Switchable electron-rich biindolizine-based macrocycles: synthesis and redox properties

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New redox-active cyclophanes, incorporating electrochemically switchable biindolizine units in combination with π-electron-rich hydroquinol units in the ether bridges, have been synthesized by intra- and inter-molecular cyclisation. The electrochemical properties of the cyclophanes, investigated by cyclic voltammetry (CV), are reported. Cyclophanes 5a/6a and 7a, containing 1,4-dioxyphenylene units, showed three reversible redox steps as expected. In contrast, intramolecular interactions occur for cyclophanes 5b/6b and 7b, containing 1,5-dioxynaphthylene as part of the cyclophane ring system. Compounds 5b/6b displayed changes in their electrochemical behaviour upon addition of 2,4,7-trinitrofluoren-9-one but, in general, no influence of potential guests on the half-wave potentials of the biindolizine unit could be established. To have additional possibilities of supramolecular interactions, new 2,2′-heterocycle-disubstituted biindolizines 8 and 9 have been synthesized, which in CV signals a complexation of copper near to the biindolizine redox unit.

Introduction

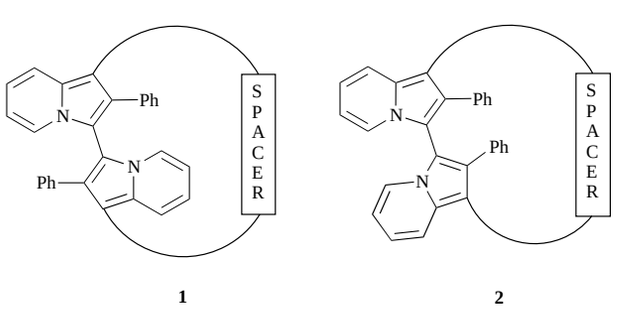
In supramolecular chemistry considerable attention has been paid to the synthesis of host compounds containing switchable functionalities. Those functionalities enable supramolecules to react reversibly on an input of *e.g.* thermal, photochemical or electrochemical energy by changing their main properties, such as size, shape, electronic structure, complexing behaviour *etc*. Such sensitive cyclophanes can act, for example, as molecular switches[1] or shuttles[2] and they are of great interest for new sensor developments and for modern technologies, based on molecular processes.

Our interest is focused on the synthesis and characterisation of redox active cyclophanes based on biindolizines.[3] In contrast to well known compounds such as ferrocenes,[4] tetrathiofulvalenes[5] and paraquat derivatives[6] biindolizines have so far received relatively little attention despite the fact that they are rather stable two-step redox systems[7] with well investigated electrochemical behaviour. Herein we describe new results in using biindolizines as building blocks for redoxactive cyclophanes.

Results and discussion

Synthesis

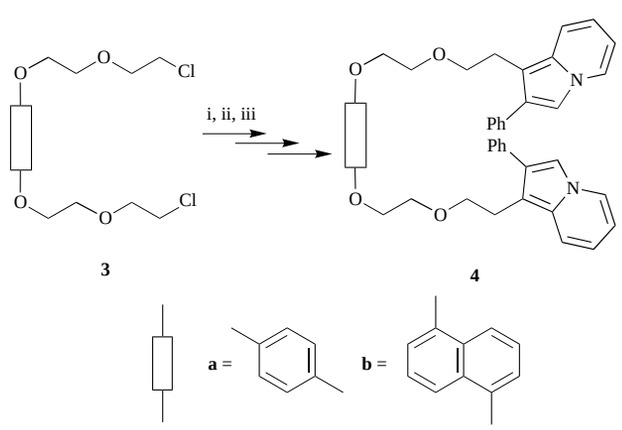
Recently we reported on the synthesis of diastereoisomeric triethylenglycol-bridged biindolizines **1** and **2** [spacer = –(CH_2-$CH_2O)_3CH_2CH_2$–].[3] One of the two isolated isomers (**1**, main product) proved to have a reversible redox system with half wave potentials (obtained by CV), corresponding to that of biindolizines reported in the literature.[7] For active host–guest interactions, especially with organic guests, the synthesized cyclophanes are not favoured because of their rather strained structure. Incorporation of 1,4-dioxyphenylene or 1,5-dioxynaphthylene ring systems should lead to larger cyclophanes, having potential as hosts for organic guests. Furthermore, a combination of the above-mentioned electron-rich aromatic π-systems with our previously investigated electron-rich biindolizines should lead to possibilities of π–π-interactions with potential guests as for example electron-deficient aromatic compounds. In addition, such dioxy aromatic compounds should allow monitoring of potential host–guest interactions both at the biindolizine system, by means of cyclic voltammetry, and the spacer site.



