Self-association of a 1,3,4-oxadiazole-containing dendrimer

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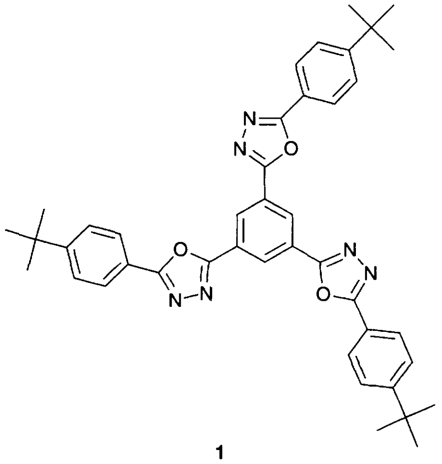
A first-generation dendrimer, which consists of electron-deficient benzene and oxadiazole rings, forms π-stacks in solution as evidenced by NMR and vapour-pressure osmometry

Electron-transporting materials are of general interest because of their potential applications in electrophotography (photocopiers, laser printers)[1] and, increasingly so in recent years, in electroluminescent devices based on organic fluorescent dyes and polymers.[2] 1,3,4-Oxadiazole derivatives in particular, for example **1**[2a] (formally a zeroth-generation dendrimer),[3] have been used in light-emitting diodes. Charge transport through thin (< 100 nm) layers of such materials occurs predominantly by a hopping mechanism. The multiple branches of a dendrimer increase the probability that charges may find an energetically favoured pathway when hopping from one molecule to another. Electron-transporting dendrimers are therefore estimated to be superior to comparable linear oligomers/polymers.[4] This theoretical prediction may now be experimentally verified with **8**, the first and simplest oxadiazole-containing dendrimer. Aryl iodide **3** is the starting material for the synthesis of **8** and can be prepared in three steps from 5-iodoisophthalic acid[5] (Scheme 1). The *tert*-butyl substituents are essential for good solubility of **3** (and later of **8**) in, *e.g.* chloroform. Furthermore, they also simplify the interpretation of ^{1}H NMR spectra, which makes it easier to detect impurities.

The key step in the synthesis of **8** (Scheme 2) is a palladium-catalysed carbonylation, a reaction used only once before for the preparation of polyhydrazides.[6] Precursor **6** is thus formed in a single step from **3**, 1,3,5-benzenetricarboxylic acid trihydrazide **4**[7] ßand carbon monoxide with *N*-methylpyrrolidone (NMP) as solvent, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as base and palladium(II) chloride–$Ph_2P(m\text{-}C_6H_4SO_3Na)$ **5** as catalyst.[8]† The seven-component reaction proceeds in remarkably good yields (80–90% after filtration of the crude product over silica gel). Carboxylate **7** is the sole major by-product (8–15% based on **3**) and is formed from **3**, CO, DBU and traces of moisture.

Despite the good solubility of **6** in $CDCl_3$ or C_6D_6 its ^{1}H NMR spectra in these solvents show broad and structureless signals for aromatic as well as *tert*-butyl protons. As the lineshape is independent of the NMR frequency, dynamic processes can be ruled out. Self-association caused by intermolecular hydrogen bonding remains therefore the most likely cause. Sharp signals are finally observed when the NMR spectrum is run in $(CD_3)_2SO$.[9] Chromatographic purification of **6** is hampered by the fact that on silica gel (with dichloromethane–methanol as eluent) the colourless **6** partially converts to a yellow mixture of compounds. An explanation might be the formation of an additional –C(OH)=N–N=C(OH)– π system through tautomerisation of a former hydrazide –C(=O)–NH–NH–C(=O)– group.[10] The process is reversible, and **6** can be regained upon addition of a drop of hydrochloric acid. The triple ring closure, which is necessary for the conversion of **6** into **8**, cannot be achieved with phosphoryl chloride. This (as has been noted occasionally in the preparation of **3** from **2**) is caused by traces of NMP that can be identified by NMR even after excessive purification of **6**. Chlorosulfonic acid proves to be a better choice provided that the reaction temperature is kept well below 100 °C because otherwise *tert*-butyl groups are cleaved off. The purification of **8** proceeds smoothly and involves



