Bidirectional Association of Branched Noncovalent Complexes of Tetrazoles and 1,3,5-Tris(4,5-dihydroimidazol-2-yl)benzene in Solution

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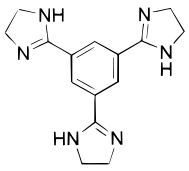
Noncovalent 3:1 complexes were obtained by combining acidic tetrazoles with the tribasic 1,3,5-tris(4,5-dihydroimidazol-2-yl)benzene (**1**). A branched structure and the use of solubilizing groups ensured that the resulting complexes dissolved in a range of nonpolar organic solvents. An X-ray crystal structure analysis of a model complex with tetrazole showed a completely planar, C_3-symmetrical, hydrogen-bonded molecule that salt-packed along the crystallographic *c* axis with an interplanar spacing of 3.31 Å. Model binding studies between a tetrazolate and a protonated 1,3-bis(4,5-dihydroimidazol-2-yl)benzene allowed an association constant of 2470 ± 400 M^{-1} to be measured in the competitive solvent mixture $CDCl_3/CD_3OD$ (97:3). The ionic nature and the extended planarity of the tetrazole complexes' core favored the formation of supramolecular stacks not only in the solid, but also in (nonpolar) solution. Self-association was evidenced by NMR and CD spectroscopy as well as by vapor-pressure osmometry.

Introduction

Self-assembly has become of great interest to chemists stimulated by Nature's ability to perfectly control the formation of stable aggregates in solution.[1] A number of recent examples emphasize how even high-molar-mass supramolecular molecules[2] and polymers[3] can be obtained in solution through the noncovalent interactions between small building blocks. A judicious combination of compounds with suitable functional headgroups that are capable of molecular recognition thus bypasses many purification problems that are frequently encountered during the chemical synthesis of large molecules. We wondered whether it might be possible to combine two different association processes (viz., the self-assembly of a disk-shaped complex by strong hydrogen-bonding, followed by stacking of the disks) for the supramolecular organization of small building blocks in solution.

Various acidic heterocycles have acted as substitutes for carboxylic acids in drug design,[4] but they have hardly found use in supramolecular chemistry. In medicinal chemistry, tetrazoles are the most frequently encountered bioisosteres[5] of carboxylic acids. The two functional groups have comparable acidity and binding properties,[6] with the tetrazole being more resistant against metabolic degradation. In two recent reports we described the formation of simple 3:1 complexes between carboxylic acids and tris(imidazoline) base **1** in nonpolar solvents,



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such as chloroform or benzene.[7] We now found that replacement of the carboxylic acid by a tetrazole gives

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(2) For recent examples, see: (a) Yang, J.; Marenday, J.-L.; Geib, S. J.; Hamilton, A. D. *Tetrahedron Lett.* **1994**, *35*, 3665−3668. (b) Whitesides, G. M.; Simanek, E. E.; Mathias, J. P.; Seto, C. T.; Chin, D. N.; Mammen, M.; Gordon, D. M. *Acc. Chem. Res.* **1995**, *28*, 37−44. (c) Marsh, A.; Silvestri, M.; Lehn, J.-M. *Chem. Commun.* **1996**, 1527−1528. (d) Zimmerman, S. C.; Zeng, F.; Reichert, D. E. C.; Kolotuchin, S. V. *Science* **1996**, *271*, 1095−1098. (e) Huck, W. T. S.; Hulst, R.; Timmerman, P.; van Veggel, F. C. J. M.; Reinhoudt, D. N. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1006−1008. (f) Stupp, S. I.; LeBonheur, V.; Walker, K.; Li, L. S.; Huggins, K. E.; Keser, M.; Amstutz, A. *Science* **1997**, *276*, 384−389. (g) Zimmerman, S. C.; Wang, Y.; Bharathi, P.; Moore, J. S. *J. Am. Chem. Soc.* **1998**, *120*, 2172−2173. (h) Kenda, B.; Diederich, F. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 3152−3156. (i) Park, H. S.; Lin, Q.; Hamilton, A. D. *J. Am. Chem. Soc.* **1999**, *121*, 8−13.

(3) (a) Sijbesma, R. P.; Beijer, F. H.; Brunsveld, L.; Folmer, B. J. B.; Hirschberg, J. H. K. K.; Lange, R. F. M.; Lowe, J. K. L.; Meijer, E. W. *Science* **1997**, *278*, 1601−1604. (b) Percec, V.; Ahn, C.-H.; Barboiu, B. *J. Am. Chem. Soc.* **1997**, *119*, 12978−12979. (c) Zimmerman, N.; Moore, J. S.; Zimmerman, S. C. *Chem. Ind. (London)* **1998**, 604−610. (d) Yamaguchi, N.; Nagvekar, D. S.; Gibson, H. W. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 2361−2364.

(4) Tetrazole drugs have found practical use as angiotension II converting enzyme antagonists in the treatment of hypertension: Wittenberger, S. J. *Org. Prep. Proc. Int.* **1994**, *26*, 499−531.

(5) For a definition of the term "bioisostere" see: Patrick, G. L. *An Introduction to Medicinal Chemistry*; Oxford University Press: Oxford, 1995; p 328.

(6) 5-Aryltetrazoles have pK_a values comparable to those of their corresponding benzoic acids. The pK_a of, for example, benzoic acid is 4.25 and that of 5-phenyltetrazole is 4.32: Abraham, M. H.; Duce, P. P.; Prior, D. V.; Barratt, D. G.; Morris, J. J.; Taylor, P. J. *J. Chem. Soc., Perkin Trans. 2* **1989**, 1355−1375. For comparison, protonated 2-phenylimidazoline has a pK_a of 9.88 similar to those of alkylamines: Fernández, B.; Perillo, I.; Lamdan, S. *Ibid.* **1973**, 1371−1374. The differences in pK_a values are large enough for proton transfer to be expected in polar solvents. In fact, neutralization takes place in aqueous solution on combining **1** and 3 equiv of a water-soluble tetrazole.

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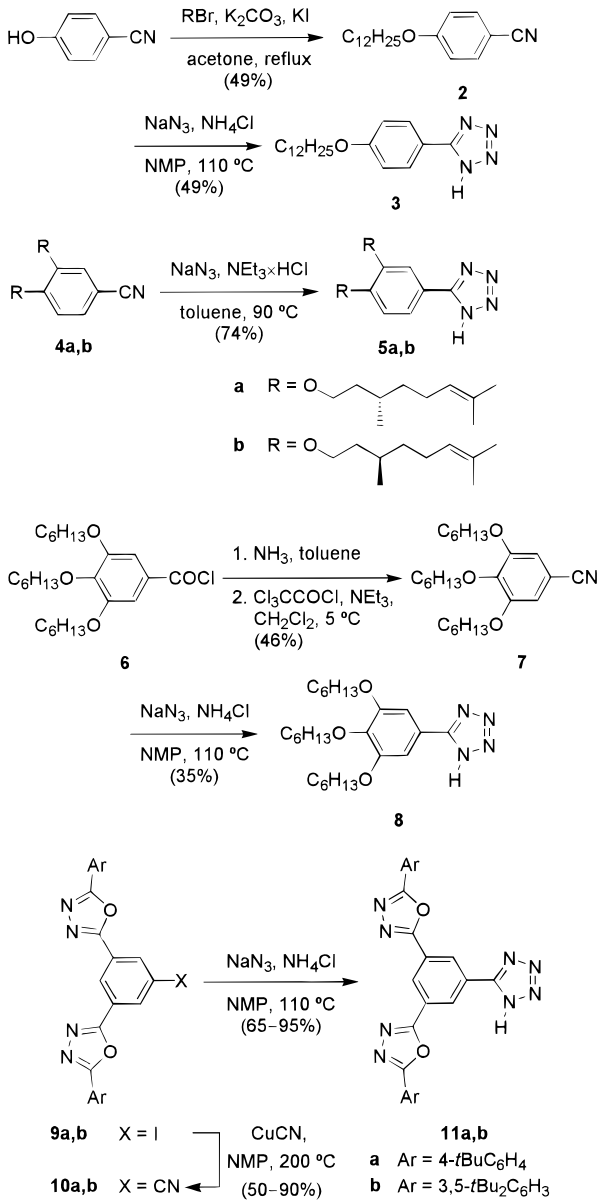
Scheme 1

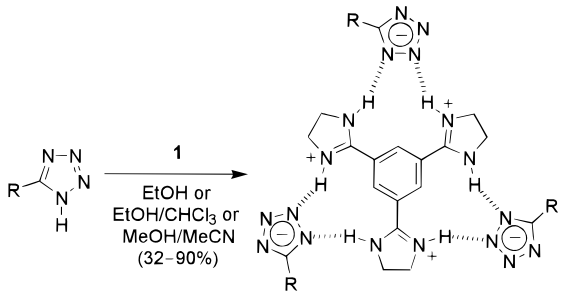


similar 3:1 salts, but that, in addition, tetrazole complexes further organized to columnar supramolecular assemblies *in the crystal and in solution*. A sufficient degree of branching, increased molar masses (between 1300 and 2500 g mol^{-1}), and a judicious choice of solubilizing groups largely helped to inhibit crystallization.[8] Thus, solubility was warranted despite strong self-association, and a stacking process could be studied in solution over a wide concentration range without complications by precipitating aggregates.

