A Platinum Open Access Journal for Organic Chemistry

Paper

Free to Authors and Readers

DOAJ Seal

Arkivoc **2021**, part x, 0-0

to be inserted by editorial office

Facile conversion of 1,2-dicyanobenzene into chiral bisamidines

Mariano Goldberg,[a] Masaki Nakajima,[a] Michael Bolte,[b] and Michael W. Göbel*[a]

[a]*Institute for Organic Chemistry and Chemical Biology, Goethe University Frankfurt, Max-von-Laue-Str. 7, D-60438 Frankfurt am Main, Germany*

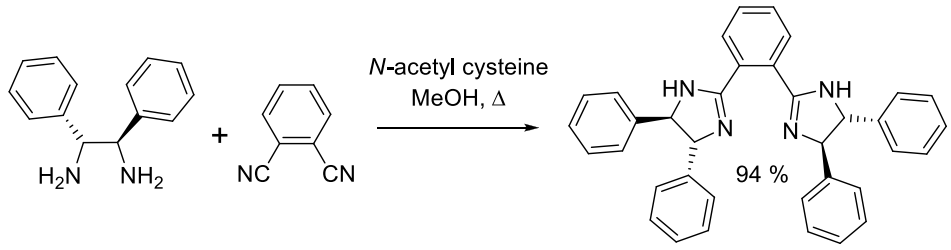
[b]*Institute for Inorganic and Analytical Chemistry, Goethe University Frankfurt, Max-von-Laue-Str. 7, D-60438 Frankfurt am Main, Germany*

Email: M.Goebel@chemie.uni-frankfurt.de

Received mm-dd-yyyy **Accepted Manuscript** mm-dd-yyyy **Published on line** mm-dd-yyyy

Abstract

Nucleophilic catalysis by *N*-acetyl cysteine permits the smooth reaction of 1,2-diarylethylene-1,2-diamines with 1,2-dicyanobenzene forming chiral bisamidines in yields up to 94% in a single step. Such bisamidines can be used as Brønsted bases or, in the protonated state, as electrophilic catalysts to promote Diels-Alder reactions with medium levels of enantioselectivity.



Keywords: Anthrone, BAr^F_4 salts, Dane's diene, organocatalysis, steroid skeleton, thiol catalysis

Introduction

Chiral amidines and guanidines are versatile compounds that have been applied many times in studies on molecular recognition[1-6] and enantioselective catalysis.[7-24] Our group, for example, has introduced the bisamidines **1** and **2** (Figure 1).[25,26] In the protonated state, these compounds promote Diels-Alder reactions as electrophilic catalysts.[27] The geometry of compound **1** was designed to coordinate cyclic 1,2 diketones, carboxylates, or nitronates by hydrogen bonds.[25] The monocation of compound **2**, in contrast, has NH groups converging towards a single carbonyl oxygen.[26] It is a weaker electrophile compared to the dication of **1**. A second protonation of **2** occurs at the central carbon, a formal enamine. C-protonation interrupts conjugation and is thermodynamically unfavorable. Accordingly, the dication of **2** tends to react as a Brønsted acid. The chiral guanidine **3** has been used for enantioselective Brønsted base catalyzed reactions.[28]

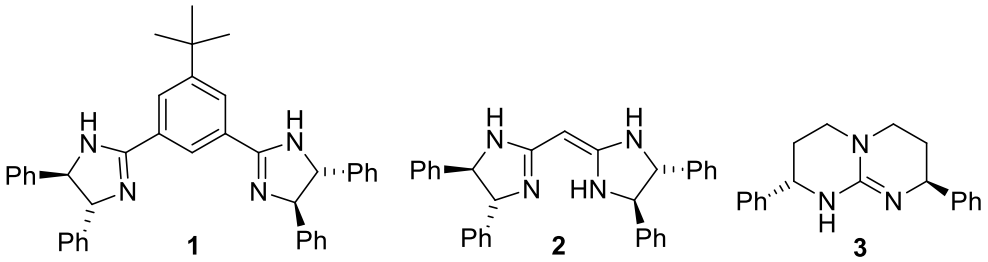


Figure 1. Structures of the chiral bisamidines **1** and **2** and of the guanidine **3**.

In the current study, we describe a one-step synthesis of bisamidines characterized by the general structure **6** (Figure 2). N-permethylated analogs of **6** have been previously described by Wilhelm.[23,24] However, the cyclic amidines were prepared in a different way from aldehydes and diamines by subsequent oxidation of the aminal.[19,20,29] Compared to compound **1**, the new bisamidines are based on a 1,2-phenylene linker bringing the nitrogens closer together as in compound **2**. However, due to a lack of direct conjugation, the bisamidines **6** can be doubly protonated without problems and isolated as their chloride or tetraaryl borate salts. Two preliminary examples show how the compounds may be used as chiral Brønsted bases or, in the dicationic states, as electrophilic catalysts.

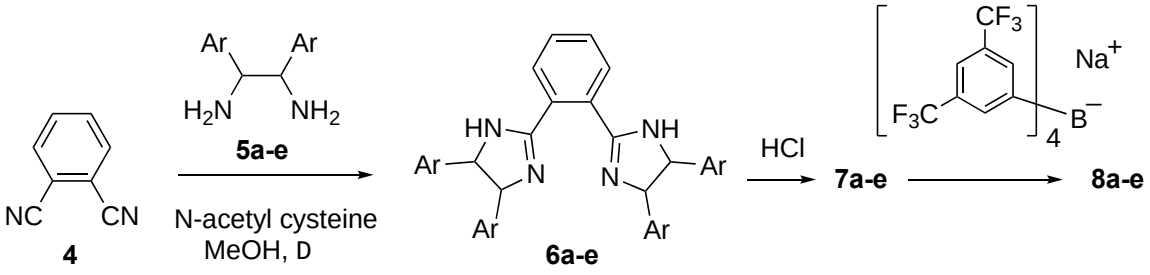


Figure 2. Preparation of bisamidines **6a-e** from phthalonitrile **4**. **5a**/**6a**: Ar = Ph, *R*,*R* enantiomer (94% of **6a** after 22 h); **5b**/**6b**: Ar = 2-hydroxyphenyl, *R*,*R* enantiomer (64% of **6b** after 8 h reflux + 15 h r.t.); **5c**/**6c**: Ar = 2-naphthyl, *S*,*S* enantiomer (20% of **6c** after 26 h); **5d**/**6d**: Ar = *p*-biphenyl, *S*,*S* enantiomer (65% of **6d** after 25 h); **5e**/**6e**: Ar = 1-naphthyl, *S*,*S* enantiomer (36% of **6e** after 37 h). Numbers **7a-e** refer to the hydrochlorides of **6a-e** and **8a-e** to the BAr^F_4 salts.

Results and Discussion

The obvious starting material for the synthesis of bisamidines **6** is 1,2-dicyanobenzene **4** (Figure 2). This compound, however, has a tendency to form phthalocyanines. In the presence of NaOMe, for example, we observed the formation of dark blue solutions. To avoid such byproducts, we used *N*-acetyl cysteine as a nucleophilic catalyst.[30,31] In the presence of 1.2 equivalents of this thiol, the conversion of **4** into bisamidine **6a** can be achieved in 94% yield simply by refluxing with 2.2 equivalents of diamine **5a** in dry methanol. No colored byproducts are formed. The yield of bisamidines however drops with increasing steric demand of the diamines (Figure 3). While diamines **5a** and **5b** are commercial compounds, **5c-e** had to be prepared by stereoselective reactions.[32] In the present study, we have applied the method of Chin based on a [3,3]-sigmatropic rearrangement of bisimines formed from aldehydes and (*R*,*R*)-diamine **5b** yielding the (*S*,*S*)-configurated products **5c-e**.[33]