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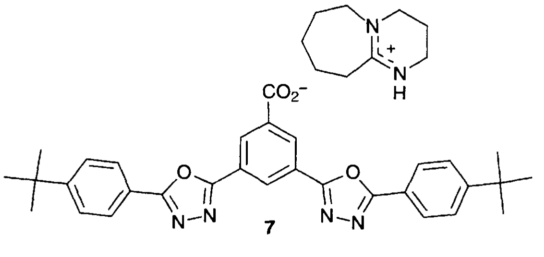

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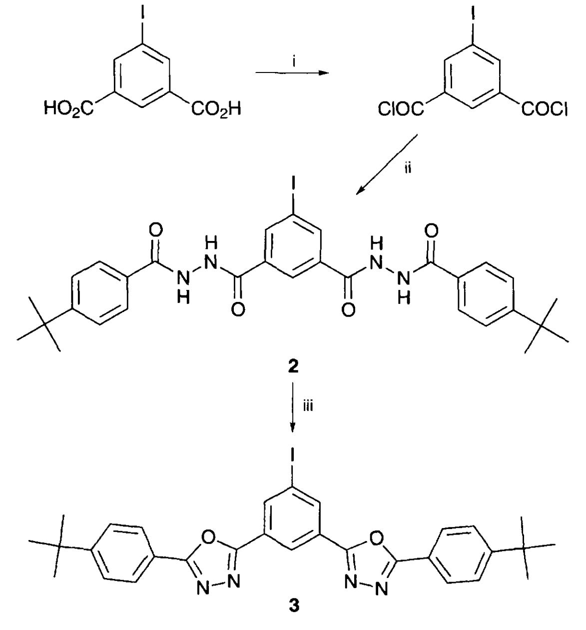
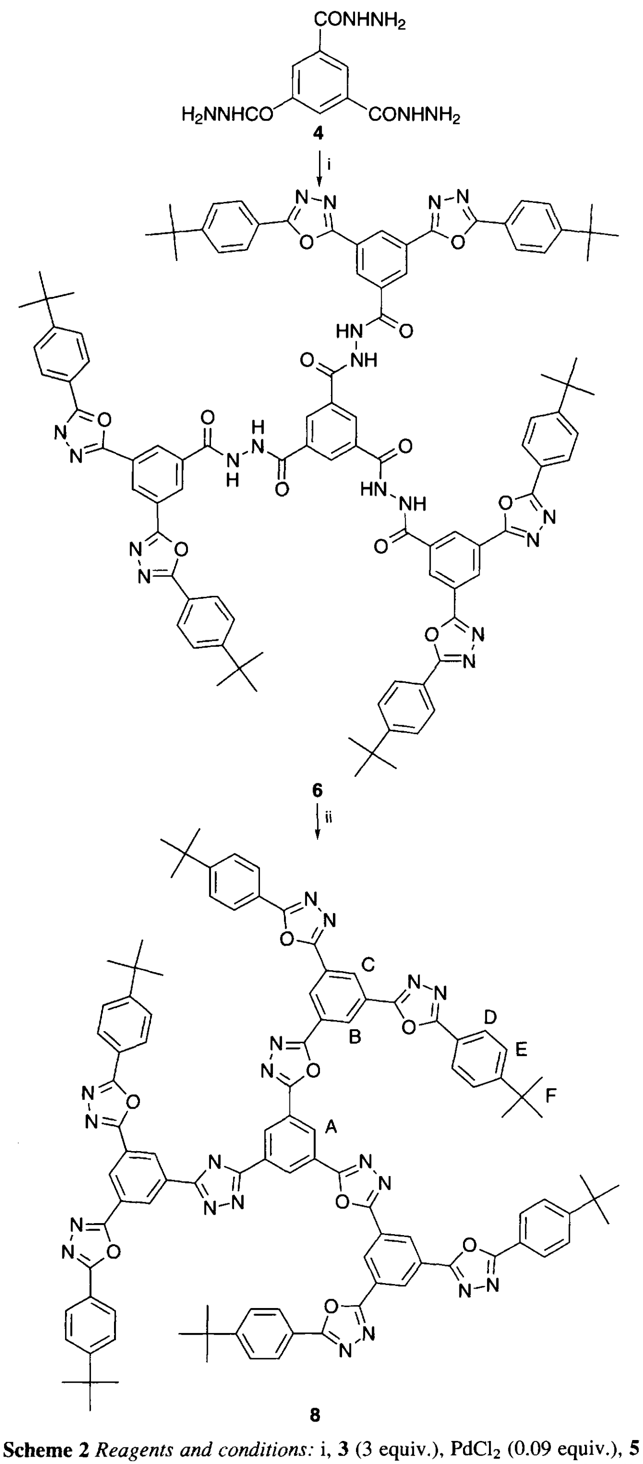