Results

Synthesis. Nitriles **2** and **4** were prepared by alkylation of commercially available mono- and dihydroxybenzonitriles (Scheme 1). Nitrile **7** was derived from an acid chloride precursor that was first converted to an amide and then dehydrated using a literature procedure.[9] Oxadiazole-substituted benzonitriles **10a**,**b** were obtained from two previously reported aryl iodide derivatives[10] after replacing the iodide by CN using copper(I) cyanide[11] in boiling *N*-methylpyrrolidone (NMP). Tetrazoles were prepared from the corresponding nitriles by 1,3-cycloaddition of NH_4N_3[12,13] or triethylammonium azide.[14] Yields were satisfactory in most cases; for derivatives with more than one long alkoxy side chain reaction times had to be prolonged since the addition of azide to electron-rich nitriles proceeds more slowly.[12]

Scheme 2



12	tetrazole	12	tetrazole
a	R = H	e	5a
b	R = C_6H_5	f	5b
c	R = 4-*t*BuC_6H_4	g	8
d	3	h	11a
		i	11b

All tetrazole complexes were easily prepared by simply dissolving a 3:1 mixture of a tetrazole and tris(imidazoline) **1**[7,15] in warm ethanol or, alternatively, combinations of a good solvent with a less volatile nonsolvent, such as $CHCl_3$/EtOH (**12h**,**i**) or MeOH/MeCN (**12a**), prior to concentration of the solution. All complexes **12** crystallized after a concentrated solution was cooled to room temperature, and one recrystallization usually provided analytically pure samples (Scheme 2).

Crystal Structure of a Model Complex. Needles suitable for X-ray crystallography were obtained after slow evaporation of a methanolic solution of complex **12a**. The X-ray crystal structure of this model complex shows a planar, C_3-symmetrical molecule (Figure 1a). Each tetrazole forms three hydrogen bonds, two of which are between nitrogen atoms N-12 and N-13 of the tetrazole

(7) (a) Kraft, A.; Fröhlich, R. *Chem. Commun.* **1998**, 1085−1086. (b) Kraft, A. *J. Chem. Soc., Perkin Trans. 1* **1999**, 705−714. For a related report on carboxylic acid complexes with a tris(tetrahydropyrimidine) base see: (c) Kraft, A.; Reichert, A. *Tetrahedron* **1999**, *55*, 3923−3930.

(8) Such a strategy has previously been used for ensuring the solubility of shape-persistent dendrimers and other large disk-shaped molecules: (a) Moore, J. S. *Acc. Chem. Res.* **1997**, *30*, 402−413. (b) Palmans, A. R. A.; Vekemans, J. A. J. M.; Fischer, H.; Hikmet, R. A.; Meijer, E. W. *Chem. Eur. J.* **1997**, *3*, 300−307.

(9) Saednya, A. *Synthesis* **1985**, 184−185.

(10) Kraft, A. *Liebigs Ann./Recueil* **1997**, 1463−1471.

(11) Newman, M. S.; Boden, H. *J. Org. Chem.* **1961**, *26*, 2525.

(12) For general overviews of tetrazole syntheses, see: (a) Butler, R. N. In *Comprehensive Heterocyclic Chemistry, A Review of the Literature 1982−1995*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Storr, R. C., Eds.; Pergamon: Exeter, 1996; Vol. 4, pp 621−678. (b) Meier, H. R.; Heimgartner, H. In *Methoden der Organischen Chemie (Houben-Weyl), Hetarene III/Teil 4*; Schaumann, E., Ed.; Georg Thieme Verlag: Stuttgart, 1994; Vol. E8d/4, pp 664−795.

(13) For applications of tetrazoles as intermediates in the synthesis of 1,3,4-oxadiazole-based electron-transporting materials, see: (a) Bettenhausen, J.; Strohriegl, P. *Macromol. Rapid Commun.* **1996**, *17*, 623−631. (b) Bettenhausen, J.; Strohriegl, P. *Adv. Mater.* **1996**, *8*, 507−510.

(14) Koguro, K.; Oga, T.; Mitsui, S.; Orita, R. *Synthesis* **1998**, 910−914.

(15) (a) Kränzlein, G.; Bastian, H. (IG Farben). German Patent D. R. P. 695473, 1937; *Chem. Abstr.* **1941**, *35*, 141b. (b) Kraft, A.; Osterod, F. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1019−1025.

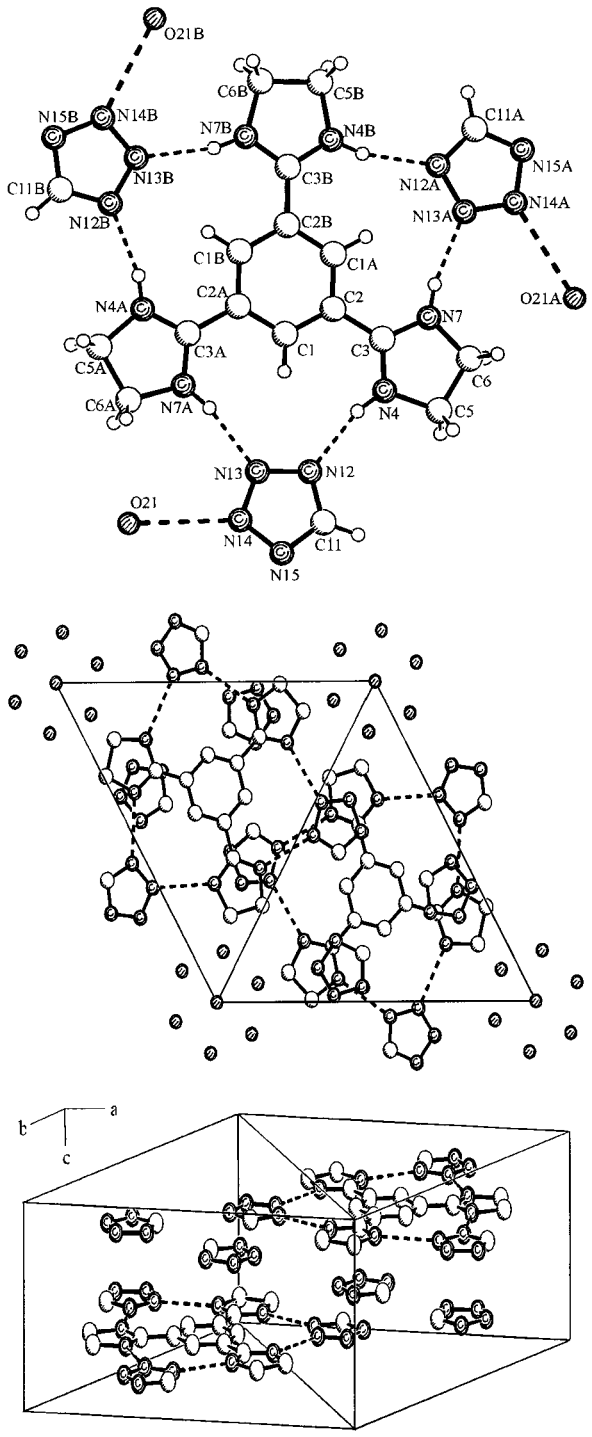


Figure 1. (a, top) Crystal structure of **12a**. (b, middle) Molecular arrangement in the unit cell, viewed along the crystallographic *c* axis (hydrogen atoms not shown). (c, bottom) Side view showing stacking interactions in the crystal structure of **12a** (water molecules have been omitted for clarity).

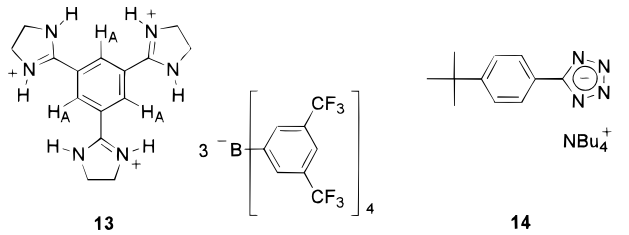
and the NH groups of the binding imidazolines;[16] the inclusion of four water molecules per molecule of complex in crystals of **12a** accounts for a third hydrogen bond between the tetrazole's N-14 and one of the H_2O molecules. Contacts close to the sum of the van der Waals radii (2.7 Å) are observed between $H_{A,\ benzene\ ring}\cdots N\text{-}12_{tetrazole}$ and $H_A\cdots N\text{-}13_{tetrazole}$ (2.60 and 2.62 Å).

The planar complex stacks along the crystallographic *c* axis with an interplanar distance of 3.31 Å, whereby the negatively charged tetrazolates salt-pack above and below imidazolinium cations (Figure 1b,c). The sliding distance between a 3:1 complex relative to its nearest neighbor in an adjacent plane is 6.93 Å. Whether this is general for tetrazole−**1** complexes or due to solvent inclusion and crystal packing effects has to be verified by other crystal structures and is currently the subject of further investigations.

Properties of Tetrazole Complexes. Most tetrazole complexes **12** were easily obtained in analytical purity; however, the included solvent (mostly water) was sometimes difficult to remove as the crystal structure of **12a** has already demonstrated. Whereas the solubility of tris(imidazoline) **1** is negligible and that of most tetrazoles is low in nonpolar organic solvents, complexes with sufficient solubilizing groups and/or a considerable degree of branching dissolved easily in chloroform. A simple *tert*-butyl group (**12c**) was clearly insufficient in providing solubility in $CHCl_3$. In contrast, the solubility of complexes **12e**−**i** in $CHCl_3$ was quite high (>200 mg mL^{-1}).