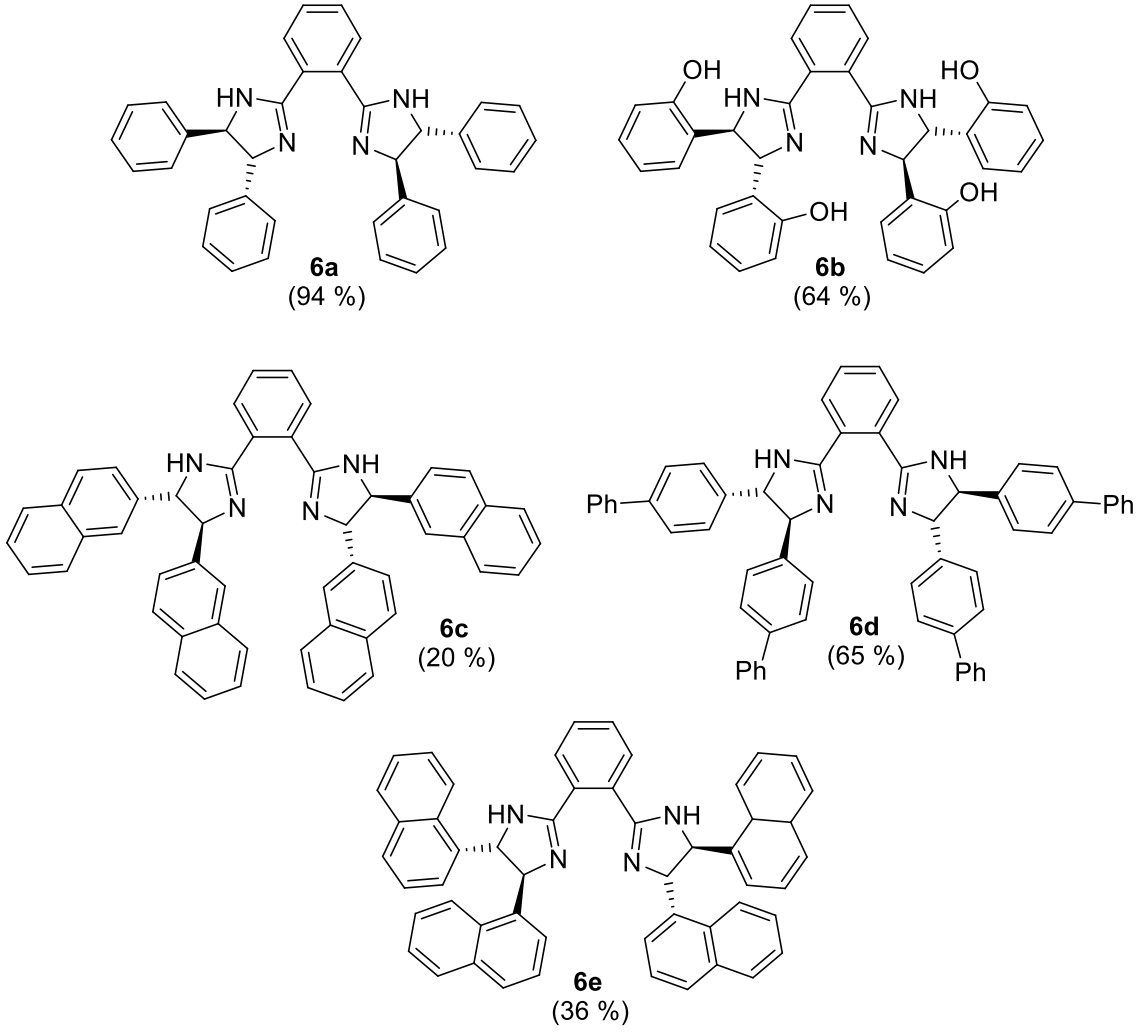


Figure 3. Structures of bisamidines **6a-e** and yields when prepared from phthalonitrile **4** and bisamines **5a-e**.

Crystals of high quality could be obtained by slow diffusion of *n*-pentane into a solution of bisamidine **6a** in EtOAc. The crystal structure (Figure 4 and Supporting Information) shows the close proximity of the

amidine nitrogens that, in the doubly protonated form, may accommodate and activate a carbonyl guest molecule.

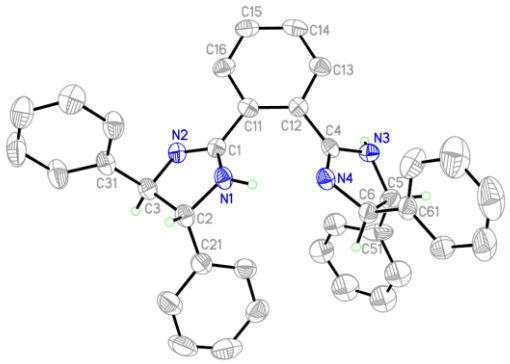


Figure 4. Crystal structure of bisamidine **6a**.

Initially we speculated the OH groups present in bisamidine **6b** might form additional hydrogen bonds with a substrate thus causing increased electrophilic activation. NMR evidence, however, does not support this idea: The NH signals of the other bisamidines in DMSO appear around 8.50 ppm and shift to 12.0 ppm upon protonation with HCl. In the 2-hydroxyphenyl analog, the NH signal moves from 9.61 (**6b**) to 11.26 ppm (**7b**). Interestingly, bisamidine protonation also induces a major shift of the OH signal from 3.17 (**6b**) to 10.28 ppm (**7b**) indicating hydrogen bonds between NH as donor and OH as acceptor. A similar type of intramolecular H-bonds is well known from TADDOLs.[34] Thus, in contrast to other bisamidine hydrochlorides **7** and $BAr^F{}_4$ salts **8**, OH but no longer NH groups are expected to act as H-bond donors in the 2-hydroxyphenyl analogs **7b** and **8b**.

The Diels-Alder reaction of Dane's diene **9** and diketone **10** has been suggested decades ago as a synthetic approach towards steroids (Figure 5).[35] Depending on solvents, the cycloaddition may preferentially form the constitutional isomers *rac*-**13** or *rac*-**14** [36] which slowly tautomerize forming compounds *rac*-**15** and *rac*-**16**. In the presence of chiral Lewis acids, isomer **13** can be obtained with excellent constitutional and enantioselectivity. This reaction represents the key step in one of the total syntheses of estrone.[37] Hydrogen bond mediated association of diketone **10** to amidinium ions also accelerated the cycloaddition with Dane's diene [38] and low to medium levels of enantioselective control were observed in the presence of chiral amidines.[39] The $BAr^F{}_4$ salt of bisamidine **1** (100 mol%) for example selectively formed the correct constitutional isomer *ent*-**15** with *ee* values ranging from 14% at 5 °C, 25% at -16 °C and up to 47% at -70 °C.[25] Using a specifically designed axially chiral amidine, the reaction could be further optimized yielding 24% for the complete multistep synthesis from Dane's diene **9** to enantiopure (+)-estrone.[40] In the present study, we have repeated this well established reaction in the presence of $BAr^F{}_4$ salt **8a** (20 mol%): In toluene at -20 °C diketone *ent*-**13** was formed in 65% yield with 28% *ee*. This result comes close to the selectivities observed for bisamidine **1**. However, it is clearly inferior to the variant using the axially chiral amidine.

Cycloadditions of Dane's diene and compounds **11** and **12** are further options to synthesize (+)-estrone from diene **9**. Both reactions can be catalyzed with excellent stereoselectivities by protonated chiral oxazaborolidines.[41,42] Although mono carbonyl groups should nicely fit into the cationic cleft of $BAr^F{}_4$ salt **8a**, we could not detect any product from the reaction of **9** and **11**. Similarly, even after 3 days at 40 °C (10 mol% **8a**, CH_2Cl_2) not more than 9% of the racemic cycloadduct could be isolated from a test reaction of **9** and

cyclopentenone **12**. Thus, in comparison to protonated oxazaborolidines, the bisamidinium salts seem to be less potent electrophilic catalysts.

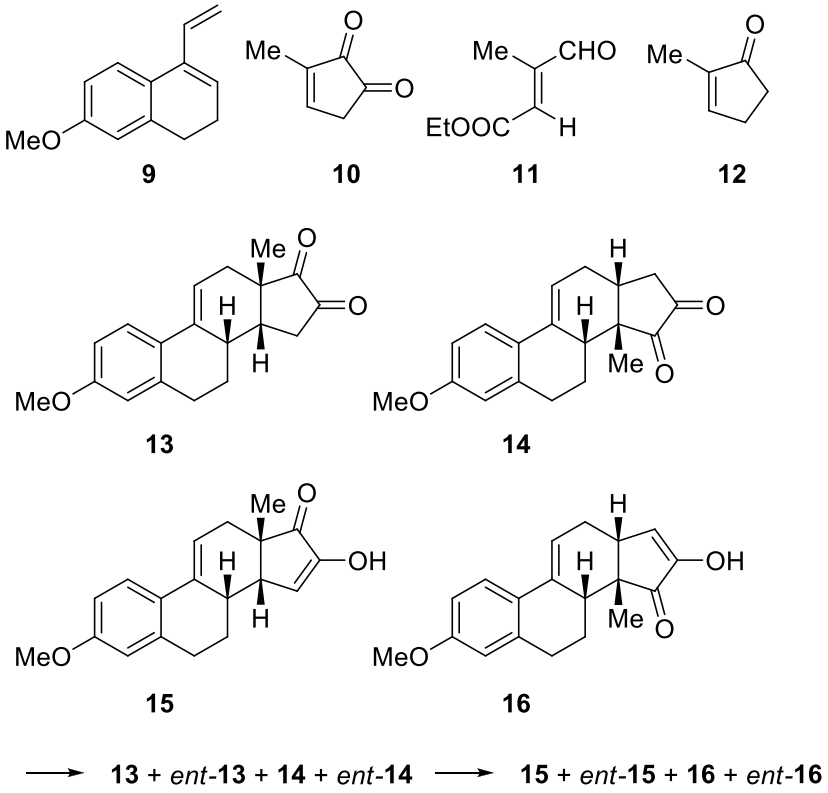


Figure 5. Dane's diene **9** and dienophiles **10** – **12** previously used in total syntheses of estrone.