1 **2**

Scheme 1

The synthesis of the planned cyclophanes proceeded in close analogy to the recently described one[3] using 1,4-bis[2-(2-chloroethoxy)ethoxy]benzene **3a**[8] and the new 1,5-bis[2-(2-chloroethoxy)ethoxy]naphthalene **3b** as starting spacer materials.

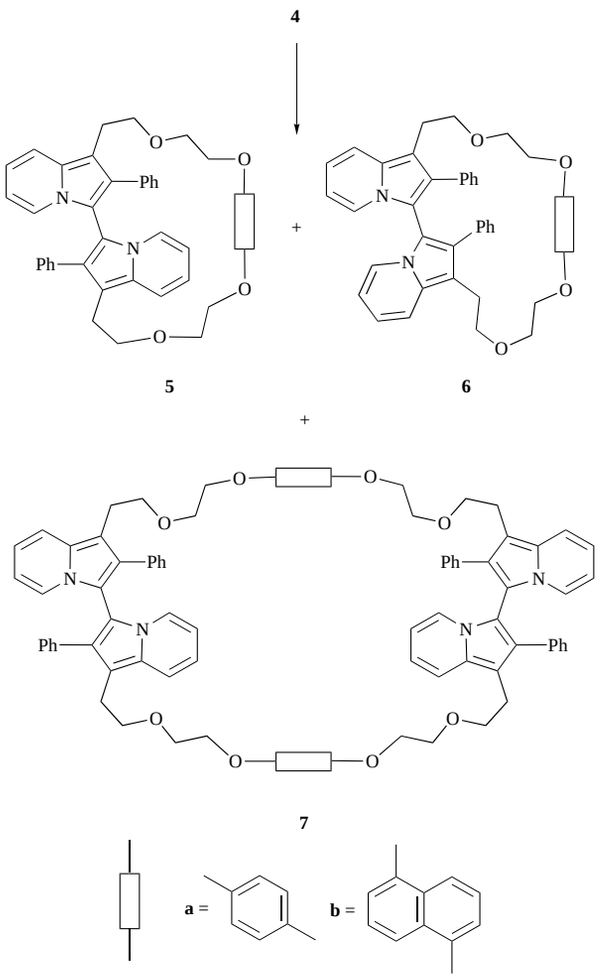


Scheme 2 *Reagents and conditions*: i, α-picoline, BuLi, Et_2O, THF, 0 °C; ii, ω-bromoacetophenone, KI, acetone, reflux; iii, $NaHCO_3$, H_2O, reflux

The desired macrocycles contain elements of chirality as a result of the ansa-chirality of cyclophanes and the reported atropisomerism of 3,3′-biindolizines. In accordance with our

previously obtained results we expected the formation of symmetrical cyclophanes of type **1** as major products and of **2** as unsymmetrical minor ones. Dependent on the dilution conditions, this intramolecular cyclisation should be accompanied by intermolecular coupling of two molecules of **4**, leading to dimers of type **7**.