No molecular ions could be detected by mass spectrometry using chemical ionization, fast atom bombardment, or matrix-assisted laser desorption/ionization. An attempt to determine the molar mass of complex **12g** by gel-permeation chromatography (GPC) in CH_2Cl_2 at 25 °C failed owing to extreme broadening; elution of both components of the complex occurred long after the elution peaks of low-molar-mass standards. This observation strongly suggested that adhesion to the column material took place[17] since the tetrazole itself was easily analyzed by GPC.

Support for the formation of 3:1 complexes in nonpolar solution could, nevertheless, be obtained by Job's method of continuous variation[18] and by vapor-pressure osmometry (VPO). When we determined the stoichiometry of the complex formed by protonated tris(imidazoline) **13** and the tetrabutylammonium salt **14**, the maximum of the



Job plot was observed at a mole fraction of 0.25 as expected for a 3:1 complex (Figure 2).[19] For additional confirmation, the number-average molar mass M_n of several complexes was measured in $CHCl_3$ at 35 °C by

(16) An alternative binding geometry for some or all of the tetrazole ligands cannot be entirely excluded where the heterocycle's second and third nitrogen atoms hydrogen bond to the imidazoline-NH groups. Although we failed to obtain crystals of a tetrazole complex other than **12a** that were suitable for X-ray crystallography, such a binding arrangement was found in the crystal structures of two related complexes between a tetrazole and 1,3,5-tris(3,4,5,6-tetrahydropyrimidin-2-yl)benzene (A. Kraft, R. Fröhlich, unpublished results).

(17) A similar observation has been made for polymeric amidine bases which adhere to phosphated and passivated metal surfaces: Wulff, G.; Schönfeld, R. *Adv. Mater.* **1998**, *10*, 957−959.

(18) (a) Job, P. *Ann. Chim.* **1928**, *9*, 113−203. (b) Blanda, M. T.; Horner, J. H.; Newcomb, M. *J. Org. Chem.* **1989**, *54*, 4626−4636.

(19) The insolubility of tetrakis[3,5-bis(trifluoromethyl)phenyl]borate **13** in neat chloroform made addition of acetonitrile necessary. Since self-association of tetrazole complexes was not suppressed under these conditions, Job's analysis had to be conducted at low concentration (10^{-3} M). Even with acetonitrile as cosolvent, the H_A chemical shift of a 3:1 complex did not significantly differ from that in neat chloroform, suggesting that complexation remained largely unaffected.

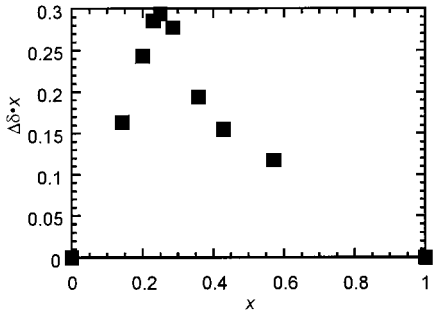


Figure 2. Job plot for the protonated tris(imidazoline) **13** binding tetrazolate **14**. The mole fraction x of **13** is defined as [**13**]/([**13**] + [**14**]). The total concentration was maintained at 10^{-3} M in $CDCl_3/CD_3CN$ (6:1),[19] and the change in the H_A chemical shift $\Delta\delta = \delta_{obsd} - \delta_0$ was determined for various compositions (δ_0 is the chemical shift of the H_A singlet in **13**).

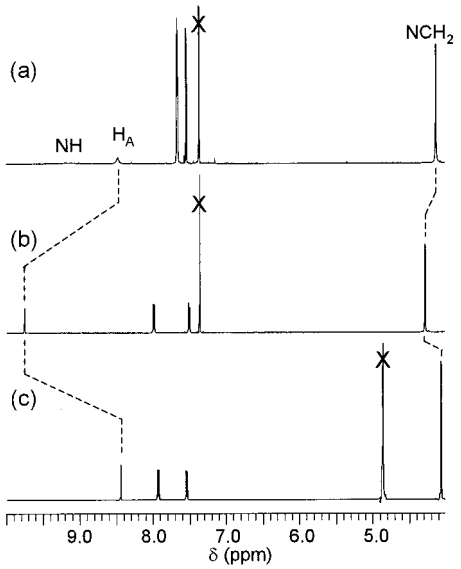
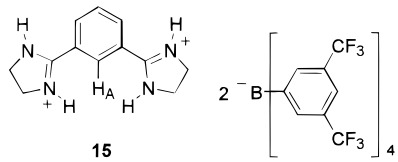


Figure 3. ^1H NMR spectra (500 MHz, 25 °C) of (a) **13** in $CDCl_3/CD_3CN$ (6:1), (b) **12c** in $CDCl_3/CD_3CN$ (6:1), and (c) **12c** in CD_3OD.

VPO. At concentrations in the range of 8−67 mM, we found M_n values of 1650 g mol^{-1} for **12g** and 2350 g mol^{-1} for **12i** (both against polystyrene 2000 as standard) that correlated well with the respective calculated molar masses of 1622 and 2259 g mol^{-1}.

^{1}H NMR Spectra. The H_A and NH resonances of tetrakis[3,5-bis(trifluoromethyl)phenyl]borate salt **13** in a $CDCl_3/CD_3CN$ (6:1) solvent mixture[19] were observed at $\delta = 8.48$ and $\delta = 9.1$, respectively (Figure 3a). All tetrazole complexes showed comparable ^1H NMR chemical shifts at $\delta \approx 8.6$ for the H_A signal in typical polar solvents, such as DMSO-d_6, CD_3OD (Figure 3c), or D_2O.[20] In contrast, complexes that dissolved in nonpolar solvents (in which dissociation became negligible) gave rise to an H_A signal at much lower field ($\delta \approx 9.9$ in $CDCl_3$) as illustrated by Figure 3b. Such a large downfield shift of $\Delta\delta \approx 1.4$ for the aromatic H_A signal cannot be explained by simple solvent effects alone. It is attributed to close tetrazole-N···H_A contacts and to the presence of an electric dipole field induced by the tetrazolate−imidazolinium ion pairs that both result from complexation.[21] A broad NH singlet at $\delta \approx 12-13$ in $CDCl_3$ is characteristic for hydrogen bonding. This signal is, however, too broad to be followed during NMR titration or dilution experiments, especially at lower concentrations.

Determination of Complexation Constants. The ^1H NMR chemical shifts of tetrazole complexes **12d**,**g**,**h** in $CDCl_3$ remained unchanged upon dilution to 10^{-5} M, indicating that dissociation did not occur to any noticeable extent even at this low concentration. Few cases allow all three association constants for a 3:1 complex to be derived from a single measurement, for example, when the association process is highly cooperative. We therefore decided on binding studies between a tetrazolate and bis(imidazoline)s **15** and **16**, since these model compounds only give rise to 1:1 and 2:1 complexes.



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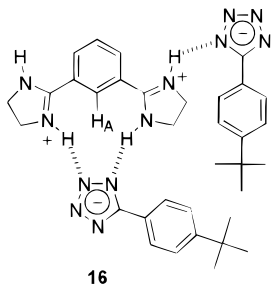

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It was found that the H_A signals of bis(imidazoline)s were also sensitive to the extent of complexation. When protonated bis(imidazoline) **15** was titrated with increasing amounts of tetrazolate **14** in $CDCl_3/CD_3CN$ (6:1), the H_A signal shifted downfield continuously until 1 equiv of tetrazolate had been added. Excess **14** caused an upfield shift of the H_A signal. The resulting deviation of the NMR titration curve from a hyperbolic shape pointed to the formation of 2:1 complexes. Although the data can be analyzed in principle, we decided to avoid the complication of 2:1 complex formation by adding a more polar cosolvent (methanol) in a sufficient amount that 1:1 binding was still taking place, whereas binding of a second tetrazolate was suppressed. ^1H NMR dilution studies[22] were therefore conducted with an equimolar mixture of **14** and **15** in the more competitive solvent mixture $CDCl_3/CD_3OD$ (97:3). Figure 4 shows that binding could indeed be interpreted by a 1:1 host−guest complex formation, allowing an association constant K_a of 2470 ± 400 M^{-1} to be calculated. A similar NMR dilution experiment, this time with the easily accessible and defined 2:1 complex **16**, gave a comparable binding isotherm and association constant (2100 ± 500 M^{-1}) although the observed binding curve started to deviate, not surprisingly, from a theoretical 1:1 isotherm once the concentration exceeded 10^{-2} M.

(20) The chemical shift of tetrazole complexes in polar solvents was almost identical to the chemical shift of salts of protonated **1** containing noncoordinating anions, such as **1**·3HCl ($\delta_H \approx 8.6$ in CD_3OD and D_2O) or **13** ($\delta_H = 8.57$ in CD_3OD), and suggests that tetrazole complexes dissociate completely in these solvents.

(21) Günther, H. *NMR−Spektroskopie*, 3rd ed.; Thieme: Stuttgart, 1992; pp 92−94.