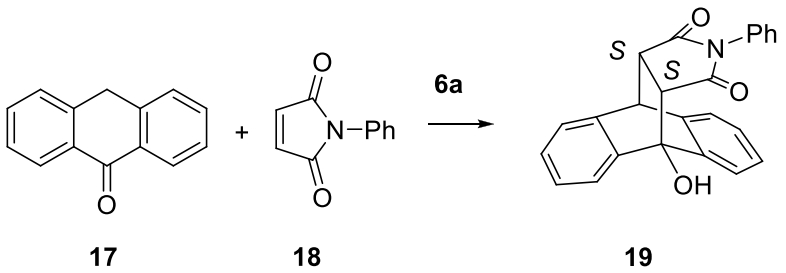


Figure 6. The enolate of anthrone **17** reacts in a Brønsted base induced cycloaddition with dienophile **18**.

Deprotonation of anthrone **17** forms an electron rich diene which readily undergoes Diels-Alder reactions with dienophils such as **18** (Figure 6).[43] When conducted with a chiral Brønsted base in nonpolar solvents, chiral ion pairs are formed and the cycloaddition can show high levels of enantioselectivity.[14,44-49] We have previously used this reaction to evaluate the chiral guanidine **3** and observed *ee* values of product **19** around 30%.[28] Based on this protocol, we have now tested bisamidine **6a**. In the presence of 10 mol% of **6a** in THF, 86% of product **19** with 46% *ee* could be isolated. No subsequent base induced retro aldol reaction occured as observed in the presence of guanidine **3**. The *ee* of product **19** increased to 84% upon recrystallization.

Conclusions

By nucleophilic catalysis with *N*-acetyl cysteine, the conversion of 1,2-dicyano benzene **4** into chiral bisamidines becomes a simple and effective procedure. Recent advances in the synthesis of enantiopure 1,2-disubstituted ethylene-1,2-diamines further increase the usefulness of this method.[32,33] The resulting products **6a-e** have some potential as chiral Brønsted bases. When converted into salts with non-coordinating counterions, BAr^F_4 salts **8a-e** can also play a role as chiral hydrogen bond donors. Like Lewis acids, they can activate substrates for Diels-Alder reactions. However, they are clearly less potent as protonated oxazaborolidines. Furthermore, bisamidines **1** and **6** may be of interest as chiral ligands in coordination chemistry.

Experimental Section

General. Column chromatography: silica gel (60 Å pore size, 0.04- 0.063 mm particle size). Proton nuclear magnetic resonance (^{1}H NMR) and carbon nuclear magnetic resonance spectra (^{13}C-NMR) were recorded with Bruker AV 250 (^{1}H: 250 MHz) or Bruker AV 300 (^{1}H: 300 MHz; ^{13}C: 75.5 MHz) or Bruker AV 500 (^{1}H: 500 MHz; ^{13}C: 125.8 MHz) NMR spectrometers. Chemical shifts for protons are reported in parts per million (δ scale) and internally referenced to the proton resonances of the solvent ($CDCl_3$: δ 7.26, d_6-DMSO: δ 2.50). Chemical shifts for carbon are reported in parts per million (δ scale) and referenced to the carbon resonances of the solvent ($CDCl_3$: δ 77.00, d_6-DMSO: δ 39.51). Data are represented as follows: chemical shift, multiplicity (s singlet, bs broad singlet, d doublet, t triplet, q quartet, m multiplet, dd double doublet), coupling constants in Hz, and integration. ESI-MS spectra were obtained on a Fisons VG Plattform II. HRMS spectra were recorded on a MALDI LTQ Orbitrap mass spectrometer from Thermo Scientific.

1,2-Bis((4*R*,5*R*)-4,5-diphenyl-4,5-dihydro-1*H*-imidazol-2-yl)-benzene (6a). To a solution of phthalonitrile **4** (169 mg, 1.32 mmol, 1.0 equiv.) and *N*-acetyl cysteine (258 mg, 1.58 mmol, 1.2 equiv.) in dry methanol (20 mL) at rt (argon atmosphere) was added (1*R*,2*R*)-1,2-diphenylethylenediamine **5a** (618 mg, 2.91 mmol, 2.2 equiv.). The solution was stirred at rt for 2 h and then heated to reflux for 22 h. After the mixture was cooled to rt, the solution was evaporated under reduced pressure and the residue purified by silica gel chromatography (EtOAc/MeOH 10:1 + 1% NEt_3) to give **6a** as a colourless solid (645 mg, 1.24 mmol, 94%). R_f 0.29 (EtOAc/MeOH 10:1 + 1% NEt_3); mp 210 – 212 °C; $[\alpha]_D^{20}$ +174 (*c* 1.0, MeOH); ^{1}H NMR (500 MHz, DMSO-d_6, δ): 8.27 (bs, 2 H, exchange with D_2O), 7.91-7.89 (m, 2 H), 7.65-7.63 (m, 2 H), 7.30-7.23 (m, 20 H), 4.71 (broad, 4 H); ^{13}C NMR (126 MHz, DMSO-d_6, δ): 164.1, 143.9, 130.8, 129.9, 129.8, 128.5, 127.2, 126.6, 79.9, 69.5; MS (ESI, *m/z*): 519.25 [*M* + H]$^+$; HRMS (MALDI, *m/z*): [*M* + H]$^+$ calcd for $C_{36}H_{31}N_4$, 519.25432; found, 519.25383. Crystal structure: See Supporting Information.

(4*R*,4'*R*,5*R*,5'*R*)-2,2'-(1,2-Phenylene)bis(4,5-diphenyl-4,5-dihydro-1*H*-imidazol-3-ium) chloride (7a). To a solution of bisamidine **6a** (0.62 g, 1.20 mmol, 1.0 equiv.) in dry CH_2Cl_2 (20 mL) at rt (argon atmosphere) was added hydrogen chloride solution (1.26 mL, 2.52 mmol, 2.1 equiv., 2.0 M in Et_2O). The clear solution was stirred at rt for 1.5 h, evaporated under reduced pressure and dried *in vacuo* to obtain **7a** as a light yellow solid (0.71 g, 1.20 mmol, quant.). ^{1}H NMR (300 MHz, DMSO-d_6, δ): 12.00 (bs, 4 H), 8.25-8.22 (m, 2 H), 8.09-8.06 (m, 2 H), 7.46-7.29 (m, 20 H), 5.36 (s, 4 H); ^{13}C NMR (75 MHz, DMSO-d_6, δ): 164.0, 137.1, 133.7, 132.1, 128.9, 128.8, 127.6, 122.9, 69.9.

