CH_2Cl_2 (20 mL) and NH_4OH (20 mL) were added. The organic layer was washed, dried and the solvent removed. The residue was purified by flash chromatography on silica gel [EtOAc, EtOAc:MeOH (5%)] to afford a mixture of the corresponding mono-, di-, tri- and tetra-imidazole substituted products in very low yields (see, Table 6.2), which were identified by mass spectrometry EI-MS.

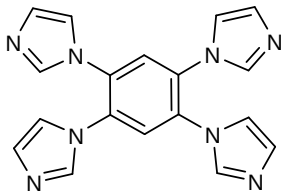
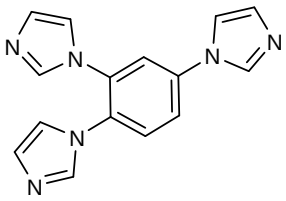
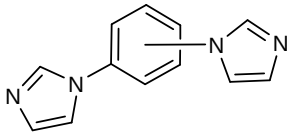
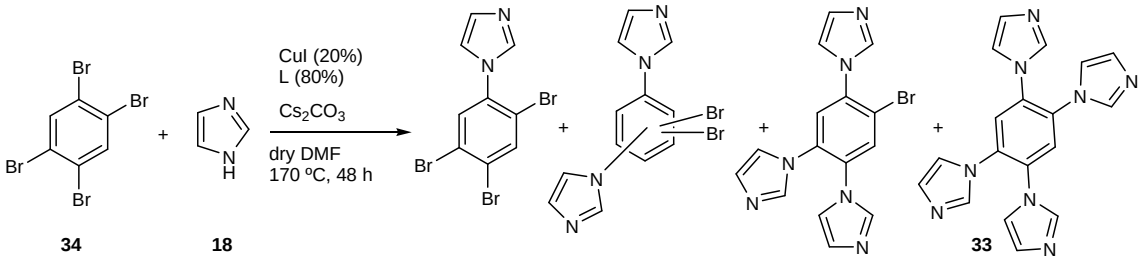
Compound	**A**	**B**	**C**
t_R (min)	18.63	12.57	9.71
			
EI-MS *m/z* (%)	341 (100) [$M^{+\cdot}$-1] 275 (19) [$M^{+\cdot}$-Im]	275 (100) [$M^{+\cdot}$-1] 209 (7) [$M^{+\cdot}$-Im]	210 (100) [$M^{+\cdot}$] 143 (8) [$M^{+\cdot}$-Im]

Figure 6.2.1

Table 6.2. Attempted preparation of 1,2,4,5-tetra(*N*-imidazolyl)benzene **33** from aryl halide **34**[a]



34 **18** **33**

Entry	L	Solvent	T (ºC)	Time (h)	Yield (%) [b]
1	A	Dioxane	95	24	—
2[c]	B	DMF	170	48	—
3	B	DMF	170	48	[d]

[a]All reactions 0.5 M with respect to 1,2,4,5-tetrabromobenzene **34** unless otherwise noted. [b]Isolated yield after chromatographic purification. [c]With 10 mol% CuI and 40 mol% **L**. [d]A mixture of the corresponding mono-, di-, tri- and tetraimidazole substituted products was observed by EI-MS (see, Figure 6.2.1).

6.3. SYNTHESIS OF DICATIONIC IMIDAZOLIUM SALTS 8-12·2X

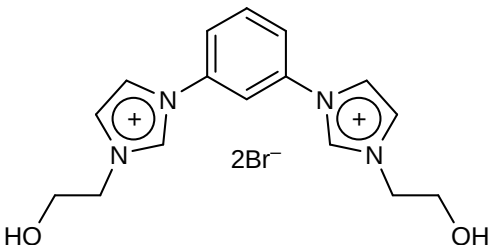
Materials

Solvents: Acetonitrile, Acetonitrile/NH_3(g), DMF (dry with molecular sieves), DMSO (anhydrous with molecular sieves), ethanol and THF were distilled prior to use and dried.

Commercially available products: 2-Bromoethanol, 1-bromo-2-chloroethane, 2-(bromomethyl)pyridine hydrobromide **38·HBr**, 2,4-bis(chloromethyl)-1,3,5-trimethylbenzene **39**, 1-methyl-1*H*-imidazole **45a**, diethyl malonate **46**, diphenylphosphine, hexafluorophosphoric acid solution, 48% hydrobromic acid, iodine, K_2CO_3, K*t*-BuO, $NaBH_4$, NaCN, NaOH and 95-98% sulfuric acid.

6.3.1. BIS(FOSFINO-IMIDAZOLIUM) SALT 8·2Br

- **1,3-Bis[3-(2-hydroxyethyl)-1-imidazolio]benzene dibromide 36·2Br**



An oven-dried two-necked round bottom 10 mL flask was back-filled with argon and charged with a magnetic stirrer bar, 1,3-bis(1-imidazolyl)benzene **5a** (0.15 g, 0.74 mmol), 2-bromoethanol (0.51 mL, d=1.763 g/mL, 7.14 mmol), and dry CH_3CN (5 mL). The reaction mixture was stirred magnetically at reflux for 24 h. The solvent was evaporated and the residue was treated several times with anhydrous acetone in an ultrasonic bath. The precipitate was filtered in vacuo to give 0.26 g (79% yield) of **36·2Br** as a white solid. Mp 176-177 ºC.

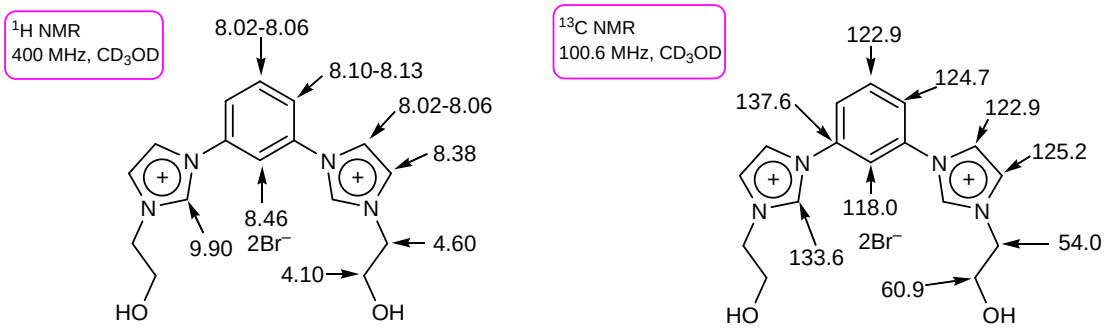
^{1}H NMR (400 MHz, CD_3OD): δ (ppm) 4.10 (t, *J*=5.02, 4H, C*H*$_2$OH), 4.60 (t, *J*=5.02, 4H, C*H*$_2$Imi), 8.02-8.06 (m, 3H, Aryl, Imi), 8.10-8.13 (m, 2H, Aryl), 8.38 (d, *J*=2.10 Hz , 2H, Imi), 8.46 (t, *J*=2.10 Hz, 1H, Aryl), 9.90 (s, 2H, Imi).

^{13}C NMR (100.6 MHz, CD_3OD): δ (ppm) 54.0 (*C*H$_2$Imi), 60.9 (*C*H$_2$OH), 118.0 (Aryl), 122.9 (Aryl, Imi), 124.7 (Aryl), 125.2 (Imi), 133.6 (Imi), 137.6 (*C*q).

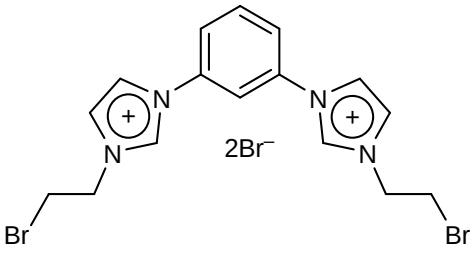
IR (KBr): ν (cm^{-1}) 1066 (C-O), 1548 (C=N), 3315 (O-H).

ESI(+)-MS *m/z* (%): 149.9 (100) $[M]^{2+}$, 380.3 (1) $[M+Br]^{+}$.

Anal. Calcd for $C_{16}H_{20}Br_2N_4O_2 \cdot H_2O$: C, 40.19; H, 4.64; N, 11.72. Found: C, 40.16; H, 4.25; N, 11.76.



- **1,3-Bis[3-(2-bromoethyl)-1-imidazolio]benzene dibromide 35b·2Br**



An oven-dried two-necked round bottom 10 mL flask was back-filled with argon and charged with a magnetic stirrer bar, **36·2Br** (1.20 g, 2.61 mmol) and 48% hydrobromic acid (7.04 mL, d=1.490 g/mL, 62.59 mmol). The reaction mixture was stirred magnetically at reflux for 24 h. The solvent was evaporated and the residue was treated several times with anhydrous acetone in an ultrasonic bath. The precipitate was filtered in vacuo to give 1.23 g (81% yield) of the title compound **35b·2Br** as a white solid. Mp 218-219 ºC.

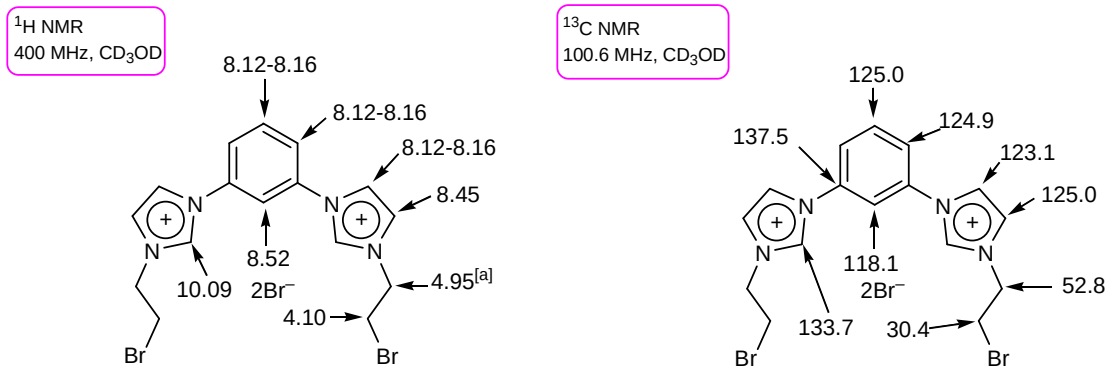
^{1}H NMR (400 MHz, CD_3OD): δ (ppm) 4.10 (t, *J*=5.9 Hz, 4H, C*H*$_2$Br), 4.95 (t, 4H, C*H*$_2$Imi), 8.12-8.16 (m, 5H, Aryl, Imi), 8.45 (d, *J*=2.1 Hz, 2H, Imi), 8.52 (t, *J*=2.1 Hz, 1H, Aryl), 10.09 (s, 2H, Imi).

^{13}C NMR (100.6 MHz, CD_3OD): δ (ppm) 30.4 (*C*H$_2$Br), 52.8 (*C*H$_2$Imi), 118.1 (Aryl), 123.1 (Imi), 124.9 (Aryl), 125.0 (Aryl, Imi), 133.7 (Imi), 137.5 (*C*q).

IR (KBr): ν (cm^{-1}) 1555 (C=N).

ESI(+)-MS *m/z* (%): 212.9 (100) $[M]^{2+}$, 506.8 (4) $[M+Br]^{+}$.

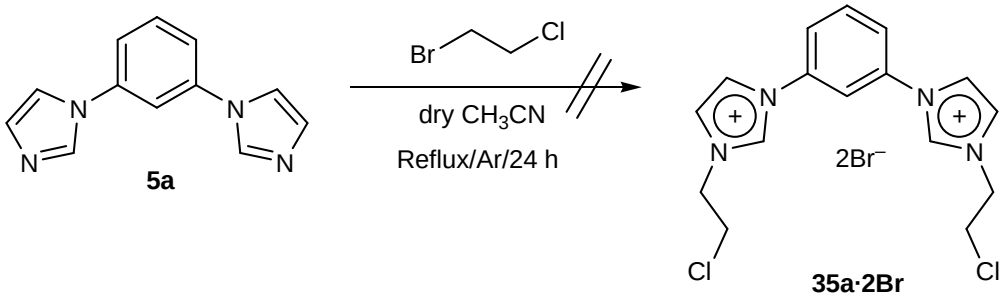
Anal. Calcd for $C_{16}H_{18}Br_4N_4$: C, 32.80; H, 3.10; N, 9.56. Found: C, 32.45; H, 3.10; N, 9.36.



[a]Signal is not completely observed (under CD_3OD)

- **Attempted preparation of 1,3-Bis[3-(2-chloroethyl)-1-imidazolio] benzene dibromide 35a·2Br**

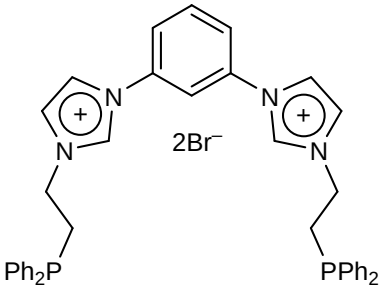
An oven-dried two-necked round bottom 10 mL flask was back-filled with argon and charged with a magnetic stirrer bar, 1,3-bis(1-imidazolyl)benzene **5a** (0.060 g, 0.29 mmol), 1-bromo-2-chloroethane (0.24 mL, d=1.723 g/mL, 2.90 mmol), and dry CH_3CN (2 mL). The reaction mixture was stirred magnetically at reflux for 24 h. The solvent was evaporated and the residue was treated several times with anhydrous acetone in an ultrasonic bath. The precipitate was filtered in vacuo and identified as a mixture of starting material and **35a·2Cl** by TLC. Purification performed by flash chromatography on alumina [EtOAc/MeOH (8:2)] was not successful.



5a **35a·2Br**

Scheme 6.7

- **1,3-Bis{3-[(2-diphenylphosphino)ethyl]-1-imidazolio}benzene dibromide 8·2Br**



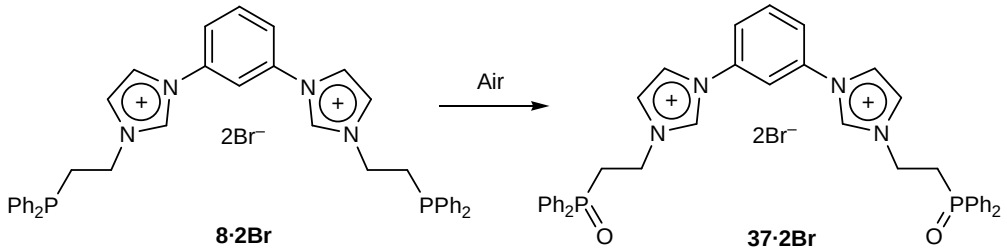
A mixture of $KPPh_2$, which was freshly prepared by a mixture of K*t*-BuO (0.16 g, 1.43 mmol) and $HPPh_2$ (0.26 mL, d=1.070 g/mL, 1.50 mmol) in anhydrous and desgassed DMSO (1 mL) was stirred for about 30 min at room temperature under a stream of argon. A red solution was formed. Then, a 2 mL DMSO solution of **35b·2Br** (0.40 g, 0.68 mmol) was added dropwise. After addition, the solution was allowed to react for 3 h at room temperature. The solvent was removed completely under vacuum. Desgased methanol (10 mL) was added to quench excess $KPPh_2$. The methanol was then removed under vacuum. A mixture of dichloromethane/water (1:1) (25 mL) was added. The organic layer was separated, and the aqueous phase was washed with another portions of dichloromethane (2 × 25 mL). After the combined organic extracts were dried over anhydrous Na_2SO_4 and filtered, the solvent was then removed completely under high vacuum to give a crude oily product which was treated several times with anhydrous diethyl ether in an ultrasonic bath. The precipitate was filtered in vacuo under argon atmosphere to give 0.30 g (55% yield) of the title compound **8·2Br** as a white solid.

^{1}H NMR (400 MHz, CD_3OD): δ (ppm) 2.52-2.59 (m, 4H, C*H*$_2$PPh$_2$), 3.84-3.94 (m, 4H, C*H*$_2$), 6.51-7.44 (m, 28H, Aryl, Imi).

^{13}C NMR (100.6 MHz, CD_3OD): δ (ppm) 30.0 (*C*H_2Br), 30.7 (*C*H_2Imi), 45.4, 117.4, 122.6, 124.4, 125.1, 128.7, 128.9, 130.2, 130.4, 131.6, 131.8, 131.9, 132.3, 132.8, 133.6, 133.8, 134.0, 134.2, 137.3.

In this case, it was not possible to carry out the assignment of the signals in ^{1}H and ^{13}C NMR spectrums due to their high complexity, probably as a result of product's oxidation in solution.

Caution: The compound **8·2Br** was handled and stored under argon atmosphere since it is extremely air-sensitive. However, in few days the oxidated product **37·2Br** was observed.



Scheme 6.8

1,3-Bis{3-[(2-diphenylphosphoryl)ethyl]-1-imidazolio}benzene dibromide 37·2Br:

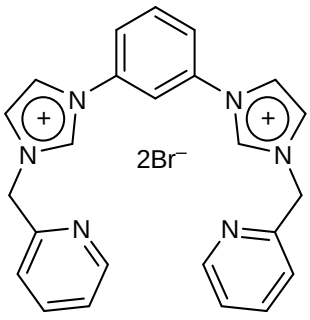
IR (KBr): ν (cm^{-1}) 1175 (P=O).

EI-MS *m/z* (%):

124 (25) [O=PPh], 201 (89) [O=PPh$_2$], 215 (5) [CH$_2$-O=PPh$_2$], 229 (11) [CH$_2$-CH$_2$-O=PPh$_2$]

6.3.2. BIS(PYRIDYL-IMIDAZOLIUM) SALTS 9·2X

- **1,3-Bis[3-(2-pyridylmethyl)-1-imidazolio]benzene dibromide 9·2Br**



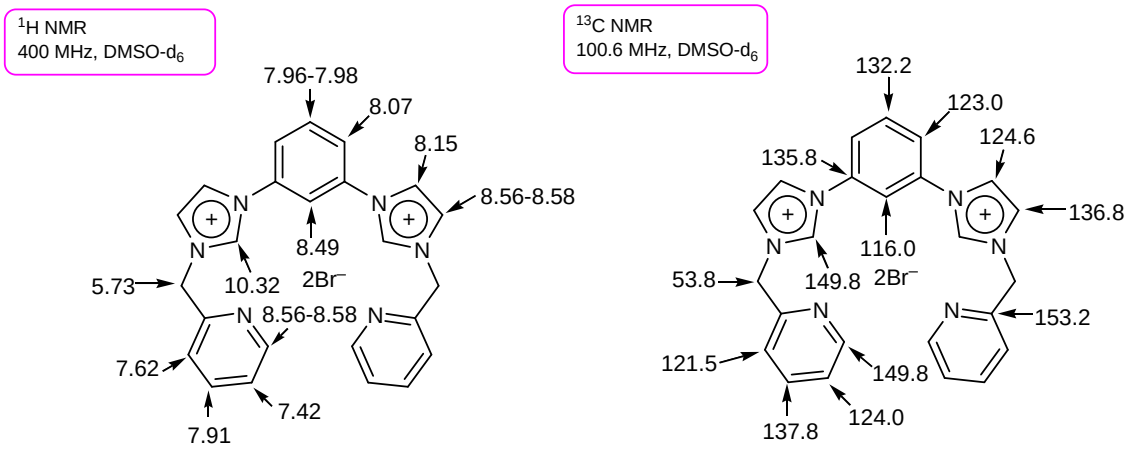
2-(Bromomethyl)pyridine hydrobromide **38·HBr** (0.32 g, 1.25 mmol) was neutralized at 0 ºC for 1 h using saturated aqueous solution of sodium carbonate (5 mL). The liberated 2-(bromomethyl)pyridine **38** was extracted into diethyl ether (3 × 5 mL) at 0 ºC, dried (with anhydrous Na_2SO_4) and filtered. 1,3-bis(1-imidazolyl)benzene **5a** (0.11 g, 0.50 mmol) in dry acetonitrile (10 mL) was added at 0 ºC to the filtrate using a transfer, and the solution was stirred magnetically at reflux for 12 h. The solvent was evaporated under reduced pressure, and the formed red oil was treated several times with EtOAc in an ultrasonic bath to eliminate the excess of

5a. The resulting hygroscopic red oily product was dried in vacuo to give 0.28 g (99% yield) of the title compound **9·2Br**.

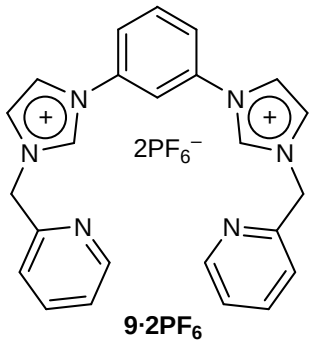
^{1}H NMR (400 MHz, DMSO-d$_6$): δ (ppm) 5.73 (s, 4H, C*H*$_2$pyr), 7.42 (ddd, *J*=7.55, 4.86, 1.00 Hz, 2H, *H*$_5$ pyr), 7.62 (d, *J*=7.81, 2H, *H*$_3$ pyr), 7.91 (dt, *J*=7.72, 7.70, 1.80 Hz, 2H, *H*$_4$ pyr), 7.96-7.98 (m, 1H, Aryl), 8.07 (dd, *J*=8.27, 1.89 Hz, 2H, Aryl), 8.15 (s, 2H, Imi), 8.49 (s,1H, Aryl), 8.56-8.58 (m, 4H, *H*$_6$ pyr, Imi), 10.32 (s, 2H, Imi).