Scheme 1 *Reagents and conditions:* i, $(COCl)_2$, DMF, toluene, 60 °C, 3 h, 85–88%; ii, 4-*tert*-butylbenzhydrazide (2 equiv.), NMP, 2 d, 20 °C, 83–96%; iii, $POCl_3$, 115 °C, 2 h, 72–87%



Scheme 2 *Reagents and conditions:* i, **3** (3 equiv.), $PdCl_2$ (0.09 equiv.), **5** (0.27 equiv.), DBU (3.6 equiv.), NMP, CO, 100 °C, 1–2 d, 80–90%; ii, $ClSO_3H$, 40 °C, 2–3 d, 10–31%. The protons of **8** are marked A–F for signal assignment.

column chromatography and recrystallisation from chloroform.‡

The ^1H NMR spectra of **8** in $CDCl_3$ show characteristic signals at $\delta \approx 9$ for the protons at the trisubstituted benzene rings, the singlet at lowest field being assigned to the protons (H_A) of the core (Fig. 1). A closer look reveals that the chemical shifts of the aromatic protons show a surprising dependence on concentration, temperature and solvent. Especially the signal of the H_A protons varies from δ_H 9.30 to δ_H 8.91 (in $CDCl_3$) or even to δ_H 8.33 (in CH_2Cl_2) when the concentration of **8** is increased from 10^{-3} to 10^{-1} mol dm^{-3}. At the same time linewidths increase notably. Up-field shift and signal broadening are considered as strong evidence for self-association of the dendrimer by π–π interactions in solution.[11] This tendency towards π-stacking seems to be a consequence of the accumulation of electron-deficient (hetero)aromatic π-systems in dendrimer **8**.[12]

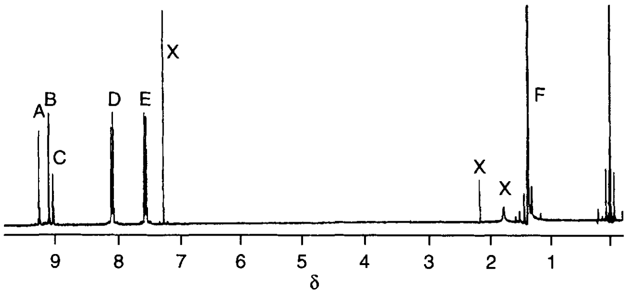


Fig. 1 ^1H NMR spectrum (300 MHz) of **8** in $CDCl_3$ (0.015 mol dm^{-3}). Solvent and impurities (acetone, water) are marked by X.

With the assumption of an equilibrium between dimer $(\mathbf{8})_2$ and free **8**, computer simulations allowed dimerisation constants (K_D) to be estimated.[13] Association is weak in chloroform (K_D = 1.4 dm^3 mol^{-1}), noticeable in dichloromethane (K_D = 10 dm^3 mol^{-1}) and stronger in pyridine (K_D > 30 dm^3 mol^{-1}). In aromatic solvents such as C_6D_6 or [$^2H_8$]toluene all ^1H NMR signals of **8** are dramatically broadened and shifted to higher field. These apparently extended aggregates can be broken up by raising the temperature (to 80 °C), resulting in sharp NMR signals and chemical shifts close to those in $CDCl_3$ solutions. It has to be emphasised that the ^1H NMR signals of model compound **1** show only a negligible chemical shift dependence ($\Delta\delta < 0.1$). Furthermore, no comparable behaviour has been reported for literature-known aromatic dendrimers.[14]

Vapour-pressure osmometry in CH_2Cl_2 at 25 °C independently confirms the self-association of **8**. The deviation from ideal behaviour (as compared to **1** or benzil as standard) is larger and the number of osmotically active molecules is smaller than expected for a non-associating system. Calculations indicate that trimers and tetramers are present besides dimers at higher concentration.

MALDI-TOF (matrix-assisted laser desorption ionisation and time-of-flight) mass spectra of **8** are in accordance with these investigations and show, apart from the molecular-ion peak, quite intense peaks for both dimer and trimer. This is the first hint that π-stacking also plays a role in solid **8**. Implications for electron-transport properties will soon be tested. Syntheses and investigations of further 1,3,4-oxadiazole-containing highly-branched compounds are in progress.