(4*R*,4'*R*,5*R*,5'*R*)-2,2'-(1,2-Phenylene)bis(4,5-diphenyl-4,5-dihydro-1*H*-imidazol-3-ium) tetrakis(3,5-bis(trifluoromethyl)phenyl)borate (8a). To a solution of bisamidinium chloride **7a** (0.69 g, 1.17 mmol, 1.0 equiv.) in dry methanol (40 mL) at rt (argon atmosphere) was added sodium tetrakis[3,5-bis(trifluormethyl)phenyl]borate (2.07 g, 2.34 mmol, 2.0 equiv.). The clear solution was stirred at rt for 1.5 h and evaporated under reduced pressure. The residue was dissolved in CH_2Cl_2, washed with brine and the aqueous phase was extracted several times with CH_2Cl_2. The combined organic phase was dried over Na_2SO_4, evaporated under reduced pressure and dried *in vacuo* to obtain **8a** as colourless foam (2.51 g, 1.12 mmol, 96%). ^{1}H NMR (300 MHz, DMSO-d_6, δ): 11.43 (bs, 4 H), 8.19 (bs, 2 H), 8.12 (bs, 2 H), 7.68 (bs, 8 H), 7.62-7.61 (bm, 16 H), 7.47-7.37 (m, 20 H), 5.48 (bs, 4 H); ^{13}C NMR (75 MHz, DMSO-d_6, δ): 163.6, 160.9 (q, $J_{11B\text{-}13C}$ 49.2 Hz, BAr^F_4), 136.8, 134.0 (BAr^F_4), 132.0, 129.0, 128.4 (qq, $J_{13C\text{-}19F}$ 31.6, 2.8 Hz, BAr^F_4), 127.7, 124.0 (q, $J_{13C\text{-}19F}$ 272.5 Hz, peaks at 129.4, 125.8, 122.2, 118.6, BAr^F_4), 117.6 (septet, $J_{13C\text{-}19F}$ 3.6 Hz, BAr^F_4).

1,2-Bis((4*R*,5*R*)-4,5-di-(2'-hydroxyphenyl)-4,5-dihydro-1*H*-imidazol-2-yl)benzene (6b). To a solution of phthalonitrile **4** (227 mg, 1.77 mmol, 1.0 equiv.) and *N*-acetyl cysteine (344 mg, 2.11 mmol, 1.2 equiv.) in dry methanol (30 mL) at rt (argon atmosphere) was added (1*R*,2*R*)-1,2-bis(2-hydroxyphenyl)ethylenediamine **5b** (950 mg, 3.89 mmol, 2.2 equiv.). The solution was heated to reflux for 8 h and then stirred at rt overnight. The solution was evaporated under reduced pressure and the residue purified by silica gel chromatography (EtOAc/MeOH 10:1 + 2% NEt_3) to give **6b** as light yellow solid (658 mg, 1.13 mmol, 64%). R_f 0.04-0.18 (EtOAc/MeOH 10:1 + 2% NEt_3); ^{1}H NMR (500 MHz, DMSO-d_6, δ): 9.61 (bs, 2 H), 7.84-7.81 (m, 2 H), 7.64-7.62 (m, 2 H), 7.34 (d, *J* 7.2 Hz, 4 H), 7.03 (td, *J* 7.7, 1.7 Hz, 4 H), 6.75 (dd, *J* 8.1, 0.9 Hz, 4 H), 6.67 (td, *J* 7.5, 1.0 Hz, 4 H), 5.22 (s, 4 H), 3.17 (s, 4 H); ^{13}C NMR (126 MHz, DMSO-d_6, δ): 163.3, 154.8, 130.0, 129.6, 127.8, 127.6, 119.0, 115.2, 48.6; MS (ESI, *m/z*): 583.17 [*M* + H]$^+$; HRMS (MALDI, *m/z*): [*M* + H]$^+$ calcd for $C_{36}H_{31}N_4O_4$, 583.23398; found, 583.23425.

(4*R*,4'*R*,5*R*,5'*R*)-2,2'-(1,2-Phenylene)bis(4,5-bis(2-hydroxy-phenyl)-4,5-dihydro-1*H*-imidazol-3-ium) chloride (7b). To a solution of bisamidine **6b** (0.57 g, 0.98 mmol, 1.0 equiv.) in a mixture of dry CH_2Cl_2 (40 mL) and dry methanol (5 mL) at rt (argon atmosphere) was added hydrogen chloride solution (0.98 mL, 1.96 mmol, 2.0 equiv., 2.0 M in Et_2O). The clear solution was stirred at rt for 3 h, evaporated under reduced pressure and dried *in vacuo* to obtain **7b** as light orange foam (0.64 g, 0.98 mmol, quant.). ^{1}H NMR (300 MHz, DMSO-d_6, δ): 11.26 (bs, 4 H), 10.28 (bs, 4 H), 8.04-7.94 (m, 4 H), 7.34 (dd, *J* 7.7, 1.5 Hz, 4 H), 7.21 (td, *J* 7.5, 1.6 Hz, 4 H), 7.03 (dd, *J* 8.1, 0.9 Hz, 4 H), 6.79 (td, *J* 7.5, 1.0 Hz, 4 H), 5.47 (s, 4 H); ^{13}C NMR (75 MHz, DMSO-d_6, δ): 162.8, 155.7, 133.1, 130.0, 129.9, 128.8, 124.7, 123.4, 119.1, 115.9, 64.7.

(4*R*,4'*R*,5*R*,5'*R*)-2,2'-(1,2-Phenylene)bis(4,5-bis(2-hydroxy-phenyl)-4,5-dihydro-1*H*-imidazol-3-ium) tetrakis-(3,5-bis(trifluoro-methyl)phenyl)borate (8b). To a solution of bisamidinium chloride **7b** (0.64 g, 0.98 mmol, 1.0 equiv.) in dry methanol (40 mL) at rt (argon atmosphere) was added sodium tetrakis[3,5-bis(trifluormethyl)-phenyl]borate (1.74 g, 1.96 mmol, 2.0 equiv.). The clear solution was stirred at rt for 1.5 h and evaporated under reduced pressure. The residue was dissolved in CH_2Cl_2, washed with brine and the aqueous phase was extracted several times with CH_2Cl_2. The combined organic phase was dried over Na_2SO_4, evaporated under reduced pressure and dried *in vacuo* to obtain **8b** as colourless foam (2.17 g, 0.94 mmol, 96%). ^{1}H NMR (300 MHz, DMSO-d_6, δ): 11.00 (s, 4 H), 10.07 (s, 4 H), 8.07-8.04 (m, 2 H), 7.94-7.91 (m, 2 H), 7.70 (bs, 8 H), 7.62 (bm, 16 H), 7.38 (dd, *J* 7.6, 1.4 Hz, 4 H), 7.24 (td, *J* 7.2, 1.5 Hz, 4 H), 6.93 (dd, *J* 8.1, 0.8 Hz, 4 H), 6.84 (td, *J* 7.3, 0.7 Hz, 4 H), 5.52 (s, 4 H); ^{13}C NMR (75 MHz, DMSO-d_6, δ): 162.9, 161.0 (q, $J_{11B\text{-}13C}$ 9.8 Hz, BAr^F_4), 155.6, 134.0 (BAr^F_4), 133.4, 130.1, 130.0, 129.1, 128.5 (qq, $J_{13C\text{-}19F}$ 31.4, 2.8 Hz, BarF4), 124.7, 124.0 (q, $J_{13C\text{-}19F}$ 272.8 Hz, peaks at 129.4, 125.8, 122.2, 118.6, BAr^F_4), 123.6, 119.3, 117.5 (septet, $J_{13C\text{-}19F}$ 3.4 Hz, BAr^F_4), 115.8, 64.6; ^{19}F NMR (471 MHz, DMSO-d_6, δ): - 61.86; MS (ESI, *m/z*): [M + H]$^+$ 583.20; MS (ESI, *m/z*): 863.26 [$(BAr^F_4)^-$]; HRMS (MALDI, *m/z*): [M + H]$^+$ calcd for $C_{36}H_{31}N_4O_4$, 583.23398, found, 583.23443.

(1*S*,2*S*)-1,2-Di(naphthalen-2-yl)ethane-1,2-diammonium chloride (5c · 2 HCl). To a solution of ((*R*,*R*)-1,2-bis-(2-hydroxyphenyl)-1,2-diamino-ethane **5b** (1.22 g, 4.99 mmol, 1.00 equiv.) in DMSO (25 mL) was added naphthalene 2-carbaldehyde (1.87 g, 11.97 mmol, 2.40 equiv.), then stirred for 19 h at rt and then water (75 mL) and Et_2O were added. The phases were separated, the combined organic layers were dried over Na_2SO_4 and evaporated under reduced pressure. The orange solid residue was dissolved in THF (70 mL) and concentrated HCl (37%, 1.5 mL) was added. The reaction mixture was stirred for 19 h, the precipitate was filtered off and washed with cold THF. The residue was dried *in vacuo* to afford the hydrochloride of **5c** as a colourless solid (1.40 g, 3.63 mmol, 73%). mp 245 – 246 °C; ^{1}H NMR (300 MHz, DMSO-d_6, δ): 9.50 (bs, 6 H), 8.00 (d, *J* 1.1 Hz, 2 H), 7.83-7.75 (m, 6 H), 7.55 (dd, *J* 7.8, 1.7 Hz, 2 H), 7.51-7.45 (m, 4 H), 5.42 (bs, 2 H); ^{13}C NMR (75 MHz, DMSO-d_6, δ): 132.7, 132.2, 130.7, 128.8, 128.1, 127.9, 127.5, 126.9, 126.6, 125.5, 56.9; MS (ESI, *m/z*): 296.14 [M + H^+ – NH_3]; HRMS (MALDI, *m/z*): [M + H^+ – NH_3] calcd for $C_{22}H_{18}N$, 296.14338; found 296.14301.