^{13}C NMR (100.6 MHz, DMSO-d$_6$): δ (ppm) 53.8 (*C*H$_2$pyr), 116.0 (Aryl), 121.5 (*C*$_3$ pyr), 123.0 (Aryl), 124.0 (*C*$_5$ pyr), 124.6 (Imi), 132.2 (Aryl), 135.8 (*C*q), 136.8 (Imi), 137.8 (*C*$_4$ pyr), 149.8 (Imi, *C*$_6$ pyr), 153.2 (*C*q).

ESI(+)-MS *m/z* (%): 197.0 (100) $[M]^{2+}$, 475.1 (2) $[M+Br]^{+}$.



- **1,3-Bis[3-(2-pyridylmethyl)-1-imidazolio]benzene dihexafluorophosphate 9·2PF$_6$**



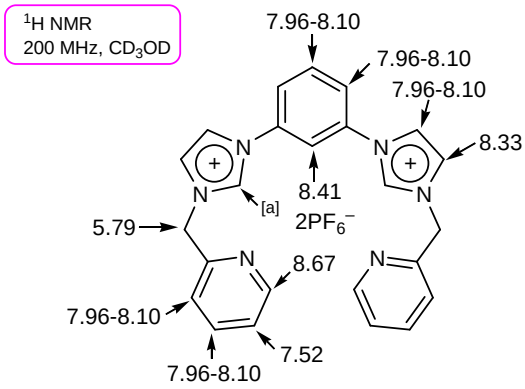
9·2PF$_6$

A solution of dicationic **9·Br** (0.15 g, 0.27 mmol) in 96% ethanol (50 mL) was passed through a column packed with a strongly basic anion-exchange resin (Ion exchanger Amberlite® IRA-400, hydroxide form). The neutral eluates were acidified to pH=6 with an hexafluorophosphoric acid solution, and the resulting solution was concentrated to dryness to afford the hexafluorophosphate **9·2PF$_6$** as an

hygroscopic red oil (0.18 g, 97% yield).

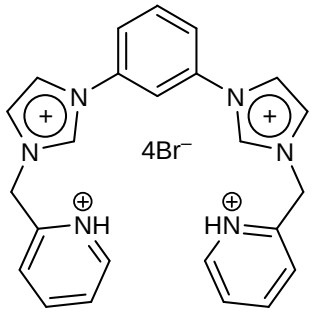
^{1}H NMR (200 MHz, CD_3OD): δ (ppm) 5.79 (s, 4H, C*H*$_2$pyr), 7.52 (dd, *J*=7.6, 1.0 Hz, 2H, *H*$_5$ pyr), 7.96-8.10 (m, 9H, *H*$_3$ pyr, *H*$_4$ pyr, Aryl, Imi), 8.33 (d, *J*=2.0, 2H, Imi), 8.41 (s,1H, Aryl), 8.67 (d, *J*=4.7, 2H, *H*$_6$ pyr).

ESI(+)-MS *m/z* (%): 197.0 (100) $[M]^{2+}$, 539.1 (8) $[M+PF_6]^+$.



[a]No signal observed due to H/D exchange

- **1,3-Bis[3-(2-pyridylmethyl)-1-imidazolio]benzene dibromide dihydrobromide 9·2Br·2HBr**



9·2Br·2HBr

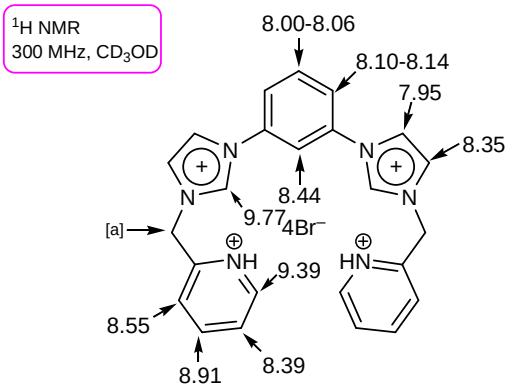
An oven-dried two-necked round bottom 10 mL flask was back-filled with argon and charged with a magnetic stirrer bar, 1,3-bis(1-imidazolyl)benzene **5a** (0.21 g, 1 mmol), 2-(bromomethyl)pyridine hydrobromide **38·HBr** (0.53 g, 2.10 mmol), and dry acetonitrile (10 mL). The reaction mixture was stirred magnetically at reflux for 24 h. After cooling to room temperature, a precipitate was formed which was filtered off, washed with small amounts of acetonitrile, and dried in vacuo to give 0.51 g (71% yield) of **9·2Br·2HBr** as a white solid. Mp >300 ºC.

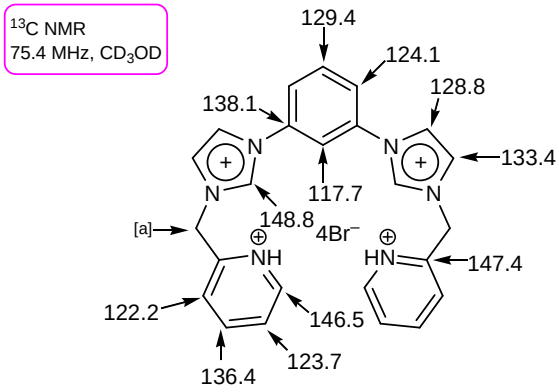
^{1}H NMR (300 MHz, CD_3OD): δ (ppm) 7.95 (dd, *J*=0.6 Hz, *J*=2.0, 2H, Imi), 8.00-8.06 (m, 1H, Aryl), 8.10-8.14 (m, 2H, Aryl), 8.35 (t, *J*=2.0, 2H, Imi), 8.39 (td, 2H, *J*=1.5, *J*=6.2, *H*$_5$ pyr), 8.44 (t, *J*=2.0, 1H, Aryl), 8.55 (ddd, *J*=0.6, *J*=1.5, *J*=8.0, 2H, *H*$_3$ pyr), 8.91 (dt, *J*=1.5, *J*=8.0, 2H, *H*$_4$ pyr), 9.39 (ddd, *J*=0.6, *J*=1.5, *J*=6.2, 2H, *H*$_6$ pyr), 9.77 (t, *J*=1.5, 2H, Imi).

^{13}C NMR (75.4 MHz, CD_3OD): δ (ppm) 117.7 (Aryl), 122.2 (*C*$_3$ pyr), 123.7 (*C*$_5$ pyr), 124.1 (Aryl), 128.8 (Imi), 129.4 (Aryl), 133.4 (Imi), 136.4 (*C*$_4$ pyr), 138.1 (*C*q), 146.5 (*C*$_6$ pyr), 147.4 (*C*q), 148.8 (Imi).

ESI(+)-MS *m/z* (%): peaks arising from molecular fragmentation were observed.

Anal. Calcd for $C_{24}H_{24}Br_4N_6 \cdot 4\ H_2O$: C, 36.57; H, 4.09; N, 10.66. Found: C, 36.33; H, 3.69; N, 11.05.

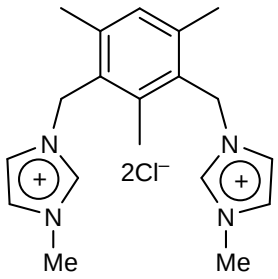




[a]No signal observed due to H/D exchange

6.3.3. BIS(METHYLENE-IMIDAZOLIUM) SALTS 10a,b·2X

- **1,3-Bis[(3-methyl-1-imidazolio)methyl]-2,4,6-trimethylbenzene dichloride 10a·2Cl**



A solution of 2,4-bis(chloromethyl)-1,3,5-trimethylbenzene **39** (1.54 g, 7.09 mmol) and 1-methyl-1*H*-imidazole **45a** (15.41 mL, d=1.035 g/mL, 194.33 mmol) was stirred at reflux temperature under argon atmosphere for 30 min. After cooling to room temperature and reduction of the volume, the brown residue was treated several times with dry acetone in an ultrasonic bath and the white solid obtained was filtered off and dried under reduced pressure to give the title compound **10a·2Cl** (2.22 g, 81% yield). Mp 264-266 ºC.

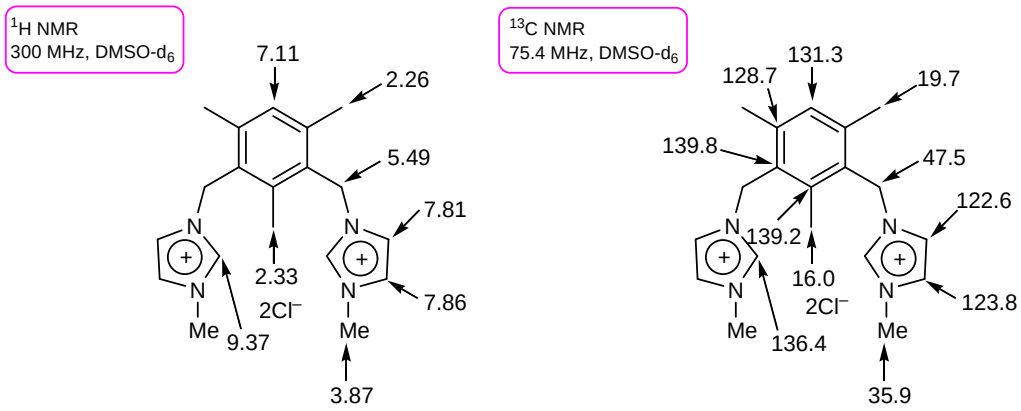
^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm) 2.26 (s, 6H, CH_3), 2.33 (s, 3H, CH_3), 3.87 (s, 6H, CH_3Imi), 5.49 (s, 4H, CH_2), 7.11 (s, 1H, Aryl), 7.81 (s, 2H, Imi), 7.86 (s, 2H, Imi), 9.37 (s, 2H, Imi).

^{13}C NMR (75.4 MHz, DMSO-d_6): δ (ppm) 16.0 (*C*H_3), 19.7 (*C*H_3), 35.9 (*C*H_3Imi), 47.5 (*C*H_2), 122.6 (Imi), 123.8 (Imi), 128.7 (*C*q), 131.3 (Aryl), 136.4 (Imi), 139.2 (*C*q), 139.8 (*C*q).

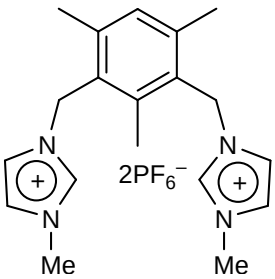
IR (KBr): ν (cm^{-1}) 1562 (C=N).

ESI(+)-MS *m/z* (%): 155.2 (100) $[M]^{2+}$, 345.9 (14) $[M+Cl]^{+}$.

The NMR spectroscopic data and elemental analysis are in accordance with those reported in literature <04EJOC695>.



- **1,3-Bis[(3-methyl-1-imidazolio)methyl]-2,4,6-trimethylbenzene dihexafluorophosphate 10a·2PF$_6$**



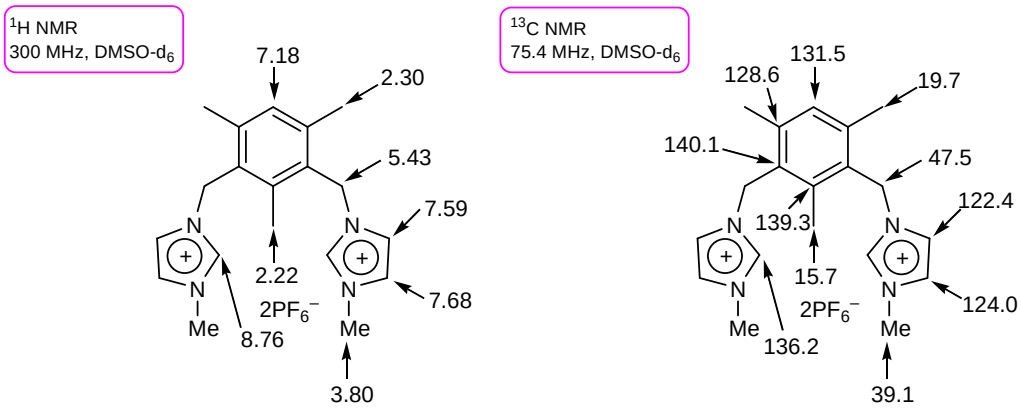
A solution of dicationic **10a·2Cl** (0.52 g, 1.38 mmol) in 96% ethanol (100 mL) was passed through a column packed with a strongly basic anion-exchange resin (Ion exchanger Amberlite® IRA-400, hydroxide form). The neutral eluates were acidified to pH=3 with an hexafluorophosphoric acid solution, and the resulting solution was concentrated to dryness to afford the hexafluorophosphate **10a·2PF$_6$** (0.82 g, 98% yield). Mp 180-182 ºC.

^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm) 2.22 (s, 3H, CH_3), 2.30 (s, 6H, CH_3), 3.80 (s, 6H, CH_3Imi), 5.43 (s, 4H, CH_2), 7.18 (s, 1H, Aryl), 7.59 (s, 2HImi), 7.68 (s, 2H, Imi), 8.76 (s, 2H, Imi).

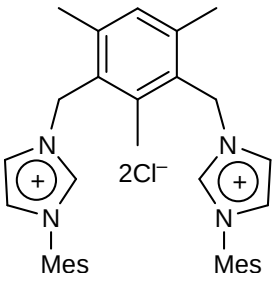
^{13}C NMR (75.4 MHz, DMSO-d_6): δ (ppm) 15.7 (*C*H_3), 19.7 (*C*H_3), 39.1 *C*H_3Imi), 47.5 (*C*H_2), 122.4 (Imi), 124.0 (Imi), 128.6 (*C*q), 131.5 (Aryl), 136.2 (Imi), 139.3 (*C*q), 140.1 (*C*q).

IR (KBr): ν (cm^{-1}) 835 (P-F), 1578 (C=N).

ESI(+)-MS *m/z* (%): 287.4 (100) $[M]^{2+}$.



- **1,3-Bis[(3-mesityl-1-imidazolio)methyl]-2,4,6-trimethylbenzene dichloride 10b·2Cl**



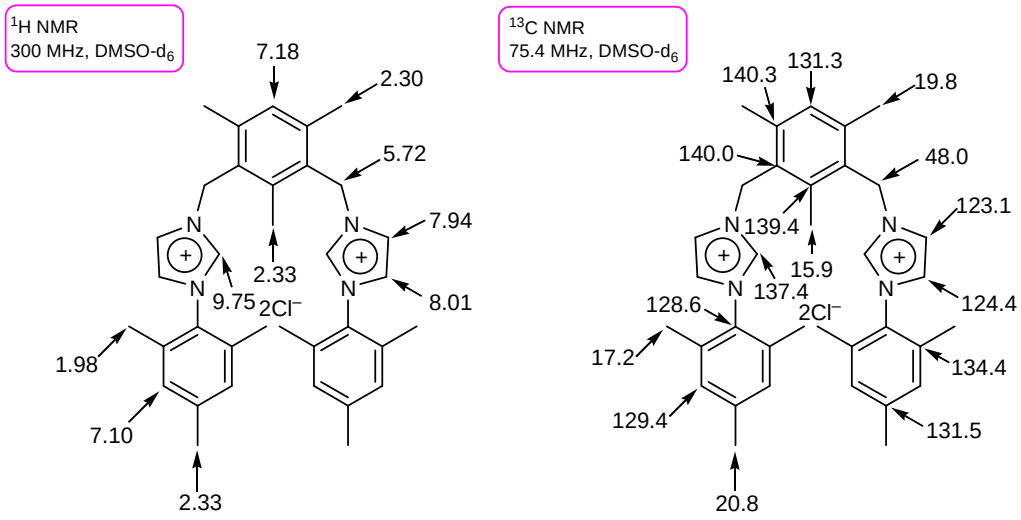
A solution of 2,4-bis(chloromethyl)-1,3,5-trimethylbenzene **39** (1.08 g, 4.98 mmol) and 1-(2,4,6-trimethylphenyl)-1*H*-imidazole **45b** (1.85 g, 9.95 mmol) in dry DMF (10 mL) was stirred at 100 ºC under argon atmosphere for 12 h. After cooling to room temperature and reduction of the volume, the brown residue was treated several times with dry acetone in an ultrasonic bath and the white solid obtained was filtered off and dried under reduced pressure to give the title compound **10b·2Br** (2.86 g, 98% yield). Mp 190-192 ºC.

^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm) 1.98 (s, 12H, CH_3), 2.30 (s, 6H, CH_3), 2.33 (s, 9H, CH_3), 5.72 (s, 4H, CH_2), 7.10 (s, 4H, Aryl), 7.18 (s, 1H, Aryl), 7.94 (s, 2H, Imi), 8.01 (s, 2H, Imi), 9.75 (s, 2H, Imi).

^{13}C NMR (100.6 MHz, DMSO-d_6): δ (ppm) 15.9 (*C*H_3), 17.2 (*C*H_3), 19.8 (*C*H_3), 20.8 (*C*H_3), 48.0 (*C*H_2), 123.1 (Imi), 124.4 (Imi), 128.6 (*C*q), 129.4 (Aryl), 131.3 (Aryl), 131.5 (*C*q), 134.4 (*C*q), 137.4 (Imi), 139.4 (*C*q), 140.0 (*C*q), 140.3 (*C*q).

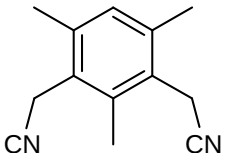
IR (KBr): ν (cm^{-1}) 1553 (C=N).

ESI(+)-MS *m/z* (%): 259.4 (100) $[M]^{2+}$, 554.2 (14) $[M+Cl]^{+}$.



6.3.4. BIS(ETHYLENE-IMIDAZOLIUM) SALTS 11a,b·2Br

- **2,4,6-Trimethylphenylene-1,3-diacetonitrile 42**



To a suspension of 2,4-bis(chloromethyl)-1,3,5-trimethylbenzene **39** (5 g, 23 mmol) in dry DMSO (15 mL), was added sodium cyanide (4.51 g, 92 mmol). The reaction mixture was stirred at room temperature under argon atmosphere for 24 h. The resulting yellow solution was added to 250 mL of water and the precipitation of a white solid was induced, which was washed with water, and dried under vacuum at 40 ºC to afford **42** as a white solid (4.24 g, 93% yield). Mp 169-171 ºC.

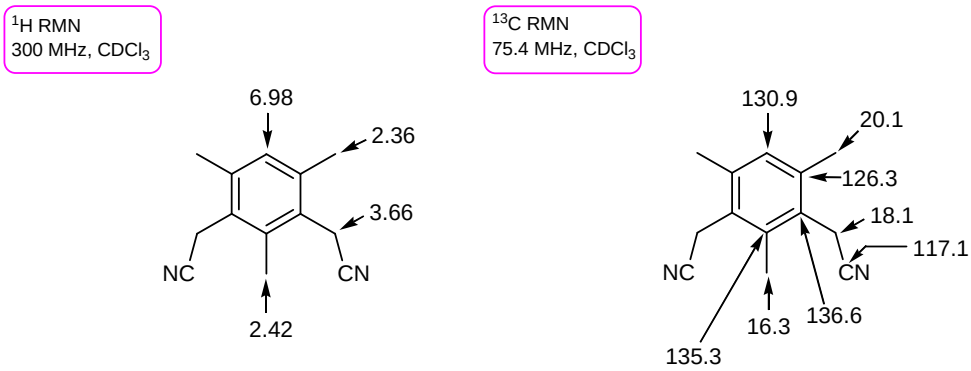
^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 2.36 (s, 6H, C*H*$_3$), 2.42 (s, 3H, C*H*$_3$), 3.66 (s, 4H, C*H*$_2$CN), 6.98 (s, 1H, Aryl).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 16.3 (*C*H$_3$), 18.1 (*C*H$_2$CN), 20.1 (*C*H$_3$), 117.1 (*C*N), 126.3 (*C*q), 130.9 (Aryl), 135.3 (*C*q), 136.6 (*C*q).

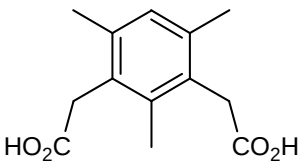
IR (KBr): ν (cm^{-1}) 2250 (CN).

EI-MS: *m/z* (%):171 (100) [$M^{+\cdot}$-7], 198 (48) [$M^{+\cdot}$], 199 (8) [$M^{+\cdot}$+1].

The NMR spectroscopic data is in accordance with those reported in literature <99JMC4485>.



- **2,4,6-Trimethylphenylene-1,3-diacetic acid 43**



To 40 mL of water was added dropwise concentrated sulfuric acid (35 mL). The exothermic reaction was cooled to 50 ºC and then was added **42** (3.50 g, 17.65 mmol). The resulting mixture was heated at reflux temperature for 12 h. The white suspension was cooled to room temperature and added to ice. A white solid was precipitated, filtered and dried under vacuum at 40 ºC to give **43** (4.10 g, 98% yield). Mp 232-234 ºC.

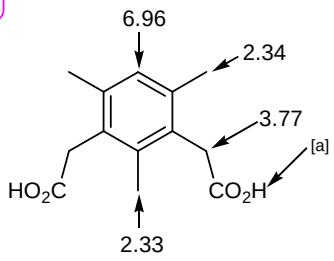
^{1}H NMR (400 MHz, CD_3OD): δ (ppm) 2.33 (s, 3H, C*H*$_3$), 2.34 (s, 6H, C*H*$_3$), 3.77 (s, 4H, C*H*$_2$COOH), 6.96 (s, 1H, Aryl).