(22) (a) Wilcox, C. S. In *Frontiers in Supramolecular Chemistry and Photochemistry*; Schneider, H.-J., Dürr, H., Eds.; VCH: Weinheim, 1991; pp 123−143. (b) Macomber, R. S. *J. Chem. Educ.* **1992**, *69*, 375−378.

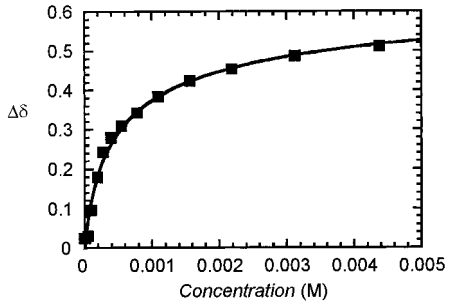


Figure 4. Changes of the chemical shift of the H_A signal upon dilution of a solution containing equimolar amounts of **14** and **15** in $CDCl_3/CD_3OD$ (97:3) at 25 °C. The curve represents the calculated isotherm for 1:1 binding.

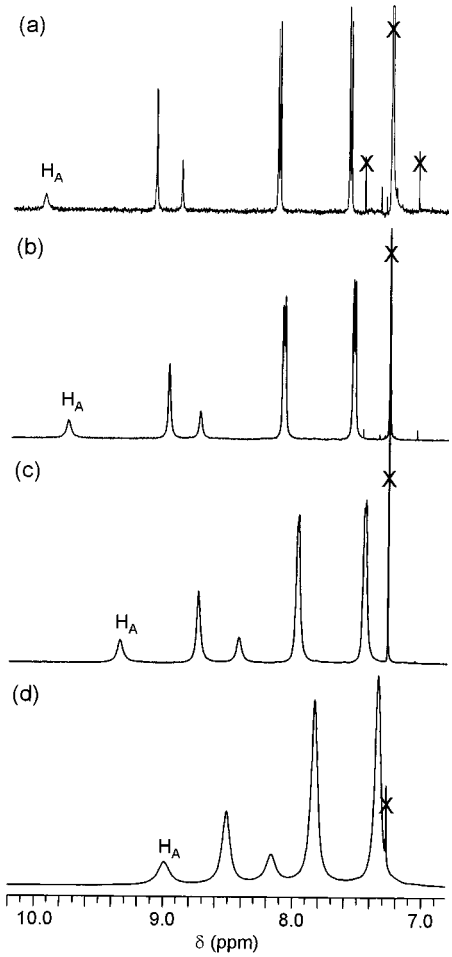


Figure 5. ^1H NMR spectra (500 MHz, $CDCl_3$, 25 °C) of **12h** at various concentrations: (a) 10^{-4} M, (b) 10^{-3} M, (c) 10^{-2} M, and (d) 10^{-1} M.

Stacking. Despite the fact that complexation was strong in chloroform, the ^1H NMR spectra of all chloroform-soluble tetrazole complexes, especially those of **12h**, changed considerably with increasing concentration in $CDCl_3$ (Figure 5). In a concentration range from 10^{-4} to 10^{-1} M, aromatic signals as well as the imidazoline-CH_2 singlet broadened and shifted upfield ($\Delta\delta$ between 0.24 and 0.95), the more so, the nearer the respective proton was to the core of the complex. Since complexation was complete at concentrations above 10^{-5} M, these observations were indicative of an additional association process. Upfield shifts in conjunction with line-broadening are diagnostic of self-association resulting from the stacking of aromatic π-systems.[23]

The formation of species with increased molar mass was supported by VPO data. The number-average molar mass of **12h** was larger than calculated for a monomeric complex (1922 g mol^{-1}), and M_n could be estimated to exceed 6000 g mol^{-1} (corresponding to an association degree of $\geq$3.3) at concentrations $\geq$0.02 M in $CHCl_3$ at 35 °C.

Assuming the isodesmic model of indefinite self-association,[23] an association constant $K_{stacking}$ of 250 $\pm$ 20 M^{-1} in neat $CDCl_3$ at 25 °C was calculated from the concentration dependence of the chemical shift of the H_A signal.[24] All NMR signals remained distinct, in accordance with a limited but ordered stacking process. Stack formation and dissociation occurred fast on the NMR time scale since only a single set of signals was detected.[25]

Self-association of complex **12g** was much less pronounced. Whereas $K_{stacking}$ was almost negligible in $CDCl_3$ (8 $\pm$ 1 M^{-1} at 25 °C), solvophobic interactions between molecules in the less polar solvent C_6D_6 raised $K_{stacking}$ to 1860 $\pm$ 420 M^{-1}. Solutions of the complex in cyclohexane-d_{12} displayed extremely broad ^1H NMR signals that made it impossible to derive an association constant by NMR measurements (Figure 6). In this context, it is interesting to note that, when association was further increased by lowering the temperature, 1 wt % solutions of **12g** in hexane formed thermally reversible gels at about −20 °C.

The extensive self-association of tetrazole complexes with long alkoxy side chains in hydrocarbon solvents suggested the possibility that the structure of a self-associating chiral complex (**12e**,**f**) may be further characterized by circular dichroism (CD). Despite the presence of six stereogenic centers in the (*S*)-configurated citronellyloxy substituents, chiral complex **12e** showed no CD effect in chloroform. In contrast, a positive Cotton effect was observed for an equally concentrated solution in cyclohexane (Figure 7). The enantiomeric complex **12f** showed an identical effect with opposite sign. E. W. Meijer and co-workers recently observed helical columnar aggregates of chiral C_3-symmetrical molecules in hydrocarbons.[26] They found pronounced CD effects even for mixtures containing a small amount of chiral ("sergeants") and an excess of achiral ("soldiers") compound which can be interpreted by the "sergeant-and-soldiers" principle.[27] No CD effect could be detected even after

(23) For a general review, see: Martin, R. B. *Chem. Rev.* **1996**, *96*, 3043−3064.

(24) The mean number of monomers per stack (i.e., the association degree) as calculated from $K_{stacking}$ was furthermore consistent with the increase in molar mass measured by VPO.

(25) Although the dynamics of association were too fast to be resolved on the NMR time scale, another dynamic process could be identified if the ^1H NMR spectra of a self-associating complex were run at the same concentration and temperature but at different NMR frequencies. Changes in line shape of the signals of the outermost substituents (viz., the OCH_2 triplet of **12g** or the AA′XX′ signals of the *para*-disubstituted phenylenes of **12h**) became then apparent at higher concentration (that is, when stack formation started to play a role), and were attributed to hindered rotation around the aryl−tetrazole C−C single bond. For a previous discussion of the rotational barrier around the C(aryl)−C(tetrazolate) bond, see: Alkorta, I.; Rozas, I.; Elguero, J. *J. Chem. Soc., Perkin Trans. 2* **1998**, 2671−2675.

(26) Palmans, A. R. A.; Vekemans, J. A. J. M.; Havinga, E. E.; Meijer, E. W. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2648−2651.

(27) Green, M. M.; Reidy, M. P. *J. Am. Chem. Soc.* **1989**, *111*, 6452−6454.

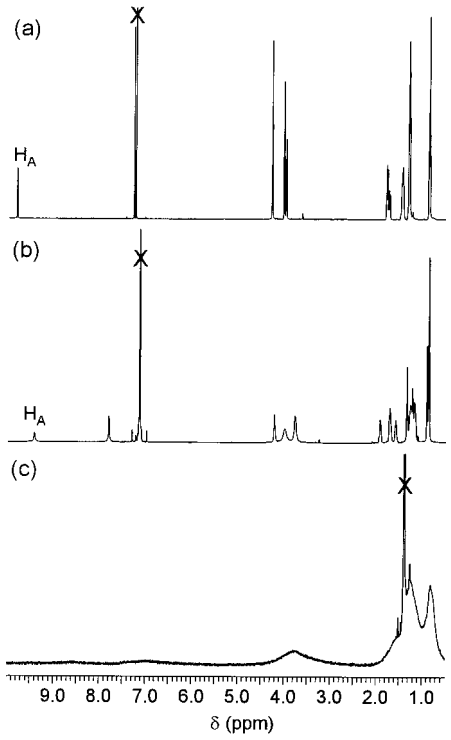


Figure 6. ^{1}H NMR spectra (500 MHz, 25 °C, 1 mg/mL) of **12g** (a) in $CDCl_3$, (b) in C_6D_6, and (c) in cyclohexane-d_{12}.

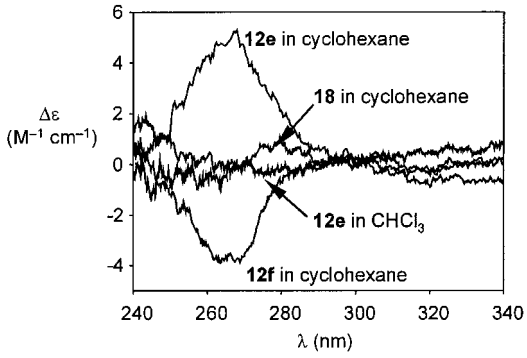


Figure 7. CD spectra of a 0.85 mM solution of **12e** in chloroform and **12e**, its enantiomer **12f**, and **18** in cyclohexane at 25 °C. All CD spectra are the average of four measurements (path length 0.1 mm).

addition of a substantial amount (30%) of chiral **12e** to achiral **12g**. This obviously resulted from extensive scrambling of chiral ligands and a loss of chiral information that is not possible in Meijer's example but can occur in hydrogen-bonded assemblies.

