Branched non-covalent complexes between carboxylic acids and two tris(amidines)

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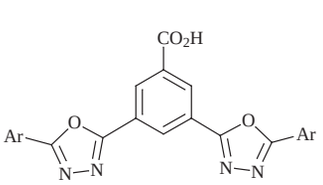
Carboxylic acids and two tris(amidine) bases formed branched 3 : 1 complexes with high solubility in chlorinated and aromatic solvents, particularly when aromatic carboxylic acids with suitable solubilising substituents were used. Whereas *N*,*N*′-diethylamidine complexes **10** proved to be difficult to isolate, the respective imidazoline complexes **14** were easily purified by crystallisation. Association constants were determined for model bis(imidazoline) complexes to be about 10^3 dm^3 mol^{-1} in the competitive solvent mixture $CDCl_3$–CD_3OD (97 : 3).

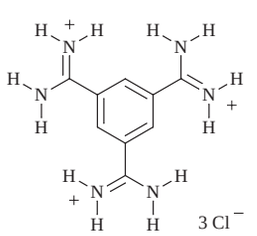
Introduction

Amidines are important basic groups in Medicinal Chemistry where they often serve as binding sites for carboxylates and phosphates, for example, in trypsin inhibitors containing arginine mimics,[1] in platelet fibrinogen receptor antagonists[2] or in drugs that interact with the minor groove of DNA.[3] A polymerisable amidine, *N*,*N*′-diethyl-4-vinylbenzamidine, has recently been applied by Wulff *et al*. in the design of molecularly imprinted polymers with esterase-like catalytic activity.[4] Hydrogen-bonding between dendrimers has been investigated by Zimmerman *et al*. who reported the strong binding of a monodendron containing an amidinium group to a dendritic host with a naphthyridine receptor.[5] Heterocyclic amidines play also an increasing rôle in various antihypertensive drugs that bind to imidazoline receptors in the central nervous system.[6] Examples in supramolecular chemistry are Anslyn's tris(aminodihydroimidazolium) receptor for citrate[7] and Hosseini's crystal structure studies of hydrogen-bonded one- and two-dimensional networks that are based on 1,2-bis(tetrahydropyrimidin-2-yl)ethane or 1,2-bis(dihydroimidazol-2-yl)ethane and various dicarboxylic acids, sulfonates and phosphates.[8]

Amidines attracted our attention when, during the preparation of an oxadiazole-containing dendrimer, we erroneously identified a DBU-derived by-product of a palladium-catalysed carbonylation as the salt of carboxylic acid **1** and DBU.[9] A purification method for complexes of carboxylic acids and DBU or other amidines was developed at a much later stage, with the effect that the false assignment, in fact, initiated our present research project on amidine complexes.



1 Ar = 4-Bu^{t}C$_6$H$_4$
2 Ar = 3,5-Bu$^t_2$C$_6$H$_3$



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In contrast to amidines, the association constant between, for example, acetic acid and a simple amine such as triethylamine is rather weak, amounting to only 3000 dm^3 mol^{-1} in chloroform.[10] Despite the single hydrogen bond, complexes between pyridines and mesogenic carboxylic acids are strong in the condensed phase below the isotropisation temperature. This type of supramolecular complex is the basis of numerous hydrogen-bonded calamitic liquid crystals.[11] Since amidine–carboxylic acid complexes are strengthened by two linear hydrogen bonds, their association constants are much larger, typically about 10^3 dm^3 mol^{-1} in DMSO.[12] The binding of carboxylic acids to a trifunctional amidine base in a 3 : 1 ratio seemed therefore to be quite promising for the self-assembly of branched or possibly even dendritic molecules. A branched structure was supposed to have a beneficial effect on the solubility of highly polar amidine derivatives in non-polar solvents in which hydrogen bonding and electrostatic ion-pair interactions should favour strong complexation. Tris(amidine) **3**[13] was the first choice for this approach. We were, however, unable to obtain **3** in sufficient purity and amount. The substituted amidine derivatives (with three *N*,*N*′-diethyl substituted amidine or imidazoline substituents) finally proved not only to be much more readily accessible, but also the resulting complexes had satisfactory solubility properties in chlorinated and aromatic solvents. Two examples will be described in this paper.

Results and discussion

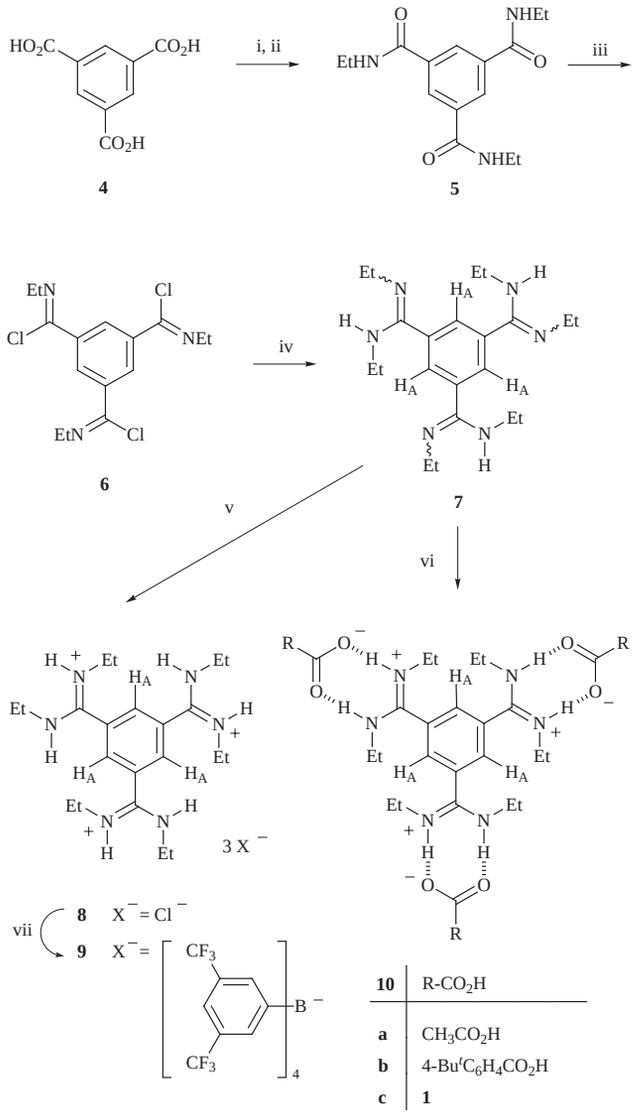
Synthesis of tris(amidine) 7, tris(imidazoline) 13 and their complexes 10 and 14

Tris(amidine) **7** was prepared in four steps from benzene-1,3,5-tricarboxylic acid (**4**). Reaction of **4** with oxalyl chloride, followed by aqueous ethylamine afforded amide **5** (Scheme 1). Imidoyl chloride **6** was obtained after treatment with $SOCl_2$, and could be converted to **7** with anhydrous ethylamine in 31% overall yield. Amidine **7** was further purified by vacuum distillation. It hydrolysed, however, slowly during prolonged storage at room temperature.

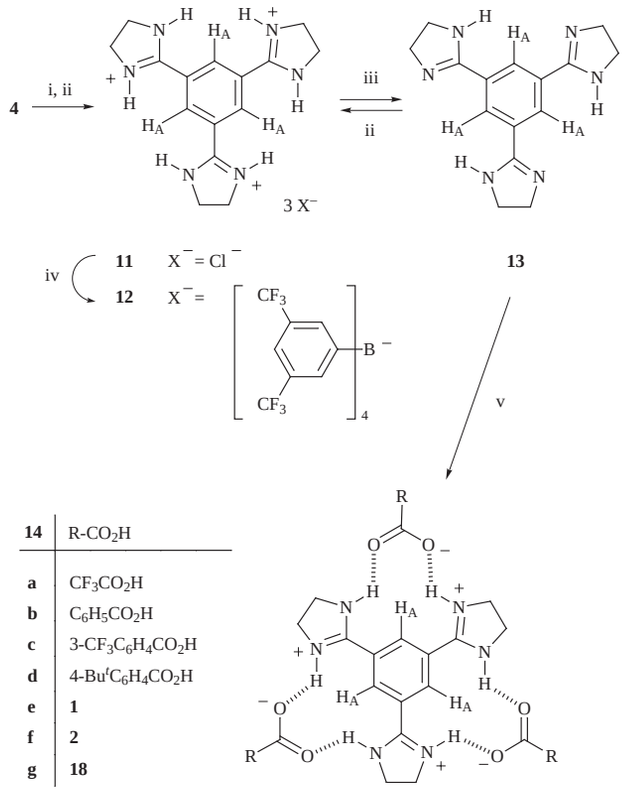
Imidazoline **13** was synthesised in a more straightforward way (Scheme 2).[14] The heterocyclic amidine derivative was obtained in one step by solution condensation of **4** with ethylenediamine and ethylenediamine dihydrochloride in boiling ethylene glycol, following a general procedure for the preparation of imidazolines.[15] The synthesis proceeded smoothly, and, after basic work-up and gradient sublimation, **13** was isolated in high purity, with yields ranging from 21 to 43%.

1,3,4-Oxadiazole-containing acids **1**, **2** and **18** were readily obtained by a reported method that used a palladium-catalysed carbonylation of aryl iodides for the conversion to the corresponding acid (Scheme 3).[9]

Amidine complexes **10** (see Scheme 1) and **14** (see Scheme 2) formed easily on dissolution of tri-basic **7** or **13** and 3 equiv. of



Scheme 1 *Reagents and conditions*: i, $(COCl)_2$, DMF, toluene, 60 °C, 3 h; ii, $EtNH_2$; iii, $SOCl_2$, reflux, 3 h; iv, $EtNH_2$, CH_2Cl_2, −10 °C, 1 h; v, HCl; vi, RCO_2H (3 equiv.), EtOH, reflux; vii, $NaB[3,5\text{-}(CF_3)_2C_6H_3]_4$ (3 equiv.), CH_3CN.



Scheme 2 *Reagents and conditions*: i, $H_2NCH_2CH_2NH_2$, $H_2NCH_2CH_2NH_2$·2HCl, TsOH, ethylene glycol, reflux, 3 h; ii, HCl; iii, NaOH; iv, $NaB[3,5\text{-}(CF_3)_2C_6H_3]_4$ (3 equiv.), CH_3CN; v, RCO_2H (3 equiv.), EtOH ($CHCl_3$), reflux.

carboxylic acid in a suitable polar solvent or solvent mixture, usually EtOH or a combination of a solvent and a less volatile non-solvent, such as EtOH–$CHCl_3$ or MeOH–MeCN. Crystallisation occurred in all cases upon cooling, if necessary, after evaporation of some of the solvent.