^{13}C NMR (100.6 MHz, CD_3OD): δ (ppm) 16.5 (*C*H$_3$), 20.5 (*C*H$_3$), 36.3 (*C*H$_2$COOH), 130.8 (Aryl), 131.3 (*C*q), 136.8 (*C*q), 137.4 (*C*q), 175.6 (*C*OOH).

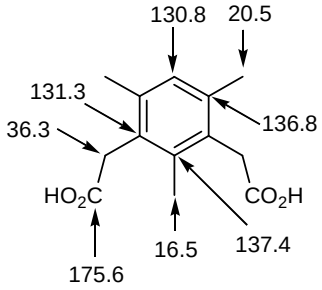
IR (KBr): ν (cm^{-1}) 1686 (C=O), 2950 (COO-H).

EI-MS: *m/z* (%): 91(41), 145 (53) [$M^{+\cdot}$-89], 191 (100) [$M^{+\cdot}$-45], 236 (66) [$M^{+\cdot}$], 237 (9) [$M^{+\cdot}$+1].

^{1}H NMR
400 MHz, CD_3OD

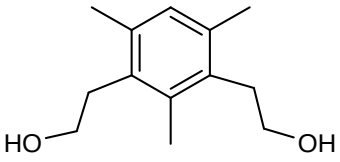


^{13}C NMR
100.6 MHz, CD_3OD



[a]No signal observed due to H/D exchange

- **2,4-Bis(2-hydroxyethyl)-1,3,5-trimethylbenzene 44**



To a suspension of $NaBH_4$ (3.01 g, 79.57 mmol) in anhydrous THF (85 mL) was added dropwise at 0 ºC under argon atmosphere, a solution of iodine (8.08 g, 31.84 mmol) in anhydrous THF (20 mL). The resulting solution was heated at reflux temperature and then was added dropwise a solution of **43** (3.76 g, 15.92 mmol) in THF(40 mL). The reaction mixture was stirred at reflux temperature for 21 h. The mixture was cooled to room temperature and then methanol was added until an orange solution was formed. After this, the solution was stirred for additional 30 minutes and was concentrated under reduced pressure to give an orange semisolid, which was diluted in aqueous 20% KOH solution (450 mL) and stirred at room temperature for 12 h. Then, the resultant solution was extracted with dichloromethane (3 × 200 mL) and the combined organic layers were dried (with anhydrous Na_2SO_4), filtered and concentrated to give **44** as a white solid (3.27 g, 99% yield). Mp 92-94 ºC.

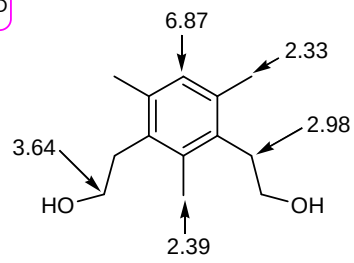
^{1}H NMR (400 MHz, CD_3OD): δ (ppm) 2.33 (s, 6H, C*H*$_3$), 2.39 (s, 3H, C*H*$_3$), 2.98 (t, *J*=7.4 Hz, 4H, C*H*$_2$), 3.64 (t, *J*=7.4 Hz, 4H, C*H*$_2$OH), 6.87 (s, 1H, Ar).

^{13}C NMR (100.6 MHz, CD_3OD): δ (ppm) 15.6 (*C*H$_3$), 20.2 (*C*H$_3$), 34.3 (*C*H$_2$), 62.0 (*C*H$_2$OH), 131.0 (Aryl), 133.7 (*C*q), 135.4 (*C*q), 136.1 (*C*q)

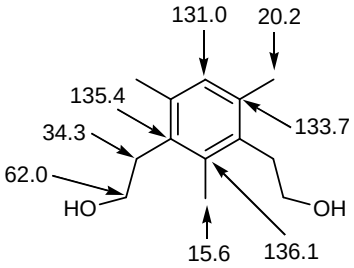
IR (KBr): ν (cm^{-1}) 1043 (C-O), 3290 (O-H).

EI-MS: *m/z* (%): 91 (22), 133 (39), 160 (37) [$M^{+\cdot}$-48], 177 (100) [$M^{+\cdot}$-31], 208 (37) [$M^{+\cdot}$], 209 (5) [$M^{+\cdot}$+1].

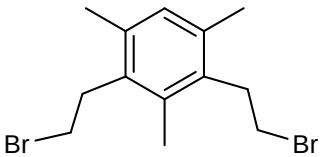
^{1}H NMR
400 MHz, CD_3OD



^{13}C NMR
100.6 MHz, CD_3OD



- **2,4-Bis(2-bromoethyl)-1,3,5-trimethylbenzene 40**

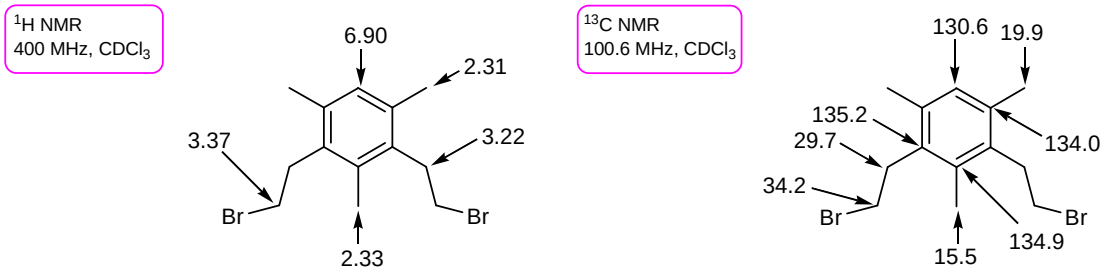


To **44** (3 g, 13.60 mmol), was added at 0 ºC 48% hydrobromic acid (11 mL, d=1.490 g/mL, 206.02 mmol). The resulting mixture was heated at reflux temperature for 3 h. The solution was cooled and then water (100 mL) was added. After this, the mixture was extracted with dichloromethane (3 × 100 mL). The combined organic layers were dried (with anhydrous Na_2SO_4), filtered and concentrated under reduced pressure to obtain **40** (3.81g, 82% yield) as a beige solid. Mp 142-144 ºC.

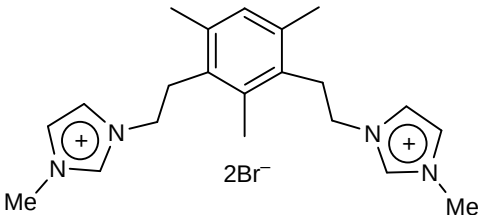
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.31 (s, 6H, C*H*$_3$), 2.33 (s, 3H, C*H*$_3$), 3.22 (t, *J*=7.4 Hz, 4H, C*H*$_2$), 3.37 (t, 4H, *J*=7.4 Hz, C*H*$_2$Br), 6.90 (s, 1H, Aryl).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 15.5 (*C*H$_3$), 19.9 (*C*H$_3$), 29.7 (*C*H$_2$), 34.2 (*C*H$_2$Br), 130.6 (Aryl), 134.0 (*C*q), 134.9 (*C*q), 135.2 (*C*q).

EI-MS: *m/z* (%): 91 (30), 115 (29), 129 (43), 145 (69), 159 (62), 239 (79) [$M^{+\cdot}$-95], 241 (81) [$M^{+\cdot}$-93], 253 (100) [$M^{+\cdot}$-81], 255 (93) [$M^{+\cdot}$-79], 334 (50) [$M^{+\cdot}$], 335 (8) [$M^{+\cdot}$+1], 336 (27) [$M^{+\cdot}$+2].



- **1,3-Bis[2-(3-methyl-1-imidazolio)ethyl]-2,4,6-trimethylbenzene dibromide 11a·2Br**



A solution of **40** (1 g, 2.99 mmol) and 1-methyl-1*H*-imidazole **45a** (6.24 mL, d=1.035 g/mL, 78.64 mmol) was stirred at reflux temperature under argon atmosphere for 30 min. After cooling to room temperature and reduction of the volume, the residue was treated several times with dry acetone in an ultrasonic bath, and the light brown solid obtained was filtered off and dried to give the title compound **11a·2Br** (1.13 g, 76% yield). Mp 137-139 ºC.

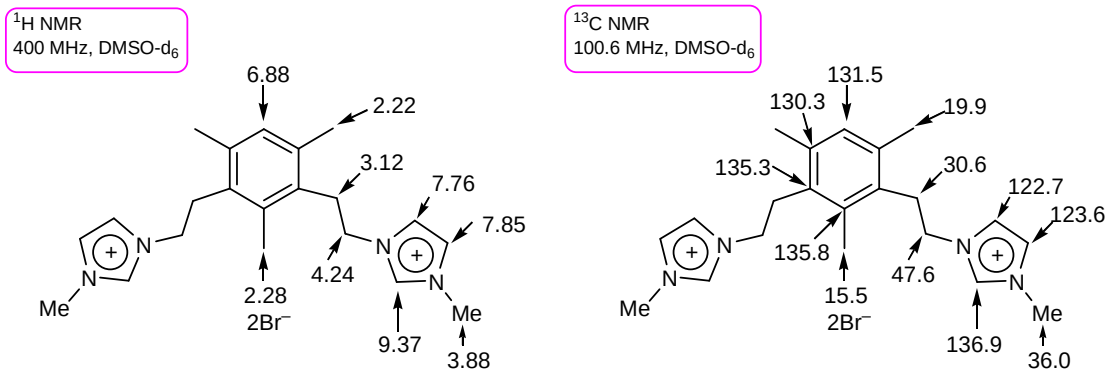
^{1}H NMR (400 MHz, DMSO-d$_6$): δ (ppm) 2.22 (s, 6H, C*H*$_3$), 2.28 (s, 3H, C*H*$_3$), 3.12 (t, 4H, *J*=6.8 Hz, 2 × C*H*$_2$), 3.88 (s, 6H, C*H*$_3$), 4.24 (t, 4H, *J*=6.8 Hz, C*H*$_2$Imi), 6.88 (s, 1H, Aryl), 7.76 (s, 2H, Imi), 7.85 (s, 2H, Imi), 9.37 (s, 2H, Imi).

^{13}C NMR (100.6 MHz, DMSO-d$_6$): δ (ppm) 15.5 (*C*H$_3$), 19.9 (*C*H$_3$), 30.6 (*C*H$_2$), 36.0 (*C*H$_3$), 47.6 (*C*H$_2$Imi), 122.7 (Imi), 123.6 (Imi), 130.3 (*C*q), 131.5 (Aryl), 135.3 (*C*q), 135.8 (*C*q), 136.9 (Imi).

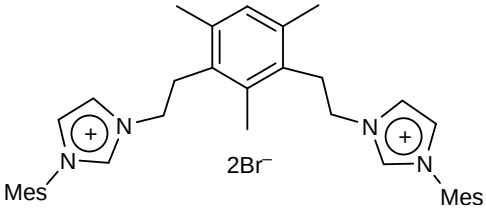
IR (KBr): ν (cm^{-1}) 1565 (C=N).

ESI(+)-MS: *m/z* (%): 169.3 (100) [M]$^{2+}$, 418.4 (2) [M+Br]$^+$.

Anal. Calcd for $C_{21}H_{30}Br_2N_4$·2 H_2O: C, 47.21; H, 6.41; N, 10.49. Found: C, 47.21; H, 6.16; N, 10.28.



- **1,3-Bis[2-(3-mesityl-1-imidazolio)ethyl]-2,4,6-trimethylbenzene dibromide 11b·2Br**



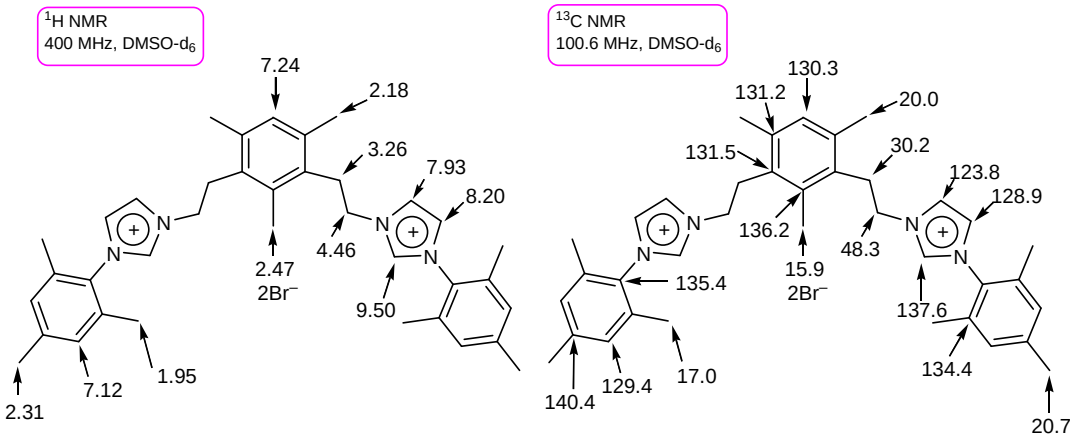
A solution of **40** (2.5 g, 7.48 mmol) and 1-(2,4,6-trimethylphenyl)-1*H*-imidazole **45b** (2.86 g, 15.33 mmol) in dry DMF (15 mL) was stirred at 100 ºC under argon atmosphere for 12 h. After cooling to room temperature and reduction of the volume, the brown residue was treated several times with dry diethyl ether in an ultrasonic bath and the hygroscopic light brown foam obtained was dried under reduced pressure to give the title compound **11b·2Br** (5.15 g, 97%). Mp 94-96 ºC.

^{1}H NMR (400 MHz, DMSO-d$_6$): δ (ppm) 1.95 (s, 12H, C*H*$_3$), 2.18 (s, 6H, C*H*$_3$), 2.31 (s, 6H, C*H*$_3$), 2.47 (s, 3H, C*H*$_3$), 3.26 (t, 4H, *J*=7.4 Hz, C*H*$_2$), 4.46 (t, 4H, *J*=7.4 Hz, C*H*$_2$Imi), 7.12 (s, 4H, Ar), 7.24 (s, 1H, Ar), 7.93 (Imi), 8.20 (Imi), 9.50 (Imi).

^{13}C NMR (100.6 MHz, DMSO-d$_6$): δ (ppm) 15.9 (*C*H$_3$), 17.0 (*C*H$_3$), 20.0 (*C*H$_3$), 20.7 (*C*H$_3$), 30.2 (*C*H$_2$), 48.3 (*C*H$_2$Imi), 123.8 (Imi), 128.9 (Imi), 129.4 (Aryl), 130.3 (Aryl), 131.2 (*C*q), 131.5 (*C*q), 134.4 (*C*q), 135.4 (*C*q), 136.2 (*C*q), 137.6 (Imi), 140.4 (*C*q).

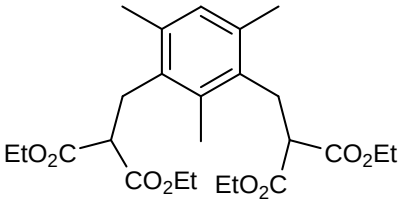
ESI(+)-MS: *m/z* (%): 273.4 (100) $[M]^{2+}$, 626.7 (11) $[M+Br]^+$.

Anal. Calcd for $C_{37}H_{46}Br_2N_4 \cdot H_2O$: C, 61.33; H, 6.68; N, 7.73. Found: C, 61.41; H, 7.01; N, 7.49.



6.3.5. BIS(PROPYLENE-IMIDAZOLIUM) SALTS 12a,b·2X

- **1,3-Bis[2,2-(diethoxycarbonyl)ethyl]-2,4,6-trimethylbenzene 47**



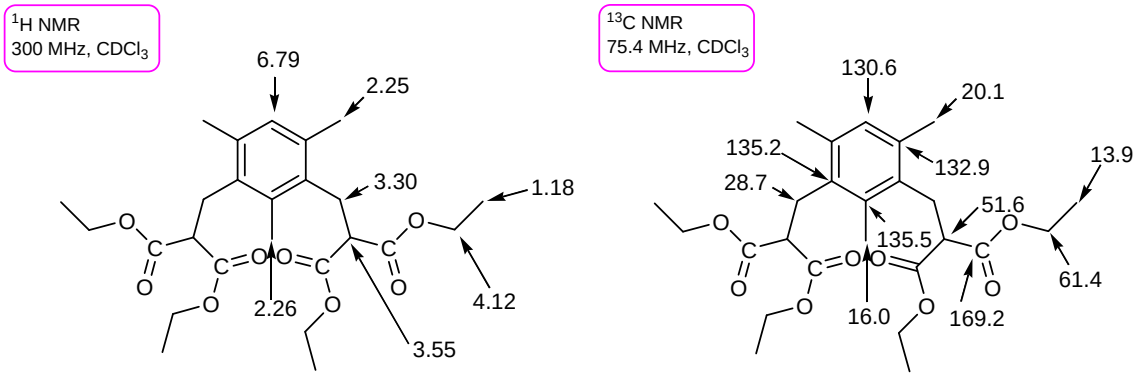
To a solution of diethyl malonate **46** (13.9 mL, d=1.060 g/mL, 92.10 mmol) and potassium carbonate (31.82 g, 230.25 mmol) in dry acetonitrile (350 mL) was added dropwise under argon atmosphere a solution of 2,4-bis(chloromethyl)-1,3,5-trimethylbenzene **39** (10 g, 46 mmol) in dry acetonitrile (200 mL). The reaction mixture was maintained under reflux for 48 h. The mixture was then cooled to room temperature and the resulting white suspension was filtered. The resulting solution was concentrated under reduced pressure, giving the desired product **47** as a yellow solid (21.18 g, 99% yield). Mp 58-60 ºC.

^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 1.18 (t, *J*=7.0 Hz, 12H, C*H*$_3$), 2.25 (s, 6H, C*H*$_3$), 2.26 (s, 3H, C*H*$_3$), 3.30 (d, *J*=7.6 Hz, 4H, C*H*$_2$), 3.55 (t, *J*=7.6 Hz, 2H, C*H*), 4.12 (q, *J*=7.0 Hz, 8H, C*H*$_2$), 6.79 (s, 1H, Aryl).

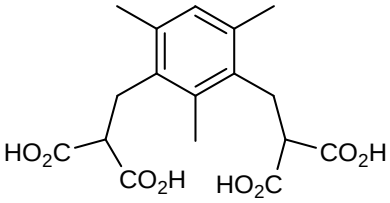
^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 13.9 (*C*H$_3$), 16.0 (*C*H$_3$), 20.1 (*C*H$_3$), 28.7 (*C*H$_2$), 51.6 (*C*H), 61.4 (O*C*H$_2$), 130.6 (Aryl), 132.9 (*C*q), 135.2 (*C*q), 135.5 (*C*q), 169.2 (*C*=O).

IR (NaCl): ν (cm^{-1}) 1283 (C-O), 1733 (C=O).

EI-MS: *m/z* (%):157 (100), 185 (70), 213 (67), 287 (65), 305 (81), 418 (41) [$M^{+\cdot}$-46], 446 (54) [$M^{+\cdot}$-18], 464 (4) [$M^{+\cdot}$].



- **1,3-Bis[2,2-(dicarboxy)ethyl]-2,4,6-trimethylbenzene 48**



To a solution of **47** (21.39 g, 46.05 mmol) in ethanol (400 mL) was added dropwise under argon atmosphere a solution of pulverized sodium hydroxide (27.63 g, 690.75 mmol) in ethanol (200 mL). The reaction mixture was maintained under reflux for 12 h. The resulting suspension was concentrated under reduced pressure to obtain a white solid, which was dissolved in water (200 mL). The resulting solution was made acidic with 5 N HCl and extracted with ethyl acetate (3 × 300 mL). The combined organic layers were dried (with anhydrous Na_2SO_4), filtered and concentrated to dryness to obtain **48** as a white solid (16.22 g, 99% yield). Mp 202-204 ºC.

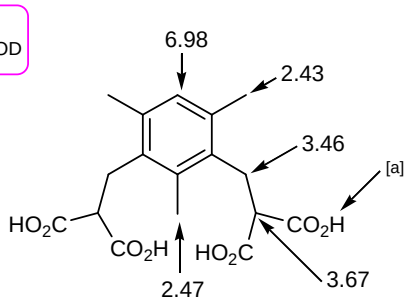
^{1}H NMR (300 MHz, CD_3OD): δ (ppm) 2.43 (s, 6H, C*H*$_3$), 2.47 (s, 3H, C*H*$_3$), 3.46 (d, *J*=7.3 Hz, 4H, C*H*$_2$), 3.67 (t, *J*=7.3 Hz, 2H, C*H*), 6.98 (s, 1H, Aryl)

^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 16.3 (*C*H$_3$), 20.4 (*C*H$_3$), 30.0 (*C*H$_2$), 53.0 (*C*H), 131.6 (Aryl), 134.5 (*C*q), 136.1 (*C*q), 136.6 (*C*q), 173.0 (*C*=O).

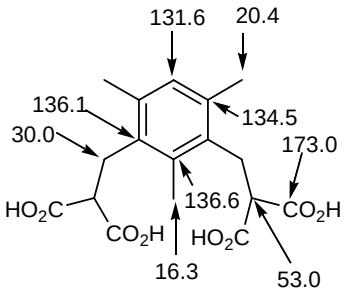
IR (KBr): ν (cm^{-1}) 1702 (C=O), 3008 (COO-H).

EI-MS: *m/z* (%):145 (65), 205 (100), 246 (31), 264 (49) [$M^{+\cdot}$-88].