Dehydrocyclisation of 0.6–0.7 mmol of the bridged biindolizines **4a** and **4b** with potassium hexacyanoferrate in ethanol–toluene (500 ml) produced diastereoisomeric mixtures of **5a** and **6a** (overall yield 62%) and **5b** and **6b** (overall yield 72%). Under these conditions the dimer compounds **7a** and **7b**



Scheme 3

were formed in yields of 13 and 6%, respectively. Compounds **7a** and **7b**, surprisingly, were formed as highly symmetric single diastereoisomers. Unfortunately, both diastereoisomeric mixtures of the desired cyclophanes **5a/6a** (1 : 10) and **5b/6b** (1 : 6) turned out to be inseparable by HPLC and other means.

Structural characterization of the cyclophanes

NMR Spectroscopy. The structure of the isolated compounds was confirmed by ^{1}H, ^{1}H COSY, GHSQC (gradient hetero single quantum coherence), GHMQC (gradient hetero multi quantum coherence) and by homodecoupling experiments. Cyclisation of starting materials **4** resulted in a strong shift of aromatic protons to higher field in the ^{1}H NMR spectra of cyclisation products **5** and **6**. This shift, seemingly, is a result of a constrained close proximity and π–π-stacking between the aromatic and the heteroaromatic ring systems inside of the cyclophanes **5** and **6**. Dimers **7** show a smaller shift of only some aromatic protons to higher field, maybe because of a better spatial separation of the different aromatic units in **7** as a direct result of the larger ring size.

The recorded ^{1}H NMR spectra of the inseparable mixtures

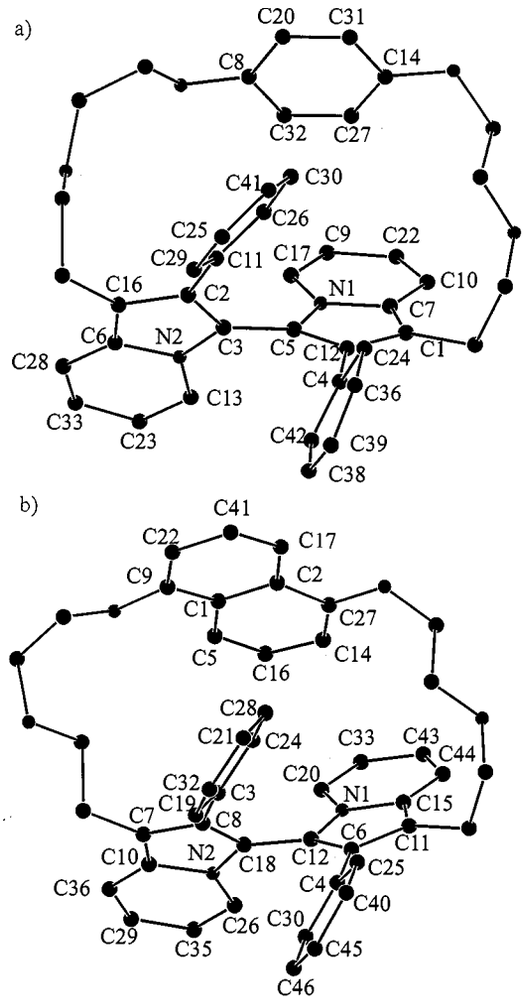


Fig. 1 Cellgraph diagrams of (a) **6a** and (b) **6b**

of **5a/6a** and **5b/6b** are rather complex. Homodecoupling experiments revealed, that in contrast to the previously obtained results[3] (**1** as major and **2** as minor isomer) the major isomers formed in this case are the unsymmetrical compounds **6**.

For dimers of type **7** two diastereoisomers are possible. The quality of the crystals obtained was not sufficient for X-ray crystallographic measurements of **7a** and **7b**. Nevertheless, from the results of NMR spectroscopy it is quite obvious, that all four indolizine units in **7a** and **7b** are equivalent and that these compounds possess the highest symmetry. The amount of the other diastereoisomer in the mother liquids of **7a** and **7b** in every case was <5% (determination by ^{1}H NMR).