Thermal Properties. According to differential scanning calorimetry (DSC) measurements and polarization optical microscope studies, various aryl-substituted tetrazole complexes underwent a melting transition to a liquid-crystalline mesophase. Depending on substitution, melting temperatures ranged between 140 °C (**12d**,**g**) and 230 °C (**12h**). Chiral complexes **12e**,**f** were found to be waxy at room temperature and became birefringent once sheared. Unfortunately, all tetrazole complexes were thermally unstable and started to rapidly decompose at their isotropization temperatures, especially when samples were heated above 200 °C for longer than a few minutes. This thermal instability hampered our attempts to obtain recognizable textures by annealing.[28]

Discussion

Like carboxylic acids, tetrazoles with their comparable acidity are equally capable of forming 3:1 complexes with tris(imidazoline) **1**. The crystal structure of tetrazole complex **12a** revealed a completely planar and C_3-symmetrical arrangement that was in stark contrast to the structure of a recently published complex between **1** and trifluoroacetic acid in which each carboxylate bound differently and twisted out of the plane containing the central benzene ring.[7] Unlike a carboxylate, the smaller tetrazolate fits quite easily into the gap between two *meta*-positioned imidazolines. The influence on the association constant K_a was, however, marginal. In the competitive solvent mixture $CDCl_3/CD_3OD$ (97:3), 5-(*p*-*tert*-butylphenyl)tetrazolate ($K_a = 2470 \pm 400$ M^{-1}, $\Delta G° = 19.4$ kJ mol^{-1}) was found to bind only slightly better to our model bis(imidazoline) **15** than benzoate[7] ($K_a = 990 \pm 230$ M^{-1}, $\Delta G° = 17.1$ kJ mol^{-1}).

The major consequence of the planarity of the complex is a tendency of the molecules to stack not only in the crystal (Figure 1), but also in solution. As we report in this paper, various tetrazole complexes (**12d**−**h**) self-associate in chloroform and other nonpolar solvents, always provided that solubilizing groups and a certain degree of branching counteract the formation of insoluble aggregates.

Recently, J. S. Moore and co-workers found that shape-persistent dendrimers[29] and macrocycles[8a] have a similar inclination toward π-stacking. At about the same time, E. W. Meijer and co-workers reported strong self-association for large disk-shaped molecules.[8b,30] Both groups suggested that a planarized core strongly promotes stacking in solution. We are now able to show that such a disk-shaped structure can be assembled through a simple association process prior to stack formation.

Self-association of complexes **12d**−**h** in various solvents was evident from NMR, VPO, and CD measurements. Since aryl-substituted tetrazoles[31] and 1,3,4-oxadiazoles[32] are flat π-systems, we attribute the considerable ^{1}H NMR upfield shifts and the more than 3-fold increase in number-average molar mass M_n for **12h** to the stacking of the complex's extended planar core. Increased line widths of NMR signals were in accord with the expected slowing of the rates of motion and a shortening of the T_2 relaxation times once the molecules

(28) After being heated from room temperature to above the melting point, complex **12g** exhibited a very fine texture. Slow (between 0.2 and 0.5 °C/min) cooling from the isotropic liquid phase resulted in the growth of homeotropic digitized stars. Such a dendritic growth was followed by the development of birefringent pseudofocal conic or fanlike textures. Although this is characteristic for the formation of a columnar liquid-crystalline mesophase, the required low cooling rates caused rapid decomposition and discoloration that led to the disappearance of the developing texture owing to a continuous drop in the clearing temperature (Kraft, A.; Osterod, F.; Peters, L.; Reichert, A. *Polym. Mater. Sci. Eng.* **1999**, *80*, 18−19). Investigations toward the improvement of thermal stability and X-ray diffraction studies of potentially liquid-crystalline carboxylic acid and tetrazole complexes with **1** are underway.

(29) Pesak, D. J.; Moore, J. S. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1636−1639.

(30) Similarly, a polystyrene−oligothiophene−polystyrene triblock copolymer also shows aggregation in solution owing to an extended planar π-system: Hempenius, M. A.; Langeveld-Voss, B. M. W.; van Haare, J. A. E. H.; Janssen, R. A. J.; Sheiko, S. S.; Spatz, J. P.; Möller, M.; Meijer, E. W. *J. Am. Chem. Soc.* **1998**, *120*, 2798−2804.

(31) This is illustrated by a crystal structure of 5-(4-hydroxyphenyl)-tetrazole: Gallardo, H.; Begnini, I. M.; Vencato, I. *Acta Crystallogr.* **1997**, *C53*, 143−144.

(32) *C.f.* Tokuhisa, H.; Era, M.; Tsutsui, T. *Adv. Mater.* **1998**, *10*, 404−407.

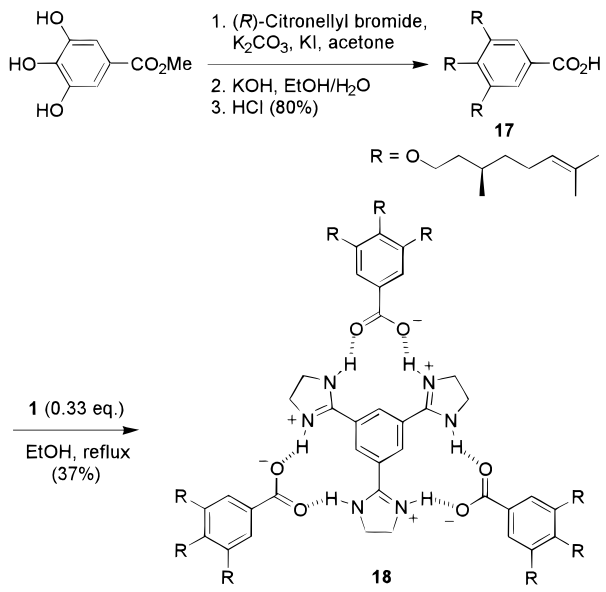
associate. Solubility of **12h** was still high in $CHCl_3$, up to 300 mg/mL, despite a high $K_{stacking}$ value of 250 ± 20 M^{-1}. The lower tendency of complex **12g** toward self-association may be readily explained by a reduced surface area of the aromatic π-system since **12g** has twelve (hetero)aromatic rings less than **12h**. In the case of complex **12i**, the additional bulky *tert*-butyl groups impeded self-association almost completely.

The attractive forces that can give rise to stack formation are salt-packing effects and $\pi-\pi$ interactions between the (hetero)aromatic rings. The former are clearly observed in the packing of **12a** in the crystal lattice. Considering that a first-generation dendrimer of similar structure and size was found to have a relatively low $K_{stacking}$ value of 2 M^{-1} in chloroform if $\pi-\pi$ interactions alone were responsible for the stacking process,[10] electrostatic interactions may therefore present the dominating contribution toward the self-association of **12h**. The upfield shifts that are observed in the ^{1}H NMR spectra may then be attributed to the increasing compensation of positive charges by stacking with negative charges at higher concentrations. Such an additional dipolar field could still be supported by $\pi-\pi$ overlap between aromatic and heteroaromatic rings.[33]

Much higher concentrations were necessary before alkoxyphenyl-substituted complexes **12d**−**g** showed noticeable signs of self-association in $CHCl_3$. On the other hand, these complexes dissolved easily in nonpolar solvents. Extensive self-association was evident from very broad ^{1}H NMR signals in cyclohexane (Figure 6). In this solvent, chiral complex **12e** with its six stereogenic centers displayed a small, but significant, circular dichroism. The same effect, but with opposite sign, was found for the enantiomeric complex **12f**. The absence of a Cotton effect for a solution of **12e** in $CHCl_3$ at the same concentration correlated, in fact, with our NMR investigations according to which no significant self-association took place at the concentration used for measuring the CD spectrum. For comparison, the ^{1}H NMR signals of a chiral carboxylic acid complex **18** (Scheme 3) were still resolved in cyclohexane, and it was not possible to detect a CD effect under the same conditions used for tetrazoles **12e**,**f** (Figure 7). Obviously, the nonplanar conformation of carboxylic acid complexes seriously restricted the extent of self-association.

As with most tetrazoles and especially their anions,[12] the tetrazole complexes had limited thermal stability and

Scheme 3



they decomposed rapidly on melting to an isotropic liquid. Differential scanning calorimetry measurements and polarization optical microscope studies indicated that several complexes, especially those with long alkoxy side chains (**12d**−**g**), possessed a liquid-crystalline (possibly columnar) mesophase that will be the subject of further investigations in due course.[34]

Conclusion

In summary, this study demonstrates how binding interactions between tetrazoles and tris(imidazoline) **1** result in complexes **12** and how self-assembly was followed by self-association. The tetrazole−**1** complexes were found to stack both *in the crystal and in solution*. Ordered macromolecules are thus accessible through a combination of two association processes that occur within and orthogonal to the plane of the complex's core without interference between both noncovalent interactions (hydrogen bonding and salt-packing). We trust that these findings open up an avenue toward other ordered columnar structures (e.g., supramolecular liquid crystals). It should further allow us to even mimic the self-assembly principle used by Nature for numereous noncovalently linked superstructures, such as the tobacco mosaic virus in which the self-assembly of a small protein generates the protein coat for the virus's RNA.[35]

Experimental Section

General Methods. All solvents were distilled prior to use. DSC: heating rate 10 °C/min. Cr = crystalline phase, M = liquid-crystalline mesophase, and I = isotropic liquid. VPO measurements were performed in $CHCl_3$ at 35 °C against benzil or polystyrene standards (Fluka, Switzerland) as reference. The number-average molar mass M_n was determined for solutions in a concentration range between about 8 and 60 mg of complex/g of $CHCl_3$.