^{1}H NMR
300 MHz, CD_3OD

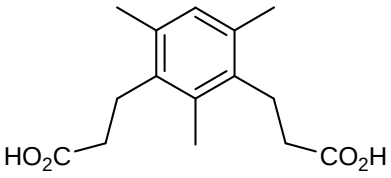


^{13}C NMR
75.4 MHz, CD_3OD



[a]No signal observed due to H/D exchange

- **1,3-Bis(2-carboxyethyl)-2,4,6-trimethylbenzene 49**



48 (16.22 g, 46.04 mmol) was heated for 12 h until reaching melting temperature. The resulting brown residue was treated with saturated potassium carbonate aqueous solution to basic pH. The resulting solution was extracted with ethyl acetate (1 × 250 mL) and the organic layer was washed with saturated potassium carbonate aqueous solution (3 × 100 mL). The aqueous layers were combined, acidified with 5 N HCl and extracted with ethyl acetate (3 × 300 mL). The organic part was dried (with anhydrous Na_2SO_4), filtered and concentrated under reduced pressure to give **49** as a beige solid (9.88 g, 81% yield). Mp 158-160 ºC.

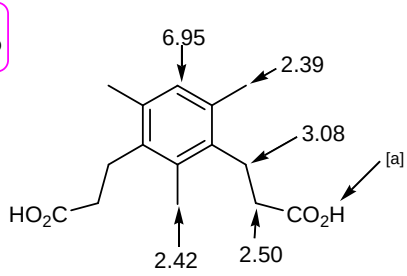
^{1}H NMR (300 MHz, CD_3OD): δ (ppm) 2.39 (s, 6H, C*H*$_3$), 2.42 (s, 3H, C*H*$_3$), 2.50 (t, *J*=7.3 Hz, 4H, C*H*$_2$COOH), 3.08 (t, *J*=7.3 Hz, 4H, C*H*$_2$), 6.95 (s, 1H, Aryl).

^{13}C NMR (75.4 MHz, CD_3OD): δ (ppm) 15.2 (*C*H$_3$), 19.9 (*C*H$_3$), 26.5 (*C*H$_2$), 36.6 (*C*H$_2$COOH), 131.2 (Aryl), 134.9 (*C*q), 136.4 (*C*q), 176.9 (*C*=O).

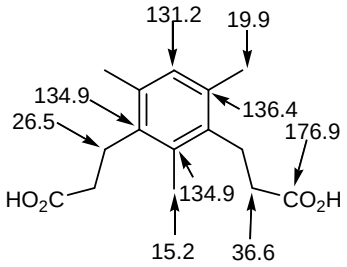
IR (KBr): ν (cm^{-1}) 1739 (C=O), 2968 (COO-H).

EI-MS: *m/z* (%):145 (65), 205 (100) [$M^{+\cdot}$-59], 246 (30) [$M^{+\cdot}$-18], 264 (48) [$M^{+\cdot}$,48].

^{1}H NMR
300 MHz, CD_3OD

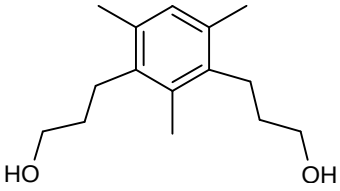


^{13}C NMR
75.4 MHz, CD_3OD



[a]No signal observed due to H/D exchange

- **1,3-Bis(3-hydroxypropyl)-2,4,6-trimethylbenzene 50**



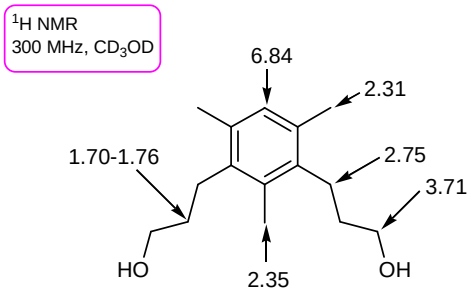
To a suspension of $NaBH_4$ (1.43 g, 37.85 mmol) in anhydrous THF (40 mL) was added dropwise at 0 ºC under argon atmosphere, a solution of iodine (3.84 g, 15.14 mmol) in anhydrous THF (10 mL). The resulting solution was heated at reflux temperature and then was added dropwise a solution of **49** (2 g, 7.57 mmol) in THF (20 mL). The reaction mixture was stirred at reflux temperature for 21 h. The mixture was cooled to room temperature and then methanol was added until an orange solution was formed. After this, the solution was stirred for additional 30 minutes and was concentrated under reduced pressure to give an orange semisolid, which was diluted in aqueous 20% KOH solution (200 mL) and stirred at room temperature for 12 h. Then, the resultant solution was extracted with dichloromethane (3 × 150 mL) and the combined organic layers were dried (with anhydrous Na_2SO_4), filtered and concentrated to give **50** as a white solid (1.76 g, 98% yield). Mp 128-130 ºC.

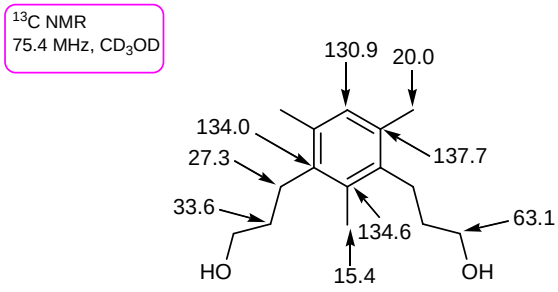
^{1}H NMR (300 MHz, CD_3OD): δ (ppm) 1.70-1.76 (m, 4H, C*H*$_2$), 2.31 (s, 6H, C*H*$_3$), 2.35 (s, 3H, C*H*$_3$), 2.75 (t, *J*=6.8 Hz, 4H, ArylC*H*$_2$), 3.71 (t, *J*=6.8 Hz, 4H, C*H*$_2$OH), 6.84 (s, 1H, Aryl).

^{13}C NMR (75.4 MHz, CD_3OD): δ (ppm) 15.4 (*C*H$_3$), 20.0 (*C*H$_3$), 27.3 (Aryl*C*H$_2$), 33.6 (*C*H$_2$), 63.1 (*C*H$_2$OH), 130.9 (Aryl), 134.0 (*C*q), 134.6 (*C*q), 137.7 (*C*q).

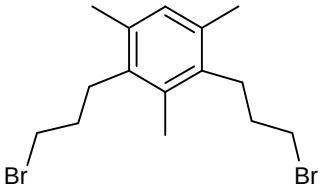
IR (KBr): ν (cm^{-1}) 1058 (C-O), 3376 (O-H).

EI-MS: *m/z* (%):71 (36), 133 (93), 147 (86) [$M^{+\cdot}$-89], 191 (100) [$M^{+\cdot}$-45], 236 (64) [$M^{+\cdot}$], 237 (12) [$M^{+\cdot}$+1].





- **1,3-Bis(3-bromopropyl)-2,4,6-trimethylbenzene 41**

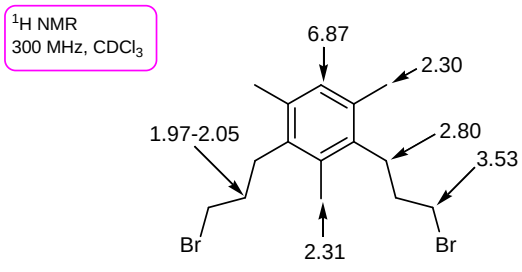


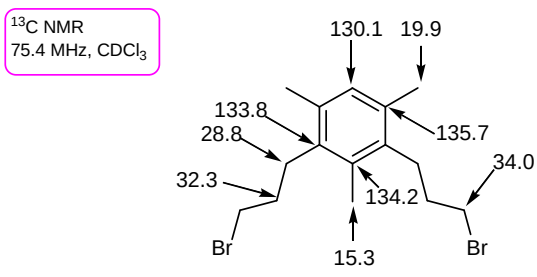
To **50** (6.34 g, 26.84 mmol), was added at 0 ºC 48% hydrobromic acid (21.5 mL, d=1.490 g/mL, 402.70 mmol). The resulting mixture was heated at reflux temperature for 12 h. The solution was cooled and then water (100 mL) was added. After this, the mixture was extracted with dichloromethane (3 × 250 mL). The organic layers were combined, dried (with anhydrous Na_2SO_4), filtered and concentrated under reduced pressure to obtain **41** (8.56 g, 88% yield) as a brown oil. Mp 58-60 ºC.

^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 1.97-2.05 (m, 4H, C*H*$_2$), 2.30 (s, 6H, C*H*$_3$), 2.31 (s, 3H, C*H*$_3$), 2.80 (t, *J*=6.8 Hz, 4H, ArylC*H*$_2$), 3.53 (t, *J*=6.8 Hz, 4H, C*H*$_2$Br), 6.87 (s, 1H, Aryl).

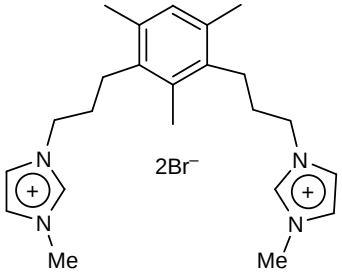
^{13}C NMR(75.4 MHz, $CDCl_3$): δ (ppm) 15.3 (*C*H$_3$), 19.9 (*C*H$_3$), 28.8 (Aryl*C*H$_2$), 32.3 (*C*H$_2$), 34.0 (*C*H$_2$Br), 130.1 (Aryl), 133.8 (*C*q), 134.2 (*C*q), 135.7 (*C*q).

EI-MS: *m/z* (%):147 (29), 253 (100) [$M^{+\cdot}$-109], 255 (98) [$M^{+\cdot}$-107], 362 (25) [$M^{+\cdot}$], 363 (4) [$M^{+\cdot}$+1], 364 (12) [$M^{+\cdot}$+2].





- **1,3-Bis[3-(3-methyl-1-imidazolio)propyl]-2,4,6-trimethylbenzene dibromide 12a·2Br**



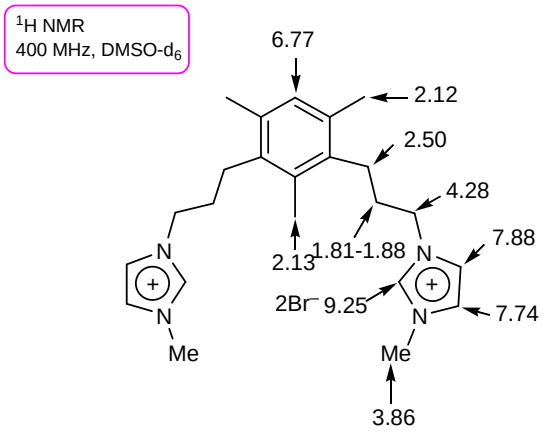
A solution of **41** (0.50 g, 1.38 mmol) and 1-methyl-1*H*-imidazole **45a** (0.30 mL, d=1.035 g/mL, 3.80 mmol) was stirred at reflux temperature under argon atmosphere for 30 min. After cooling to room temperature and reduction of the volume, the brown residue was treated several times with dry acetone in an ultrasonic bath and dried under reduced pressure to give the title compound **12a·2Br** (0.70 g, 97% yield) as an hygroscopic beige foam.

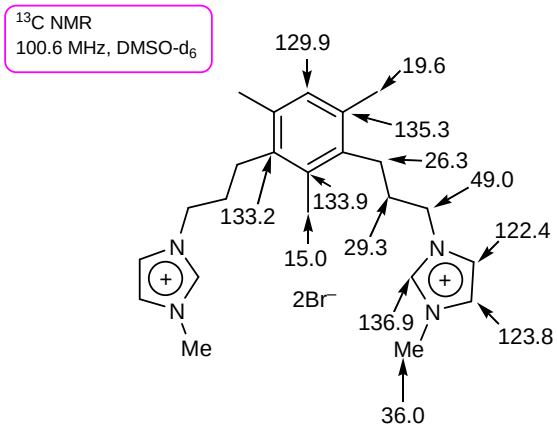
^{1}H NMR (400 MHz, DMSO-d$_6$): δ (ppm) 1.81-1.88 (m, 4H, C*H*$_2$), 2.12 (s, 6H, C*H*$_3$), 2.13 (s, 3H, C*H*$_3$), 2.50 (bs, 4H, ArylC*H*$_2$), 3.86 (s, 6H, C*H*$_3$Imi), 4.28 (t, *J*=7.0, 4H, C*H*$_2$Imi), 6.77 (s, 1H, Aryl), 7.74 (s, 2H, Imi), 7.88 (s, 2H, Imi), 9.25 (s, 2H, Imi).

^{13}C NMR (100.6 MHz, DMSO-d$_6$): δ (ppm) 15.0 (*C*H$_3$), 19.6 (*C*H$_3$), 26.3 (Aryl*C*H$_2$), 29.3 (*C*H$_2$), 36.0 (CH$_3$Imi), 49.0 (*C*H$_2$Imi), 122.4 (Imi), 123.8 (Imi), 129.9 (Aryl), 133.2 (*C*q), 133.9 (*C*q), 135.3 (*C*q), 136.9 (Imi).

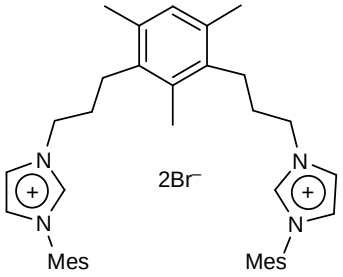
ESI(+)-MS: *m/z* (%):183.3 (100) [M]$^{2+}$, 446.5 (3) [M+Br]$^{+}$.

Anal. Calcd for $C_{23}H_{34}Br_2N_4$·3.5 H_2O: C, 46.87; H, 7.01; N, 9.51. Found: C, 47.27; H, 6.89; N, 9.15.





- **1,3-Bis[3-(3-mesityl-1-imidazolio)propyl]-2,4,6-trimethylbenzene dibromide 12b·2Br**



A solution of **41** (0.50 g, 1.38 mmol) and 1-(2,4,6-trimethylphenyl)-1*H*-imidazole **45b** (0.53 g, 2.83 mmol) in dry DMF (3 mL) was stirred at 100 ºC under argon atmosphere for 12 h. After cooling to room temperature and reduction of the volume, the brown residue was treated several times with dry acetone in an ultrasonic bath and the white solid obtained was filtered off and dried to give the title compound **12b·2Br** (0.78 g, 77% yield). Mp 218-220 ºC.

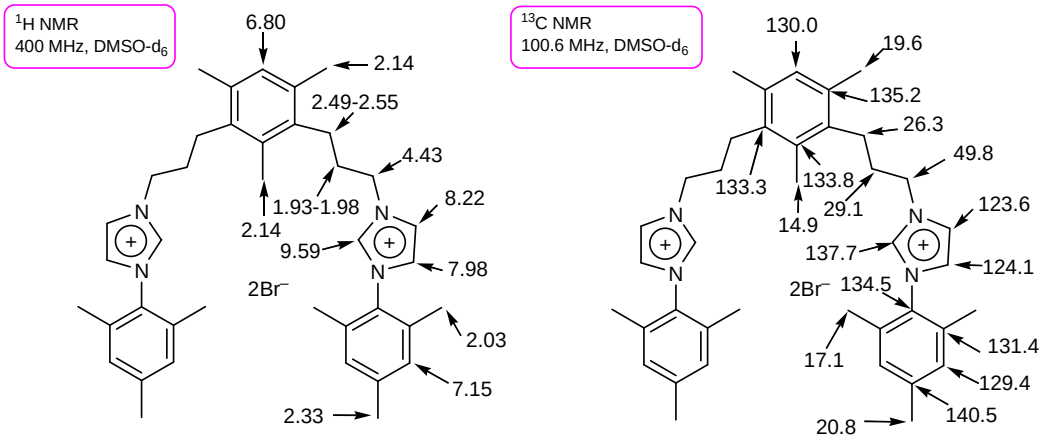
^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 1.93-1.98 (m, 4H, C*H*$_2$), 2.03 (s, 12H, C*H*$_3$), 2.14 (s, 9H, C*H*$_3$), 2.33 (s, 6H, C*H*$_3$), 2.49-2.55 (m, 4H, ArylC*H*$_2$), 4.43 (t, *J*=7.0 Hz, 4H, C*H*$_2$Imi), 6.80 (s, 1H, Aryl), 7.15 (s, 4H, Aryl), 7.98 (s, 2H, Imi), 8.22 (s, 2H, Imi), 9.59 (s, 2H, Imi).

^{13}C NMR (100.6 MHz, DMSO-d_6): δ (ppm) 14.9 (*C*H$_3$), 17.1 (*C*H$_3$), 19.6 (*C*H$_3$), 20.8 (*C*H$_3$), 26.3 (Aryl*C*H$_2$), 29.1 (*C*H$_2$), 49.8 (*C*H$_2$Imi), 123.6 (Imi), 124.1 (Imi), 129.4 (Aryl), 130.0 (Aryl), 131.4 (*C*q), 133.3 (*C*q), 133.8 (*C*q), 134.5 (*C*q), 135.2 (*C*q), 137.7 (Imi), 140.5 (*C*q).

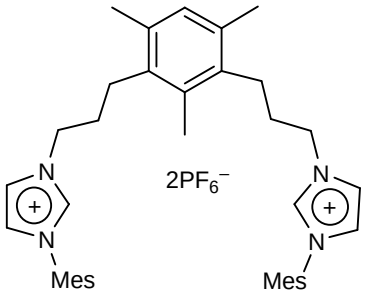
IR (KBr): ν (cm^{-1}) 1547 (C=N).

ESI(+)-MS: *m/z* (%):287.4 (100) $[M]^{2+}$, 654.8 (8) $[M+Br]^{+}$.

Anal. Calcd for $C_{39}H_{50}Br_2N_4 \cdot H_2O$: C, 62.77; H, 7.11; N, 6.81. Found: C, 62.78; H, 7.01; N, 7.09.



- **1,3-Bis[3-(3-mesityl-1-imidazolio)propyl]-2,4,6-trimethylbenzene dihexafluorophosphate 12b·2PF$_6$**

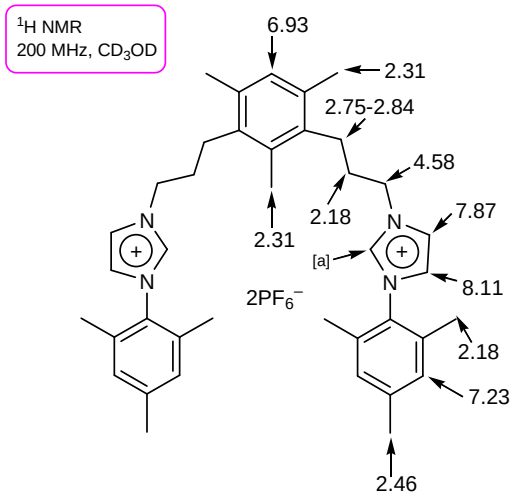


A solution of dicationic **12b·2Br** (0.15 g, 0.20 mmol) in 96% ethanol (50 mL) was passed through a column packed with a strongly basic anion-exchange resin (Ion exchanger Amberlite® IRA-400, hydroxide form). The neutral eluates were acidified to pH=3 with a hexafluorophosphoric acid solution, and the resulting solution was concentrated to dryness to afford the hexafluorophosphate **12b·2PF$_6$** (0.12 g, 71% yield). Mp 218-220 ºC.

^{1}H NMR (200 MHz, CD_3OD): δ (ppm) 2.18 (s, 16H, C*H*$_3$, C*H*$_2$), 2.31 (s, 9H, C*H*$_3$), 2.46 (s, 6H, C*H*$_3$), 2.75-2.84 (m, 4H, ArylC*H*$_2$), 4.58 (t, *J*=7.0 Hz, 4H, C*H*$_2$Imi), 6.93 (s, 1H, Aryl), 7.23 (s, 4H, Aryl), 7.87 (d, *J*=1.9 Hz, 2H, Imi), 8.11 (d, *J*=1.9 Hz, 2H, Imi).

IR (KBr): ν (cm^{-1}) 958 (P-F).

ESI(+)-MS *m/z* (%): 287.4 (100) $[M]^{2+}$.



[a]No signal observed due to H/D exchange

6.4. SYNTHESIS OF IMIDAZOLIUM-OXAZOLINE SALTS AND BIS(OXAZOLINES)

Materials

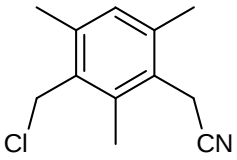
Solvents: Acetonitrile, chlorobenzene, dichloromethane, 1,4-Dioxane, DMF (dry with molecular sieves), DMSO (anhydrous with molecular sieves), IPA and THF were distilled prior to use and dried.

Commercially available products: 2,4-bis(chloromethyl)-1,3,5-trimethyl-benzene **39**, 1-methyl-1*H*-imidazole **45a**, diethyl malonate **46**, 2-amino-2-methyl-1-propanol **53**, *S*-(+)-2-amino-3-methyl-1-butanol **(*S*)-58**, triethylamine (anhydrous with molecular sieves), $CaCO_3$, cadmium acetate dihydrate, NaCN, NaOH, phosphorous tribromide, 95-98% sulfuric acid and thionyl chloride.

The following products were prepared according to the literature: 1,3-dimesitylimidazolium chloride **IMes·HCl** <99JA9889> and 1,3-bis(2,6-diisopropylphenyl)imidazolium chloride **IPr·HCl** <99JA9889>.