X-Ray crystallographic structure analysis of compounds 6a and 6b

In order to ascertain the conformation of the main cyclisation products, we obtained the crystal structures of **6a** and **6b** by manual selection of crystals. These cyclophanes are not symmetric, because both indolizine units are located on the same site of the whole cyclophane system.

The angle between the two least-squares planes marked by the indolizine groups is 59.51° for **6a** and 55.60° for **6b**, respectively and corresponds to the angle found for unbridged 3,3′-biindolizines. This means, that steric problems play only a secondary role during cyclisation and that in contrast to the formation of **1** and **2**, in the case of **5** and **6** the statistically favoured latter conformation is preferred. The appropriate angle for the unsymmetrical diastereoisomer of type **2** [spacer = $-(CH_2CH_2O)_3CH_2CH_2-$] was 108°.[3] According to these results the longer bridges in **6a** and **6b** allow a normal position of the

indolizine units each to the other. Therefore the observed π–π-stacking in ^{1}H NMR spectra should not be the primary result of an abnormal tension within the cyclophane ring.

One of the main purposes of the structural study was to determine the intramolecular distances between the C–C bond, connecting the two indolizine units, and the 1,4-dioxyphenylene or 1,5-dioxynaphthylene rings on the opposite site, respectively. The values of these distances are for **6a** 5.13 Å [C(3)–C(8)] and 5.48 Å [C(5)–C(14)]. Similar distances in **6b** amounted 5.14 Å [C(12)–C(27)] and 5.47 Å [C(18)–C(1)]. From the observed distances the incorporation of small electron-deficient guest molecules into the cyclophane hosts **6a** and **6b** seemed feasible, also with regard to a possible 'enlargement' of the cavity due to a host–guest interaction. For the appropriate dimers **7a** and **7b** an interaction with bulkier guests was expected.

Cyclic voltammetry

Cyclic voltammetry (CV) was employed to study the redox behaviour of the prepared compounds and to detect possible host–guest interactions. The redox behaviour of the isolated cyclophanes **5a/6a**, **5b/6b**, **7a** and **7b** was investigated with a voltage sweep rate of 0.1 V s^{-1}. We were not able to differentiate between the electrochemical behaviour of the single diastereoisomers in mixtures **5a/6a** or **5b/6b**. As reported previously,[3] the EE-mechanisms for diastereoisomers were similar. Only in the case where one of the diastereoisomers was able to undergo an EC-mechanism (for example at lower sweep rates) was the electrochemistry changed significantly. We found no evidence for an EC-mechanism of our cyclophanes on carrying out several multi-sweep experiments.

Half-wave potentials of the redox waves of diastereoisomeric mixtures **5/6** and of pure dimers **7** (see Table 1) were obtained by averaging the cathodic and anodic peak potentials.[9] Cyclic voltammograms recorded in the solvent–electrolyte systems CH_2Cl_2–tetrabutylammonium hexafluorophosphate (TBAHFP) or CH_3CN–TBAHFP for **5a/6a**, **5b/6b**, **7a** and **7b** (Fig. 2) in the voltage range 0–1 V showed two stable reversible one-electron oxidation steps at approximately $E^{I}_{\frac{1}{2}} = 0.5$ V and $E^{II}_{\frac{1}{2}} = 0.9$ V. That means, every cyclophane in this part of the cyclovoltammogram displayed the typical redox behaviour of the incorporated biindolizine units.[7]

One additional reversible oxidation step around 1.4 V was found for the mixture of **5a** and **6a** and for the pure diastereoisomer **7a** (see Fig. 2a), which is in accordance with the reported reversible one-electron oxidation potential for the production of a cation radical from hydroquinone ether systems.[11,12] The peak separation for anodic and cathodic processes of the monomeric mixture **5a/6a** and of dimer **7a** ΔE_p was in the range 71–96 mV. The deviations from the theoretically expected value (59 mV) for a reversible redox reaction are explained by distortions due to solution resistance effects and electronic smoothing of data. The ratio of the appropriate peak currents was close to 1 for all three oxidation steps.