DBU–Carboxylic acid complexes

A literature survey revealed that strong DBU–carboxylic acid interactions in solution have been noted before.[16] Various DBU–carboxylic acid complexes **19a**–**c** were obtained analytically pure after crystallisation of an equimolar mixture of DBU and the acid component from a suitable non-polar solvent (*e.g.* CH_3CN). The complexes were quite hygroscopic and decomposed on silica gel. Nevertheless, complexes **19b**–**c** were stable enough to exhibit peaks of about 12% intensity for DBU·**1** + H^+ and DBU·**2** + H^+, respectively, in the mass spectra after chemical ionisation with NH_3.

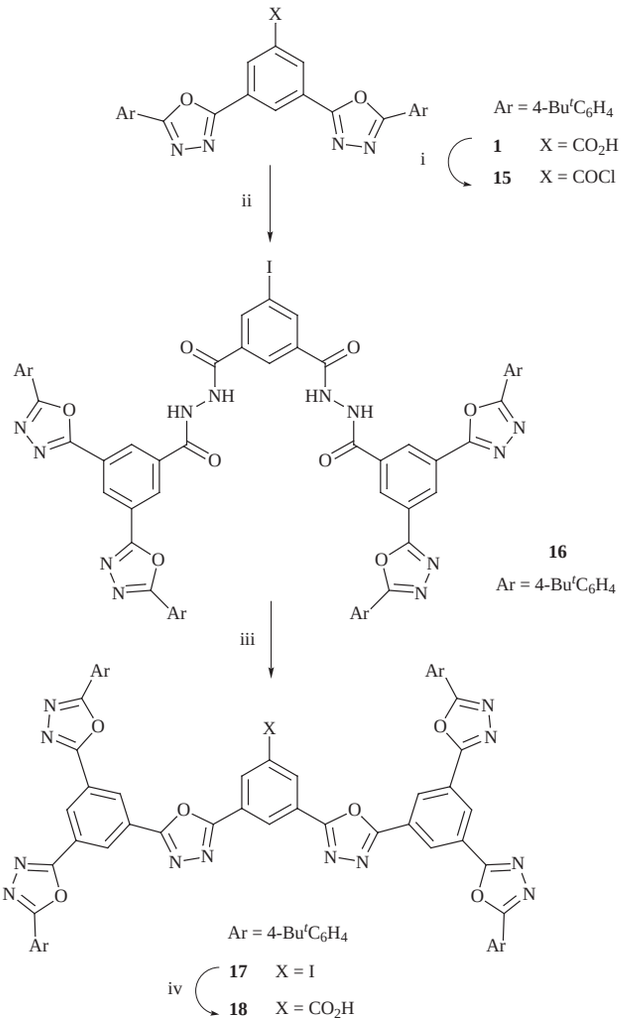
Comparison of the NMR data made it clear that the previously isolated by-product during the preparation of an oxadiazole-containing dendrimer[9] could not be the DBU salt **19b** of carboxylic acid **1**, but had to be a structural isomer instead. A second review of the analytical data suggested amide **21** as a possible alternative. The covalently linked amide **21** was therefore prepared independently by coupling of acid chloride **15** and amine **20**, a literature-known hydrolysis product of DBU that forms when DBU is treated with aqueous hydroxide (Scheme 4).[17] The resulting amide **21** was found to be identical to a sample isolated after one of our earlier carbonylation reactions. How it was formed in the first place and whether the DBU batch used was contaminated with **20** or decomposed during the reaction is unclear at present.

Complex properties

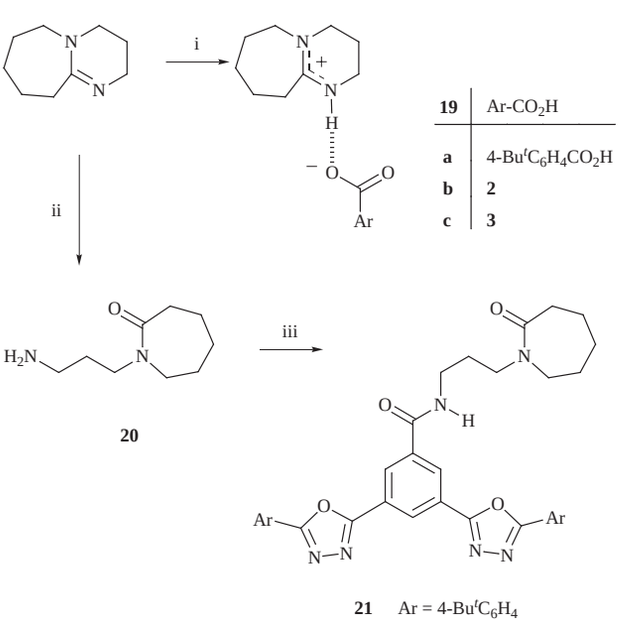
It should be noted that the basicity of amidines varies considerably. Whereas the pK_a of *N*,*N*′-dimethyl-4-chlorobenzamidine hydrochloride (11.41 in 50% alcohol)[15] is almost as large as that of benzamidinium salts (11.6 in water)[18] or DBU–H^+ (12.9 in water),[19] the pK_a of a heterocyclic amidine derivative, such as protonated 2-phenylimidazoline, tends to be significantly smaller (9.64 in 50% alcohol).[15] The differences in pK_a values of carboxylic acids and protonated amidines were supposed to be large enough for proton transfer to occur, thus ensuring that, in non-polar solvents, amidine–carboxylic acid complexes consist of close ion pairs formed by negatively charged carboxylates and amidinium cations. In fact, neutralisation takes place in aqueous and ethanolic solution on combining, for example, **13** and 3 equiv. of a water-soluble acid.

Most complexes derived from amidine **7** were highly soluble in a variety of polar and non-polar solvents.† All investigated

† The high solubility of such complexes may be used to advantage for the chromatographic purification of carboxylic acids, such as **1** or **18**, that are notorious for their low solubility in most solvents. Concentrated solutions of the crude acids and amidine **7** could be made in CH_2Cl_2 or $CHCl_3$, which were then transferred to a silica gel column. Gradient elution allowed the non-polar by-products to be removed first before the complex was destroyed with a more polar eluent (in the case of **1**, elution of the acid required CH_2Cl_2–MeOH, 9:1). Under these conditions most of the amidine remained adsorbed on the silica, but any traces could be quantitatively removed by acidic aqueous work-up of the acid-containing fractions.



Scheme 3 *Reagents and conditions*: i, $(COCl)_2$, DMF, toluene, 60–110 °C, 7 h; ii, 5-iodoisophthalic dihydrazide, NMP, 25 °C, 15 h; iii, $ClSO_3H$, 25 °C, 18 h; iv, $LiOH·H_2O$, $PdCl_2$, $Ph_2P(m\text{-}C_6H_4SO_3Na)$, NMP, CO, 100 °C, 1 d, then HCl.



Scheme 4 *Reagents and conditions*: i, $ArCO_2H$, MeOH, reflux; ii, KOH, MeOH–H_2O, 25 °C, 40 h; iii, **15**, NMP, 20 °C, 15 h.

complexes **10** were rather difficult to crystallise, probably yet another consequence of the large number of solubilising ethyl groups. Their tendency to include solvents or moisture during crystallisation and slow hydrolysis made purification of the amidine complexes cumbersome. A different amidine derivative was accordingly sought that did not have these drawbacks.

Imidazoline complexes **14** were usually obtained free of solvent impurities. Although tris(imidazoline) **13** scarcely dissolves in non-acidic polar solvents (<2 mg cm^{-3} in methanol or water), the solubility of its complexes in chloroform is surprisingly high, extending to 40–50 mg cm^{-3} for **14e** and even to >100 mg cm^{-3} for **14c**,**d**,**f**. The insolubility of **14b** in neat $CHCl_3$ emphasises that the acid component must have suitable solubilising groups. Complexes **14c**–**f** do not self-associate in chloroform or benzene to any extent.‡ It was, however, reported earlier that amidocarboxylic acids give rise to inter-complex hydrogen bonding in solution.[20]

In contrast to DBU salts **19b**–**c**, none of the complexes **10**, **14** or **23** were stable enough under various conditions tried for mass spectrometry (chemical ionisation, fast atom bombardment or matrix-assisted laser desorption/ionisation), allowing only molecular ions and fragments of the components to be detected. One reason may be that, when **10a**, **14a**, **19a** or **23** were heated under vacuum, only the DBU salt could be sublimed without decomposition. An attempt to determine the molar mass of complexes **10c** or **14f** by gel permeation chromatography in CH_2Cl_2 or THF at 25 °C also failed. In fact, both complexes and their components eluted as extensively broadened peaks long after the low-molar mass standards used. This was not observed with the corresponding acids on their own and suggests that **10c** and **14f** adhered to the column material. Such an adhesion effect of amidines is not without precedence and has been observed by others before.[21]

Support for the formation of 3:1 complexes in non-polar solution could, nevertheless, be obtained by Job's method of continuous variation[22] and vapour-pressure osmometry studies. The insolubility of tetrakis[3,5-bis(trifluoromethyl)phenyl]-borate salts **9** and **12** (obtained from the corresponding hydrochlorides by ion exchange) in neat chloroform made it necessary to add a polar co-solvent. When the stoichiometry of the complexes formed by tris(amidine) **9**§ or tris(imidazoline) **12** and tetramethylammonium benzoate was determined in a $CDCl_3$–CD_3CN (6:1) mixture, the maximum of the Job plot was observed in both cases at a mole fraction of 0.25, as would be expected for 3:1 complexes (Fig. 1). Vapour-pressure osmometry studies in $CHCl_3$ at 34 °C (against benzil or polystyrene 2000 as standard) also supported 3:1 stoichiometry. The experimentally determined number average molar mass values M_n for complexes **10b**–**c** and **14c**–**f** were in good agreement with the calculated molar masses (see Experimental).