(1*S*,2*S*)-1,2-Di(naphthalen-2-yl)ethane-1,2-diamine (5c). A suspension of **5c** · 2 HCl (1.21 g, 3.14 mmol, 1.00 equiv.) in CH_2Cl_2 (50 mL) was thoroughly mixed with aqueous NaOH (2 M, 50 mL). The phases were separated, the combined organic layers were dried over Na_2SO_4 and evaporated under reduced pressure. The residue was dried *in vacuo* to afford **5c** as light grey solid (0.95 g, 3.04 mmol, 97%). mp 143 – 146 °C; ^{1}H NMR (300 MHz, DMSO-d_6, δ): 7.79-7.69 (m, 8 H), 7.46 (dd, *J* 8.4, 1.6 Hz, 2 H), 7.42-7.36 (m, 4 H), 4.18 (s, 2 H), 2.13 (bs, 4 H); ^{13}C NMR (75 MHz, DMSO-d_6, δ): 142.5, 132.7, 131.9, 127.5, 127.3, 126.9, 126.1, 125.7, 125.5, 125.2, 62.1.

1,2-Bis((4*S*,5*S*)-4,5-di(naphthalen-2-yl)-4,5-dihydro-1*H*-imidazol-2-yl)benzene (6c). To a solution of phthalonitrile **4** (0.18 g, 1.39 mmol, 1.0 equiv.) and *N*-acetyl cysteine (0.27 g, 1.67 mmol, 1.2 equiv.) in dry methanol (40 mL) at rt (argon atmosphere) was added diamine **5c** (0.91 g, 2.91 mmol, 2.1 equiv.). The solution was heated to reflux for 26 h. After the reaction was cooled to rt the solution was evaporated under reduced pressure and the residue purified by silica gel chromatography (CH_2Cl_2/MeOH 50:1 + 0.1% NH_3) to give **6c** as a yellow solid (0.20 g, 0.28 mmol, 20%). R_f 0.20 (CH_2Cl_2/MeOH 50:1 + 1% NH_3); mp 225-227 °C; ^{1}H NMR (500 MHz, DMSO-d_6, δ): 8.55 (bs, 2 H), 8.04-8.02 (m, 2 H), 7.83 (d, *J* 8.1 Hz, 4 H), 7.78 (d, *J* 8.5 Hz, 4 H), 7.73-7.70 (m, 10 H), 7.50 (d, *J* 8.5 Hz, 4 H), 7.46 (t, *J* 7.4 Hz, 4 H), 7.39 (t, *J* 7.6 Hz, 4 H), 5.01 (bs, 4 H); ^{13}C NMR (126 MHz, DMSO-d_6, δ): 164.3, 141.2, 132.9, 132.4, 130.9, 130.0, 129.9, 128.3, 127.7, 127.5, 126.1, 125.8, 125.1, 54.9; MS (ESI, *m/z*): 719.31 [*M* + H^+]; HRMS (MALDI, *m/z*): [*M* + H]$^+$ calcd for $C_{52}H_{39}N_4$, 719.31692; found, 719.31780.

(4*S*,4'*S*,5*S*,5'*S*)-2,2'-(1,2-Phenylene)bis(4,5-di(naphthalen-2-yl)-4,5-dihydro-1*H*-imidazol-3-ium) chloride (7c). To a solution of bisamidine **6c** (0.18 g, 0.25 mmol, 1.0 equiv.) in dry CH_2Cl_2 (25 mL) at rt (argon atmosphere) was added hydrogen chloride in Et_2O (0.27 mL, 0.54 mmol, 2.2 equiv., 2.0 M). The clear solution was stirred at rt for 2 h, evaporated under reduced pressure and dried *in vacuo* to obtain **7c** as a yellow solid (0.20 g, 0.25 mmol, quant.). ^{1}H NMR (500 MHz, DMSO-d_6, δ): 12.10 (bs, 4 H), 8.38 (bs, 2 H), 8.18 (bs, 2 H), 7.95 (s, 4 H), 7.77-7.75 (m, 8 H), 7.63 (s, 8 H), 7.51 (td, *J* 7.5, 1.1 Hz, 4 H), 7.44 (t, *J* 7.6 Hz, 4 H), 5.63 (bs, 4 H); ^{13}C NMR (126 MHz, DMSO-d_6, δ): 164.1, 134.6, 134.1, 132.9, 132.6, 128.8, 127.8, 127.6, 127.1, 126.7, 126.5, 124.9, 123.1, 70.2.

(4*S*,4'*S*,5*S*,5'*S*)-2,2'-(1,2-Phenylene)bis(4,5-di(naphthalen-2-yl)-4,5-dihydro-1*H*-imidazol-3-ium) tetrakis(3,5-bis(trifluoro-methyl)phenyl)borate (8c). To a solution of bisamidinium chloride **7c** (0.17 g, 0.21 mmol, 1.0 equiv.) in dry methanol (24 mL) at rt (argon atmosphere) was added sodium tetrakis[3,5-bis(trifluormethyl)-phenyl]borate (0.37 g, 0.42 mmol, 2.0 equiv.). The clear solution was stirred at rt for 2 h and evaporated under reduced pressure. The residue was dissolved in CH_2Cl_2, washed with brine and the aqueous phase was extracted several times with CH_2Cl_2. The combined organic phase was dried over Na_2SO_4, evaporated under reduced pressure and dried *in vacuo* to obtain **8c** as a light yellow foam (0.46 g, 0.19 mmol, 90%). ^{1}H NMR (500 MHz, CD_3CN, δ): 9.53 (bs, 2 H), 8.30-8.28 (m, 2 H), 8.12 (bm, 2 H), 7.86-7.83 (m, 12 H), 7.75 (d, *J* 8.1 Hz, 4

H), 7.70 (bm, 16 H), 7.67 (bs, 8 H), 7.56-7.46 (m, 12 H), 5.67 (bs, 4 H); ^{13}C NMR (126 MHz, CD_3CN, δ): 165.4, 162.7 (q, $J_{11B\text{-}13C}$ 49.8 Hz, $BAr^F{}_4$), 135.7 ($BAr^F{}_4$), 134.5, 134.2, 133.0, 130.4, 130.0 (qq, $J_{13C\text{-}19F}$ 31.5, 2.9 Hz, $BAr^F{}_4$), 129.0, 128.9, 128.2, 128.0, 127.9, 125.5 (q, $J_{13C\text{-}19F}$ 271.8 Hz, peaks at 128.8, 126.6, 124.5, 122.3, $BAr^F{}_4$), 125.3, 118.8 (septet, $J_{13C\text{-}19F}$ 3.8 Hz, $BAr^F{}_4$), 118.4, 72.1.

(1*S*,2*S*)-1,2-Di(biphenyl-4-yl)ethane-1,2-diammonium chloride (5d · 2 HCl). To a solution of ((*R*,*R*)-1,2-bis-(2-hydroxyphenyl)-1,2-diamino-ethane **5b** (0.710 g, 2.91 mmol, 1.00 equiv.) in DMSO (15 mL) was added 4-phenylbenzaldehyde (1.21 g, 6.65 mmol, 2.40 equiv.), then stirred for 12 h at rt. Workup and imine hydrolysis were carried out as described for **5c** to yield the hydrochloride of **5d** as a colorless solid (1.22 g, 96%). mp 236 – 238 °C (decomp.); $[\alpha]_D^{20}$ +63 (*c* 1.0, MeOH); ^{1}H NMR (250 MHz, DMSO-d_6, δ): 9.14 (bs, 6 H), 7.69-7.58 (m, 8 H), 7.48-7.33 (m, 10 H), 5.10 (s, 2 H); ^{13}C NMR (75 MHz, DMSO-d_6, δ): 140.6, 138.9, 134.0, 132.2, 129.5, 129.0, 127.9, 126.6, 56.3; MS (ESI, *m/z*): 348.3 [M + H$^+$ – NH_3], 365.0 [M + H$^+$].