6.4.1. IMIDAZOLIUM-OXAZOLINE SALTS 13a-c AND (*S*)-14a,b

- **[3-(chloromethyl)-2,4,6-trimethylphenyl]acetonitrile 52**



To a suspension of 2,4-bis(chloromethyl)-1,3,5-trimethylbenzene **39** (5 g, 23 mmol) in dry DMSO (15 mL), was added sodium cyanide (1.13 g, 23 mmol). The reaction mixture was stirred at room temperature under argon atmosphere for 12 h. The mixture was poured into water (250 mL) and the resulting precipitate was filtered, washed with water, and dried under vacuum. Purification by flash chromatography on silica gel [hexanes/EtOAc, mixtures of increasing polarity) provided **52** as a white solid (1.63 g, 34% yield). Mp 105-107 ºC.

^{1}H NMR (200 MHz, $CDCl_3$): δ (ppm) 2.36 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 2.46 (s, 3H, CH_3), 3.65 (s, 2H, CH_2CN), 4.67 (s, 2H, CH_2Cl), 6.96 (s, 1H, Aryl).

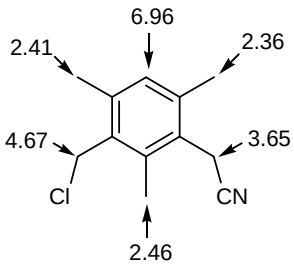
^{13}C NMR (50.3 MHz, $CDCl_3$): δ (ppm) 15.6 (*C*H_3), 18.1 (*C*H_2CN), 19.4 (*C*H_3), 20.3 (*C*H_3), 41.3 (*C*H_2Cl), 117.2 (*C*N), 126.0 (*C*q), 130.7 (Aryl), 132.7 (*C*q), 136.2 (*C*q), 137.0 (*C*q), 137.4 (*C*q).

IR (KBr): ν (cm^{-1}) 1444 (C-Cl), 2248 (CN).

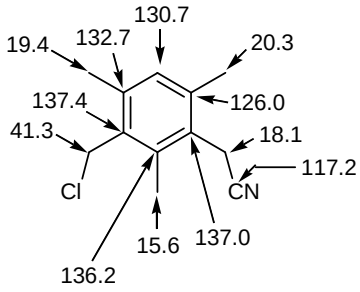
EI-MS: *m/z* (%):145 (29) [$M^{+\cdot}$-62], 172 (100) [$M^{+\cdot}$-5], 207 (20) [$M^{+\cdot}$], 208 (3) [$M^{+\cdot}$+1], 209 (6) [$M^{+\cdot}$+2].

The NMR spectroscopic data is in accordance with those reported in literature <99JMC4485>.

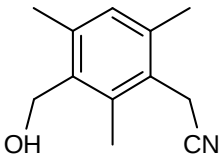
^{1}H NMR
200 MHz, $CDCl_3$



^{13}C NMR
50.3 MHz, $CDCl_3$



- **[3-(Hydroxymethyl)-2,4,6-trimethylphenyl]acetonitrile 51**



To a stirred solution of **52** (0.69 g, 3.30 mmol) in dry dioxane (20 mL) was added a suspension of $CaCO_3$ (1.70 g, 17.01 mmol) in water (20 mL).The mixture was then heated to reflux temperature for 12 h. The resulting white suspension was cooled to room temperature, acidified with 5 N HCl and extracted with ethyl acetate (3 × 100 mL). The combined organic layers were washed with a saturated aqueous solution of Na_2CO_3 (3 × 100 mL), dried (with anhydrous Na_2SO_4), and the solvent was evaporated to dryness to provide **51** (0.62 g, 99% yield) as a yellow solid. Mp 120-122 °C.

^{1}H NMR (200 MHz, $CDCl_3$): δ (ppm) 2.34 (s, 3H, C*H*$_3$), 2.37 (s, 3H, C*H*$_3$), 2.43 (s, 3H, C*H*$_3$), 3.63 (s, 2H, C*H*$_2$CN), 4.69 (s, 2H, C*H*$_2$OH), 6.93 (s, 1H, Aryl).

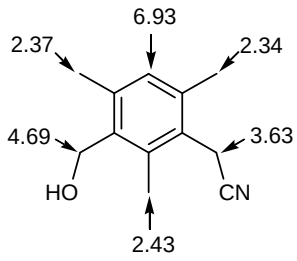
^{13}C NMR (50.3 MHz, $CDCl_3$): δ (ppm) 15.6 (*C*H_3), 18.0 (*C*H_2CN), 19.5 (*C*H_3), 20.1 (*C*H_3), 59.2 (*C*H_2OH), 117.4 (*C*N), 125.7 (*C*q), 130.5 (Aryl), 135.2 (*C*q), 136.2 (*C*q), 136.3 (*C*q), 137.2 (*C*q).

IR (KBr): ν (cm^{-1}) 2249 (CN), 3297 (O-H).

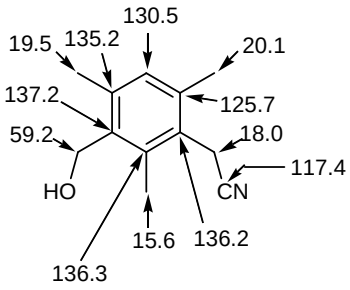
EI-MS: *m/z* (%): 171 (100) [$M^{+\cdot}$-18], 189 (24) [$M^{+\cdot}$].

Anal Calcd for $C_{12}H_{15}NO \cdot 0.25$ EtOAc: C, 73.90; H, 8.11; N, 6.63. Found: C, 73.90; H, 8.06; N, 6.86.

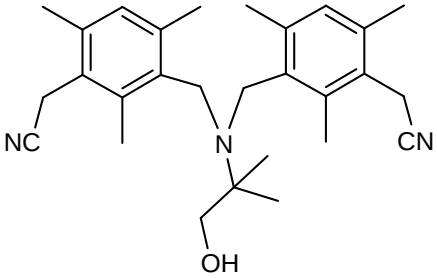
^{1}H NMR
200 MHz, $CDCl_3$



^{13}C NMR
50.3 MHz, $CDCl_3$



- **3-{[(3-Cyanomethyl-2,4,6-trimethylbenzyl)-2-(2-hydroxy-1,1-dimethylethyl)amino]methyl}-2,4,6-trimethylphenyl)acetonitrile 54**



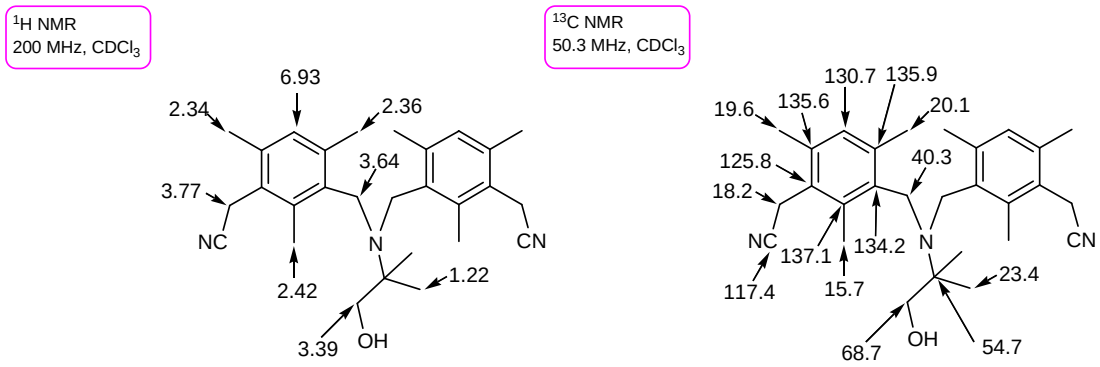
A solution of $Cd(OAc)_2 \cdot 2H_20$ (0.08 g, 0.30 mmol), **52** (1.25 g, 6.02 mmol) and 2-amino-2-methyl-1-propanol **53** (1.08 mL, d=0.934 g/mL, 11.29 mmol) in chlorobenzene (25 mL) was stirred at reflux temperature under an argon atmosphere for 7 days. The resulting solution was evaporated to dryness. The resulting orange oil was purified by column chromatography on silica gel [EtOAc/methanol, mixtures of increasing polarity] to provide **54** (1.08 g, 42% yield) as a yellow oil.

^{1}H NMR (200 MHz, $CDCl_3$): δ (ppm) 1.22 (s, 6H, $C(CH_3)_2$), 2.34 (s, 6H, CH_3), 2.36 (s, 6H, CH_3), 2.42 (s, 6H, CH_3), 3.39 (s, 2H, CH_2OH), 3.64 (s, 4H, CH_2N), 3.77 (s, 4H, CH_2CN), 6.93 (s, 2H, Aryl).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 15.7 (CH_3), 18.2 (CH_2CN), 19.6 (CH_3), 20.1 (CH_3), 23.4 (CH_3), 40.3 (CH_2N), 54.7 (*C*q), 68.7 (CH_2OH), 117.4 (*C*N), 125.8 (*C*q), 130.7 (Aryl), 134.2 (*C*q), 135.6 (*C*q), 135.9 (*C*q), 137.1 (*C*q).

IR (KBr): ν (cm^{-1}) 2252 (CN), 3161 (O-H).

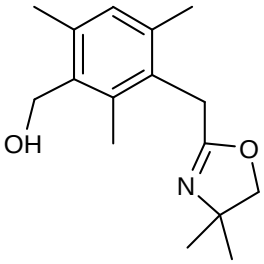
CI-MS: *m/z* (%): 432 (100) [$M^{+\cdot}$+1].



- **Attempted preparation of [3-(Hydroxymethyl)-2,4,6-trimethylphenyl] acetic acid 55**

A mixture of **51** (0.59 g, 3.12 mmol), H_2SO_4 (2.93 mL, 95-98% w/w) and water (3.51 mL) was stirred and heated at reflux temperature for 6 h. The reaction mixture was cooled to room temperature and poured into ice. The resulting brownish solid was filtered, washed with cold water and dried under vacuum, obtaining a solid mixture of unidentified compounds.

- **{3-[(4,4-Dimethyl-4,5-dihydro-2-oxazolyl)methyl]-2,4,6-trimethylphenyl} methanol 56**



A solution of $Cd(OAc)_2 \cdot 2H_20$ (0.60 g, 2.25 mmol), **51** (0.85 g, 4.49 mmol) and 2-amino-2-methyl-1-propanol **53** (0.81 mL, d=0.934 g/mL, 8.53 mmol) in chlorobenzene (80 mL) was stirred at reflux temperature under an argon atmosphere for 7 days. The resulting solution was evaporated to dryness. The resulting orange oil was purified by column chromatography on silica gel [hexanes/EtOAc, mixtures of increasing polarity] to provide **56** (0.61 g, 52% yield) as a yellow oil.

^{1}H NMR (200 MHz, $CDCl_3$,): δ (ppm) 1.21 (s, 6H, C(CH_3)$_2$), 2.31 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 3.61 (s, 2H, CH_2oxazoline), 3.86 (s, 2H, OCH_2), 4.66 (s, 2H, CH_2OH), 6.87 (s, 1H, Aryl).

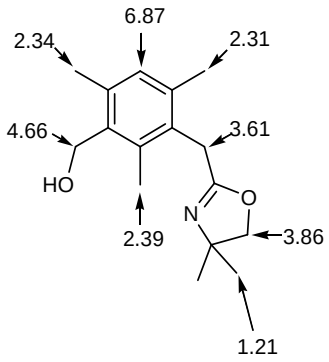
^{13}C NMR (50.3 MHz, $CDCl_3$): δ (ppm) 15.6 (*C*H_3), 19.6 (*C*H_3), 20.4 (*C*H_3), 28.2 (*C*H_3), 29.2 (*C*H_2oxazoline), 59.3 (*C*H_2OH), 66.7 (*C*$(CH_3)_2$), 79.1 (O*C*H_2), 130.1 (Aryl), 130.4 (*C*q), 134.8 (*C*q), 135.7 (*C*q), 136.8 (*C*q), 136.9 (*C*q), 163.9 (*C*=N).

IR (NaCl): ν (cm^{-1}) 1658 (C=N), 3345 (O-H).

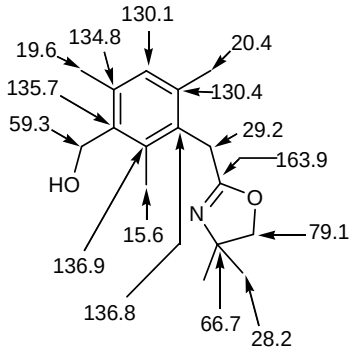
EI-MS: *m/z* (%): 242 (100) [$M^{+\cdot}$-19], 261 (60) [$M^{+\cdot}$].

Anal. Calcd for $C_{16}H_{23}NO_2$·0.25 EtOAc: C, 72.05; H, 8.89; N, 4.94. Found: C, 72.23; H, 8.98; N, 5.32.

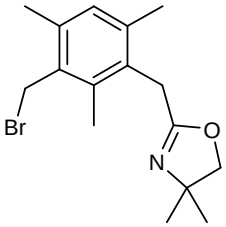
^{1}H NMR
200 MHz, $CDCl_3$



^{13}C NMR
50.3 MHz, $CDCl_3$



- **2-[3-(Bromomethyl)-2,4,6-trimethylbenzyl]-4,4-dimethyl-4,5-dihydro-oxazole 57**

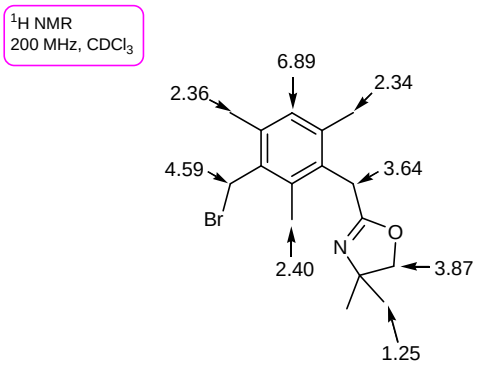


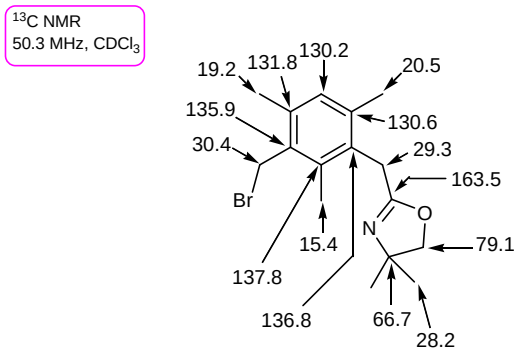
To a solution of **56** (0.55 g, 1.94 mmol) in anhydrous THF (30 mL) was added PBr_3 (0.18 mL, d=2.88 g/mL, 1.94 mmol) at –20 ºC under an argon atmosphere. This was stirred for 1 h. The reaction mixture was washed with an ice-cold saturated aqueous solution of $NaHCO_3$ (30 mL), and the aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried (with anhydrous Na_2SO_4), filtered and evaporated under reduced pressure to yield **57** (0.62 g, 99%) as a yellow oil, which was subjected to the next step without further purification.

^{1}H NMR (200 MHz, $CDCl_3$): δ (ppm) 1.25 (s, 6H, C(C*H*$_3$)$_2$), 2.34 (s, 3H, C*H*$_3$), 2.36 (s, 3H, C*H*$_3$), 2.40 (s, 3H, C*H*$_3$), 3.64 (s, 2H, C*H*$_2$oxazoline), 3.87 (s, 2H, OC*H*$_2$), 4.59 (s, 2H, C*H*$_2$Br), 6.89 (s, 1H, Aryl).

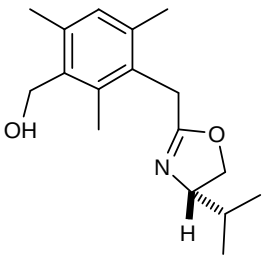
^{13}C NMR (50.3 MHz, $CDCl_3$): δ (ppm) 15.4 (*C*H_3), 19.2 (*C*H_3), 20.5 (*C*H_3), 28.2 (*C*H_3), 29.3 (*C*H_2oxazoline), 30.4 (*C*H_2Br), 66.7 (*C*$(CH_3)_2$), 79.1 (O*C*H_2), 130.2 (Aryl), 130.6 (*C*q), 131.8 (*C*q), 135.9 (*C*q), 136.8 (*C*q), 137.8 (*C*q), 163.5 (*C*=N).

EI-MS: *m/z* (%): 244 (100) [$M^{+\cdot}$-80], 245 (19) [$M^{+\cdot}$-79], 324 (4) [$M^{+\cdot}$].





- **3-{[(4*S*)-4-Isopropyl-4,5-dihydro-2-oxazolyl]methyl}-2,4,6-trimethyl-phenylmethanol (*S*)-59**



A solution of $Cd(OAc)_2{\cdot}2H_20$ (0.70 g, 2.64 mmol), **51** (1 g, 5.28 mmol) and (*S*)-(+)-2-amino-3-methyl-1-butanol **(*S*)-58** (1.04 g, 10.04 mmol) in chlorobenzene (25 mL) was stirred at reflux temperature under an argon atmosphere for 7 days. The resulting solution was evaporated to dryness. The resulting orange oil was purified by column chromatography on neutral aluminum oxide [hexanes/EtOAc, using mixtures of increasing polarity] to give **(*S*)-59** (0.77 g, 53%) as a white solid. Mp 112-114 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 0.83 (d, *J*=6.8 Hz, 3H, *i*-Pr), 0.91 (d, *J*=6.8 Hz, 3H, *i*-Pr), 1.67-1.79 (m, 1H, *i*-Pr), 2.33 (s, 3H, C*H*$_3$), 2.36 (s, 3H, C*H*$_3$), 2.37 (s, 3H, C*H*$_3$), 3.66 (s, 2H, C*H*$_2$oxazoline), 3.81-3.92 (m, 2H, OC*H*$_2$), 4.10-4.19 (m, 1H, NC*H*), 4.70 (s, 2H, C*H*$_2$OH), 6.89 (s, 1H, Aryl).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 15.7 (*C*H_3), 17.7 (*C*H_3), 18.8 (*C*H_3), 19.5 (*C*H_3), 20.4 (*C*H_3), 29.1 (*C*H_2oxazoline), 32.2 (*C*H), 59.6 (*C*H_2OH), 66.7

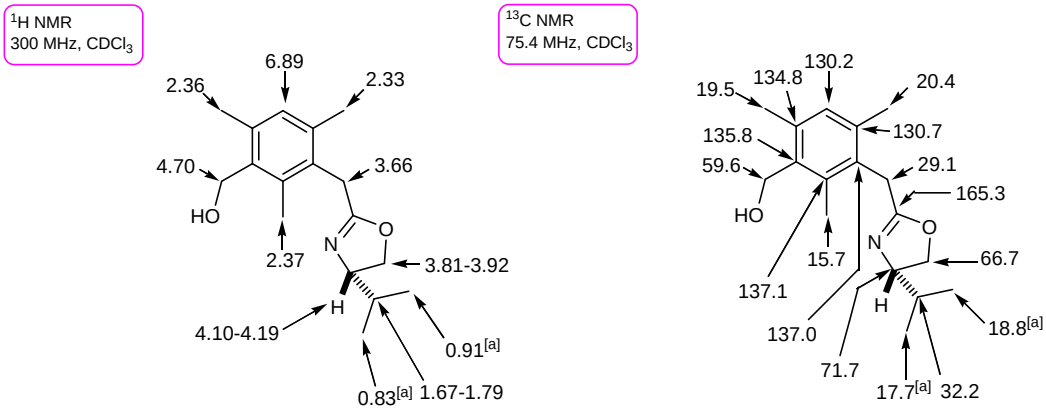
(OCH_2), 71.7 (NCH), 130.2 (Aryl), 130.7 (*C*q), 134.8 (*C*q), 135.8 (*C*q), 137.0 (*C*q), 137.1 (*C*q), 165.3 (*C*=N).

IR (KBr): ν (cm^{-1}) 1651 (C=N), 3191 (O-H).

EI-MS: *m/z* (%): 256 (100) [$M^{+\cdot}$-19], 275 (69) [M^{+}].

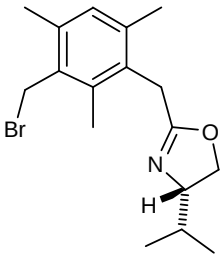
Anal. Calcd for $C_{17}H_{25}NO_2$: C, 74.12; H, 9.15; N, 5.09. Found: C, 74.19; H, 9.26; N, 5.24.

$[\alpha]^{25}_D$ –36.0 (*c* 1.0, CH_3OH).



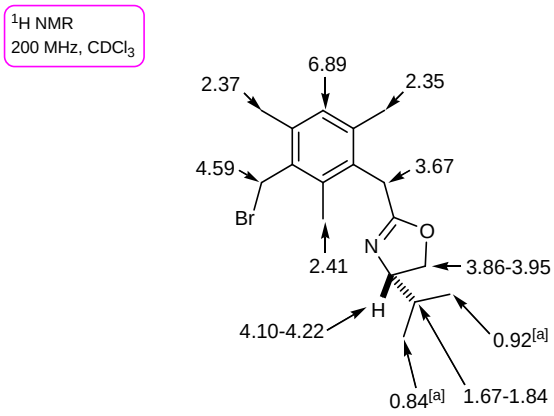
[a]Interchangeable signals

- **(4*S*)-2-[3-(Bromomethyl)-2,4,6-trimethylbenzyl]-4-isopropyl-4,5-dihydro-oxazole (*S*)-60**



To a solution of **(*S*)-59** (0.45 g, 1.62 mmol) in anhydrous THF (25 mL) was added PBr_3 (0.15 mL, d=2.88 g/mL, 1.94 mmol) at –20ºC under argon atmosphere. This was stirred for 1 h. The reaction mixture was washed with an ice-cold saturated aqueous solution of $NaHCO_3$ (30 mL), and the aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried (with anhydrous Na_2SO_4), filtered and evaporated under reduced pressure to give **(*S*)-60** (0.54 g, 99%) as a yellow oil, which was subjected to the next step without further purification.