^{1}H NMR Spectra of amidine 7 and its complexes

Broad signals are observed in the high field ^{1}H and ^{13}C NMR spectra of **7**. As with other substituted amidines, slow proton exchange between tautomers[23] and/or hindered rotation around the C–NEt bond[24] can account for the observation of two sets of broad singlets for the *N*-ethyl protons at 500 MHz at room temperature. The barrier to rotation in, *e.g.*, *N*,*N*′-dimethylacetamidine (38–105 kJ mol^{-1}) is known to be in the same range as that of amides.[25] It should be noted that the structure of unsubstituted and *N*-monoalkylated or *N*,*N*′-dialkylated amidines differs in the twist angle between the aryl ring and the amidine group which is reported to be close to 0° in the former, but increases up to 62° in substituted amidines.[26,27]

‡ Self-association is observed in hexane or cyclohexane. Solubility in these highly non-polar solvents requires benzoic acids with long alkoxy side chains, as is the case for a complex formed by **13** and 3,4,5-tris(dodecyloxy)benzoic acid: A. Kraft and A. Reichert, unpublished results.

§ Since the ^{1}H NMR signals of the tris(amidine) broadened extensively upon addition of benzoate, the signal of the benzoate proton *para* to the carboxylate group was used for the Job plot.

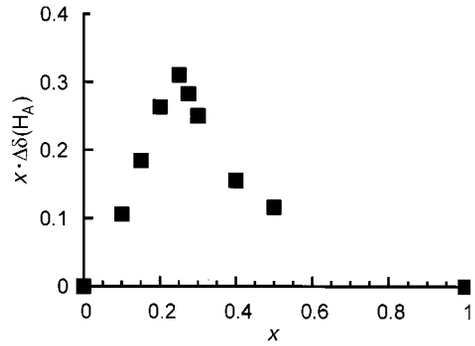


Fig. 1 Job plot for **12** binding tetramethylammonium benzoate. The total concentration was maintained at 10^{-3} mol dm^{-3} in $CDCl_3$–CD_3CN (6:1). The mole fraction x is defined as [**12**]/([**12**] + [NMe_4PhCO_2]). The maximum of the Job plot at a mole fraction x of 0.25 is consistent with a 3:1 complex stoichiometry in this solvent mixture (for a 2:1 complex, *i.e.* on partial dissociation, the maximum would have been expected at $x = 0.33$).

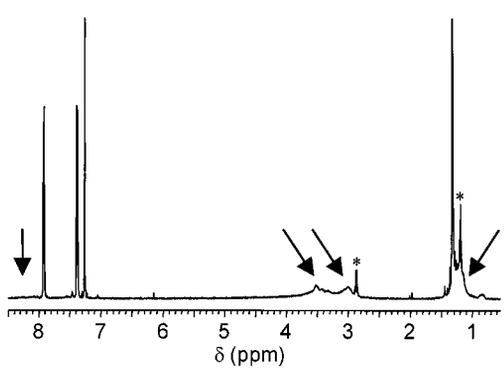


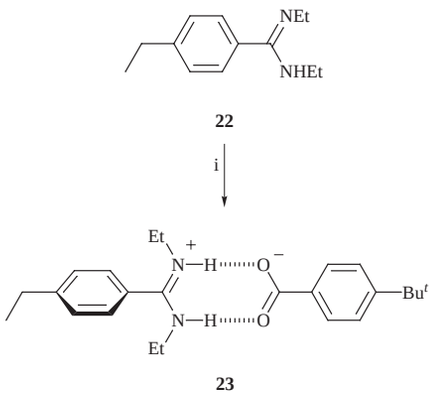
Fig. 2 ^{1}H NMR spectrum (500 MHz, 25 °C) of **10b** in $CDCl_3$. Arrows indicate the aromatic and *N*-ethyl signals of the amidine component. Signals of an amide impurity are marked by an asterisk; the amount of hydrolysis product increases slowly with time upon standing at room temperature.

The crystal structure of *N*,*N*′-dimethylbenzamidine furthermore shows a preference for the (*E*,*Z*)-configuration at the C–N amidine bonds.[26]

Simple space-filling model studies imply that **7** (and, even more so, its complexes **10**) cannot be planar. The presence of three substituted amidine groups next to a benzene ring generates a variety of possible stereoisomers and conformers. Low temperature ^{1}H NMR spectra (−40 °C, $CDCl_3$, 300 MHz) of **7** accordingly show three major singlets for the aromatic H_A protons at $\delta_H = 7.22$, 7.26 and 7.43 in the ratio 2:3:5 and an even more complicated pattern for the *N*-ethyl triplets and quartets, consistent with a complex mixture of tautomers and rotamers. The *N*-ethyl signals simplify to a quartet and a triplet at lower ^{1}H NMR frequency (90 MHz), in a protic solvent (CD_3OD) and at higher temperature (100 °C in [$^2H_6$]DMSO), indicating fast exchange on the NMR timescale under these conditions.

On the other hand, the ^{1}H NMR spectrum of the protonated amidines **8** and, to a lesser extent, **9** show two sets of sharp signals for the *N*-ethyl and NH protons, consistent with an (*E*,*Z*)-stereochemistry at the partial C–N double bond.[25] A high rotational barrier is also apparent from the vicinal spin-spin coupling between amide NH and N–CH_2 protons observed for **8**.

Complexation of an amidine with carboxylic acids requires exclusive (*E*,*E*)-stereochemistry at the amidine C–N bond which should be easily identified by NMR. Nevertheless, the 300 and 500 MHz ^{1}H NMR spectra of complexes **10** show again broad singlets for both the tris(amidine)'s aliphatic and aromatic protons at room temperature (Fig. 2). The lineshapes are influenced by temperature and NMR frequency, and the samples have to be heated to 100 °C until the NMR signals in [$^2H_6$]DMSO become sharp again. We note that the H_A signal of **10** at $\delta_H \approx 8.2$ is also considerably broadened. Hindered rotation around the Ar–$C_{amidine}$ bond therefore becomes the most likely explanation resulting from congestion of the three substituted amidine groups at the 1,3,5 positions of the same benzene core. For comparison, monoamidine complex **23** (Scheme 5)



Scheme 5 *Reagents and conditions*: i, 4-Bu^t$C_6H_4CO_2H$, EtOH, reflux.

displays only a single set of relatively sharp ^{1}H NMR signals for its *N*-ethyl protons at 500 MHz in $CDCl_3$. A similar dynamic behaviour has been reported for 2,4,6-tris(dialkylamino)-*s*-triazines in which the sterically crowded alkyl groups of the dialkylamino substituents perform correlated rotations.[28]

^{1}H NMR Spectra of the complexes with imidazoline 13

None of these complications can occur with conformationally rigid heterocyclic amidines. The ^{1}H NMR chemical shift of the aromatic H_A protons of **13** ($\delta_H = 8.23$ in CD_3OD) is characteristic for benzene derivatives with three weakly electron-withdrawing substituents. Protonation with HCl leads to slight downfield shifts ($\delta_H \approx 8.6$ in CD_3OD and D_2O, $\delta_H = 8.93$ in [$^2H_6$]DMSO). Similarly, the H_A and NH resonances of borate **12** with its non-coordinating counter-anion are found at $\delta_H = 8.48$ and 9.1, respectively, even in the less polar $CDCl_3$–CD_3CN (6:1) solvent mixture [Fig. 3(a)]. Protonation of **13** with carboxylic acids gives 3:1 salts that show comparable ^{1}H NMR chemical shifts for the H_A signal ($\delta_H \approx 8.6$) in polar solvents, such as [$^2H_6$]DMSO, CD_3OD or D_2O. In contrast, when a complex, *e.g.* **14**, has sufficient solubilising groups that it dissolves in non-polar solvents in which dissociation can be considered to be negligible, its H_A signal is found at much lower field ($\delta_H \approx 10.1$ in $CDCl_3$ and $\delta_H \approx 10.0$ in C_6D_6) as illustrated by Fig. 3(b). Such large downfield shifts of $\Delta\delta \approx 1.5$ for an aromatic proton signal cannot be explained by simple solvent effects alone, but are attributed to the binding of each carboxylate to the NH groups of two imidazolines in a bridged arrangement. As was previously confirmed by the crystal structure of model complex **14a**, this binding geometry results in carboxylate–O···H_A contacts (2.26–2.63 Å for the shorter, 2.77–3.40 Å for the longer distance) close to the sum of the van der Waals radii (2.6 Å).[14] Both the field induced by the nearby dipole of the carboxylate–imidazolinium ion pair and close contacts then explain the unusual deshielding of the H_A resonance. The crystal structure of **14a** further demonstrated that the complex lacks symmetry and that it is non-planar. Owing to the size of the carboxylate group, two carboxylates have to twist considerably out of the plane of an almost planar tris(imidazoline) core.

Determination of association constants

In all cases, complex association and dissociation was fast on

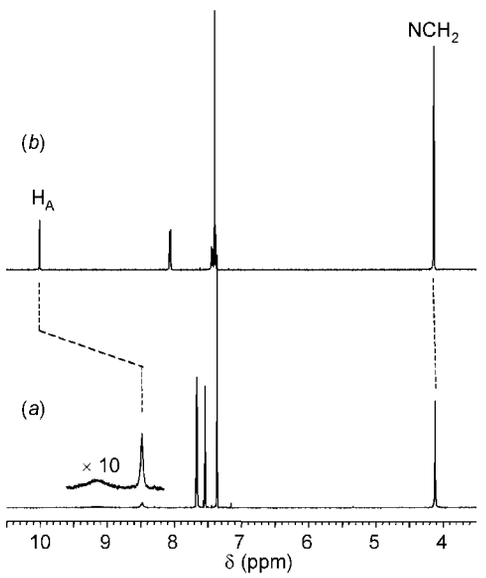


Fig. 3 ^{1}H NMR spectra (500 MHz) of (*a*) **12** and of (*b*) **14b** in $CDCl_3$–CD_3CN (6:1) showing the difference in the H_A chemical shift in the presence of a non-coordinating counter-anion (**12**) and benzoate (**14b**).

the NMR timescale. A broad singlet at $\delta_H \approx 12$–13 (for **10a**–**c** and **14c**–**g** in $CDCl_3$ or C_6D_6) can be assigned to the NH protons and indicates strong hydrogen bonding. The signal is, however, too broad to be followed during NMR titrations, especially at lower concentrations. According to Wulff and Schönfeld, the association constant of an amidine–carboxylic acid complex similar to **23** exceeds 10^6 dm^3 mol^{-1} in $CDCl_3$ at 25 °C.[21] It was expected that imidazoline complexes would show weaker binding since non-linear hydrogen bonds are involved.