Cyclic voltammograms of the cyclophanes with dioxynaphthylene bridges in dichloromethane differ from those with dioxyphenylene bridges especially in the electrochemical behaviour of the appropriate donor bridges (see Fig. 2b). The third oxidation step for **5b/6b** is irreversible. For tetrathiafulvalene-based redox-active cyclophanes with a similar bridge a reversible oxidation step was reported in the literature.[7] In addition, the cyclic voltammogram of the mixture **5b/6b** in CH_2Cl_2–TBAHFP displays a small superimposed reversible redox step in the region of the first half-wave potential. This system is not present in the oxidation wave during the first scan and must be a result of additional processes.

The irreversibility of the third oxidation step for **5b/6b** is a result of a strong interaction between the 1,5-dioxynaphthylene unit and the biindolizine switch. This interaction becomes evident by pointing out major differences between the first and all following scans of **5b/6b** (Fig. 3a). The peak potential for the third oxidation step of the first scan amounts to 1329 mV. All consecutive scans show a potential of 1370 mV, that means, we observe here a shift of 41 mV for one and the same peak potential. The reduction cycles are similar for all three measured scans, but the peak separation (ΔE_p value) for the formal redox wave E^{II} amounts already to 131 mV and for E^{I} now a superimposed redox step is visible. The first oxidation of the 1,5-dioxynaphthylene spacer unit causes a change in the redox behaviour of the whole cyclophane system of **5b/6b**, which is permanent for all consecutive redox circles in CV.

Dimer **7b** (Fig. 2b) displays four reversible oxidation steps at approximately 0.5, 0.8, 1.0 and 1.2 V, the last two with significantly lower intensities (peak currents). We can only speculate on the nature of this phenomenon. The size of the molecule and the intensity of redox waves $E^{III}_{\frac{1}{2}}$ and $E^{IV}_{\frac{1}{2}}$ in comparison with $E^{I}_{\frac{1}{2}}$ and $E^{II}_{\frac{1}{2}}$ indicate the possibility of an intramolecular stacking of the two dioxynaphthylene units causing here a stepwise oxidation and reduction process of two single dioxynaphthylene bridges, whereas the redox processes for the two biindolizine units isolated from each other proceed simultaneously.

Table 1 Half-wave potentials $E_{\frac{1}{2}}$/V obtained by cyclic voltammetry in CH_2Cl_2 sweeping with 0.1 V s^{-1} (second scan)

	$E^{I}_{\frac{1}{2}}$	$E^{II}_{\frac{1}{2}}$	$E^{III}_{\frac{1}{2}}$	$E^{IV}_{\frac{1}{2}}$
5a/6a	0.54	0.92	1.46	
5b/6b	0.50[a]	0.83	1.37[b]	
7a	0.49	0.81	1.37	
7b	0.47	0.76	0.99	1.21
9	0.57	0.91		

[a] Cathodic peak potential (two superimposed reduction peaks with maximum at 0.23 V due to additional electrochemical reaction during reduction process. [b] Irreversible.