^{1}H NMR (200 MHz, $CDCl_3$): δ (ppm) 0.84 (d, *J*=6.8 Hz, 3H, *i*-Pr), 0.92 (d, *J*=6.8 Hz, 3H, *i*-Pr), 1.67-1.84 (m, 1H, *i*-Pr), 2.35 (s, 3H, C*H*$_3$), 2.37 (s, 3H, C*H*$_3$), 2.41 (s, 3H, C*H*$_3$), 3.67 (s, 2H, C*H*$_2$oxazoline), 3.86-3.95 (m, 2H, OC*H*$_2$), 4.10-4.22 (m, 1H, NC*H*), 4.59 (s, 2H, C*H*$_2$Br), 6.89 (s, 1H, Aryl).



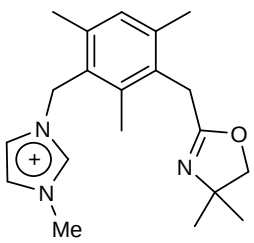
[a]Interchangeable signals

⇨ **General procedure for preparation of oxazolinyl-imidazolium salts 13a-c and (*S*)-14a,b**

(Bromomethylaryl)oxazoline **57** or **(*S*)-60** (1 equivalent) and *N*-substituted imidazoles **45a-c** (1.1-1.5 equiv) were dissolved in dry DMF and heated to 80 °C under an argon atmosphere for 12 h, and the solvent was then removed under vacuum. The white solids obtained were washed several times with diethyl ether and used without further purification. The yields were not optimized.

- **1-[3-(4,4-Dimethyl-4,5-dihydro-2-oxazolyl)methyl-2,4,6-trimethylbenzyl]-3-methylimidazolium bromide 13a**

The above procedure was followed using oxazoline **57** (0.50 g, 1.54 mmol), 1-methyl-1*H*-imidazole **45a** (0.18 mL, d=1.035 g/mL, 2.31 mmol) and dry DMF (5 mL). The product was obtained as an hygroscopic solid (0.58 g, 93 % yield).



^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 1.18 (s, 6H, C(C*H*$_3$)$_2$), 2.24 (s, 6H, C*H*$_3$), 2.31 (s, 3H, C*H*$_3$), 3.58 (s,

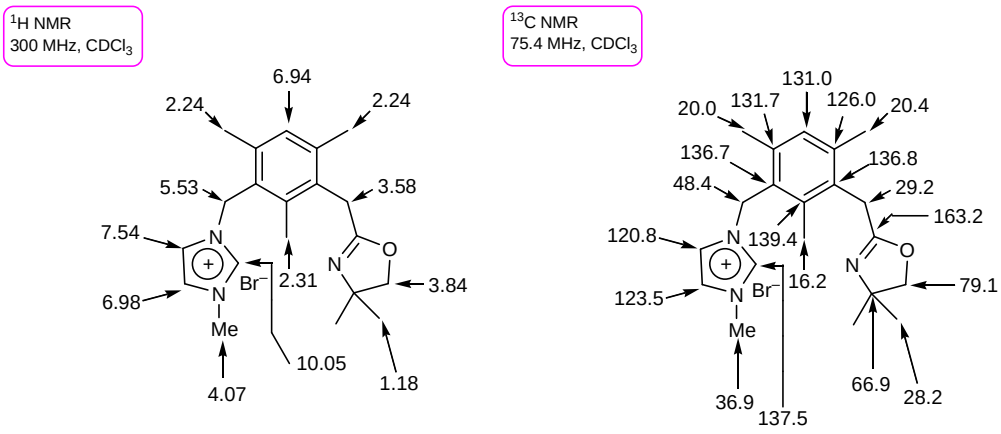
2H, C*H*$_2$oxazoline), 3.84 (s, 2H, OC*H*$_2$), 4.07 (s, 3H, C*H*$_3$Imi), 5.53 (s, 2H, C*H*$_2$Imi), 6.94 (s, 1H, Aryl), 6.98 (s, 1H, Imi), 7.54 (s, 1H, Imi), 10.05 (s, 1H, Imi).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 16.2 (*C*H$_3$), 20.0 (*C*H$_3$), 20.4 (*C*H$_3$), 28.2 (*C*H$_3$), 29.2 (*C*H$_2$oxazoline), 36.9 (*C*H$_3$Imi), 48.4 (*C*H$_2$Imi), 66.9 (*C*(CH$_3$)$_2$), 79.1 (OC*H*$_2$), 120.8 (Imi), 123.5 (Imi), 126.0 (*C*q), 131.0 (Aryl), 131.7 (*C*q), 136.7 (*C*q), 136.8 (*C*q), 137.5 (Imi), 139.4 (*C*q), 163.2 (*C*=N).

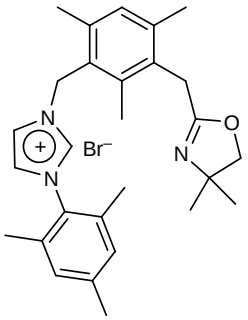
IR (NaCl): ν (cm^{-1}) 1733 (C=N).

ESI(+)-MS: *m/z* (%): 326 (100) [M]$^+$, 731 (2) [2M+Br]$^+$.

Anal. Calcd for $C_{20}H_{28}BrN_3O \cdot 1.5\ H_2O$: C, 55.43; H, 7.21; N, 9.70. Found: C, 55.83; H, 7.18; N, 9.30.



- **1-[3-(4,4-Dimethyl-4,5-dihydro-2-oxazolyl)methyl-2,4,6-trimethylbenzyl]-3-(2,4,6-trimethylphenyl)imidazolium bromide 13b**



The above procedure was followed using oxazoline **57** (0.73 g, 2.24 mmol), 1-mesityl-1*H*-imidazole **45b** (0.46 g, 2.46 mmol) and dry DMF (6 mL). The product was obtained as a white solid (0.94 g, 82 % yield). Mp 148-150 °C.

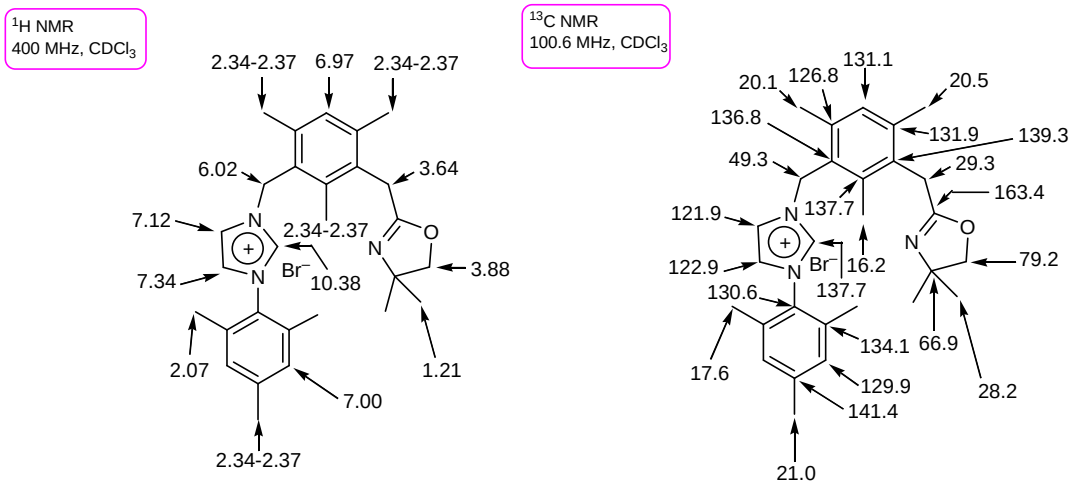
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.21 (s, 6H, C(C*H*$_3$)$_2$), 2.07 (s, 6H, C*H*$_3$), 2.34-2.37 (m, 12H, C*H*$_3$), 3.64 (s, 2H, C*H*$_2$oxazoline), 3.88 (s, 2H, OC*H*$_2$), 6.02 (s, 2H, C*H*$_2$Imi), 6.97 (s, 1H, Aryl), 7.00 (s, 2H, Aryl), 7.12 (s, 1H, Imi), 7.34 (s, 1H, Imi), 10.38 (s, 1H, Imi).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 16.2 (*C*H_3), 17.6 (*C*H_3), 20.1 (*C*H_3), 20.5 (*C*H_3), 21.0 (*C*H_3), 28.2 (*C*H_3), 29.3 (*C*H_2oxazoline), 49.3 (*C*H_2Imi), 66.9 (*C*$(CH_3)_2$), 79.2 (O*C*H_2), 121.9 (Imi), 122.9 (Imi), 126.8 (*C*q), 129.9 (Aryl), 130.6 (*C*q), 131.1 (Aryl), 131.9 (*C*q), 134.1 (*C*q), 136.8 (*C*q), 137.7 (Imi), 137.7 (*C*q), 139.3 (*C*q), 141.4 (*C*q), 163.4 (*C*=N).

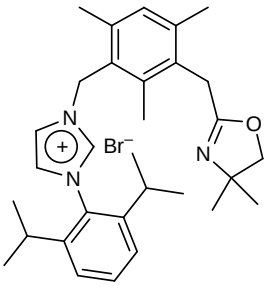
IR (KBr): ν (cm^{-1}) 1734 (C=N).

ESI(+)-MS: *m/z* (%): 430 (100) $[M]^+$, 941 (1) $[2M+Br]^+$.

Anal. Calcd for $C_{28}H_{36}BrN_3O \cdot 1.5\ H_2O$: C, 62.56; H, 7.31; N, 7.82. Found: C, 62.27; H, 7.27; N, 7.42.



- **1-[3-(4,4-Dimethyl-4,5-dihydro-2-oxazolyl)methyl-2,4,6-trimethylbenzyl]-3-(2,6-diisopropylphenyl)imidazolium bromide 13c**



The above procedure was followed using oxazoline **57** (0.59 g, 1.81 mmol), 1-(2,6-diisopropylphenyl)-1*H*-imidazole **45c** (0.46 g, 1.99 mmol) and dry DMF (5 mL). The product was obtained as a white solid (0.71 g, 71 % yield). Mp 132-134 °C.

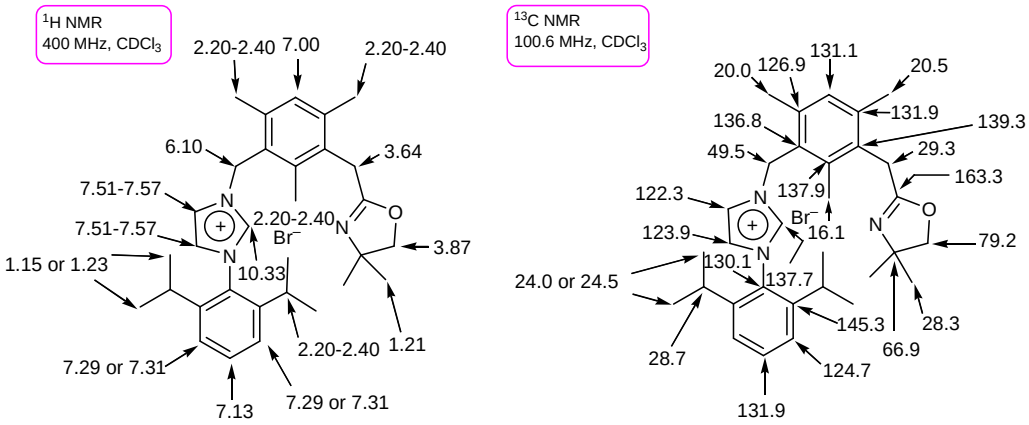
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.15 (d, *J*=6.8 Hz, 6H, *i*-Pr), 1.21 (s, 6H, C(C*H*$_3)_2$), 1.23 (d, *J*=6.8 Hz, 6H, *i*-Pr), 2.20-2.40 (m, 11H, Aryl, C*H*$(CH_3)_2$), 3.64 (s, 2H, C*H*$_2$oxazoline), 3.87 (s, 2H, OC*H*$_2$), 6.10 (s, 2H, C*H*$_2$Imi), 7.00 (s, 1H, Aryl), 7.13 (s, 1H, Aryl), 7.29 (s, 1H, Aryl), 7.31 (s, 1H, Aryl), 7.51-7.57 (m, 2H, Imi), 10.33 (s, 1H, Imi).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 16.1 (*C*H_3), 20.0 (*C*H_3), 20.5 (*C*H_3), 24.0 (*C*H_3), 24.5 (*C*H_3), 28.3 (*C*H_3), 28.7 (*C*H(CH_3)$_2$), 29.3 (*C*H_2oxazoline), 49.5 (*C*H_2Imi), 66.9 (*C*(CH_3)$_2$), 79.2 (O*C*H_2), 122.3 (Imi), 123.9 (Imi), 124.7 (Aryl), 126.9, 130.1, 131.1 (Aryl), 131.9 (Aryl), 131.9 (*C*q), 136.8 (*C*q), 137.7 (Imi), 137.9 (*C*q), 139.3 (*C*q), 145.3 (*C*q), 163.3 (*C*=N).

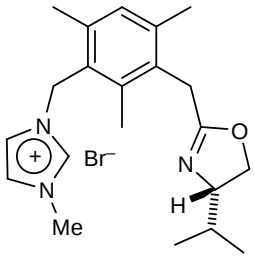
IR (KBr): ν (cm^{-1}) 1735 (C=N).

ESI(+)-MS: *m/z* (%): 472 (100) $[M]^+$, 1025 (2) $[2M+Br]^+$.

Anal. Calcd for $C_{31}H_{42}BrN_3O{\cdot}2\ H_2O$: C, 63.26; H, 7.88; N, 7.14. Found: C, 63.35; H, 7.86; N, 6.74.



- **1-{3-[(4S)-4-Isopropyl-4,5-dihydro-2-oxazolyl]methyl-2,4,6-trimethyl-benzyl}-3-methylimidazolium bromide (*S*)-14a**



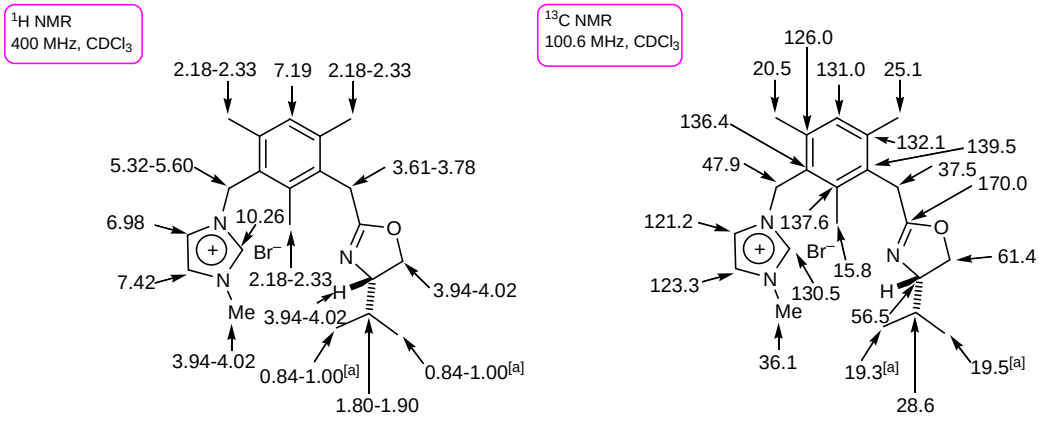
The above procedure was followed using oxazoline **(*S*)-60** (0.52 g, 1.53 mmol), 1-methyl-1*H*-imidazole **45a** (0.18 mL, d=1.035 g/mL, 2.31 mmol) and dry DMF (4 mL). The product was obtained as an hygroscopic solid (0.44 g, 68 % yield, ^{1}H NMR purity = 80%).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.84-1.00 (m, 6H, *i*-Pr), 1.80-1.90 (m, 1H, *i*-Pr), 2.18-2.33 (m, 9H, C*H*$_3$), 3.61-3.78 (m, 2H, C*H*$_2$oxazoline), 3.94-4.02 (m, 6H, C*H*$_3$Imi, NC*H*, OC*H*$_2$), 5.32-5.60 (s, 2H, C*H*$_2$Imi), 6.98 (s, 1H, Imi), 7.19 (s, 1H, Aryl), 7.42 (s, 1H, Imi), 10.26 (s, 1H, Imi).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 15.8 (*C*H_3), 19.3 (*C*H_3), 19.5 (*C*H_3), 20.5 (*C*H_3), 25.1 (*C*H_3), 28.6 (*C*H), 36.1 (*C*H_3Imi), 37.5 (*C*H_2oxazoline), 47.9

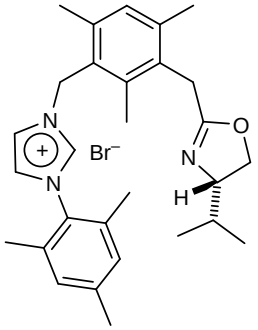
(*C*H$_2$Imi), 56.5 (N*C*H), 61.4 (O*C*H$_2$), 121.2 (Imi), 123.3 (Imi), 126.0 (*C*q), 130.5 (Imi), 131.0 (Aryl), 132.1 (*C*q), 136.4 (*C*q), 137.6 (*C*q), 139.5 (*C*q), 170.0 (*C*N).

ESI(+)-MS: *m/z* (%): 358 (100) $[M + H_2O]^+$, 762 (2) $[2M+Br]^+$.



[a]Interchangeable signals

- **1-{3-[(4*S*)-4-Isopropyl-4,5-dihydro-2-oxazolyl]methyl-2,4,6-trimethyl-benzyl}-3-(2,4,6-trimethylphenyl)imidazolium bromide (*S*)-14b**



The above procedure was followed using oxazoline **(*S*)-60** (0.23 g, 0.69 mmol), 1-mesityl-1*H*-imidazole **45b** (0.14 g, 0.75 mmol) and dry DMF (2 mL). The product was obtained as a white solid (0.27 g, 75 % yield). Mp 130-132 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): δ(ppm) 0.82 (d, *J*=1.0 Hz, 3H, *i*-Pr), 0.86 (d, *J*=1.0 Hz, 3H, *i*-Pr), 1.74-1.86 (m, 1H, *i*-Pr), 2.04-2.09 (m, 6H, C*H*$_3$), 2.24-2.42 (m, 12H, C*H*$_3$), 3.47-3.94 (m, 4H, C*H*$_2$oxazoline, OC*H*$_2$), 4.08-4.28 (m, 1H, NC*H*), 5.76-6.09 (m, 2H, C*H*$_2$Imi), 6.95-7.05 (m, 3H, Aryl), 7.09-7.20 (m, 1H, Imi), 7.31-7.39 (m, 1H, Imi), 9.91-10.54 (m, 1H, Imi).

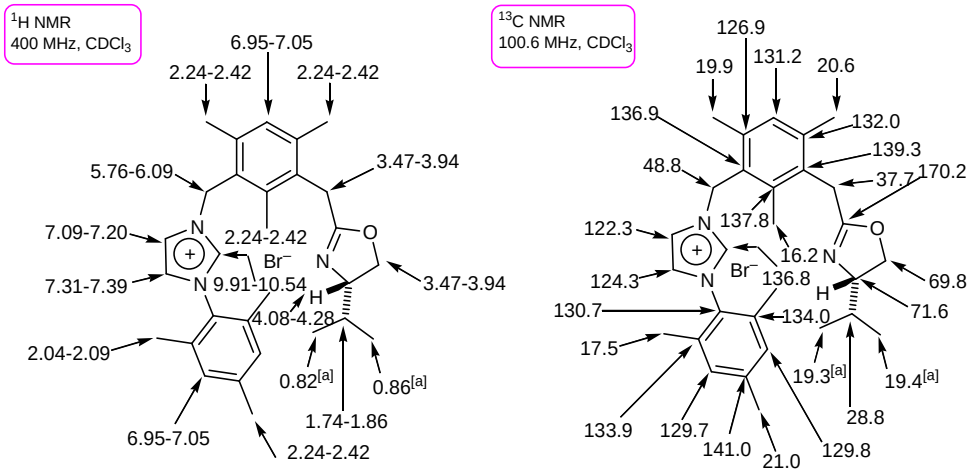
^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 16.2 (*C*H$_3$), 17.5 (*C*H$_3$), 19.3 (*C*H$_3$), 19.4 (*C*H$_3$), 19.9 (*C*H$_3$), 20.6 (*C*H$_3$), 21.0 (*C*H$_3$), 28.8 (*C*H), 37.7 (*C*H$_2$oxazoline), 48.8 (*C*H$_2$Imi), 69.8 (O*C*H$_2$), 71.6 (N*C*H), 122.3 (Imi), 124.3 (Imi), 126.9 (*C*q), 129.7 (Ar), 129.8 (Ar), 130.7 (*C*q), 131.2 (Ar), 132.0 (*C*q), 133.9 (*C*q), 134.0 (*C*q), 136.8 (Imi), 136.9 (*C*q), 137.8 (*C*q), 139.3 (*C*q), 141.0 (*C*q), 170.2 (*C*=N).

IR (KBr): ν (cm^{-1}) 1731(C=N).

ESI(+)-MS: *m/z* (%): 444 (53) $[M]^+$, 462 (100) $[M+H_2O]^+$.