The ^{1}H NMR chemical shifts of imidazoline complexes **14c**–**f** in $CDCl_3$ remain almost unchanged ($\Delta\delta < 0.1$) over a concentration range of 10^{-1} to 10^{-5} mol dm^{-3} and, for example, when a solution of **14f** in $CDCl_2CDCl_2$ is heated to 120 °C; in the latter case, the H_A signal shifted even further downfield. Although the tris(imidazoline) complexes show some line-broadening below 10^{-3} mol dm^{-3}, this may be caused by traces of residual water. Addition of a polar co-solvent (*e.g.* CD_3OD) resulted in a gradual upfield shift of the H_A signal and was attributed to the onset of complex dissociation as well as to the increased solvent polarity.

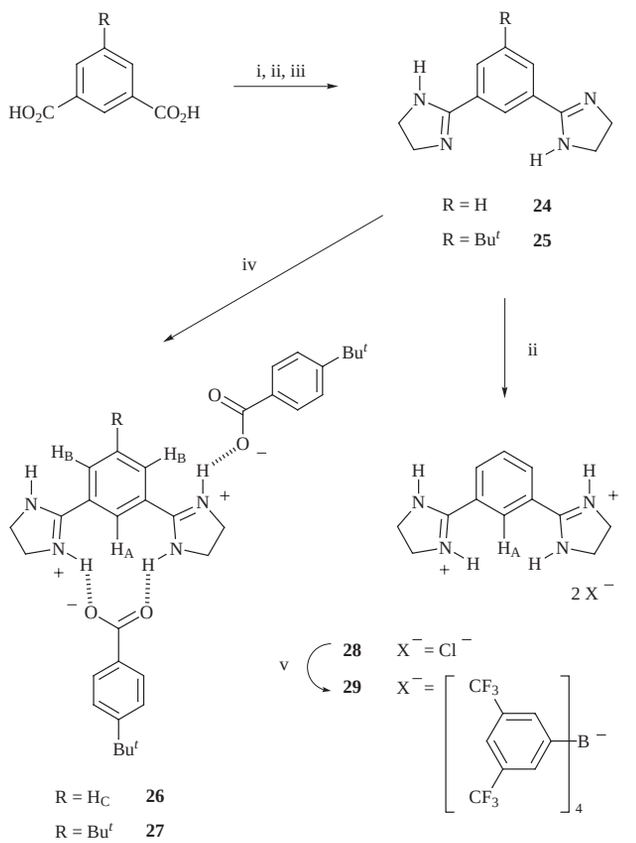
Association constants for a 3:1 complex can only be derived in a few special cases, for example when the association process is highly cooperative. The binding of a carboxylate between two imidazolinium groups was therefore studied with bis(imidazoline) model compounds **26**, **27** and **29**, since in these cases only 1:1 and 2:1 complexes are possible. It was found that the H_A signals of these bis(imidazolines) were also sensitive to the extent of complexation.

When protonated bis(imidazoline) **29** was titrated with tetrabutylammonium benzoate in $CDCl_3$–CD_3CN mixtures in which **29** was sufficiently soluble, it was noticed that under these conditions 2:1 complexes formed with increasing benzoate:**29** ratio. This complication could be avoided by ^{1}H NMR dilution experiments.[29] An association constant K_a in excess of 10^4 dm^3 mol^{-1} was derived from the dilution of an equimolar ratio of **29** and tetrabutylammonium benzoate in $CDCl_3$–CD_3CN (6:1). Similar dilution studies in a more competitive solvent mixture, $CDCl_3$–CD_3OD (97:3), gave a K_a of 990 ± 230 dm^3 mol^{-1}. Since model 2:1 complexes **26** and **27** were easily accessible (Scheme 6), both complexes with their defined host–guest ratio were also subjected to dilution studies. The change in $\delta(H_A)$ with varying concentration could be evaluated as simple 1:1 host–guest complex formation. As might be expected, some deviations from hyperbolic dependence of δ as a function of the concentration were observed for H_C and, with increasing concentration, also for the H_B and N-CH_2 (but not H_A) signals since these protons are affected by the onset of weak binding of a second carboxylate. Association constants K_a for various model systems are listed in Table 1 and were found to be in good agreement with previous results. The smaller K_a and reduced chemical shift for complex **27** is attributed to a slight change in binding geometry accompanied by interference of the sterically demanding *tert*-butyl group during complexation.

Table 1 Summary of binding constants of imidazoline receptors[a]

Compound	Solvent[a]	K_a/dm^3 mol^{-1}	$\Delta\delta$	H followed
26	A	800 ± 100	0.79	H_A
	A	780 ± 110	0.30	H_B
27	A	510 ± 50	0.87	H_A
29[b]	B	59400 ± 7200	1.11	H_A
29[b]	A	990 ± 230	1.13	H_A (ref. 14)

[a] Binding constants were determined by ^{1}H NMR dilution studies at 25 °C in either solvent A [$CDCl_3$–CD_3OD (97:3)] or B [$CDCl_3$–CD_3CN (6:1)]. [b] A 1:1 ratio of **29**:tetrabutylammonium benzoate was used.



Scheme 6 *Reagents and conditions*: i, $H_2NCH_2CH_2NH_2$, H_2NCH_2-CH_2NH_2·2HCl, TsOH, ethylene glycol, reflux, 3 h; ii, HCl; iii, NaOH; iv, 4-Bu^{t}C$_6$H$_4$CO$_2$H (2 equiv.), EtOH, reflux; v, NaB[3,5-(CF$_3$)$_2$C$_6$H$_3$]$_4$ (2 equiv.), CH_3CN.

Towards dendritic structures

Despite the fact that several routes to first-generation 1,3,4-oxadiazole-containing dendrimers have already been developed,[9,30] all our efforts to prepare the second-generation dendrimer failed so far. It was therefore of interest whether or not non-covalent binding, such as between carboxylic acid **19** and a tris(amidine) base, may be a suitable alternative. Such an approach had already been used successfully for the complexation of a branched amidocarboxylic acid,[20] and should be equally applicable to other monodendrons.

Complex **14g** was obtained after precipitation and centri-

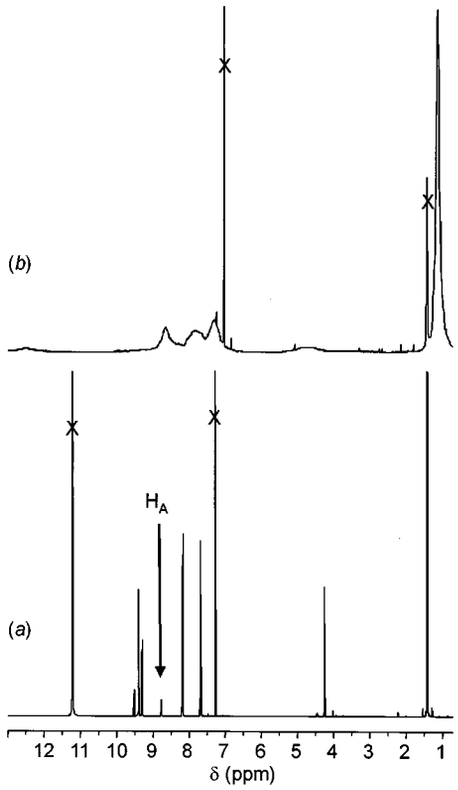


Fig. 4 ^{1}H NMR spectra (500 MHz) of **14g** in (*a*) $CDCl_3$–CF_3CO_2D and in (*b*) $CDCl_3$ (1.5 mg cm^{-3}). The broadened signals in neat $CDCl_3$ are a result of strong self-association. Protonation with trifluoroacetic acid breaks up all stacking interaction between the oxadiazole-containing ligands. The large excess of a carboxylic acid also causes the H_A signal to shift upfield. Solvent and water signals are marked by X.

fugation. Although **14g** is strictly speaking not a dendrimer, the complex has at least a comparable shape and degree of branching. Low solubility (up to 10 mg cm^{-3}), a tendency to precipitate, and broad ^{1}H NMR signals in $CDCl_3$ even at a concentration as low as 10^{-5} mol dm^{-3} were accompanied by upfield shifts of the aromatic signals and downfield shifts of the N–CH_2 singlet with increasing concentration, thus indicating strong self-association (stacking) of the extended π-system. All non-covalent interactions between the components of the complex were then broken up by the addition of trifluoroacetic acid.[20] The purity and correct stoichiometric ratio of the complex could thus be checked by a ^{1}H NMR spectrum of the complex in $CDCl_3$–CF_3CO_2D (6:1) which showed the expected sharp signals of the dissociated complex and the protonated components (Fig. 4). These results indicate that complexation of a monodendron with a carboxylic acid group at the focal point is indeed possible, but again emphasise that extended π-systems induce self-association and π-stacking interactions.

Conclusions

Tris(amidine) bases **7** and **13** easily formed 3:1 salts with carboxylic acids. Suitable solubilising groups ensured that these salts are soluble in non-polar solvents in which complexation through hydrogen bonding is strong. Some preparative difficulties arose because of the hydrolytic instability of **7** and the tendency of the corresponding amidine complexes **10** to include solvents. Imidazoline complexes **14**, on the other hand, fulfilled the criteria of both easy accessibility and purification. Applications of this complexation principle, especially by using carboxylic acids with specific functions, are currently being pursued and concentrate on the substitution of carboxylic acids with acidic heterocycles as well as the design of liquid-crystalline complexes¶ and the development of strongly self-associating systems with columnar superstructures.

Experimental

General

All solvents were distilled prior to use. Melting points: Olympus BH-2 polarisation microscope with a Linkam THMS600 hot stage and a TMS91 temperature controller. DSC: Mettler DSC 30 with TC 11/TA 4000 Processor (10 °C min^{-1}; K: crystalline, X: unidentified phase transition, I: isotropic liquid). NMR: Varian VXR 300, Bruker DRX 500, Varian Unity plus (^{13}C: 150 MHz). TMS was used as internal standard in the NMR measurements. The multiplicities of ^{13}C signals were determined by DEPT experiments. IR: Perkin-Elmer Ratio Recording Infrared Spectrophotometer 1420, Bruker Vector 22 FT-IR. EI-MS: Varian MAT 311 A (70 eV). CI-MS: Finnigan INCOS 50. MALDI-TOF-MS were measured at the University of Münster with 2,5-dihydroxybenzoic acid as matrix. Elemental analyses: Pharmaceutical Institute of the Heinrich Heine University, Düsseldorf. VPO: Knauer vapour-pressure osmometer. The number-average molar mass M_n was determined for solutions in a concentration range between 10 and 30 mg g^{-1}. Compounds **1**,[20] **11**,[20] **13**,[20] **14a**,[14] **14d**,[20] **14e**,[14] **20**,[17] **22**,[4] Ph_2P-(*m*-$C_6H_4SO_3Na$)[31] and sodium tetrakis[3,5-bis(trifluoromethyl)-phenyl]borate[32] were prepared as described in the literature.