(1*S*,2*S*)-1,2-Di(biphenyl-4-yl)ethane-1,2-diamine (5d). Diamine **5d** was prepared as described above for compound **5c**. From 600 mg of hydrochloride 447 mg (89%) of amine **5d** were obtained as a slightly colored solid. mp 190 – 192 °C; ^{1}H NMR (250 MHz, $CDCl_3$, δ): 7.60-7.53 (m, 8 H), 7,46-7.33 (m, 10 H), 4.21 (s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$, δ): 142.7, 141.0, 140.1, 128.9, 127.5, 127.4,127.16, 127.12, 61.7.

1,2-Bis((4*S*,5*S*)-4,5-di([1,1'-biphenyl]-4-yl)-4,5-dihydro-1*H*-imidazol-2-yl)benzene (6d). To a solution of phthalonitrile **4** (246 mg, 1.92 mmol, 1.0 equiv.) and *N*-acetyl cysteine (375 mg, 2.30 mmol, 1.2 equiv.) in dry methanol (40 mL) at rt (argon atmosphere) was added diamine **5d** (1.54 g, 4.23 mmol, 2.2 equiv.). The solution was heated to reflux for 25 h. After the reaction was cooled to rt the solution was evaporated under reduced pressure and the residue purified by silica gel chromatography (CH_2Cl_2/MeOH 50:1 + 0.1% NH_3) to give **6d** as light yellow foam (1.03 g, 1.25 mmol, 65%). R_f 0.28 (CH_2Cl_2/MeOH 25:1); ^{1}H NMR (300 MHz, DMSO-d_6, δ): 8.42 (bs, 2 H), 7.99-7.96 (m, 2 H), 7.70-7.67 (m, 2 H), 7.61-7.57 (m, 16 H), 7.43-7.37 (m, 16 H), 7.36-7.30 (m, 4 H), 4.83 (bs, 4 H); ^{13}C NMR (126 MHz, C_6D_6, δ): 165.9, 143.5, 141.6, 141.0, 131.6, 131.3, 130.8, 129.5, 128.1, 128.0, 127.8, 127.7, 75.6; MS (ESI, *m/z*): 823.42 [*M* + H]$^+$; HRMS (MALDI, *m/z*): [*M* + H]$^+$ calcd for $C_{60}H_{47}N_4$, 823.37952; found, 823.37916.

(4*S*,4'*S*,5*S*,5'*S*)-2,2'-(1,2-Phenylene)bis(4,5-di([1,1'-biphenyl]-4-yl)-4,5-dihydro-1*H*-imidazol-3-ium) chloride (7d). To a solution of bisamidine **6d** (0.89 g, 1.08 mmol, 1.0 equiv.) in dry CH_2Cl_2 (40 mL) at rt (argon atmosphere) was added hydrogen chloride solution (1.14 mL, 2.28 mmol, 2.1 equiv., 2.0 M in Et_2O). The clear solution was stirred at rt for 3 h, evaporated under reduced pressure and dried *in vacuo* to obtain **7d** as yellow solid (0.97 g, 1.08 mmol, quant.). ^{1}H NMR (300 MHz, DMSO-d_6, δ): 11.95 (bs, 4 H), 8.26 (bs, 2 H), 8.13 (bs, 2 H), 7.67-7.59 (m, 24 H), 7.44-7.33 (m, 12 H), 5.55 (bs, 4 H); ^{13}C NMR (126 MHz, DMSO-d_6, δ): 164.3, 140.6, 139.2, 136.1, 133.9, 132.4, 129.0, 128.4, 127.7, 127.2, 126.6, 123.0, 69.5, 54.9.

(4*S*,4'*S*,5*S*,5'*S*)-2,2'-(1,2-Phenylene)bis(4,5-di([1,1'-biphenyl]-4-yl)-4,5-dihydro-1*H*-imidazol-3-ium) tetrakis(3,5-bis(tri-fluoromethyl)phenyl)borate (8d). To a solution of bisamidinium chloride **7d** (0.94 g, 1.05 mmol, 1.0 equiv.) in dry methanol (40 mL) at rt (argon atmosphere) was added sodium tetrakis[3,5-bis(trifluormethyl)-phenyl]borate (1.86 g, 2.10 mmol, 2.0 equiv.). The clear solution was stirred at rt for 3 h and evaporated under reduced pressure. The residue was dissolved in CH_2Cl_2, washed with brine and the aqueous phase was extracted several times with CH_2Cl_2. The combined organic phase was dried over Na_2SO_4, evaporated under reduced pressure and dried *in vacuo*. After NMR-spectra showed only 1 equiv. of the $BAr^F{}_4$ anion, the whole procedure was repeated with 1 equiv. of tetrakis[3,5-bis(trifluormethyl)phenyl]borate to obtain **8d** as colourless foam (2.40 g, 0.94 mmol, 90%). ^{1}H NMR (500 MHz, CD_3CN, δ): 8.17-815 (m, 2 H), 8.01-7.99 (m, 2 H), 7.71 (bt, 16 H), 7.67 (s, 8 H), 7.65 (s, 8 H), 7.61-7.59 (m, 8 H), 7.48 (d, *J* 8.3 Hz, 8 H), 7.44-7.40 (m, 8 H), 7.38-7.35 (m, 4 H), 5.32 (bs, 4 H); ^{13}C NMR (126 MHz, CD_3CN, δ): 165.4, 162.7 (q, $J_{11B\text{-}13C}$ 49.9 Hz, $BAr^F{}_4$), 142.5, 140.9, 138.9, 135.7 ($BAr^F{}_4$), 134.7, 132.2, 130.1, 130.0 (qq, $J_{13C\text{-}19F}$ 31.5, 2.9 Hz, $BAr^F{}_4$), 128.9, 128.8,

128.7, 127.9, 125.5 (q, $J_{13C\text{-}19F}$ 272.0 Hz, peaks at 126.6, 124.5, 122.3, BarF4), 118.8 (septet, $J_{13C\text{-}19F}$ 3.8 Hz, $BAr^F{}_4$), 118.4, 72.5 ppm.

1,2-Bis((4*S*,5*S*)-4,5-di(naphthalen-1-yl)-4,5-dihydro-1*H*-imidazol-2-yl)benzene (6e). To a solution of phthalonitrile **4** (0.11 g, 0.87 mmol, 1.0 equiv.) and *N*-acetyl cysteine (0.17 g, 1.04 mmol, 1.2 equiv.) in dry methanol (50 mL) at rt (argon atmosphere) was added (1*S*,2*S*)-1,2-di(naphthalen-1-yl)ethane-1,2-diamine **5e** (0.60 g, 1.92 mmol, 2.2 equiv.).[33] The solution was heated to reflux for 37 h. After the reaction was cooled to rt the solution was evaporated under reduced pressure and the residue purified by silica gel chromatography (CH_2Cl_2/MeOH 50:1 + 1% NH_3) to give **6e** as a yellow foam (0.22 g, 0.31 mmol, 36%). R_f 0.14 (CH_2Cl_2/MeOH 50:1 + 1% NH_3); ^{1}H NMR (300 MHz, CD_2Cl_2, δ): 8.01-7.98 (m, 2 H), 7.77 (bt, *J* 8.5 Hz, 8 H), 7.58 (dd, *J* 7.2, 0.9 Hz, 4 H), 7.43-7.34 (m, 10 H), 7.30 (ddd, *J* 8.1, 7.0, 1.0 Hz, 4 H), 6.99 (ddd, *J* 8.5, 7.0, 1.3 Hz, 4 H), 5.55 (bs, 4 H); ^{13}C NMR (75 MHz, CD_2Cl_2, δ): 165.1, 139.9, 134.5, 131.5, 131.02, 131.0, 130.8, 129.1, 128.5, 126.2, 126.1, 126.0, 124.8, 124.0, 71.0; MS (ESI, *m/z*): 719.39 [*M* + H$^+$]; HRMS (MALDI, *m/z*): [*M* + H]$^+$ calcd for $C_{52}H_{39}N_4$, 719.31692; found, 719.31648.