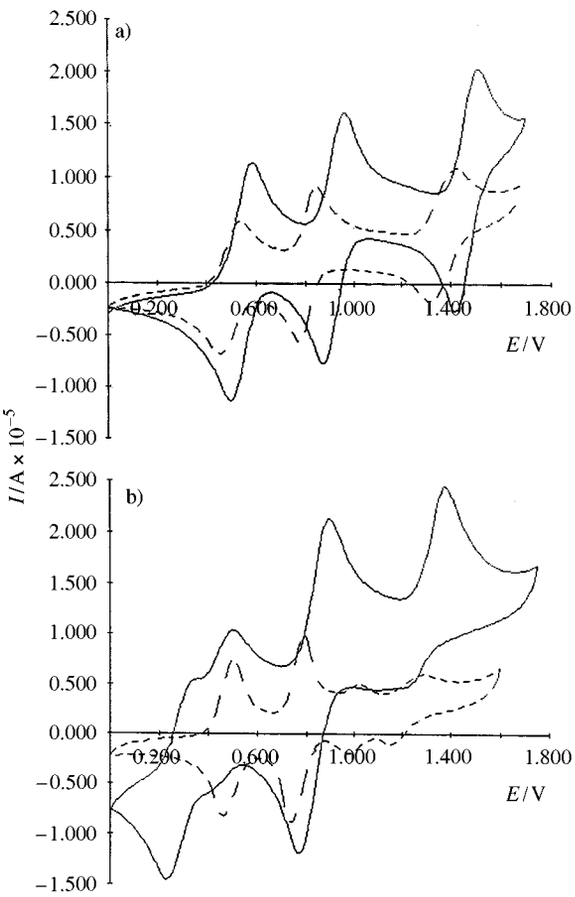


Fig. 2 Cyclic voltammograms of (a) **5a/6a** (6 mg) (solid line) and **7a** (6 mg) (dashed line) and (b) **5b/6b** (6 mg) (solid line) and **7b** (6 mg) (dashed line) in CH_2Cl_2 (20 ml)–0.1 M TBAHFP sweeping with 0.1 V s^{-1}

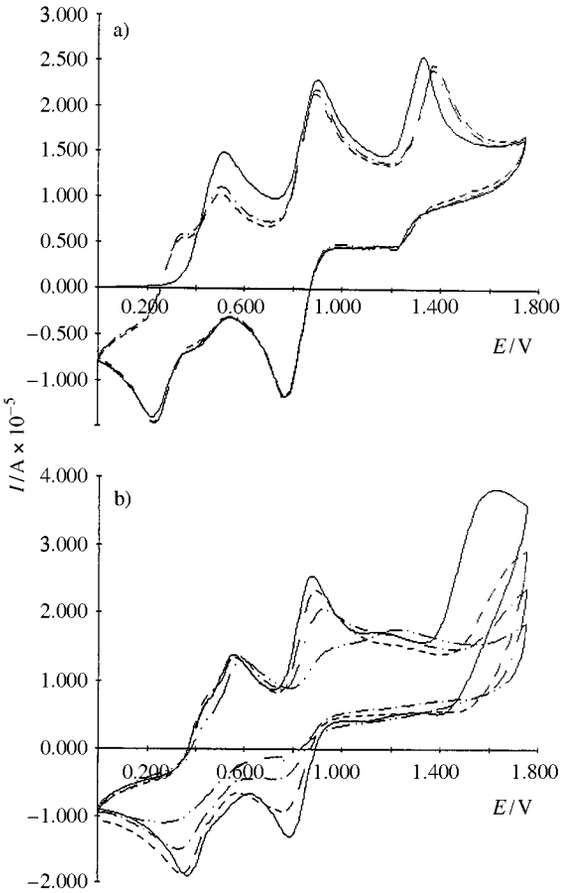


Fig. 3 Cyclic voltammograms of **5b/6b** (13 mg) in (a) CH_2Cl_2 (20 ml)–0.1 M TBAHFP in a multisweep ($v = 0.1$ V s^{-1}) experiment (three scans without delay): 1 scan (solid line), 2 scan (dashed line) and 3 scan (dotted line); and (b) Me_3CN (20 ml)–0.1 M TBAHFP (solid line) and addition of 1 equiv. (– – –), 2 equiv. (–·–·) and 3 equiv. (–··–··) 2,4,7-trinitrofluoren-9-one