3,5-Bis[5-(3,5-di-*tert*-butylphenyl)-1,3,4-oxadiazol-2-yl]benzoic acid 2

Synthesis as described previously[20] for **1** with 3,5-bis[5-(3,5-di-*tert*-butylphenyl)-1,3,4-oxadiazol-2-yl]-1-iodobenzene[9b] (5.73 g, 8.00 mmol), lithium hydroxide hydrate (504 mg, 12.0 mmol), $PdCl_2$ (81.8 mg, 0.461 mmol), NMP (20 cm^3) and carbon monoxide. Chromatography (silica gel, CH_2Cl_2–MeOH, 9:1) gave **2** (3.00 g, 59%) as a colourless solid, mp 358–360 °C (from MeOH) [Found: C, 73.8; H, 7.3; N, 9.1%; $C_{39}H_{46}N_4O_4$ (634.82) requires C, 73.8; H, 7.3; N, 8.8%]; ν_{max} (KBr)/cm^{-1} 3500–2700, 2950, 1715, 1620, 1590, 1540, 1245, 1230, 740, 700; δ_H(300 MHz, $CDCl_3$) 1.42 (s, CH_3), 7.67 (br s, 2 H), 8.03 (br s, 4 H, C_6H_3), 9.12 (br s, 2 H), 9.14 (br s, 1 H, $C_6H_3CO_2H$); δ_C(125 MHz, $CDCl_3$–[$^2H_6$]DMSO, 6:1) 31.3 (CH_3), 35.0 [$C(CH_3)_3$], 121.3, 126.4, 128.1, 130.5 (arom. CH), 122.8, 125.4, 152.0, 163.0, 166.0 (*ipso*-C, C=O, 2 signals missing); *m/z* (CI, NH_3) 652 (M + NH_4^+, 12%), 536, 535 (M + H^+, 47, 82), 251 (19), 234, 233 (23, 100); R_f(ethyl acetate) 0.13.

N,*N*′,*N*″-Triethylbenzene-1,3,5-tricarboxamide 5

Benzene-1,3,5-tricarbonyl chloride (prepared by the reaction of **4** with oxalyl chloride and a catalytic amount of DMF in toluene at 60 °C) (16.8 g, 63.4 mmol) was added dropwise to ice-cold aqueous ethylamine (70%, 80 cm^3, 1 mol). After stirring for 15 min, the mixture was diluted with water (300 cm^3) and conc. HCl (40 cm^3). The colourless precipitate was collected by suction filtration, washed with water and methanol, and dried (16.4 g, 89%), mp 292 °C [Found: C, 61.8; H, 7.2; N, 14.4; $C_{15}H_{21}N_3O_3$ (291.34) requires C, 61.8, H 7.3; N, 14.4%]; ν_{max} (KBr)/cm^{-1} 3330, 3300, 3250, 3060, 2860, 2820, 1640, 1580, 1540, 1295, 1140, 710, 695; δ_H(300 MHz, [$^2H_6$]DMSO) 1.15 (t, *J* 7.1, CH_3), 3.32 (dq, *J* 7.1, 5.4, NH-C*H*$_2$), 8.38 (s, C_6H_3), 8.70 (t, *J* 5.4, NH); δ_C(75 MHz, [$^2H_6$]DMSO) 14.7 (CH_3), 34.2

¶ Several complexes described in this paper showed a liquid-crystalline mesophase with a "sandy" texture above the melting transition, but only on first heating. Most samples started to rapidly decompose at the clearing temperature (*ca.* 240 °C for complexes from simple benzoic acids **14c**–**d**, and, as a consequence of the more extended aromatic π-systems, >270 °C for **14e**–**g**). These findings demonstrate that (presumably columnar) liquid-crystalline mesophases are possible by non-covalent complexation of suitable acids with **13**.

(CH_2), 128.2 (C_6H_3), 135.1 (*ipso*-C), 165.2 (C=O); *m*/*z* (EI, 70 eV) 291 (M^+, 89%), 262 (57), 247 (100), 220 (29).

N,*N*′,*N*″-Triethylbenzene-1,3,5-tricarboximidoyl trichloride 6

A solution of **5** (5.69 g, 19.5 mmol) in $SOCl_2$ (30 cm^3) was heated to reflux for 3 h. Excess $SOCl_2$ was then removed by distillation. The residual oil was dried *in vacuo*, extracted with hexane and filtered. After concentrating the filtrate *in vacuo* and drying, the oil was crystallised from hexane to yield 4.43 g (65%) of **6** as a colourless solid, mp 82 °C [Found: C, 51.9; H, 5.4; N, 12.0; $C_{15}H_{18}N_3Cl_3$ (346.68) requires C, 52.0; H, 5.2; N, 12.1%]; ν_{max} (KBr)/cm^{-1} 2860, 2820, 1650, 1425, 1340, 1160, 995, 895, 670; δ_H(300 MHz, $CDCl_3$) 1.36 (t, *J* 7.3, CH_3), 3.77 (q, N–CH_2), 8.66 (s, C_6H_3); δ_C(75 MHz, $CDCl_3$) 14.6 (CH_3), 49.0 (CH_2), 131.4 (C_6H_3), 136.5 (*ipso*-C), 140.1 (C=N); *m*/*z* (CI, NH_3) 365, 363 (M + NH_4^+, 7, 7%), 348, 346 (M + H^+, 16, 18), 312, 310 (M^+ − Cl, 77, 100), 246 (17).

1,3,5-Tris(*N*,*N*′-diethylcarbamimidoyl)benzene 7

A solution of **6** (8.60 g, 24.8 mmol) in CH_2Cl_2 (20 cm^3) was added dropwise to a solution of dry ethylamine (13.0 cm^3, 198 mmol) in CH_2Cl_2 (50 cm^3) at −20 °C. After stirring at −10 °C for 1 h and then at room temperature overnight, the solution was concentrated *in vacuo* and dried. The residue was dissolved in water (50 cm^3). After addition of NaOH (10 g), the mixture was extracted with ethyl acetate (3 × 40 cm^3). The combined organic extracts were concentrated *in vacuo* and dried to give an orange-red oil. Distillation (Kugelrohr, 240–250 °C/0.05 mbar) furnished **7** as a colourless solid (5.18 g, 56%), mp 42–46 °C [Found: C, 67.4; H, 9.7; N, 22.4; $C_{21}H_{36}N_6$ (372.56) requires C, 67.7; H, 9.7; N, 22.6%]; ν_{max} (KBr)/cm^{-1} 3314, 2967, 1628, 1528; δ_H(300 MHz, CD_3OD) 1.12 (br t, *J* 7.2, CH_3), 3.13 (br q, N–CH_2), 7.24 (s, H_A); δ_H(300 MHz, [$^2H_6$]DMSO, 100 °C) 1.04 (t, *J* 7.1, CH_3), 3.08 (q, N–CH_2), 7.07 (s, H_A); δ_C(75 MHz, CD_3OD) 16.0 (br, CH_3), 41.0 (br, N–CH_2), 128.5 (arom. CH), 137.5 (*ipso*-C), 161.0 (C=N); *m*/*z* (CI, NH_3) 374, 373 (M + H^+, 25, 100%). Hydrochloride **8** was obtained as a light yellow solid after dissolving **7** in aqueous HCl and freeze-drying, mp 80 °C; δ_H(500 MHz, [$^2H_6$]DMSO) 1.13 (t, *J* 7.2, CH_3), 1.27 (t, *J* 7.2, CH_3), 3.23 (tt, *J* 7.2, 5.7, CH_2), 3.46 (approx. quintet, *J* 6.8, CH_2), 8.17 (s, C_6H_3), 9.42 (t, *J* 5.7, NH), 10.04 (br t, NH). A solution of **8** (22.1 mg, 0.0442 mmol) and NaB[3,5-$(CF_3)_2C_6H_3$]$_4$ (117 mg, 0.133 mmol) in CH_3CN (4 cm^3)–water (2 cm^3) was concentrated *in vacuo*. The residue was then taken up in CH_3CN (2 cm^3), membrane-filtered and concentrated again *in vacuo*. Drying at 70 °C/10^{-4} mbar yielded **9** (84 mg, 64%) as a colourless glass (Found: C, 47.4; H, 2.7; N, 3.1; $C_{117}H_{75}B_3F_{72}N_6$ requires C, 47.4; H, 2.6; N, 2.8%); ν_{max} (KBr)/cm^{-1} 1653, 1357, 1281, 1128; δ_H(500 MHz, $CDCl_3$–CD_3CN, 6:1) 1.15 (br s, 18 H), 1.30 (br s, 18 H, CH_3), 3.18 (br s, 12 H), 3.39 (br s, 12 H, NCH_2), 7.55 (br s, 12 H), 7.67 [br m, 24 H, $(CF_3)_2C_6H_3$], 7.73 (s, 3 H, H_A), 7.83 (br s, 3 H, NH), 7.95 (br s, 3 H, NH).