I thank the Fonds der Chemischen Industrie for a Liebig fellowship (1993–1994), Professor G. Wulff for generous support, Professor J. Moser and Mr D. Kirsch for MALDI-TOF-MS measurements and Ms H. Fürtges for help in the preparation of starting materials.

Footnotes

† Water-soluble triphenylphosphane derivative **5** was easily removed by aqueous work-up. The tendency of **6** to contain impurities complicated any chromatographic removal of triphenylphosphane, which is usually employed in Pd-catalysed carbonylations.

‡ All compounds were characterised by microanalysis (**6** as monohydrate), IR, NMR and MS.

Selected data for **3**: mp 220–221 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 1.39 (s, CH_3), 7.57, 8.10 (AA′XX′, C_6H_4), 8.63 (d, J 1.5 Hz, 2 H), 8.81 (t, 1 H, C_6H_3); MS (CI, NH_3, negative ions): m/z (%) 604 (M^-, 39), 477 ($M^- - I$, 19), 127 (I^-, 100); R_f(SiO_2, hexane–ethyl acetate, 2 : 1) 0.35; R_f(dichloromethane–methanol, 9 : 1) 0.85.

For **6**: mp 267–270 °C; ^1H NMR [300 MHz, $(CD_3)_2SO$]: δ 1.35 (s, CH_3), 7.68, 8.14 (AA′XX′, C_6H_4), 8.82 [s, 3 H, $C_6H_3(CO)_3$], 8.91 (d, J 1.6 Hz, 6 H), 8.92 (t, 3 H, C_6H_3), 11.23 (br s, 3 H, NH), 11.38 (br s, 3 H, NH); ^{13}C NMR [75 MHz, $(CD_3)_2SO$]: δ 30.7 (CH_3), 34.8 [$C(CH_3)_3$], 126.1, 126.7 (C_6H_4), 128.1, 130.0 (br) (C_6H_3, 1 signal missing), 120.2, 125.0, 133.4, 134.4, 155.2, 162.4, 163.5, 164.5, 164.9 (*ipso*-C, C=O); IR (KBr): ν 3450 m (br), 3240s (br), 2950s, 1650s (br), 1250s (br), 1110s, 1010s, 840s, 720s; MALDI-TOF-MS (2,5-dihydroxybenzoic acid matrix): *m/z* 1767 ($M + H^+$), 1247; R_f(ethyl acetate) 0.82; R_f(dichloromethane–methanol, 9 : 1) 0.30.

For **8**: DSC (heating rate 10 K min^{-1}) T_{cryst} 264 °C, mp 396 °C (decomp.); ^{1}H NMR (300 MHz, $CDCl_3$, 0.011 mol dm^{-3}): δ 1.38 (s, H_F), 7.55, 8.08 (AA′XX′, H_D and H_E), 9.02 (t, *J* 1.5 Hz, 3 H, H_C), 9.08 (d, 6 H, H_B), 9.24 (s, 3 H, H_A); ^{13}C NMR (75 MHz, $CDCl_3$, 0.059 mol dm^{-3}): δ 31.1 (CH_3), 35.1 [$C(CH_3)_3$], 126.1, 126.9 (C_6H_4), 127.0, 127.1, 127.9 (C_6H_3), 120.2, 125.4, 125.9, 126.3, 155.8, 162.1, 163.1, 163.5, 165.3 (*ipso*-C); IR (KBr): ν 3060w, 2950s, 1610s, 1545s, 1490s, 1265m, 1240m, 1110m, 840s, 800s, 780s, 720s; UV (CH_2Cl_2): λ_{max} 298 nm (ε 246000 dm^3 mol^{-1} cm^{-1}); MALDI-TOF-MS: *m/z* 1713 (100%, $M + H^+$), 3427 (14%, M_2^+), 5138 (7%, M_3^+); R_f(ethyl acetate) 0.0; R_f(dichloromethane–ethanol, 100 : 3) 0.17. The molar mass was measured by vapour-pressure osmometry in $CHCl_3$ at 40 °C at a concentration range low enough to exclude self-association: 1650 g mol^{-1} (against benzil), 1740 g mol^{-1} (against **1** as standard).

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Received, 13th September 1995; Com. 5/06042G