Anal. Calcd for $C_{29}H_{38}BrN_3O \cdot 1.5\ H_2O$: C, 63.15; H, 7.49; N, 7.62. Found: C, 63.08; H, 7.45; N, 7.22.

$[\alpha]^{25}_D$ +4.7 (*c* 1.0, CH_3OH).



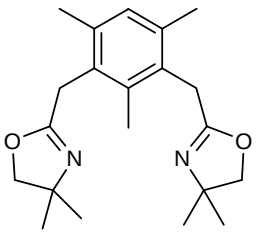
[a]Interchangeable signals

6.4.2. BIS(OXAZOLINES) 15 AND (*S*,*S*)-17

⇨ General procedure for preparation of bis(oxazolines) 15 and (*S,S*)-17

A solution of $Cd(OAc)_2 \cdot 2H_2O$ (0.05 or 0.5 equivalents), dinitrile **42** (1 equiv) and amino alcohol **53** or **(*S*)-58** (3.75 equivalents) in chlorobenzene (25 mL) was stirred at reflux temperature under an argon atmosphere for 7 days, and the solvent was then removed under vacuum. The oily residue was purified by column chromatography on silica gel with hexanes/EtOAc/methanol mixtures of increasing polarity as eluents.

- **1,3-Bis[(4,4-dimethyl-4,5-dihydro-2-oxazolyl)methyl]-2,4,6-trimethyl-benzene 15**



The above procedure was followed using $Cd(OAc)_2 \cdot 2H_2O$ (0.07 g, 0.25 mmol), dinitrile **42** (1 g, 5.05 mmol), 2-amino-2-methyl-1-propanol **53** (1.80 mL, d=0.934 g/mL, 18.90 mmol) and chlorobenzene (25 mL). The product was obtained as a yellow solid (1.36 g, 79% yield). Mp 100-102 °C.

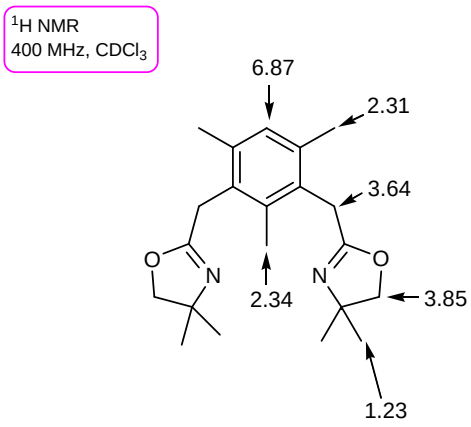
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.23 (s, 12H, CH_3), 2.31 (s, 6H, CH_3), 2.34 (s, 3H, CH_3), 3.64 (s, 4H, CH_2oxazoline), 3.85 (s, 4H, OCH_2), 6.87 (s, 1H, Aryl).

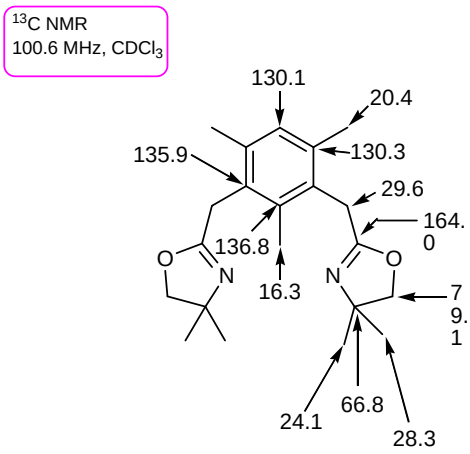
^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 16.3 (*C*H_3), 20.4 (*C*H_3), 24.1 (*C*H_3), 28.3 (*C*H_3), 29.6 (*C*H_2oxazoline), 66.8 (*C*$(CH_3)_2$), 79.1 (O*C*H_2), 130.1 (Aryl), 130.3 (*C*q), 135.9 (*C*q), 136.8 (*C*q), 164.0 (*C*=N).

IR (KBr): ν (cm^{-1}) 1658 (C=N).

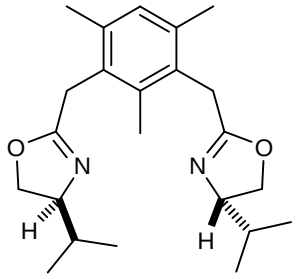
EI-MS: *m/z* (%): 342 (100) [$M^{+\cdot}$].

Anal. Calcd for $C_{21}H_{30}N_2O_2$: C, 73.65; H, 8.83; N, 8.18. Found: C, 73.68; H, 8.77; N, 8.18.





- **1,3-Bis{[(4*S*)-4-isopropyl-4,5-dihydro-2-oxazolyl]methyl}-2,4,6-trimethyl-benzene (*S*,*S*)-17**



The above procedure was followed using $Cd(OAc)_2 \cdot 2H_2O$ (0.67 g, 2.52 mmol), dinitrile **42** (1 g, 5.05 mmol), (*S*)-(+)-2-amino-3-methyl-1-butanol **(*S*)-58** (1.95 g, 18.90 mmol), and chlorobenzene (25 mL). The product was obtained as a yellow solid (1.10g, 59% yield). Mp 80-82 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.83 (d, *J*=6.8

Hz, 6H, *i*-Pr), 0.91 (d, *J*=6.8 Hz, 6H, *i*-Pr), 1.68-1.80 (m, 2H, *i*-Pr), 2.32 (s, 6H, C*H*$_3$), 2.37 (s, 3H, C*H*$_3$), 3.66 (s, 4H, C*H*$_2$oxazoline), 3.84-3.91 (m, 4H, OC*H*$_2$), 4.11-4.21 (m, 2H, NC*H*), 6.88 (s, 1H, Aryl).

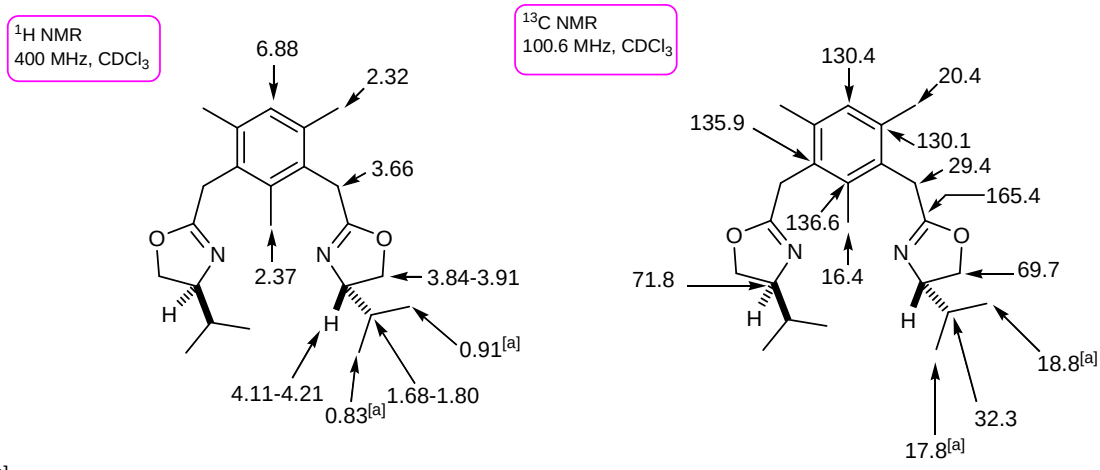
^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 16.4 (*C*H$_3$), 17.8 (*C*H$_3$), 18.8 (*C*H$_3$), 20.4 (*C*H$_3$), 29.4 (*C*H$_2$oxazoline), 32.3 (*C*H), 69.7 (OC*H*$_2$), 71.8 (NC*H*), 130.1 (*C*q), 130.4 (Aryl), 135.9 (*C*q), 136.6 (*C*q), 165.4 (*C*=N).

IR (KBr): 1661 (C=N).

EI-MS: *m/z* (%): 370 (100) [M^+].

Anal. Calcd for $C_{23}H_{34}N_2O_2 \cdot 0.67\ H_2O$: C, 72.20; H, 9.31; N, 7.32. Found: C, 72.19; H, 9.16; N, 7.57.

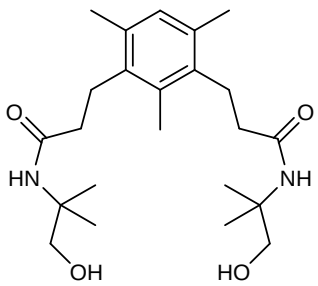
$[\alpha]^{25}_D$ –0.87 (*c* 1.0, CH_3OH).



[a]Interchangeable signals

6.4.3. BIS(OXAZOLINE) 16

- **1,3-Bis[*N*-{(2-hydroxy-1,1-dimethyl)ethyl}propanamide]-2,4,6-trimethyl-benzene 61**



Thionyl chloride (3.60 mL, d=1.64 g/mL, 49.57 mmol) was added to **49** (0.72 g, 2.71 mmol) under argon atmosphere at room temperature. The resulting mixture was stirred at 60 ºC for 4 h and then was concentrated under reduced pressure to eliminate excess of thionyl chloride. The resulting orange solid

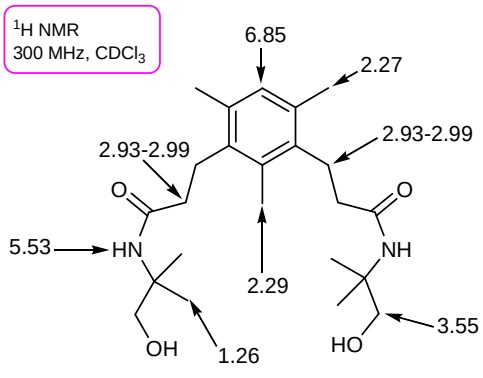
was taken into dry dichloromethane (7 mL), cooled to 0 ºC and to the resulting solution was added dropwise a solution of 2-amino-2-methyl-1-propanol **53** (1.03 mL, d=0.934 g/mL, 10.84 mmol) and anhydrous triethylamine (1.51 mL, d=0.730 g/mL, 10.84 mmol) in dry dichloromethane (5 mL). The reaction mixture was allowed to warm to room temperature and stirred overnight. Dichloromethane (10 mL) was added and the solution washed with aqueous sodium hydrogen carbonate (2 × 25 mL) and brine (1 × 25 mL). The organic layer was dried (with anhydrous Na_2SO_4), filtered and concentrated to give an orange foam, which was purified by flash chromatography on silica gel eluting with [hexanes, hexanes/EtOAc and EtOAc/methanol, mixtures of increasing polarity] affording **61** as a brown oil (0.41 g, 37% yield).

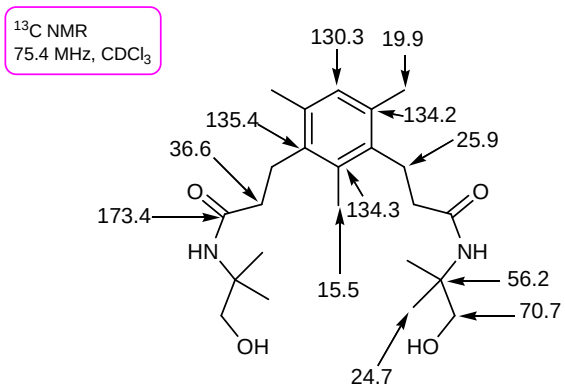
^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 1.26 (s, 12H, C*H*$_3$), 2.27 (s, 6H, C*H*$_3$), 2.29 (s, 3H, C*H*$_3$), 2.93-2.99 (m, 8H, C*H*$_2$, C*H*$_2$C=O), 3.55 (s, 4H, C*H*$_2$OH), 5.53 (bs, 2H, N*H*), 6.85 (s, 1H, Aryl).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 15.5 (*C*H$_3$), 19.9 (*C*H$_3$), 24.7 (*C*H$_3$), 25.9 (*C*H$_2$), 36.6 (*C*H$_2$C=O), 56.2 (*C*(CH$_3$)$_2$), 70.7 (*C*H$_2$OH), 130.3 (Aryl), 134.2 (*C*q), 134.3 (*C*q), 135.4 (*C*q), 173.4 (*C*=O).

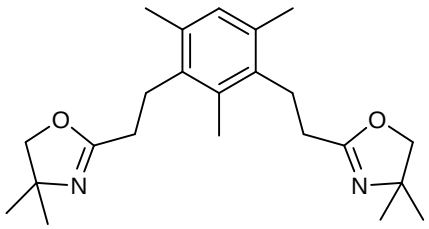
IR (NaCl): 1649 (C=O), 3310 (N-H).

CI-MS: *m/z* (%): 407 (100) [$M^{+\cdot}$].





- **1,3-Bis[(4,4-dimethyl-4,5-dihydro-2-oxazolyl)ethyl]-2,4,6-trimethyl-benzene 16**



61 (0.35 g, 0.86 mmol) was treated under argon atmosphere with thionyl chloride (10 mL, d=1.64 g/mL, 137.85 mmol). The mixture was stirred at room temperature for 4 h and then was concentrated under reduced pressure to remove most of the thionyl chloride. The resulting brown foam was dissolved in dry dichloromethane (25 mL) and stirred with 10% aqueous sodium hydroxide solution (25 mL) overnight. After phase separation, the organic layer was washed with brine (3 × 50 mL), dried (with anhydrous Na_2SO_4), filtered and evaporated to yield **16** as a brown oil (0.31 g, 96% yield).

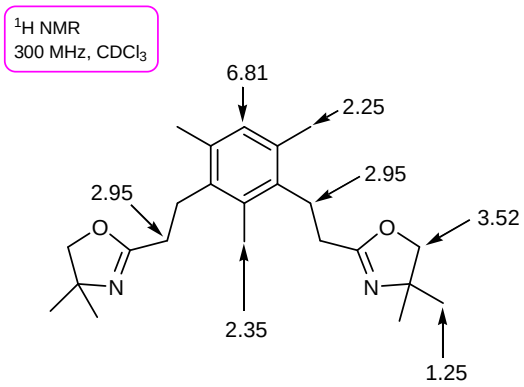
^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 1.25 (s, 12H, C*H*$_3$), 2.25 (s, 6H, C*H*$_3$), 2.35 (s, 3H, C*H*$_3$), 2.95 (bs, 8H, C*H*$_2$), 3.52 (s, 4H, OC*H*$_2$), 6.81 (s, 1H, Aryl).

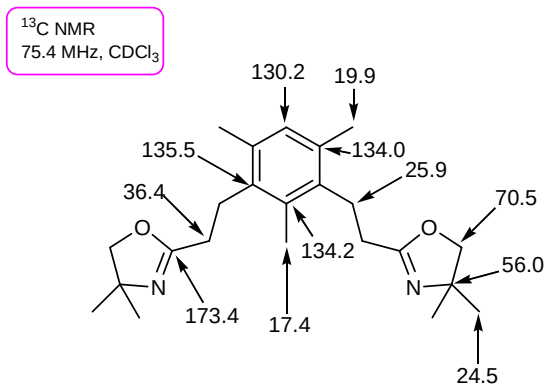
^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 17.4 (*C*H$_3$), 19.9 (*C*H$_3$), 24.5 (*C*H$_3$), 25.9 (*C*H$_2$), 36.4 (*C*H$_2$oxazoline), 56.0 (*C*(CH$_3$)$_2$), 70.5 (O*C*H$_2$), 130.2 (Aryl), 134.0 (*C*q), 134.2 (*C*q), 135.5 (*C*q), 173.4 (*C*=N).

IR (NaCl): ν (cm^{-1}) 1647 (C=N).

CI-MS: *m/z* (%): 371 (100) [M^+].

Anal. Calcd for $C_{23}H_{34}N_2O_2 \cdot 1.5\ CH_2Cl_2$: C, 59.10; H, 7.49; N, 5.63. Found: C, 58.80; H, 7.30; N, 5.24.





6.5. EVALUATION AS A LIGANDS IN CATALYST SYSTEMS GENERATED *in situ*

Materials

Solvents: Acetonitrile, dichloromethane, 1,4-Dioxane, DMF (dry with molecular sieves), DMSO (anhydrous with molecular sieves), IPA and THF were distilled prior to use and dried.

Commercially available products: phenylboronic acid **27e**, 4-bromoanisole, 4'-bromoacetofenona, 4'-chloroacetophenone, 4-chlorotoluene, Cs_2CO_3, K*t*-BuO, $PdCl_2$, $Pd_2(dba)_3$ and $Pd(OAc)_2$.

⇨ General Protocol Used for Suzuki-Miyaura Reaction with Pd (II) of Imidazolium-Oxazoline Salts 13a-c and (*S*)-14b and Bis(Oxazoline) 15

Under an argon atmosphere, a Schlenk tube was charged with 1,4-dioxane (3 mL), $Pd(OAc)_2$, ligand and Cs_2CO_3 (2 mmol). After 2 h at 80 ºC, the reaction mixture was cooled to room temperature and the aryl halide (1 mmol) and arylboronic acid (1.5 mmol) were added in turn. The Schlenk tube was heated at 80 ºC and stirred for 2 h. The mixture was then allowed to cool to room temperature, filtered through a pad of Celite® an dried. It was subsequently concentrated and finally purified by flash chromatography on silica gel.

Results are compiled in Chapter 4, Table 4.1

⇨ General Protocol Used for Suzuki-Miyaura Reaction with Dication 8·2Br

An oven-dried two-necked round bottom 25 mL flask was back-filled with argon and charged with a magnetic stirrer bar, $Pd(OAc)_2$ or $Pd_2(dba)_3$, ligand precursor, Cs_2CO_3 (2 mmol) and 1,4-dioxane (1.5 mL). After 2 h at 80 ºC, the reaction mixture was cooled to room temperature and the aryl halide (1 mmol), phenylboronic acid **27e** (1.5 mmol) and 1,4-dioxane (1.5 mL) were added in

turn. The resulting mixture was heated at 80 ºC for 16 h and then was allowed to cool to room temperature. The mixture was filtered through a pad of Celite®, dried, concentrated, and then purified by flash chromatography on silica gel.

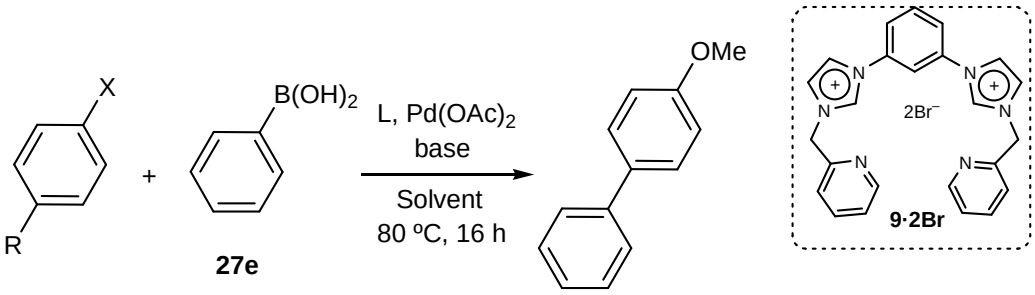
Results and conditions are compiled in Chapter 4, Table 4.2

⇨ **General Protocol Used for Suzuki-Miyaura Reaction with Dication 9·2Br**

An oven-dried two-necked round bottom 25 mL flask was back-filled with argon and charged with a magnetic stirrer bar, $Pd(OAc)_2$, ligand precursor, base (1.5 mmol) and solvent (1.5 mL). After 2 h at 80 ºC, the reaction mixture was cooled to room temperature and the aryl halide (1 mmol), phenylboronic acid **27e** (1.5 mmol) and solvent (1.5 mL) were added in turn. The resulting mixture was heated at 80 ºC for 16 h and then was allowed to cool to room temperature. The mixture was filtered through a pad of Celite®, dried, concentrated, and then purified by flash chromatography on silica gel.

Results and conditions are compiled in Table 6.3

Table 6.3. Results of the Suzuki-Miyaura reactions between aryl halides and phenylboronic acid **27e** using an *in situ* catalyst system[a]



Entry	R	X	L	Base	mol % Pd		Solvent	Yield [b,c] (%)
1	COMe	Br	**IMes·HCl**	Cs_2CO_3	1	[2L/Pd]	IPA	38
2		Br	**9·2Br**	Cs_2CO_3	1	[L/Pd]	IPA	[d]
3		Br	**IMes·HCl**	K-*t*BuO	1	[2L/Pd]	IPA	72
4		Br	**9·2Br**	K-*t*BuO[e]	1	[L/Pd]	IPA	24
5	Me	Cl	**IMes·HCl**	Cs_2CO_3	2.5	[2L/Pd]	Dioxane	16
6		Cl	**9·2Br**	Cs_2CO_3	2.5	[L/Pd]	Dioxane[f]	[d,g]
7		Cl	**9·2Br**	Cs_2CO_3	2.5	[L/Pd]	Dioxane + MeOH	[g]
8		Cl	**9·2Br**	Cs_2CO_3	2.5	[L/Pd]	DMF	[g]
9		Cl	**IPr·HCl**	K-*t*BuO	2	[2L/Pd]	Dioxane	9
10		Cl	**9·2Br**	K-*t*BuO	2	[L/Pd]	Dioxane	[d,g]

[a]Reaction conditions: aryl halide (1 mmol), phenylboronic acid **27e** (1.5 mmol), Cs_2CO_3 (2 mmol) or K-*t*BuO (1.5 mmol), [Ligand/Pd], solvent (3 mL), 80 ºC, 16 h. [b]Isolated yields alter chromatographic purification. [c]Average of two runs. [d]Starting materials were recovered. [e]K-*t*BuO (2.4 mmol) [g]No identified decomposition products were observed.[f]Solubility problems of **L** in solvent.