1,3,5-Tris(4,5-dihydro-1*H*-imidazol-2-yl)benzene 13 and borate salt 12

For preparation and analytical data, see ref. 20; δ_H(500 MHz, CD_3OD) 3.78 (s, N–CH_2), 8.23 (s, H_A). Hydrochloride **11** was obtained as a light brown solid after freeze-drying a solution of **13** in aqueous HCl; δ_H(500 MHz, CD_3OD) 4.21 (s, N–CH_2), 8.63 (s, H_A); δ_H(500 MHz, [$^2H_6$]DMSO) 4.10 (s, N–CH_2), 8.93 (s, H_A), 11.03 (br s, NH). For the preparation of **12** a solution of **11** (10.3 mg, 0.0263 mmol) and NaB[3,5-$(CF_3)_2C_6H_3$]$_4$ (69.9 mg, 0.0789 mmol) in CH_3CN (3.0 cm^3)–water (0.5 cm^3) was concentrated *in vacuo*. The residue was then taken up in CH_3CN (4 cm^3), membrane-filtered and concentrated again *in vacuo*. Drying at 80 °C/10^{-5} mbar yielded **12** (72 mg, 95%) as a colourless glass (Found: C, 45.4; H, 2.1; N, 2.9; $C_{111}H_{57}B_3F_{72}N_6 \cdot 3H_2O$ requires C, 45.5; H, 2.2; N, 2.9%); ν_{max} (KBr)/cm^{-1} 1644, 1612, 1580, 1357, 1280, 1124; δ_H(500 MHz, $CDCl_3$–CD_3CN, 6:1) 4.12 (s, 12 H, N–CH_2), 7.54 (br s, 12 H), 7.67 [br m, 24 H, $(CF_3)_2C_6H_3$], 8.48 (s, 3 H, H_A), 9.15 (br s, NH).

3,5-Bis(2-{3,5-bis[(4-*tert*-butylphenyl)-1,3,4-oxadiazol-5-yl]-phenyl}-1,3,4-oxadiazol-5-yl)iodobenzene 17

A mixture of **1** (2.92 g, 5.59 mmol), oxalyl chloride (1.46 cm^3, 16.8 mmol), dry toluene (15 cm^3) and DMF (2 drops) was stirred at 60 °C for 2 h, then at 110 °C for 5 h until gas evolution had ceased and all starting material was dissolved. The brown solution was decanted and concentrated *in vacuo* to afford **15** as a light brown residue (2.93 g, 97%), mp 245–248 °C (from toluene) [Found: C, 68.6; H, 5.4; N, 10.1. $C_{31}H_{29}ClN_4O_3$ (541.05) requires C, 68.8; H, 5.4; N, 10.4%]; ν_{max} (KBr)/cm^{-1} 2950, 1760, 1610, 1495, 1180, 840, 720; δ_H(300 MHz, $CDCl_3$) 1.40 (s, CH_3), 7.59, 8.11 (AA'XX', C_6H_4), 8.95 (d, *J* 1.6, 2 H), 9.12 (t, 1 H, C_6H_3); δ_C(75 MHz, $CDCl_3$) 31.1 (CH_3), 35.2 [*C*(CH_3)$_3$], 126.2, 127.0, 130.2, 131.1 (arom. CH), 120.3, 126.4, 135.4, 156.1, 162.0, 165.6, 167.0 (*ipso*-C, C=O); *m*/*z* (EI) 545, 543, 542 (M^+, 23, 22, 62%), 529, 527 (M^+ − CH_3, 49, 100), 255 (24), 92 (50), 91 (64). A mixture of **15** (2.93 g, 5.42 mmol), 5-iodoisophthalic dihydrazide[9b] (867 mg, 2.71 mmol) and NMP (15 cm^3) was stirred at room temperature for 15 h. The clear brown solution was then added slowly to vigorously stirred water (150 cm^3). The ochre precipitate was collected by suction filtration, washed with water and dried. After extraction with ethyl acetate and filtration through a short column of silica gel (eluent: ethyl acetate), the crude product was recrystallised from hot $CHCl_3$–EtOH to yield **16** as a colourless powder (1.53 g, 43%), mp 252–253 °C; δ_H(300 MHz, $CDCl_3$–[$^2H_6$]DMSO, 1:1) 1.38 (s, CH_3), 7.64, 8.14 (AA'XX', C_6H_4), 8.58 (d, *J* 1.6, 2 H), 8.66 (t, 1 H C_6H_3I), 8.96 (approx. s, 6 H, C_6H_3), 11.04 (s, 2 H, NH), 11.30 (s, 2 H, NH); δ_C(75 MHz, [$^2H_6$]DMSO) 30.7 (CH_3), 34.8 [*C*(CH_3)$_3$], 95.0 (C-I), 126.1, 126.7, 128.1, 139.0 (arom. CH, 2 signals missing), 120.3, 125.0, 134.2, 134.5, 155.1, 162.4, 163.4, 163.9, 164.5 (*ipso*-C, C=O); R_f(ethyl acetate) 0.84. A solution of **16** (1.48 g, 1.11 mmol) in chlorosulfonic acid (5 cm^3) was stirred at 0–5 °C for 10 min and then at 30 °C for 18 h. The pale yellow-brown solution was added dropwise to water (100 cm^3) under vigorous stirring. The resulting precipitate was collected by suction filtration, washed with water and further purified by chromatography (CH_2Cl_2–MeOH, 100:3) to give **17** as a colourless powder (952 mg, 66%) that was very soluble in CH_2Cl_2 or $CHCl_3$, but crystallised from concentrated solutions within 10 min and, once crystallised and aggregated, could only be redissolved in large amounts of solvent, mp 303–304 °C [Found: C, 64.9; H, 4.8; N, 12.8. $C_{70}H_{61}IN_{12}O_6$ (1293.24) requires C, 65.0; H, 4.8; N, 13.0%]; ν_{max} (KBr)/cm^{-1} 2950, 1610, 1545, 1490, 1265, 1250, 1235, 1110, 840, 795, 780, 720; δ_H(500 MHz, $CDCl_3$, 3 mg/0.7 cm^3) 1.40 (s, CH_3), 7.60, 8.15 (AA'XX', C_6H_4), 8.81 (d, *J* 1.6, 2 H), 9.04 (t, *J* 1.6, 1 H, C_6H_3I), 9.10 (t, *J* 1.6, 2 H), 9.12 (d, *J* 1.6, 4 H, C_6H_3); δ_C(150 MHz, $CDCl_3$) 31.1 (CH_3), 35.2 [*C*(CH_3)$_3$], 95.0 (C-I), 125.8, 126.2, 127.1, 127.4, 127.7, 138.9 (arom. CH), 120.5, 126.6, 156.0, 162.5, 163.1, 163.7, 165.7 (*ipso*-C, 2 signals missing); *m*/*z* (MALDI-TOF) 1167 (M + H^+ − I), 1189 (M + Na^+ − I), 1294 (M + H^+), 1317 (M + Na^+); R_f(CH_2Cl_2–MeOH, 100:3) 0.42.

3,5-Bis(2-{3,5-bis[(4-*tert*-butylphenyl)-1,3,4-oxadiazol-5-yl]-phenyl}-1,3,4-oxadiazol-5-yl)benzoic acid 18

Synthesis as described previously[20] for **1** with **17** (1.13 g, 0.872 mmol), lithium hydroxide monohydrate (73.2 mg, 1.74 mmol), $PdCl_2$ (10.0 mg, 0.0564 mmol), Ph_2P(*m*-$C_6H_4SO_3Na$) (67.7 mg, 0.169 mmol), NMP (10 cm^3) and carbon monoxide. Chromatography (first $CHCl_3$–ethyl acetate, 2:1, then $CHCl_3$–MeOH, 9:1†) yielded a colourless solid (804 mg, 76%), mp 387–388 °C (from $CHCl_3$–MeOH) [Found: C, 70.6; H, 5.0; N, 13.6. $C_{71}H_{62}N_{12}O_8$ (1211.36) requires C, 70.4; H, 5.2; N, 13.9%]; ν_{max} (KBr)/cm^{-1} 2964, 1731, 1615, 1547, 1494, 1269, 1241, 721;

δ_H(500 MHz, $CDCl_3$–CF_3CO_2D, 6:1) 1.42 (s, CH_3), 7.70, 8.18 (AA'XX', C_6H_4), 9.29 (d, *J* 1.5, 2 H), 9.31 (t, *J* 1.6, 2 H), 9.40 (d, *J* 1.6, 4 H), 9.51 (t, *J* 1.5, 2 H, C_6H_3); δ_C(125 MHz, $CDCl_3$–CF_3CO_2D, 6:1) 31.1 (CH_3), 35.6 [*C*(CH_3)$_3$], 127.1, 128.0, 129.4, 131.3, 133.1 (arom. CH, 1 signal missing), 118.2, 124.9, 125.5, 125.9, 132.2, 158.8, 162.7, 164.0, 164.3, 167.0, 169.3 (*ipso*-C, C=O); *m*/*z* (MALDI-TOF) 1212 (80%, M + H^+), 1235 (90, M + Na^+); R_f($CHCl_3$–MeOH, 9:1) 0.17.

N-[3-(2-Oxoazepan-1-yl)propyl]-3,5-bis[5-(4-*tert*-butylphenyl)-1,3,4-oxadiazol-2-yl]benzamide 21

Amine **20** was prepared from DBU according to a literature procedure[17] and obtained as a colourless oil after chromatography ($CHCl_3$–MeOH–conc. NH_3, 9:1:1, then $CHCl_3$–MeOH, 4:1); δ_H(500 MHz, $CDCl_3$) 1.62–1.78 (m, 8 H), 2.50 (br s, 2 H), 2.51–2.54 (m, 2 H), 2.77 (t, *J* 6.6, 2 H), 3.32–3.34 (m, 2 H), 3.47 (t, *J* 6.6, 2 H). A solution of **20** (48.6 mg, 0.286 mmol) and **15** (155 mg, 0.286 mmol) in dry NMP (4 cm^3) was stirred at 20 °C for 15 h. The solution was added dropwise to water (40 cm^3). The resulting light brown precipitate was collected by suction filtration, dried and further purified by chromatography (ethyl acetate) to yield **21** (52.1 mg, 27%) as a colourless solid with identical analytical data as the by-product reported in ref. 9.