(4*S*,4'*S*,5*S*,5'*S*)-2,2'-(1,2-Phenylene)bis(4,5-di(naphthalen-1-yl)-4,5-dihydro-1*H*-imidazol-3-ium) chloride (7e). To a solution of bisamidine **6e** (0.19 g, 0.26 mmol, 1.0 equiv.) in dry CH_2Cl_2 (20 mL) at rt (argon atmosphere) was added hydrogen chloride solution (0.28 mL, 0.56 mmol, 2.2 equiv., 2.0 M in Et_2O). The clear solution was stirred at rt for 1.5 h, evaporated under reduced pressure and dried *in vacuo* to obtain **7e** as colourless solid (0.21 g, 0.26 mmol, quant.). ^{1}H NMR (500 MHz, DMSO-d_6, δ): 12.16 (bs, 4 H), 8.39 (bs, 2 H), 8.16 (bs, 2 H), 8.06 (bd, 4 H), 7.96 (d, *J* 8.1 Hz, 8 H), 7.44-7.39 (m, 8 H), 7.34 (t, *J* 7.5 Hz, 4 H), 7.15 (t, *J* 7.5 Hz, 4 H), 6.40 (bs, 4 H); ^{13}C NMR (126 MHz, DMSO-d_6, δ): 164.0, 133.9, 133.4, 133.3, 131.8, 130.3, 129.4, 128.8, 126.5, 126.1, 125.7, 125.5, 123.2, 122.3, 65.5.

(4S,4'S,5S,5'S)-2,2'-(1,2-Phenylene)bis(4,5-di(naphthalen-1-yl)-4,5-dihydro-1*H*-imidazol-3-ium) tetrakis(3,5-bis(trifluoro-methyl)phenyl)borate (8e). To a solution of bisamidinium chloride **7e** (0.18 g, 0.23 mmol, 1.0 equiv.) in dry methanol (20 mL) at rt (argon atmosphere) was added sodium tetrakis[3,5-bis(trifluormethyl)phenyl]borate (0.41 g, 0.46 mmol, 2.0 equiv.). The clear solution was stirred at rt for 3 h and evaporated under reduced pressure. The residue was dissolved in CH_2Cl_2, washed with brine and the aqueous phase was extracted several times with CH_2Cl_2. The combined organic phase was dried over Na_2SO_4, evaporated under reduced pressure and dried *in vacuo*. After NMR-spectra showed only 1 equiv. of the $BAr^F{}_4$ anion, the whole procedure was repeated with 1 equiv. of tetrakis[3,5-bis(trifluormethyl)phenyl]borate to obtain **8e** as a yellow foam (0.56 g, 0.23 mmol, quant.). ^{1}H NMR (500 MHz, CD_3CN, δ): 8.29-8.27 (m, 2 H), 8.03 (bm, 2 H), 7.89 (d, *J* 8.2 Hz, 4 H), 7.86 (d, *J* 8.2 Hz, 4 H), 7.76 (bd, *J* 7.0 Hz, 4 H), 7.70 (bm, 16 H), 7.67 (bs, 8 H), 7.46 (dd, *J* 8.4, 7.7 Hz, 4 H), 7.34 (t, *J* 7.5 Hz, 4 H), 7.25 (bd, *J* 8.5 Hz, 4 H), 7.03 (bt, *J* 7.4 Hz, 4 H), 5.96 (bs, 4 H); ^{13}C NMR (126 MHz, CD_3CN, δ): 165.2, 162.7 (q, $J_{11B\text{-}13C}$ 49.8 Hz, $BAr^F{}_4$), 135.7 ($BAr^F{}_4$), 135.0, 132.4, 131.4, 130.4, 129.99 (qq, $J_{13C\text{-}19F}$ 31.5, 2.9 Hz, $BAr^F{}_4$), 129.97, 127.5, 127.2, 126.7, 125.7, 125.5 (q, $J_{13C\text{-}19F}$ 271.8 Hz, peaks at 128.8, 126.6, 124.5, 122.3, $BAr^F{}_4$), 123.4, 118.8 (septet, $J_{13C\text{-}19F}$ 3.9 Hz, $BAr^F{}_4$), 118.4, 68.6.

Cycloaddition of compounds 9 and 10 forming estrone precursor 13/*ent*-13 (Figure 5). The reaction was run in a closed 50 mL polyethylene vessel. To a solution of dienophile **10** (28.6 mg, 0.26 mmol, 1.0 equiv.) and $BAr^F{}_4$ salt **8a** (117 mg, 0.052 mmol, 0.2 equiv.) in dry toluene (5 mL, argon atmosphere) at -20 °C, a spatula tip of molecular sieves (3 Å) was added. After stirring for 30 min, a solution of Dane's diene **9** (54.0 mg, 0.29 mmol, 1.1 equiv.) in toluene (5 mL) was added to the mixture in one portion. The solution was stirred for 21 h at -20 °C and then the molecular sieves were filtered off. The solvent was removed *in vacuo* and the residue purified by flash column chromatography (*c*-hexane/EtOAc 10:1 → 4:1) to afford **13**/*ent*-**13** as light yellow foam (50.0 mg, 0.17 mmol, 65%, 28% *ee*, Daicel OJ, *n*-hexane/i-PrOH 10:4, 0.8 mL/min, 254 nm. Retention

time of **13**: 10.8 min (disfavored), of *ent*-**13**: 18.0 min (favored). The products were identified by comparison with authentic samples.[40]

Base induced cycloaddition of anthrone 17 and maleimide 18 forming compound 19 (Figure 6). The reaction was run in a closed 50 mL polyethylene vessel. To a solution of anthrone **17** (42.0 mg, 0.22 mmol, 1.0 equiv.) in dry THF (6 mL) at -40 °C, the catalyst **6a** (11.4 mg, 0.022 mmol, 0.1 equiv.) was added. After stirring for 30 min, maleimide **18** (38.0 mg, 0.22 mmol, 1.0 equiv.) was added to the mixture in one portion. The solution was allowed to warm up to -15 °C for 16 h and stirred for two more days at rt. The mixture was then purified by flash column chromatography (*c*-hexane/EtOAc 10:1) to afford product **19**/*ent*-**19** as a colourless solid (70.0 mg, 0.19 mmol, 86%, 46% *ee*). Single recrystallization from *c*-hexane/CH_2Cl_2 improved the *ee* to 84% (19.7 mg, 0.05 mmol, 23%, Chiralpak IA, 0.46 × 25 cm, *n*-hexane/i-PrOH 10:3 + 20% CH_2Cl_2, 0.7 mL/min, 254 nm. Retention time of **19**: 11.6 min (favored), of *ent*-**19**: 13.2 min (disfavored). The products were identified by comparison with authentic samples.[28,46]

Supplementary Material

^{1}H and ^{13}C NMR spectra, determination of enantiomeric purities by HPLC, and crystallographic information concerning bisamidine **6a**. Crystallographic data in cif format were deposited with the Cambridge Crystallographic Data Centre (deposition number 2032917) and can be obtained from the CCDC homepage (https://www.ccdc.cam.ac.uk/structures/).

References

The results described in this article originate from the PhD thesis of Dr. Mariano Goldberg:
http://publikationen.ub.uni-frankfurt.de/frontdoor/index/index/docId/55098

1. Schug, K. A.; Lindner, W. *Chem. Rev.* **2005**, *105*, 67-113. https://doi.org/10.1021/cr040603j
2. Coles, M. P. *Chem. Commun.* **2009**, 3659-3676. https://doi.org/10.1039/b901940e
3. Blondeau, P.; Segura, M.; Pérez-Fernández, R.; de Mendoza, J. *Chem. Soc. Rev.* **2007**, *36*, 198-210. https://doi.org/10.1039/b603089k
4. Mosquera, J.; Sánchez, M. I.; Valero, J.; de Mendoza, J.; Vázquez, M. E.; Mascareñas, J. L. *Chem. Commun.* **2015**, *51*, 4811-4814. https://doi.org/10.1039/c4cc09525a
5. Kurzmeier, H.; Schmidtchen, F. P. *J. Org. Chem.* **1990**, *55*, 3749-3755. https://doi.org/10.1021/jo00299a013
6. Jadhav, V.; Schmidtchen, F. P. *J. Org. Chem.* **2008**, *73*, 1077-1087. https://doi.org/10.1021/jo7021026
7. Ishikawa, T.; Kumamoto, T. *Synthesis* **2006**, *38*, 737-752. https://doi.org/10.1055/s-2006-926325
8. Selig, P. *Synthesis* **2013**, *45*, 703-718. https://doi.org/10.1055/s-0032-1318154