6.6. ATTEMPTED PREPARATION OF ORGANOMETALLIC COMPLEXES

Materials

Solvents: Acetonitrile, dichloromethane, 1,4-Dioxane, DMF (dry with molecular sieves) and DMSO (anhydrous with molecular sieves). They were distilled prior to use and dried.

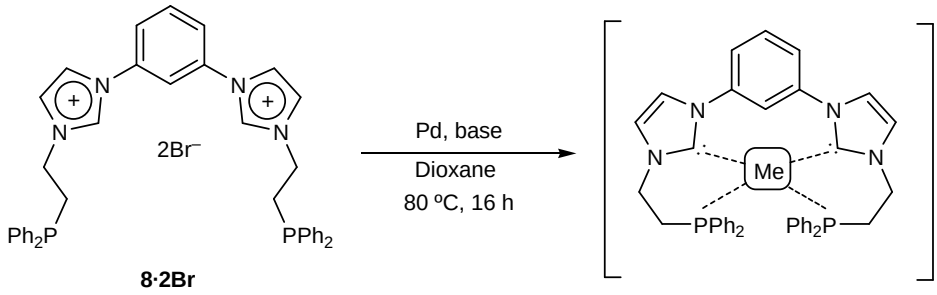
Commercially available products: 4Å molecular sieves, Ag_2CO_3, Ag_2O, Cs_2CO_3, K*t*-BuO, $PdCl_2$, $Pd_2(dba)_3$ and $Pd(OAc)_2$.

⇒ From Fosfino-Imidazolium Salt 8·2Br

Assay A: $Pd(OAc)_2$ (1.1 mmol) was added to a solution of imidazolium salt **8·2Br** (1 mmol) in dry dioxane [15 mM] under an inert atmosphere. The resulting mixture was heated at 80 ℃ for 16 h. After elimination of the solvent under reduced pressure, the remaining greenish solid was dissolved in EtOAc, filtered through a pad of Celite® to remove any elemental Pd formed during the reaction, dried and concentrated to provide a mixture of unidentified decomposition products.

Assay B: $PdCl_2$ (1.1 mmol), Cs_2CO_3 (10 mmol) and 4Å MS (1 g) were added to a solution of imidazolium salt **8·2Br** (1 mmol) in dry dioxane [15 mM] under an inert atmosphere.The resulting mixture was heated at 80 ℃ for 16 h. After elimination of the solvent under reduced pressure the remaining greenish solid was dissolved in EtOAc, filtered through a pad of Celite® to remove any elemental Pd formed during the reaction, dried and concentrated to provide a mixture of unidentified decomposition products.

Table 6.4. Attempted preparation of organometallic complexes of fosfino-imidazolium salt **8·2Br**[a]



8·2Br

Entry	[Pd]	Base	Yield (%)
1	$Pd(OAc)_2$	—	[c]
2[b]	$PdCl_2$	Cs_2CO_3	[c]

[a]Reaction conditions: **8·2Br** (1 mmol), Pd (1.1 mmol), Cs_2CO_3 (10 mmol), 1,4-dioxane, 80 ºC, 16 h. [b] 4Å MS. [c]No identified decomposition products were observed.

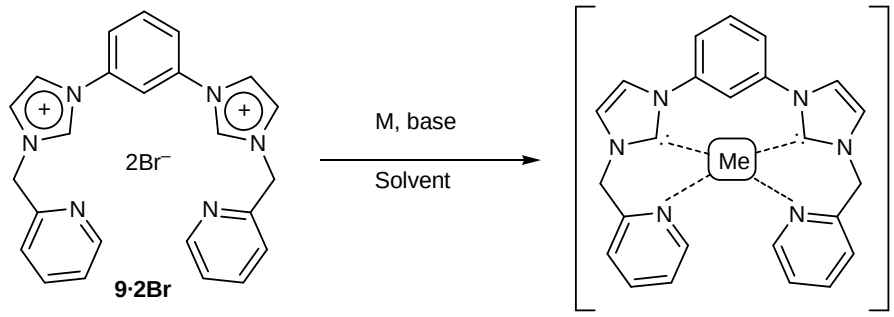
⇒ **From Pyridyl-Imidazolium Salt 9·2Br**

Silver complexes: Ag_2O or Ag_2CO_3 (1.5 mmol) and 4Å MS (1 g) were added to a solution of imidazolium salt **9·2Br** (1 mmol) in dry CH_2Cl_2, DMSO or CH_3CN [15 mM] (see, Table 6.5) under an inert atmosphere.The resulting mixture was stirred at room temeperature or heated at 40 ℃ or 60 ºC for 3-48 h (see, Table 6.5). After completion, the reaction mixture was filtered through a pad of Celite®, the volatiles were removed under reduced pressure and the solid product was washed with diethyl ether, dried *in vacuo* or purified by flash chromatography on silica gel. In all cases, mixtures of unidentified products were observed.

Pd(II) complexes: $Pd(OAc)_2$ or $PdCl_2$ (1.1 mmol), Cs_2CO_3 (10 mmol) or K-*t*BuO (2.5 mmol) were added to a solution of imidazolium salt **9·2Br** (1 mmol) in dry CH_3CN, DMSO or dioxane [15 mM] (see, Table 6.5) under an inert atmosphere. The resulting mixture was heated at different temperatures (see, Table 6.5) and for time specified in Table 6.5. After completion, the reaction mixture was filtered through a pad of Celite®, the volatiles were removed under

reduced pressure and the solid product was washed with diethyl ether, dried *in vacuo* or purified by flash chromatography on silica gel. In all cases, mixtures of unidentified products were observed.

Table 6.5. Attempted preparation of organometallic complexes of pyridyl-imidazolium salt **9·2Br**[a]



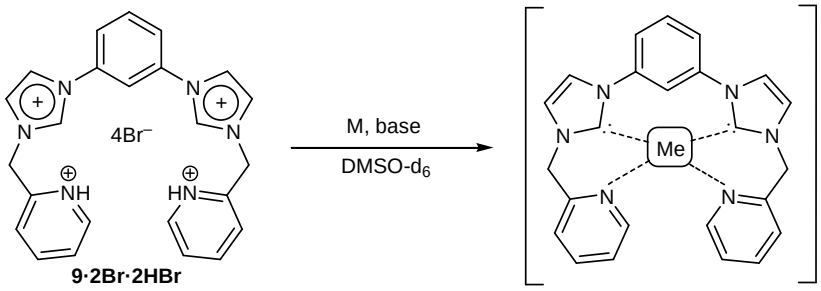
9·2Br

Entry	M	Base	Conditions	Solvent
1	Ag_2O	—	r.t/24 h/4Å MS	dry CH_2Cl_2
2	Ag_2O	—	40ºC/48 h/4Å MS	dry CH_2Cl_2
3[b]	Ag_2O	—	60ºC/2.5 h/4Å MS	DMSO
4	Ag_2CO_3	—	40 ºC/48 h/4Å MS	dry CH_2Cl_2
5	$Pd(OAc)_2$	—	40 ºC/30 min + reflux/ 22 h	dry CH_3CN
6	$Pd(OAc)_2$	—	110 ºC/22 h/sealed tub	dry CH_3CN
7	$Pd(OAc)_2$	—	50 ºC/3 h/ + 110 ºC/2 h/4Å MS	DMSO
8[c]	$Pd(OAc)_2$	Cs_2CO_3	80 ºC/5 h/4Å MS	1,4-dioxane
9	$PdCl_2$	Cs_2CO_3	90 ºC/22 h/3Å MS	dry CH_3CN
10	$PdCl_2$	K*t*-BuO	50 ºC/16 h/3Å MS	dry CH_3CN

[a]Reaction conditions: **9·2X** (1 mmol), **M**: Ag_2O or Ag_2CO_3 (1.5 mmol), $Pd(OAc)_2$ or $PdCl_2$ (1.1 mmol); **base**: Cs_2CO_3 (10 mmol) or K*t*-BuO (2.5 mmol), and solvent. [b]With **9·2PF$_6$**. [c]Low solubility of **9·2Br** in 1,4-dioxane.

⇒ From Pyridyl-Imidazolium Salt 9·2Br·2HBr

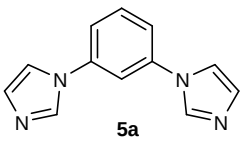
Table 6.6. Attempted preparation of organometallic complexes of pyridyl-imidazolium salt **9·2Br·2HBr**[a]



9·2Br·2HBr

Entry	M	Base	Conditions	Compound observed
1	—	Cs_2CO_3	r.t/1 h/4Å MS	**5a**
2	$PdCl_2$	Cs_2CO_3	r.t/1 h/4Å MS	**5a**
3	$PdCl_2$	—	r.t/1 h/4Å MS	**9·2Br·2HBr**
4	Ag_2O	—	r.t/1 h/4Å MS	**5a**
5	$Pd(OAc)_2$	—	r.t/1h/4Å MS	[b]
6[c]	$Pd(OAc)_2$	—	r.t/1h/4Å MS	**9·2Br·2HBr**
7[c]	$Pd(OAc)_2$	—	80 ºC/2h/4Å MS	**9·2Br·2HBr**

[a]All reactions were carried out in NMR tubs using DMSO-d_6 as a solvent, otherwise noted. [b]Decomposition product. [c]CD_3OD as a solvent.



5a

6.7. IMIDAZOLIUM SALTS: PROPERTIES

Materials

Solvents: H_2O:CH_3CN (1:1 v/v) and methanol-d_4.

1,3-Bis[(3-methyl-1-imidazolio)methyl]benzene dichloride **62a·2Cl** <02EJOC1221>, 1,3-Bis[(3-methyl-1-imidazolio)methyl]benzene dibromide **62a·2Br** <02EJOC1221>, 1,3-Bis[(3-methyl-1-imidazolio)methyl]benzene dihexafluorophosphate **62a·2PF_6** <02EJOC1221>, 1,3-Bis[(3-methyl-1-imidazolio)methyl]-5-*tert*-butylbenzene dibromide **62b·2Br** <02EJOC1221>, 1,3-Bis[(3-adamantyl-4,5-diphenyl-1-imidazolio)methyl]benzene dichloride **62c·2Cl** <02EJOC1221>, macrocycles **63a-c·2X** <06EJOC3988>, 1,3-bis(1-adamantyl)imidazolium chloride **64·Cl**, and 1,3-bis(1-adamantyl)imidazolium bromide **64·Br** were generously provided by Dra. Neus Mesquida.

1,3-Dimesitylimidazolium chloride **IMes·HCl** <99JA9889>, 1,3-bis(2,6-diisopropylphenyl)imidazolium chloride **IPr·HCl** <99JA9889> and 1-mesityl-3-(4-methoxybenzyl)imidazolium chloride **65·Cl** <06EJOC2378> were prepared according to the literature.

6.7.1. ELECTROSPRAY MASS SPECTROMETRY

Positive-ion ESI mass spectrometric analyses were performed on a Waters ZQ mass spectrometer from Micromass Instruments (Manchester, UK) at Serveis Científico-Tècnics of Universitat de Barcelona under the following experimental conditions: • Solvent: H_2O:CH_3CN (1:1, v/v) • Source temperature: 100 ºC • Focus voltage: 0-40 V • Flow rate: 1-10 $\mu L \cdot min^{-1}$ • Nebulizer gas: N_2 (60 $L \cdot h^{-1}$) • Drying gas: N_2 (416 $L \cdot h^{-1}$) • Capillary voltage: 3.5 KV. Spectra were scanned at a rate of 2 s over the mass range *m/z* 100-1500 and were recorded and processed using the MassLynx software, version 4.0 (Micromass). Mass calibration was performed with a 2 $mg \cdot mL^{-1}$ standard solution of NaI in 2-propanol/H_2O (1:1, v/v).

6.7.2. DETERMINATION OF H/D EXCHANGE RATE CONSTANT (k')

H/D exchange analyses were followed by ^{1}H NMR spectroscopy (200 MHz) over a period of 24 h at 25 ºC. In all experiments, we prepare solutions of concentration included between 13 and 5 mM of the imidazolium salt, in methanol-d_4 containing 3% water without any further additives, as the reaction medium. The rate constants (k') were deduced from plots of C-2 proton(s) integral values versus time which followed a standard pseudo-first-order kinetic and is representated by the following equation:

$$I = I_0 \cdot e^{-k't} \quad \text{or} \quad \ln I = \ln I_0 - k't \Rightarrow \boxed{k' = \frac{\ln I_0/I}{t}}$$

where:

I = C-2 proton(s) integral value of imidazolium unit versus time

$\mathbf{I_0}$ = C-2 proton(s) integral value of imidazolium unit at t = 0

k' = pseudo-first-order rate constant, expressed in $days^{-1}$

t = time, expressed in days

The mean values of the C-2 proton(s) integral of imidazolium units versus time and the rate constants of the H/D exchange of all compounds are shown Tables 6.7-6.16.

Table 6.7. Values of C-2 proton(s) integral in methanol-d_4 containing 3% water of compounds **Imes·HCl**, **IPr·HCl**, **64·X** and **65·Cl**

Time [h]	Time [days]	Integral				
		Imes·HCl	**IPr·HCl**	**64·Cl**	**64·Br**	**65·Cl**
0	0.00	0.74	0.63	1	0.99	0
1	0.04	0.72	0.63	1	0.99	0
2	0.08	0.70	0.61	1	0.99	0
3	0.13	0.68	0.61	1	0.99	0
4	0.17	0.65	0.61	1	0.99	0
5	0.21	0.64	0.61	1	0.99	0
6	0.25	0.62	0.60	1	0.99	0
24	1.00	0.35	0.57	1	0.98	0

Table 6.8. Logarithms (ln) values of C-2 proton(s) integral in methanol-d_4 containing 3% water and rate constants of the H/D exchange (k') of compounds **Imes·HCl**, **IPr·HCl**, **64·X** and **65·Cl**

Time [h]	Time [days]	ln (Integral)			
		Imes·HCl	**IPr·HCl**	**64·Cl**	**64·Br**
0	0.00	-0.301	-0.462	0.000	-0.010
1	0.04	-0.329	-0.462	0.000	-0.010
2	0.08	-0.357	-0.494	0.000	-0.010
3	0.13	-0.386	-0.494	0.000	-0.010
4	0.17	-0.431	-0.494	0.000	-0.010
5	0.21	-0.446	-0.494	0.000	-0.010
6	0.25	-0.478	-0.511	0.000	-0.010
24	1.00	-1.050	-0.562	0.000	-0.020
Gradient of linear plot (k')		-0,752	-0,092	0,000	-0,011

Table 6.9. Values of C-2 proton(s) integral in methanol-d_4 containing 3% water of compounds **9·2X**, **35b·2Br** and **36·2Br**

Time [h]	Time [days]	Integral			
		9·2Br	**9·2PF$_6$**	**35b·2Br**	**36·2Br**
0	0.00	1.50	0	1.45	1.56
1	0.04	1.48	0	1.44	1.54
2	0.08	1.47	0	1.41	1.51
3	0.13	1.46	0	1.38	1.50
4	0.17	1.46	0	1.38	1.49
5	0.21	1.45	0	1.36	1.48
6	0.25	1.43	0	1.35	1.42
24	1.00	1.28	0	1.13	1.03

Table 6.10. Logarithms (ln) values of C-2 proton(s) integral in methanol-d_4 containing 3% water and rate constants of the H/D exchange (k') of compounds **9·2X**, **35b·2Br** and **36·2Br**

Time [h]	Time [days]	ln (Integral)		
		9·2Br	**35b·2Br**	**36·2Br**
0	0.00	0.405	0.372	0.445
1	0.04	0.392	0.365	0.432
2	0.08	0.385	0.344	0.412
3	0.13	0.378	0.322	0.405
4	0.17	0.378	0.322	0.399
5	0.21	0.372	0.307	0.392
6	0.25	0.358	0.300	0.351
24	1.00	0.247	0.122	0.030
Gradient of linear plot (k')		-0.154	-0.245	-0.422

Table 6.11. Values of C-2 proton(s) integral in methanol-d_4 containing 3% water of compounds **10a,b·2X**, **11a,b·2X** , **12a,b·2X**

Time [h]	Time [days]	Integral							
		10a·2Cl	**10a·2PF$_6$**	**10b·2Cl**	**11a·2Br**	**11b·2Br**	**12a·2Br**	**12b·2Br**	**12b·2PF$_6$**
		0	1.81	1.14	1.59	1.21	1.74	1.22	0
0	0.00	0	1.81	0.40	0.58	0.76	1.34	0.06	0
1	0.04	0	1.78	0.13	0.15	0.45	1.03	0	0
2	0.08	0	1.73	0.03	0	0.24	0.75	0	0
3	0.13	0	1.73	0	0	0.14	0.57	0	0
4	0.17	0	1.70	0	0	0.11	0.43	0	0
5	0.21	0	1.67	0	0	0.06	0.32	0	0
6	0.25	0	1.42	0	0	0	0	0	0
24	1.00	0	1.42	0	0	0	0	0	0

Table 6.12. Logarithms (ln) values of C-2 proton(s) integral in methanol-d_4 containing 3% water and rate constants of the H/D exchange (k') of compounds **10a,b·2X**, **11a,b·2X** , **12a,b·2X**

Time [h]	Time [days]	ln (Integral)					
		10a·2PF$_6$	**10b·2Cl**	**11a·2Br**	**11b·2Br**	**12a·2Br**	**12b·2Br**
0	0.00	0.593	0.131	0.464	0.191	0.554	-0.199
1	0.04	0.593	-0.916	-0.545	-0.274	0.293	2.813
2	0.08	0.577	-2.040	-1.897	-0.799	0.030	
3	0.13	0.548	-3.507		-1.427	-0.288	
4	0.17	0.548			-1.966	-0.562	
5	0.21	0.531			-2.207	-0.844	
6	0.25	0.513			-2.813	-1.139	
24	1.00	0.351					
Gradient of linear plot (k')		-0.243	-28.888	-28.330	-12.039	-6.810	-72.294

Table 6.13. Values of C-2 proton(s) integral in methanol-d_4 containing 3% water of compounds **62a-c·2X**

Time [h]	Time [days]	Integral				
		62a·2Cl	**62a·2Br**	**62a·2PF_6**	**62b·2Br**	**62c·2Cl**
0	0.00	1.27	0.98	0	1.17	1.80
1	0.04	0.23	0.06	0	1.14	1.78
2	0.08	0	0.05	0	1.14	1.74
3	0.13	0	0.05	0	1.14	1.74
4	0.17	0	0	0	1.13	1.71
5	0.21	0	0	0	1.13	1.69
6	0.25	0	0	0	1.13	1.67
24	1.00	0	0	0	1.12	1.39

Table 6.14. Logarithms (ln) values of C-2 proton(s) integral in methanol-d_4 containing 3% water and rate constants of the H/D exchange (k') of compounds **62a-c·2X**

Time [h]	Time [days]	ln (Integral)			
		62a·2Cl	**62a·2Br**	**62b·2Br**	**62c·2Cl**
0	0.00	0.239	-0.020	0.157	0.588
1	0.04	-1.470	-2.813	0.131	0.577
2	0.08		-2.996	0.131	0.554
3	0.13		-2.996	0.131	0.554
4	0.17			0.122	0.536
5	0.21			0.122	0.525
6	0.25				0.513
24	1.00			0.113	0.329
Gradient of linear plot (k')		-41.009	-21.861	-0.026	-0.255

Table 6.15. Values of C-2 proton(s) integral in methanol-d_4 containing 3% water of compounds **63a-c·2X**

Time [h]	Time [days]	Integral							
		63a·2Cl	**63a·2Br**	**63b·2Cl**	**63b·2Br**	**63b·2PF$_6$**	**63c·2Cl**	**63c·2Br**	**63c·2PF$_6$**
0	0.00	1.41	0	1.67	1.58	1.48	1.86	0	1.88
1	0.04	0.46	0	1.67	1.45	1.39	1.82	0	1.74
2	0.08	0.18	0	1.67	1.31	1.20	1.82	0	1.71
3	0.13	0.07	0	1.67	1.18	1.12	1.82	0	1.71
4	0.17	0.04	0	1.67	1.08	0.97	1.82	0	1.69
5	0.21	0	0	1.67	0.96	0.84	1.82	0	1.66
6	0.25	0	0	1.67	0.89	0.73	1.82	0	1.66
24	1.00	0	0	1.67	0.14	0	1.81	0	1.40

Table 6.16. Logarithms (ln) values of C-2 proton(s) integral in methanol-d_4 containing 3% water and rate constants of the H/D exchange (k') of compounds **63a-c·2X**

Time [h]	Time [days]	ln (Integral)					
		63a·2Cl	**63b·2Cl**	**63b·2Br**	**63b·2PF$_6$**	**63c·2Cl**	**63c·2PF$_6$**
0	0.00	0.344	0.513	0.457	0.392	0.621	0.631
1	0.04	-0.777	0.513	0.372	0.329	0.599	0.554
2	0.08	-1.715	0.513	0.270	0.182	0.599	0.536
3	0.13	-2.659	0.513	0.166	0.113	0.599	0.536
4	0.17	-3.219	0.513	0.077	-0.030	0.599	0.525
5	0.21		0.513	-0.041	-0.174	0.599	0.507
6	0.25		0.513	-0.117	-0.315	0.599	0.507
24	1.00		0.513	-1.966		0.593	0.336
Gradient of linear plot (k')		-21.618	0.000	-2.434	-2.863	-0.013	-0.247