1,3-Bis(4,5-dihydro-1*H*-imidazol-2-yl)benzene 24 and conversion to salts 28 and 29

Isophthalic acid (3.22 g, 19.4 mmol), ethylenediamine (4.25 cm^3, 63.6 mmol), ethylenediamine dihydrochloride (8.46 g, 63.6 mmol), toluene-*p*-sulfonic acid (296 mg, 1.54 mmol) and ethylene glycol (15 cm^3) were heated to reflux for 3 h. About half of the ethylene glycol was then slowly removed by distillation. The residual solution was concentrated to dryness at reduced pressure (100 °C/0.1 mbar). The residue was dissolved in water (100 cm^3)–conc. HCl (3 cm^3). Addition of 50% aqueous NaOH (10 cm^3) gave a brown precipitate which was purified by another reprecipitation. Sublimation (230 °C/0.04 mbar) afforded yellow crystals (809 mg, 19%), mp 255–256 °C (lit.,[33] 244 °C; lit.,[34] 234–235 °C) [Found: C, 67.1; H, 6.7; N, 26.2; $C_{12}H_{14}N_4$ (214.27) requires C, 67.3; H, 6.6; N, 26.2%]; ν_{max} (KBr)/cm^{-1} 3157, 1615, 1568, 1492, 1467, 1267, 980, 700; δ_H(500 MHz, CD_3OD) 3.77 (s, N–CH_2), 7.51 (t, *J* 7.9, 1 H), 7.90 (dd, *J* 7.9, 1.7, 2 H), 8.12 (t, *J* 1.7, 1 H, C_6H_4); *m*/*z* (EI) 215, 214, 213 (M^+, 25, 91, 68%), 186, 185 ($M^+ - CH_2CH_2N$, 36, 100), 156 (49), 78 (33). Hydrochloride **28** was obtained as a colourless solid after freeze-drying a solution of **24** in aqueous HCl, mp 344–345 °C; δ_H(300 MHz, D_2O) 4.17 (s, N–CH_2), 7.89 (t, *J* 8.0, 1 H), 8.16 (dd, *J* 8.0, 1.7, 2 H), 8.22 (t, *J* 1.7, 1 H, C_6H_4); δ_C(75 MHz, D_2O) 47.8 (N–CH_2), 126.6 (*ipso*-C), 130.5, 133.6, 136.5 (arom. CH), 168.4 (C=N). Borate salt **29** was prepared in 91% yield from **28** analogously to **12**, mp 200–202 °C (decomp.) [Found: C, 46.8; H, 1.8; N, 3.0; $C_{76}H_{40}B_2F_{48}N_4$ (1942.72) requires C, 47.0; H, 2.1; N, 2.9%]; δ_H(500 MHz, $CDCl_3$–CD_3CN, 6:1) 4.11 (s, 9 H, N–CH_2), 7.54 (br s, 9 H), 7.67 [br m, 18 H, $(CF_3)_2C_6H_3$], 7.80 (t, *J* 8.2, 1 H), 8.02 (dd, *J* 8.2, 1.9, 2 H), 8.41 (br s, 1 H, C_6H_4), 8.9 (br s, NH); ν_{max} (KBr)/cm^{-1} 3451, 1630, 1356, 1280, 1127.

1,3-Bis(4,5-dihydro-1*H*-imidazol-2-yl)-5-*tert*-butylbenzene 25

Preparation analogous to **24** starting from 5-*tert*-butylisophthalic acid. Sublimation (250 °C/0.03 mbar) afforded light yellow crystals (63%), mp 206–208 °C [Found: C, 70.9; H, 8.4; N, 20.6; $C_{16}H_{22}N_4$ (270.38) requires C, 71.1; H, 8.2; N, 20.7%]; ν_{max} (KBr)/cm^{-1} 2959, 2865, 1620, 1574, 1496, 987; δ_H(500 MHz, CD_3OD) 1.38 (s, CH_3), 3.78 (s, N–CH_2), 7.92 (t, *J* 1.6, 1 H), 8.01 (d, *J* 1.6, 2 H, C_6H_3); δ_C(125 MHz, CD_3OD) 31.6 (CH_3), 36.0 [*C*(CH_3)$_3$], 50.4 (N–CH_2), 124.4, 128.1 (C_6H_3), 131.2, 153.4, 167.3 (*ipso*-C, C=N); *m*/*z* (CI, NH_3) 288 (M + NH_4^+, 7%), 271 (M + H^+, 100). Hydrochloride **25**·2HCl was obtained as a light brown solid after freeze-drying a solution of **25** in aqueous HCl, mp 293–297 °C; δ_H(300 MHz, D_2O) 1.44 (s, CH_3), 4.19 (s, CH_2), 8.06 (t, *J* 1.7, 1 H), 8.22 (d, *J* 1.7, 2 H, C_6H_3).

General procedure for the preparation of the complexes

Amidine base and carboxylic acid (1, 2 or 3 equiv., depending on the number of amidine groups) were dissolved in hot ethanol (40 cm^3 $mmol^{-1}$), to which, if necessary (as in the case of **14e**–**g**), a certain amount of $CHCl_3$ (5–10 cm^3) was added as co-solvent. After filtration of the hot solution and concentration, the crude product was crystallised from the solvent (mixture) indicated for each complex.

Complex 10a. Yield: quant., oil; ν_{max} (KBr)/cm^{-1} 1651, 1574, 1402, 1343, 1288; δ_H(300 MHz, [$^2H_6$]DMSO, 100 °C) 1.07 (t, *J* 7.1, N–CH_2CH_3), 1.84 (s, $CH_3CO_2^-$), 3.13 (q, N–CH_2), 7.30 (s, H_A).

Complex 10b. Yield: 74% (from hexane), mp 104–108 °C (Found: C, 69.3; H, 8.9; N, 8.2; $C_{54}H_{78}N_6O_6$ requires C, 71.5; H, 8.7; N, 9.3%); ν_{max} (KBr)/cm^{-1} 1653, 1589, 1541, 1385; δ_H(300 MHz, [$^2H_6$]DMSO, 100 °C) 1.10 (t, *J* 7.1, CH_3), 1.30 (s, N–CH_2CH_3), 3.17 (q, N–CH_2), 7.39 and 7.82 (AA'XX', C_6H_4), 7.49 (s, H_A); M_n (VPO, $CHCl_3$, 34 °C) 1150 g mol^{-1} (against benzil as standard; $C_{54}H_{78}N_6O_6$ requires 907.25), 1210 g mol^{-1} (against polystyrene 2000 as standard).

Complex 10c. Yield: 80% (from EtOH–MeOH–H_2O), DSC: K/184 (ΔH 11 J g^{-1})/liquid crystalline/231 (ΔH 20 J g^{-1})/I (Found: C, 69.2; H, 6.4; N, 12.7; $C_{114}H_{126}N_{18}O_{12}$·$2H_2O$ requires C, 69.3; H, 6.6; N, 12.8%); ν_{max} (KBr)/cm^{-1} 3105, 2984, 2927, 1647, 1577, 1287, 1037, 726, 687, 614; δ_H(300 MHz, [$^2H_6$]DMSO, 100 °C) 1.17 (t, *J* 7.3, N–CH_2CH_3), 1.36 [s, C(CH_3)$_3$], 3.30 (br q, *J* 7.3, N–CH_2CH_3), 7.65 and 8.08 (AA'XX', C_6H_4), 7.86 (s, H_A), 8.27 (t, *J* 1.6, 1 H), 8.75 (d, *J* 1.6, 2 H, $C_6H_3CO_2^-$); M_n (VPO, $CHCl_3$, 34 °C) 2290 g mol^{-1} (against benzil as standard; $C_{114}H_{126}N_{18}O_{12}$ requires 1940.38), 2410 g mol^{-1} (against polystyrene 2000 as standard).

Complex 14a. Yield: quant. (complex **14a** was obtained by concentrating the mixture and drying under vacuum until excess trifluoroacetic acid was removed); δ_H(500 MHz, CD_3CN) 4.08 (s, N–CH_2), 9.31 (s, H_A), 11.25 (s, NH).

Complex 14b. Yield: 72% (from EtOH), decomp. >240 °C (Found: C, 65.0; H, 5.6; N, 12.9; $C_{36}H_{36}N_6O_6$·H_2O requires C, 64.9; H, 5.7; N, 12.6%); ν_{max} (KBr)/cm^{-1} 1637, 1600, 1575, 1385, 1292, 718, 671; δ_H(500 MHz, $CDCl_3$–CD_3CN, 6:1) 4.15 (s, N–CH_2), 7.39 (m, 6 H), 7.44 (m, 3 H), 8.07 (m, 6 H, C_6H_5), 10.06 (s, H_A).

Complex 14c. Yield: 38% (from MeOH), DSC: K/172 (ΔH 25 J g^{-1})/liquid crystalline/250 (ΔH 19 J g^{-1})/*I* (decomp.) [Found: C, 55.1; H, 3.6; N, 10.1; $C_{39}H_{33}F_9N_6O_6$ (852.71) requires C, 54.9; H, 3.9; N, 9.9%]; ν_{max} (KBr)/cm^{-1} 1637, 1615, 1579, 1395, 1326, 1278, 1123, 691; δ_H(300 MHz, $CDCl_3$) 4.19 (s, N–CH_2), 7.52 (br m), 7.69 (br m), 8.26 (br m), 8.35 (br s, $C_6H_4CF_3$), 10.06 (s, H_A), 13.0 (br s, NH); M_n (VPO, $CHCl_3$, 34 °C) 790 g mol^{-1} (against benzil as standard), 835 g mol^{-1} (against polystyrene 2000 as standard).

Complex 14d. Yield: 60% (from EtOH), DSC: K/105 (ΔH 144 J g^{-1})/X/230 (ΔH 4 J g^{-1})/liquid crystalline/248 (ΔH 42 J g^{-1})/I [Found: C, 70.5; H, 7.7; N, 10.5; $C_{48}H_{60}N_6O_6$ (817.04) requires C, 70.6; H, 7.4; N, 10.3%]; ν_{max} (KBr)/cm^{-1} 2963, 1639, 1608, 1591, 1387; δ_H(500 MHz, C_6D_6) 1.28 (s, CH_3), 3.48 (s, N–CH_2), 7.49 and 8.58 (AA'XX', C_6H_4), 9.95 (s, H_A), 12.1 (br s, NH); δ_C(125 MHz, $CDCl_3$) 31.3 (CH_3), 34.8 [*C*(CH_3)$_3$], 45.4

(N–CH_2), 124.9, 129.3, 134.4 (arom. CH), 125.1, 133.9, 154.1, 162.5, 173.4 (*ipso*-C, C=N, C=O); M_n (VPO, $CHCl_3$, 35 °C) 820 g mol^{-1} (against benzil as standard), 880 g mol^{-1} (against polystyrene 2000 as standard); M_n (VPO, toluene, 50 °C) 760 g mol^{-1} (against benzil as standard).

Complex 14e. Yield: 87% (from EtOH–$CHCl_3$); DSC: K/188 (ΔH 2 J g^{-1})/X/220 (ΔH 5 J g^{-1})/liquid crystalline/274 (ΔH 4 J g^{-1})/I.