5-(4-Dodecyloxyphenyl)tetrazole (3). 4-Dodecyloxybenzonitrile[36] (10.0 g, 34.8 mmol), NaN_3 (2.49 g, 38.3 mmol), NH_4Cl (2.12 g, 39.7 mmol), and dimethylformamide (200 mL) were stirred at 110 °C for 20 h. The suspension was then poured into water (350 mL)/concentrated HCl (5 mL). The crude

(33) It should be taken into account that $\pi-\pi$ interactions between electron-deficient aromatic systems (such as with the 1,3,4-oxadiazole-containing ligand **11a**) are very favorable and may equally promote stacking interactions: (a) Hunter, C. A.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1990**, *112*, 5525−5534. (b) Zhang, J.; Moore, J. S. *Ibid.* **1992**, *114*, 9701−9702. (c) Cozzi, F.; Cinquini, M.; Annuziata, R.; Siegel, J. S. *Ibid.* **1993**, *115*, 5330−5331. (d) Hunter, C. A. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1584−1586. (e) Shetty, A. S.; Zhang, J.; Moore, J. S. *J. Am. Chem. Soc.* **1996**, *118*, 1019−1027. (f) Tobe, Y.; Utsumi, N.; Kawabata, K.; Naemura, K. *Tetrahedron Lett.* **1996**, *37*, 9325−9328.

(34) Stacking interactions are also well-known for columnar liquid-crystalline mesophases of suitably substituted condensed aromatic compounds. For recent examples, see: (a) Reference 8b. (b) van de Craats, A. M.; Warmann, J. M.; Müllen, K.; Geerts, Y.; Brand, J. D. *Adv. Mater.* **1998**, *10*, 36−38. Columnar liquid-crystalline mesophases were already reported for a number of self-assembled compounds: (c) Mariani, P.; Mazabard, C.; Garbesi, A.; Spada, G. P. *J. Am. Chem. Soc.* **1989**, *111*, 6369−6373. (d) Kleppinger, R.; Lillya, C. P.; Yang, C. *J. Am. Chem. Soc.* **1997**, *119*, 4097−4102. (e) Beginn, U.; Zipp, G.; Möller, M.; Johansson, G.; Percec, V. *Macromol. Chem. Phys.* **1997**, *198*, 2839−2852. (f) Suárez, M.; Lehn, J.-M.; Zimmerman, S. C.; Skoulios, A.; Heinrich, B. *J. Am. Chem. Soc.* **1998**, *120*, 9526−9532 and references therein.

(35) Klug, A. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 565−582.

(36) Schubert, H.; Zaschke, H. *J. Prakt. Chem.* **1970**, *312*, 494−506.

product was collected by suction filtration and recrystallized from aqueous acetone. Yield: 5.68 g (49%). Colorless solid. Mp 152−155 °C. ^{1}H NMR (500 MHz, $CDCl_3$/DMSO-d_6, 1:1): δ 0.87 (t, J = 6.9 Hz, 3 H), 1.20−1.38 (m, 16 H), 1.45 (tt, J = 7.7, 6.5 Hz, 2 H), 1.78 (tt, J = 8.2, 7.0 Hz, 2 H), 4.03 (t, J = 6.5 Hz, 2 H), 7.05 and 7.98 (AA′XX′, 4 H). ^{13}C NMR (125 MHz, $CDCl_3$/DMSO-d_6, 1:1): δ 14.0, 22.3, 25.6, 28.8, 28.90, 28.95, 29.16, 29.19, 29.22, 31.5, 67.8, 115.0, 116.3, 128.5, 161.0. MS (CI, NH_3): m/z 365 (M + NH_3 + NH_4^+, 19%), 348 (M + NH_4^+, 100), 331 (M + H^+, 76). Anal. Calcd for $C_{19}H_{30}N_4O$: C, 69.05; H, 9.15; N, 16.95. Found: C, 69.11; H, 9.07; N, 16.89. R_f (CH_2Cl_2/MeOH, 9:1) 0.27.

3,4-Bis[3,7-(*S*)-dimethyl-6-octenyloxy]benzonitrile (4a). (*S*)-Citronellyl bromide (4.38 g, 20.0 mmol), 3,4-dihydroxybenzonitrile (1.35 g, 10.0 mmol), K_2CO_3 (2.76 g, 20.0 mmol), and a pinch of KI in dry acetone (80 mL) were heated to reflux for 40 h. After filtration of the still hot suspension, the solution was concentrated, combined with CH_2Cl_2 (100 mL), filtered, and concentrated. The crude product was purified by distillation (Kugelrohr, 230 °C/0.02 mbar) and column chromatography (hexane/ethyl acetate, 20:1). Yield: 1.88 g (46%). Colorless oil. $[\alpha]^{25}_D$ −5° (c 3.5 × 10^{-3} M, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.97 (br d, 6 H), 1.20−1.28 (m, 2 H), 1.37−1.44 (m, 2 H), 1.60 (br s, 6 H), 1.68 (br s, 6 H), 1.61−1.74 (m, 4 H), 1.85−2.07 (m, 6 H), 4.00−4.10 (m, 4 H), 5.07−5.13 (m, 2 H), 6.87 (d, J = 8.8 Hz, 1 H), 7.07 (d, J = 1.9 Hz), 7.22 (dd, J = 8.8, 1.9 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 17.7, 19.6, 25.7, 29.7, 112.7, 116.0, 124.57, 124.62, 126.3 (CH, CH_3), 25.5, 35.8, 35.9, 37.14, 37.16, 67.5, 67.8 (CH_2), 103.6, 119.4, 131.3, 131.4, 149.1, 153.1 (*ipso*-C, CN). MS (CI, NH_3): m/z 429 (M + NH_4^+, 100%). IR (KBr, cm^{-1}): ν 2224. Anal. Calcd for $C_{27}H_{41}NO_2$: C, 78.78; H, 10.04; N, 3.40. Found: C, 78.60; H, 10.35; N, 3.44. R_f (CH_2Cl_2/MeOH, 9:1) 0.92.

5-[3,4-Bis(3,7-(*S*)-dimethyl-6-octenyloxy)phenyl]tetrazole (5a). A mixture of **4a** (1.25 g, 3.03 mmol), NaN_3 (260 mg, 4.00 mmol), and triethylammonium chloride (551 mg, 4.00 mmol) in toluene (10 mL) was stirred at 100 °C for 40 h. The suspension was then added to water (130 mL)/concentrated HCl (20 mL). The toluene layer was separated, and the aqueous phase was further extracted with toluene. The combined organic extracts were concentrated, and the crude product was further purified by column chromatography (first CH_2Cl_2 and then CH_2Cl_2/MeOH, 9:1). Yield: 1.01 g (74%). Colorless solid. Mp 90−93 °C. $[\alpha]^{25}_D$ −8° (c 2.2 × 10^{-3} M, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.93 (d, J = 6.3 Hz, 3 H), 0.95 (d, J = 6.3 Hz, 3 H), 1.16−1.26 (m, 2 H), 1.33−1.42 (m, 2 H), 1.58 (s, 3 H), 1.59 (s, 3 H), 1.66 (s, 3 H), 1.67 (s, 3 H), 1.58−1.72 (m, 4 H), 1.82−2.07 (m, 6 H), 4.01−4.10 (m, 4 H), 5.06−5.12 (m, 2 H), 6.93 (d, J = 8.2 Hz, 1 H), 7.56−7.82 (m, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 17.6, 19.49, 19.56, 25.69, 29.7, 112.0, 113.2, 120.7, 124.62, 124.70 (CH, CH_3), 25.49, 35.95, 36.02, 37.2, 67.6, 67.8 (CH_2), 115.8, 131.17, 131.28, 149.6, 151.9, 156.6 (*ipso*-C, C=N). MS (CI, NH_3): m/z 472 (M + NH_4^+, 100%), 455 (M + H^+, 40). Anal. Calcd for $C_{27}H_{42}N_4O_2$: C, 71.33; H, 9.31; N, 12.32. Found: C, 70.21; H, 9.46; N, 13.96. R_f (CH_2Cl_2/MeOH, 9:1) 0.48.

5-[3,4-Bis(3,7-(*R*)-dimethyl-6-octenyloxy)phenyl]tetrazole (5b). Analogous preparation as for **5a**. $[\alpha]^{25}_D$ +3° (c 3.5 × 10^{-3} M, $CHCl_3$).