9. Turočkin, A.; Honecker, R.; Raven, W.; Selig, P. *J. Org. Chem.* **2016**, *81*, 4516-4529. https://doi.org/10.1021/acs.joc.6b00283
10. Turočkin, A.; Raven, W.; Selig, P. *Eur. J. Org. Chem.* **2017**, 296-305. https://doi.org/10.1002/ejoc.201601154
11. Davis. A. P.; Dempsey, K. J. *Tetrahedron Asymmetry* **1995**, *6*, 2829-2840. https://doi.org/10.1016/0957-4166(95)00374-X
12. Kita, T.; Georgieva, A.; Hashimoto, Y.; Nakata, T.; Nagasawa, K. *Angew. Chem. Int. Ed.* **2002**, *41*, 2832-2834. https://doi.org/10.1002/1521-3773(20020802)41:15%3C2832::AID-ANIE2832%3E3.0.CO;2-Q
13. Corey, E. J.; Grogan, M. *J. Org. Lett.* **1999**, *1*, 157-160. https://doi.org/10.1021/ol990623l
14. Shen, J.; Nguyen, T. T, Goh, Y.-P.; Ye, W.; Fu. X.; Xu, J.; Tan, C.-H. *J. Am. Chem. Soc.* **2006**, *128*, 13692-13693. https://doi.org/10.1021/ja064636n
15. Leow, D.; Tan, C.-H. *Chem. Asian J.* **2009**, *4*, 488-507. https://doi.org/10.1002/asia.200800361
16. Misaki, T.; Takimoto, G.; Sugimura, T. *J. Am. Chem. Soc.* **2010**, *132*, 6286-6287. https://doi.org/10.1021/ja101216x
17. Terada, M.; Ube, H.; Yaguchi, Y. *J. Am. Chem. Soc.* **2006**, *128*, 1454-1455. https://doi.org/10.1021/ja057848d
18. Gómez-Torres, E.; Alonso, D. A.; Gómez-Bengoa, E.; Nájera, C. *Org. Lett.* **2011**, *13*, 6106-6109. https://doi.org/10.1021/ol202599h
19. Fujioka, H.; Murai, K.; Ohba, Y.; Hiramatsu, A.; Kita, Y. *Tetrahedron Lett.* **2005**, *46*, 2197-2199. https://doi.org/10.1016/j.tetlet.2005.02.025
20. Murai, K.; Fukushima, S.; Hayashi, S.; Takahara, Y.; Fujioka, H. *Org. Lett.* **2010**, *12*, 964-966. https://doi.org/10.1021/ol902958m
21. Uyeda, C.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2011**, *133*, 5062-5075. https://doi.org/10.1021/ja110842s
22. Nakamura, S.; Hyodo, K.; Nakamura, Y.; Shibata, N.; Toru, T. *Adv. Synth. Catal.* **2008**, *350*, 1443-1448. https://doi.org/10.1002/adsc.200800189
23. Jurčík, V.; Wilhelm, R. *Tetrahedron Asymmetry* **2006**, *17*, 801-810 https://doi.org/doi:10.1016/j.tetasy.2006.02.021
24. Sereda, O.; Clemens, N.; Heckel, T.; Wilhelm, R. *Beilstein J. Org. Chem.* **2012**, *8*, 1798-1803. https://doi.org/10.3762/bjoc.8.205
25. Tsogoeva, S. B.; Dürner, G.; Bolte, M.; Göbel, M. W. *Eur. J. Org. Chem.* **2003**, 1661-1664. https://doi.org/10.1002/ejoc.200200635
26. Akalay, D.; Dürner, G.; Bats, J. W.; Bolte, M.; Göbel, M. W. *J. Org. Chem.* **2007**, *72*, 5618-5624. https://doi.org/10.1021/jo070534j
27. Walvoord, R. R.; Huynh, P. N. H.; Kozlowski, M. C. *J. Am. Chem. Soc.* **2014**, *136*, 16055-16065. https://doi.org/10.1021/ja5086244
28. Goldberg, M.; Sartakov, D.; Bats, J. W.; Bolte, M.; Göbel, M. W. *Beilstein J. Org. Chem.* **2016**, *12*, 1870-1876. https://doi.org/10.3762/bjoc.12.176

29. Salerno, A.; Caterina, C.; Perillo, I. A. *Synth. Commun.* **2000**, *30*, 3369-3382. https://doi.org/10.1080/00397910008086977
30. Moser, H.; Fliri, A.; Steiger, A.; Costello, G.; Schreiber, J.; Eschenmoser, A. *Helv. Chim. Acta* **1986**, *69*, 1224-1262. https://doi.org/10.1002/hlca.19860690530
31. Lange, U. E. W.; Schäfer, B.; Baucke, D.; Buschmann, E.; Mack, H. *Tetrahedron Lett.* **1999**, *40*, 7067-7071. https://doi.org/10.1016/S0040-4039(99)01460-4
32. Zhou, M.; Li, K.; Chen, D.; Xu, R.; Xu, G.; Tang, W. *J. Am. Chem. Soc.* **2020**, *142*, 10337-10342. https://dx.doi.org/10.1021/jacs.0c04558
33. Kim, H.; Nguyen, Y.; Yen, C. P. H.; Chagal, L.; Lough, A. J.; Kim, B. M.; Chin, J. *J. Am. Chem. Soc.* **2008**, *130*, 12184-12191. https://dx.doi.org/10.1021/ja803951u
34. Seebach, D.; Beck, A. K.; Heckel, A. *Angew. Chem. Int. Ed.* **2001**, *40*, 92-138. https://doi.org/10.1002/1521-3773(20010105)40:1<92::AID-ANIE92>3.0.CO;2-K
35. Dane. E.; Schmitt, J. *Liebigs Ann. Chem.* **1939**, *537*, 246-249. https://doi.org/10.1002/jlac.19395370120
36. Singh, G. *J. Am. Chem. Soc.* **1956**, *78*, 6109-6115. https://doi.org/10.1021/ja01604a043
37. Quinkert, G.; Del Grosso, M.; Döring, A.; Döring, W.; Schenkel, R. I.; Bauch, M.; Dambacher, G. T.; Bats, J. W.; Zimmermann, G.; Dürner, G. *Helv. Chim. Acta* **1995**, *78*, 1345-1391. https://doi.org/10.1002/HLCA.19950780524
38. Schuster, T.; Kurz, M.; Göbel, M. W. *J. Org. Chem.* **2000**, *65*, 1697-1701. https://doi.org/10.1021/jo991372x
39. Schuster, T.; Bauch, M.; Dürner, G.; Göbel, M. W. *Org. Lett.* **2000**, *2*, 179-181. https://doi.org/10.1021/ol991276i
40. Weimar, M.; Dürner, G.; Bats, J. W.; Göbel, M. W. *J. Org. Chem.* **2010**, *75*, 2718-2721. https://doi.org/10.1021/jo100053j
41. Hu, Q.-Y.; Rege, P. D.; Corey, E. J. *J. Am. Chem. Soc.* **2004**, *126*, 5984-5986. https://doi.org/10.1021/ja048808x
42. Canales, E.; Corey, E. J. *Org. Lett.* **2008**, *10*, 3271-3273. https://doi.org/10.1021/ol8011502
43. Koerner, M.; Rickborn, B. *J. Org. Chem.* **1990**, *55*, 2662-2672. https://doi.org/10.1021/jo00296a024
44. Riant, O.; Kagan, H. B.; Ricard, L. *Tetrahedron* **1994**, *50*, 4543-4554. https://doi.org/10.1016/S0040-4020(01)89385-6
45. Uemae, K.; Masuda, S.; Yamamoto, Y. *J. Chem. Soc. Perkin Trans. 1* **2001**, 1002-1006. https://doi.org/10.1039/b100961n
46. Akalay, D.; Dürner, G.; Bats, J. W.; Göbel, M. W. *Beilstein J. Org. Chem.* **2008**, *4*, No. 28. https://doi.org/10.3762/bjoc.4.28
47. Zea, A.; Valerao, G.; Alba, A.; Moyano, A.; Rios, R. *Adv. Synth. Catal.* **2010**, *352*, 1102-1106. https://doi.org/10.1002/adsc.201000031
48. Bai, J. F.; Guo, Y. L.; Peng, L.; Jia, L. N.; Xu, X. Y.; Wang, L. X. *Tetrahedron* **2013**, *69*, 1229-1233.

https://doi.org/10.1016/j.tet.2012.11.011
49. Kumagai, J.; Otsuki, T.; Reddy, U. V.; Kohari, Y.; Seki, C.; Uwai, K.; Okuyama, Y.; Kwon, E.; Tokiwa, M.; Takeshita, M.; Nakano, H. *Tetrahedron Asymmetry* **2015**, 26, 1423-1429. https://doi.org/10.1016/j.tetasy.2015.10.022