Complex 14f. Yield: 56% (from EtOH–$CHCl_3$), DSC: 109/glass transition/310 (ΔH 8 J g^{-1})/liquid crystalline/323 (ΔH 42 J g^{-1})/*I* (decomp.) [Found: C, 72.3; H, 7.3; N, 11.6; $C_{132}H_{156}N_{18}O_{12}$ (2186.82) requires C, 72.5; H, 7.2; N, 11.5%]; ν_{max} (KBr)/cm^{-1} 3060, 2950, 1630, 1575, 1490, 1370, 1115, 1010, 840, 780, 720; δ_H(300 MHz, $CDCl_2CDCl_2$, 12 mg/0.7 cm^3, 120 °C) 1.37 (s, CH_3), 4.29 (s, N–CH_2), 7.55 and 8.07 (AA'XX', C_6H_4), 8.80 (t, *J* 1.7, 3 H) and 8.94 (d, *J* 1.7, 6 H, $C_6H_3CO_2^-$), 10.18 (s, H_A); δ_H(500 MHz, C_6D_6) 1.37 (s, CH_3), 3.68 (s, N–CH_2), 7.69 (br s, 6 H), 8.26 (br s, 12 H, C_6H_3), 8.69 (br s, 3 H), 9.48 (br s, 6 H, $C_6H_3CO_2^-$), 10.00 (s, C_6H_3), 13.3 (br s, 6 H, NH); δ_C(75 MHz, $CDCl_3$) 31.4 (CH_3), 35.1 [*C*(CH_3)$_3$], 45.7 (CH_2), 121.4, 126.3, 126.8, 130.7, 135.0 (arom. CH), 123.0, 125.0, 125.5, 135.0, 139.5, 152.0, 163.2, 163.7, 166.0, 171.2 (*ipso*-C, C=N, C=O).

Complex 14g. Yield: 65% (from EtOH–$CHCl_3$), DSC: K/377 (ΔH 36 J g^{-1})/liquid crystalline/391 (ΔH 10 J g^{-1})/*I* (decomp.) [Found: C, 69.7; H, 5.1; N, 15.3. $C_{228}H_{204}N_{42}O_{24}$ (3916.39) requires C, 69.9; H, 5.3; N, 15.0%]; ν_{max} (KBr)/cm^{-1} 2962, 1615, 1541, 1494, 1390, 1268, 720; δ_H(500 MHz, $CDCl_3$–CF_3CO_2D, 6:1) 1.42 (s, CH_3), 4.25 (s, NCH_2), 7.68, 8.18 (AA'XX', C_6H_4), 8.76 (br s, 3 H), 9.28 (d, *J* 1.4, 2 H), 9.30 (t, *J* 1.4, 2 H), 9.38 (d, *J* 1.4, 4 H), 9.50 (t, *J* 1.4, 1 H, C_6H_3).

Complex 19a. Yield: 30% (from toluene–hexane), hygroscopic solid that could be sublimed at 100 °C/0.02 mbar, mp 145–148 °C (Found: C, 72.0; H, 9.4; N, 8.7; $C_{20}H_{30}N_2O_2$ requires C, 72.7; H, 9.2; N, 8.5%) ν_{max} (KBr)/cm^{-1} 1650, 1590, 1544, 1385; δ_H(500 MHz, $CDCl_3$) 1.32 (s, CH_3), 1.63–1.82 (m, 6 H), 2.02 (quintet, *J* 5.8, 2 H), 2.95–2.98 (m, 2 H), 3.38–3.44 (m, 4 H), 3.54 (t, *J* 5.7, 2 H, CH_2), 7.36 and 8.02 (AA'XX', C_6H_3), 14.0 (br s, NH); δ_C(125 MHz, $CDCl_3$) 19.8, 24.2, 27.1, 29.2, 32.1, 38.1, 48.6, 54.1 (CH_2), 31.4 (CH_3), 34.7 [*C*(CH_3)$_3$], 124.4, 129.2 (arom. CH), 135.4, 152.7, 166.0, 172.9 (*ipso*-C, C=N, C=O). Owing to the strong hygroscopicity of **19a**, only fragments of the complex were observed in the CI-MS.

Complex 19b. Yield: 42%, mp 258–261 °C (decomp.) (from CH_3CN) [Found: C, 71.0; H, 7.0; N, 12.5; $C_{40}H_{46}N_6O_4$ (674.84) requires C, 71.2; H, 6.9; N, 12.5%]; ν_{max} (KBr)/cm^{-1} 2961, 1648, 1620, 1584, 1542, 1495, 1380, 1364, 1323, 722; δ_H(500 MHz, $CDCl_3$) 1.39 (s, CH_3), 1.70–1.89 (m, 6 H), 2.10 (quintet, *J* 5.7, 2 H), 3.02–3.05 (m, 2 H), 3.48–3.53 (m, 4 H, CH_2), 3.61 (t, *J* 5.7, 2 H, CH_2), 7.56 and 8.12 (AA'XX', C_6H_4), 8.98 (t, *J* 1.7, 1 H), 9.02 (d, *J* 1.7, 2 H, C_6H_3), 13.6 (br s, NH); *m*/*z* (CI, NH_3) 675 (DBU·**1** + H^+, 12%), 541, 540 (**1** + NH_4^+, 17, 56), 524, 523 (**1** + H^+, 25, 92), 305 (2DBU + H^+, 79), 153 (DBU + H^+, 100); R_f(ethyl acetate) 0.07 (smearing).

Complex 19c. Yield: 43%, mp 266–268 °C (decomp.) (from CH_3CN) (Found: C, 71.3; H, 8.0; N, 10.0; $C_{48}H_{62}N_6O_4·H_2O$ requires C, 71.6; H, 8.0; N, 10.4%); ν_{max} (KBr)/cm^{-1} 2962, 1649, 1625, 1595, 1542, 1384, 1364, 1251, 1236, 793, 703; δ_H(300 MHz, $CDCl_3$) 1.41 (s, CH_3), 1.64–1.88 (m, 6 H), 2.10 (quintet, *J* 5.7, 2 H), 3.02–3.05 (m, 2 H), 3.47–3.53 (m, 4 H, CH_2), 3.60 (t, *J* 5.7, 2 H, CH_2), 7.63 (br s, 2 H), 8.02 (br s, 4 H, arom. H), 9.00 (br s, 1 H), 9.04 (br d, *J* 1.6, 2 H, arom. H), 13.6 (br s, NH); *m*/*z* (CI, NH_3) 787 (DBU·**2** + H^+, 11%), 652 (**2** + NH_4^+, 26), 636, 635 (**2** + H^+, 22, 100), 305 (6), 153 (DBU + H^+, 4); R_f(ethyl acetate) 0.38 (smearing).

Complex 23. Yield: 70% (from hexane), mp 149–150 °C [Found: C, 75.3; H, 9.1; N, 7.1; $C_{24}H_{34}N_2O_2$ (382.54) requires C, 75.4; H, 9.0; N, 7.3%]; ν_{max} (KBr)/cm^{-1} 2967, 1643, 1383; δ_H(500 MHz, $CDCl_3$) 1.16 (t, *J* 7.3, CH_3), 1.30 (t, *J* 7.6, CH_3), 1.34 [s, C(CH_3)$_3$], 2.75 (q, *J* 7.6, Ar–CH_2), 3.05 (br q, *J* 7.2, N–CH_2), 7.23 and 7.39 (AA'XX', amidine-C_6H_4), 7.39 and 8.03 (AA'XX', $C_6H_4CO_2^-$), 12.97 (s, NH); δ_H(500 MHz, [$^2H_6$]-DMSO) 1.09 (br s, CH_3), 1.21 (t, *J* 7.6, CH_3), 1.28 [s, C(CH_3)$_3$], 2.69 (q, *J* 7.6, Ar–CH_2), 3.10 (br s, N–CH_2), 7.42 (br s, amidine-C_6H_4), 7.33 and 7.80 (AA'XX', $C_6H_4CO_2^-$), 12.9 (br s, NH).

Complex 26. Yield: 32% (from CH_3CN–MeOH), DSC: K/86 (ΔH 6 J g^{-1})/X/136 (ΔH 9 J g^{-1})/liquid crystalline/147 (ΔH 38 J g^{-1})/liquid crystalline/179 °C (ΔH 27 J g^{-1})/*I* (Found: C, 68.8; H, 7.3; N, 9.4; $C_{34}H_{42}N_4O_4·H_2O$ requires C, 69.4; H, 7.5; N, 9.5%); ν_{max} (KBr)/cm^{-1} 3159, 2962, 1614, 1589, 1541, 1384; δ_H(500 MHz, $CDCl_3$) 1.33 (s, CH_3), 4.01 (s, N–CH_2), 6.99 (t, *J* 8.0, 1 H), 7.40 and 7.96 (AA'XX', C_6H_4), 8.24 (dd, *J* 8.0, 1.6, 2 H), 9.30 (br t, 1 H, C_6H_4).

Complex 27. Yield: 61% (from CH_3CN–MeOH), mp 209–213 °C [Found: C, 72.8; H, 8.2; N, 8.9; $C_{38}H_{50}N_4O_4$ (626.84) requires C, 72.8; H, 8.0; N, 8.9%]; ν_{max} (KBr)/cm^{-1} 2963m, 1635m, 1540s, 1385s; δ_H(500 MHz, $CDCl_3$) 1.04 (s, 9 H, CH_3), 1.33 (s, 18 H, CH_3), 3.89 (s, N–CH_2), 7.39 and 7.95 (AA'XX', C_6H_4), 8.27 (d, *J* 1.5, 2 H), 9.03 (br s, 1 H, H_A).

Calculation of association constants

Non-linear regression analysis [with Kaleidagraph ver. 3.09 (Synergy Software)] was used to derive association constants K_a by the ^1H NMR dilution method.[29] In the case of 2:1 complexes, the concentration *C* (= [bis-imidazoline] = [carboxylate]/2) and the experimental ^1H NMR chemical shifts δ as well as the chemical shifts of the bis(imidazoline) host (δ_h) and the complex (δ_c) were fitted to the equation.

$$\delta = \delta_h + \frac{\delta_c - \delta_h}{2C} \cdot \left(3C + \frac{1}{K_a} - \sqrt{(3C + \frac{1}{K_a})^2 - 8C} \right).$$

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