3,4,5-Tris(hexyloxy)benzonitrile (7). A stream of gaseous NH_3 was bubbled through a solution of **6**[8b] (14.3 g, 32.4 mmol) in dry toluene (200 mL) over 3 h. The mixture was then concentrated in a vacuum, and the brown residue was recrystallized from acetone (500 mL)/water (100 mL) to yield 8.97 g (66%) of 3,4,5-tris(hexyloxy)benzamide as a colorless solid. Mp 90 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 0.82−0.93 (m, 9 H), 1.22−1.50 (m, 18 H), 1.68−1.77 (m, 6 H), 3.86 (t, J = 6.3 Hz, 2 H), 3.95 (t, J = 6.6 Hz, 4 H), 7.18 (s, 2 H), 7.30 (s, 1 H), 7.93 (s, 1 H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 13.81, 13.83, 105.8 (CH, CH_3), 22.09, 22.12, 25.20, 25.24, 28.8, 29.7, 31.0, 31.1, 68.3, 72.3 (CH_2), 139.6, 152.1, 167.3 (*ipso*-C, C=O). IR (KBr, cm^{-1}): ν 3361, 3189, 1649. MS (CI, NH_3): m/z 439 (M + NH_4^+, 100%), 422 (M + H^+, 98). Anal. Calcd for $C_{25}H_{43}NO_3$: C, 71.22; H, 10.28; N, 3.32. Found: C, 71.28; H, 10.01; N, 3.53. R_f (CH_2Cl_2/MeOH, 9:1) 0.67. A solution of trichloroacetyl chloride (2.5 mL, 22 mmol) in CH_2Cl_2 (20 mL) was added dropwise to an ice-cold solution of 3,4,5-tris(hexyloxy)benzamide (8.44 g, 20.0 mmol) and triethylamine (5.5 mL, 40 mmol) in CH_2Cl_2 (20 mL). The light yellow mixture was stirred for 30 min, then diluted with CH_2Cl_2 (20 mL), washed with 0.5 M aqueous NaOH (20 mL), 0.1 M aqueous HCl (2 × 25 mL), and water (3 × 20 mL), and dried over Na_2SO_4. The solvent was removed in a vacuum, and the crude product was purified by distillation (Kugelrohr, 230 °C/0.02 mbar) to furnish 5.60 g (69%) of a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.87−0.95 (m, 9 H), 1.27−1.54 (m, 18 H), 1.68−1.86 (m, 6 H), 3.96 (t, J = 6.4 Hz, 4 H), 4.06 (t, J = 6.6 Hz, 2 H), 6.82 (s, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.99, 14.05, 105.5 (CH, CH_3), 22.57, 22.65, 25.65, 25.69, 29.2, 30.2, 31.5, 31.7, 69.2, 73.9 (CH_2), 118.5, 140.2, 153.7, 156.6 (*ipso*-C, C=N). IR (KBr, cm^{-1}): δ 2226. MS (CI, NH_3): m/z 421 (M + NH_4^+, 100%). Anal. Calcd for $C_{25}H_{41}NO_3$: C, 74.40; H, 10.24; N, 3.47. Found: C, 74.01; H, 10.57; N, 3.97. R_f (CH_2Cl_2/MeOH, 9:1) 0.95.

5-[3,4,5-Tris(hexyloxy)phenyl]tetrazole (8). A solution of **7** (3.61 g, 8.95 mmol), NaN_3 (1.16 g, 17.9 mmol), and NH_4Cl (1.05 g, 19.7 mmol) in NMP (20 mL) was stirred at 110 °C for 8 h. The yellow-brown solution was added dropwise to water (150 mL)/concentrated HCl (2 mL) under vigorous stirring. The resulting yellow precipitate was collected by suction filtration, dried, and purified by column chromatography (CH_2Cl_2/MeOH, 10:1) to give 1.38 g (35%) of a colorless solid. Mp 92 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.80−0.95 (m, 9 H), 1.20−1.50 (m, 18 H), 1.65−1.82 (m, 6 H), 3.92 (t, J = 6.3 Hz, 2 H), 4.04 (t, J = 6.6 Hz, 4 H), 7.31 (s, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.99, 14.05, 105.5 (CH, CH_3), 22.57, 22.65, 25.65, 25.69, 29.2, 30.2, 31.5, 31.7, 69.2, 73.9 (CH_2), 118.5, 140.2, 153.7, 156.6 (*ipso*-C, C=N). MS (CI, NH_3): m/z 464 (M + NH_4^+, 100%), 447 (M + H^+, 37). Anal. Calcd for $C_{25}H_{42}N_4O_3$: C, 67.23; H, 9.48; N, 12.54. Found: C, 67.38; H, 9.63; N, 12.80. R_f (CH_2Cl_2/MeOH, 9:1) 0.33.

General Procedure for the Preparation of the Complexes. Imidazoline base **1**[15b] and tetrazole (3 equiv) were dissolved in hot ethanol (ca. 40 mL/mmol), to which, if necessary (as in the case of **12h**,**i**), a certain amount of $CHCl_3$ (5−10 mL) was added as cosolvent. After filtration of the hot solution and concentration, the crude product was crystallized from the solvent (mixture) indicated for each complex and thoroughly dried at 50−100 °C/10^{-5} mbar.

Complex 12a. Yield: 73% (MeCN/MeOH). Colorless needles. Mp 257−259 °C dec. ^{1}H NMR (500 MHz, DMSO-d_6): δ 3.82 (s, 12 H), 8.54 (s, 3 H), 8.87 (s, 3 H). Anal. Calcd for $C_{18}H_{24}N_{18}\cdot 2H_2O$: C, 40.91; H, 5.34; N, 47.70. Found: C, 40.89; H, 5.33; N, 47.97.

Complex 12d. Yield: 55% (EtOH). Light yellow solid. DSC: Cr_1 88 (ΔH 79 J g^{-1}) Cr_2 139 (ΔH 6 J g^{-1}) M 193 (ΔH 29 J g^{-1}) I_{dec}. ^{1}H NMR (500 MHz, $CDCl_3$, 10^{-3} M): δ 0.88 (m, 9 H), 1.28−1.45 (m, 48 H), 1.46 (br s, 6 H), 1.79 (br qui, 6 H), 3.99 (br t, J = 5.6 Hz, 6 H), 4.29 (br s, 12 H), 6.97 and 7.97 (AA′XX′, 12 H), 9.84 (br s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$/CD_3OD, 5:2): δ 14.2, 115.2, 128.6, 133.0 (CH, CH_3), 23.0, 26.3, 29.5, 29.66, 29.73, 29.90, 29.91, 29.93, 29.95, 29.97, 46.6, 68.5 (CH_2), 121.0, 126.7, 160.7, 161.2, 164.2 (*ipso*-C, C=N). Anal. Calcd for $C_{72}H_{108}N_{18}O_3\cdot 2H_2O$: C, 66.02; H, 8.62; N, 19.25. Found: C, 65.70; H, 8.70; N, 19.20.

Complex 12e. Yield: 50% (EtOH/MeCN). Waxy yellow solid. Clearing point: 150−162 °C dec. $[\alpha]^{25}_D$ −6° (c 7.7 × 10^{-4} M, $CHCl_3$). $[\alpha]^{25}_D$ 17° (c 7.7 × 10^{-4} M, cyclohexane). ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.97 (d, J = 5.7 Hz, 9 H), 0.98 (d, J = 5.7 Hz, 9 H), 1.18−1.29 (m, 6 H), 1.36−1.46 (m, 6 H), 1.60 (s, 9 H), 1.61 (s, 9 H), 1.67 (s, 9 H), 1.68 (s, 9 H), 1.61−1.75 (m, 12 H), 1.87−2.10 (m, 18 H), 4.05−4.15 (m, 12 H), 4.29 (s, 12 H), 5.11 (m, 6 H), 6.95 (d, J = 8.2 Hz, 3 H), 7.58 (dd, J = 8.2, 1.9 Hz, 3 H), 7.65 (d, J = 1.9 Hz, 3 H), 9.87 (s, 3 H). UV (cyclohexane): λ_{max} 254 nm (ϵ 55 200 M^{-1} cm^{-1}). Anal. Calcd for $C_{96}H_{144}N_{18}O_6\cdot H_2O$: C, 69.28; H 8.84; N, 15.15. Found: C, 68.84; H, 8.93; N, 15.45.

Complex 12f. Yield: 33% (MeCN/MeOH). Waxy yellow solid. $[\alpha]^{25}_D$ +6° (c 6.8 × 10^{-4} M, $CHCl_3$).

Complex 12g. Yield: 82% (EtOH). Light yellow crystals. DSC: Cr 73 (ΔH 28 J g^{-1}) M_1 126 (ΔH 1 J g^{-1}) M_2 146 (ΔH 3

J g^{-1}) I_{dec}. ^{1}H NMR (500 MHz, $CDCl_3$, 10^{-3} M): δ 0.88−0.93 (m, 27 H), 1.31−1.36 (m, 36 H), 1.44−1.53 (m, 18 H), 1.74−1.85 (m, 18 H), 4.00 (t, J = 6.3 Hz, 6 H), 4.06 (t, J = 6.3 Hz, 12 H), 4.31 (s, 12 H), 7.30 (s, 6 H), 9.84 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.05, 14.11, 105.4, 133.7 (CH, CH_3), 22.6, 22.7, 25.8, 39.4, 30.3, 31.6, 31.8, 45.8, 69.2, 73.5 (CH_2), 125.0, 125.3, 138.7, 153.4, 162.9, 163.2 (*ipso*-C, C═N). VPO ($CHCl_3$, 35 °C): M_n 1650 g mol^{-1} (against benzil as standard), 1800 g mol^{-1} (against polystyrene 2000 as standard). Anal. Calcd for $C_{90}H_{144}N_{18}O_9$: C, 66.64; H, 8.95; N, 15.54. Found: C, 66.46; H, 9.05; N, 15.31. R_f (CH_2Cl_2/MeOH, 9:1) 0.40 (smearing).