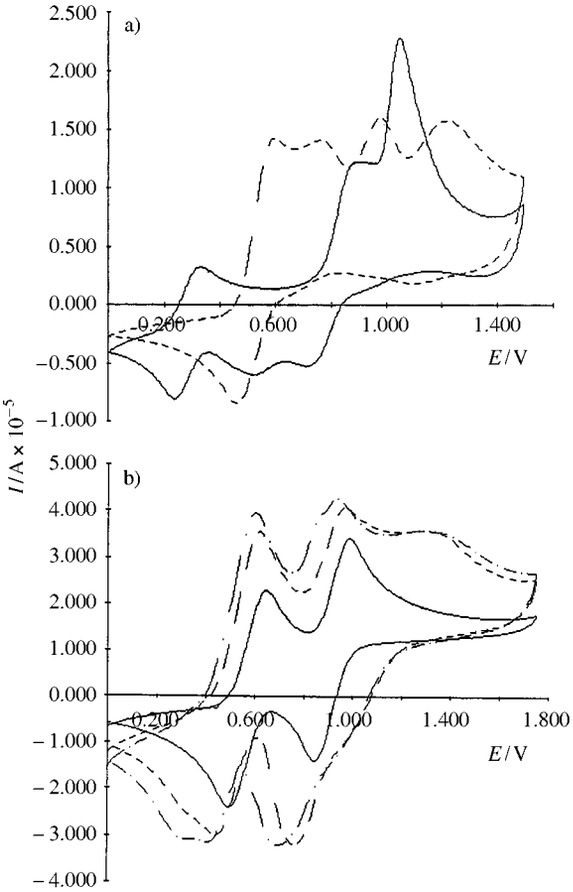
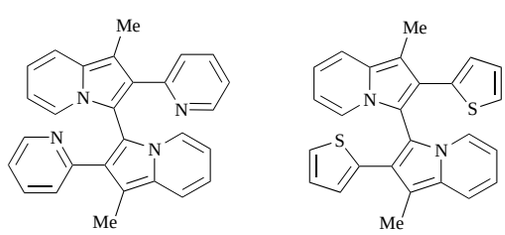


Fig. 4 Cyclic voltammograms of (a) **8** (11 mg) (dashed line), **8** and one equiv. of tetrakis(acetonitrile)copper(I) hexafluorophosphate $(Me_3CN)_4CuHFP$ (solid line) and (b) **9** (7 mg) (—), and addition of 1 mg (– – –) and 2 mg (–·–·) $(Me_3CN)_4CuHFP$ in CH_2Cl_2 (20 ml)–0.1 M TBAHFP

During CV-investigations potential electron-deficient host compounds of various sizes such as nitromethane, malononitrile, ethyl nitroacetate, nitrobenzene, 2,4,7-trinitrofluoren-9-one (TNF) and others were added. From X-ray structure analysis (monomers **6a** and **6b**) and molecular modelling (dimers **7**) it was clear, that only cyclophanes **7** are able to host the large TNF. There was no evidence for any host–guest interaction for dimers **7a** and **7b**. Surprisingly, addition of 1–4 equivalents TNF to a solution of **5b/6b** in acetonitrile caused a continuous decrease and shift of the irreversible oxidation wave of the dioxynaphthylene unit as well as of the second oxidation step of the biindolizine system (see Fig. 3b). Addition of TNF to a solution of **5a/6a** resulted only in minor changes in the intensity of the redox wave of the 1,4-dioxyphenylene spacer unit. For **5b/6b** a complexation 'from outside' must be taken into account.

To investigate the effect of a complexation near to the biindolizine system, compounds **8** and **9** were synthesized by dimerisation of 1-methyl-2-(2-pyridyl)- and 1-methyl-2-(2-thienyl)-indolizine, respectively. The starting materials were prepared in close analogy to the reported synthesis of 2-(2-pyridyl)indolizine.[13] Dimerisation of this compound, not possessing a substituent in the 1-position, should not give a reversible redox system in CV.[14]