Complex 12h. Yield: 69% (EtOH/$CHCl_3$). Colorless solid. DSC: Cr_1 194 (ΔH 5 J g^{-1}) Cr_2 232 (ΔH 4 J g^{-1}) M 250 (ΔH 5 J g^{-1}) I_{dec}. ^{1}H NMR (500 MHz, $CDCl_3$, 10^{-4} M): δ 1.39 (s, 54 H), 4.57 (s, 12 H), 7.59 and 8.14 (AA′XX′, 24 H), 8.89 (s, 3 H), 9.09 (s, 6 H), 9.95 (br s, 3 H), 12.95 (br s, 6 H). ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.36 (s, 54 H), 3.96 (br s, 12 H), 7.70 and 8.15 (AA′XX′, 24 H), 8.58 (s, 3 H), 8.73 (t after resolution enhancement, J = 1.5 Hz, 3 H), 8.93 (d after resolution enhancement, J = 1.5 Hz, 6 H). ^{13}C NMR (125 MHz, $CDCl_3$, 10^{-2} M): δ 31.1, 126.0, 126.9, 124.1, 126.7, 133.5 (CH, CH_3), 45.9 (CH_2), 35.1, 120.5, 125.1, 125.2, 132.1, 155.6, 160.6, 162.4, 163.1, 165.0 (*ipso*-C, C═N). VPO ($CHCl_3$, 35 °C): M_n 6050 g mol^{-1} (against benzil as standard), 6300 g mol^{-1} (against polystyrene 2000 as standard), 6640 g mol^{-1} (against polystyrene 5000 as standard). Anal. Calcd for $C_{108}H_{108}N_{30}O_6 \cdot 2H_2O$: C, 66.24; H, 5.76; N, 21.46. Found: C, 66.04; H, 5.74; N, 21.21.

Complex 12i. Yield: 90% (EtOH/$CHCl_3$). Colorless solid. Dec >300 °C. ^{1}H NMR (500 MHz, $CDCl_3$, 10^{-2} M): δ 1.42 (s, 108 H), 4.59 (s, 12 H), 7.66 (t, J = 1.5 Hz, 6 H), 8.03 (d, 12 H), 8.90 (t, J = 1.5 Hz, 3 H), 9.11 (d, 6 H), 9.91 (s, 3 H). VPO ($CHCl_3$, 35 °C): M_n 2350 g mol^{-1} (against benzil as standard), 2570 g mol^{-1} (against polystyrene 2000 as standard). Anal. Calcd for $C_{132}H_{156}N_{30}O_6 \cdot 2H_2O$: C, 69.09; H, 7.03; N, 18.31. Found: C, 68.92; H, 7.23; N, 18.47.

Complex 16. From 1,3-bis(4,5-dihydro-1*H*-imidazol-2-yl)-benzene[7b] and 5-(*tert*-butylphenyl)tetrazole (2 equiv).[13b] Yield: 59% (MeCN/MeOH). Colorless crystals. DSC: Cr 156 (ΔH 109 J g^{-1}) M 198 (ΔH 51 J g^{-1}) I. ^{1}H NMR (500 MHz, $CDCl_3$/CD_3OD, 13:1): δ 1.34 (s, 18), 4.16 (s, 8 H), 7.46 (t, J = 7.9 Hz, 1 H), 7.47 and 7.92 (AA′XX′, 8 H), 8.00 (dd, J = 7.9, 1.6 Hz, 2 H), 8.66 (br s, 1 H). Anal. Calcd for $C_{34}H_{42}N_{12} \cdot H_2O$: C, 64.13; H, 6.96; N, 26.39. Found: C, 63.97; H, 7.01; N, 26.24.

3,4,5-Tris[3,7-(*R*)-dimethyl-6-octenyloxy]benzoic Acid (17). Methyl gallate (1.31 g, 7.1 mmol), (*R*)-citronellyl bromide (5.00 g, 22.8 mmol), K_2CO_3 (3.15 g, 22.8 mmol), and a pinch of KI were stirred in dry acetone (50 mL) at reflux for 60 h. After filtration of the still hot suspension, the solution was concentrated. The crude product was purified by column chromatography (hexane/ethyl acetate, 9:1). Yield: 2.39 g (56%). A solution of the ester (1.10 g, 1.8 mmol) in ethanol (100 mL) was combined with a solution of KOH (0.40 g, 7.1 mmol) in water (40 mL) and heated to reflux for 3 h. The solution was acidified with HCl, concentrated, and extracted with $CHCl_3$ (100 mL). The organic extracts were concentrated in a vacuum and dried. Chromatography (CH_2Cl_2/ether, 7:1) furnished 0.86 g (80%) of a colorless oil. $[\alpha]^{25}_D$ +6° (c 2.2 × 10^{-3} M, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.94 (d, J = 6.3 Hz, 3 H), 0.96 (d, J = 7.0 Hz, 6 H), 1.15−1.29 (m, 3 H), 1.31−1.47 (m, 3 H), 1.59 (s, 3 H), 1.60 (s, 6 H), 1.67 (s, 3 H), 1.68 (s, 6 H), 1.51−1.79 (m, 6 H), 1.80−2.09 (m, 9 H), 4.00−4.15 (m, 6 H), 5.05−5.15 (m, 3 H), 7.33 (s, 2 H). ^{13}C NMR (125 Hz, $CDCl_3$): δ 17.63, 17.66, 19.4, 15.5, 25.7, 29.4, 29.6, 108.5, 124.7, 124.9 (CH, CH_3, 1 signal missing), 25.5, 36.2, 37.2, 37.2, 37.3, 67.5, 71.7 (CH_2, 1 signal missing), 123.7, 131.1, 131.3, 143.1, 152.9, 171.6 (*ipso*-C, C═O). MS (CI, NH_3): m/z 602 (M + NH_4^+, 100%), 585 (M + H^+, 10). Anal. Calcd for $C_{37}H_{60}O_5 \cdot 2H_2O$: C, 71.57; H, 10.39. Found: C, 71.13; H, 10.63. R_f (CH_2Cl_2/MeOH, 9:1) 0.60.

Complex 18. Yield: 37% (MeCN/MeOH). Waxy white solid. $[\alpha]^{25}_D$ +6° (c 9.7 × 10^{-4} M, $CHCl_3$).^{1}H NMR (500 MHz, $CDCl_3$): δ 0.94 (d, J = 6.3 Hz, 9 H), 0.95 (d, J = 7.0 Hz, 18 H), 1.12−1.28 (m, 9 H), 1.34−1.44 (m, 9 H), 1.59 (s, 27 H), 1.67 (s, 27 H), 1.50−1.77 (m, 18 H), 1.78−2.08 (m, 27 H), 3.98−4.10 (m, 18 H), 4.13 (s, 12 H), 5.10 (br s, 9 H), 7.33 (s, 6 H), 10.17 (s, 3 H).

Single-Crystal X-ray Diffraction Analysis of 12a. Crystal structure data for **12a** (single crystals were obtained after slow evaporation from MeOH through a closed vial): formula $C_{18}H_{32}N_{18}O_4$, M = 564.62, crystal dimensions 0.50 × 0.15 × 0.10 mm, $a = b$ = 14.680(2) Å, c = 6.623(1) Å, γ = 120°, V = 1236.1(4) $Å^3$, ρ_{calcd} = 1.517 g cm^{-3}, $F(000)$ = 596 e, m = 9.66 cm^{-1}, empirical absorption correction via φ scan data (0.957 ≤ C ≤ 0.999), Z = 2, hexagonal, space group $P6_3/m$ (no. 176), l = 1.54178 Å, T = 223 K, $\omega/2\theta$ scans, 2816 reflections collected ($\pm h$, $\pm k$, $+l$), [(sin θ)/λ] = 0.62 $Å^{-1}$, 925 independent and 485 observed reflections [$I \geq 2\ \sigma(I)$], 82 refined parameters, R = 0.067, wR^2 = 0.218, maximum residual electron density 0.24 (−0.35) e $Å^{-3}$, hydrogens (excluding those of the crystal water molecules) calculated and refined as riding atoms. The data set was collected with an Enraf Nonius CAD4 diffractometer. Programs used: data reduction MolEN, structure solution SHELXS-86, structure refinement SHELXL-93, graphics SCHAKAL-92 and DIAMOND.

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Supporting Information Available: Details of the X-ray crystal structure determination of **12a**, preparation of **10a**−**b**, **11a**−**b**, and **14**, NMR dilution experiment for **16** in $CDCl_3$/CD_3OD (97:3) at 25 °C, ^{1}H NMR spectra and VPO data for **12h**, ^{1}H NMR spectra and DSC data of **12g**, and ^{1}H NMR spectra of **18**. This material is available free of charge via the Internet at http://pubs.acs.org.

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