Complex formation *via* the two pyridyl-nitrogens of **8** or of the sulfur atoms in **9** should have an immediate impact on the biindolizine redox systems. CV measurements disappointingly revealed that **8** shows a non-reversible system without the redox waves, typically found for 2-phenyl or 2-methyl substituted biindolizines. But, as expected, dramatic changes in CV occur upon addition of tetrakis(acetonitrile)copper(I) hexafluorophosphate $(MeCN)_4CuHFP$, suggesting the formation of a pyridyl–N–Cu-complex (Fig. 4a).[15] We tried to quaternize the pyridyl-nitrogens of compound **9** with methyl iodide. The idea was 'to block' those nitrogens from disturbing the biindolizine-based two-step redox system. CV measurements of the resulting diiodide[16] in the system CH_2Cl_2–TBAHFP showed a reorganisation of the oxidation part of the redox system. In contrast to the electrochemical behaviour of 2,2′-dipyridyl-substituted **8**, 2,2′-dithienyl-substituted biindolizine **9** displayed the classical reversible two-step redox system (Fig. 4b). Addition of $(MeCN)_4CuHFP$ resulted in a stepwise change of the plot. The complexation process was accompanied by a colour change of the solution from pale green (pure **9**) to red–brown [addition of $(MeCN)_4CuHFP$] and can be monitored by ^1H NMR measurements (shift and widening of lines), too.



8 **9**

Conclusion

Macromolecules **5**, **6** and **7** have been synthesized as potential host molecules to form complexes with various electron-

deficient aromatic guest molecules by interactions between them and the electron-rich centres of the heterocyclic biindolizine systems or the aromatic dioxy spacer units. In addition, the aim was to control a possible host–guest interaction by means of electrochemical switching (CV). Compounds **5b/6b** with a dioxynaphthylene unit showed a remarkable change in the cyclic voltammetrical behaviour upon addition of TNF. Biindolizine **8** with 2-pyridyl-units in the 2-position interacted with $(MeCN)_4CuHFP$ to form a stable complex, but the starting material **8** itself displayed irreversible electrochemical reactions. In contrast, the stable reversible two-step redox system of the 2-thienyl-substituted derivative **9** changed only upon addition of $(MeCN)_4CuHFP$. Now work is under progress to synthesize biindolizines, which are substituted with heterocycles in the 2-position as complexation groups. An investigation of cyclophanes, based on such biindolizines, would be of interest.

Experimental

Methods

NMR data were recorded with a UNITY plus-500 spectrometer and shifts are given in ppm (internal standard TMS, coupling constants *J* are given in Hz and were taken directly from the spectra obtained). The assignments were carried out by various 2D NMR methods (H,H COSY; HSQC and HMQC) by using indirect detection and gradient techniques. Mass spectra were run on a Hewlett Packard 5985 B machine. Microanalyses were performed with a Carlo Erba Elemental Analyzer 1106. Melting points are uncorrected (Boetius apparatus). TLC was carried out on plastic plates coated with silica gel 60 F_{254} (5735) (MERCK) and chromatography on MERCK silica gel 60 (7731).

Cyclic voltammetry

Cyclic voltammetric measurements were carried out with a METROHM PGSTAT 20 potentiostat and a three-electrode single compartment cell. The working electrode was a platinum disk of 3 mm diameter, the counter electrode was a glassy carbon electrode and the reference electrode assembly was Ag/AgCl/0.1 mol dm^{-3} LiCl–ethanol/fine porosity glass disk/0.1 mol dm^{-3} Bu_4NPF_6 acetonitrile/fine porosity glass disk when the employed electrolytic solvent was acetonitrile (FLUKA, selectophore quality) or Ag/AgCl/0.1 mol dm^{-3} LiCl–ethanol/fine porosity glass disk/LiCl–ethanol/fine porosity glass disk when the employed electrolytic solvent was dichloromethane (HPLC grade). Both electrolytic solvents contained 0.1 mol dm^{-3} tetrabutylammonium hexafluorophosphate TBAHFP. Solutions were deaerated by bubbling argon through them prior to each experiment which was run under an argon atmosphere.

Materials

1,5-Bis[2-(2-chloroethoxy)ethoxy]naphthalene 3b. A suspension of 1,5-dihydroxynaphthalene (8.0 g, 50 mmol) and K_2CO_3 (20.7 g, 150 mmol) in 2,2′-dichlorodiethyl ether (88 ml, 0.75 ml) was refluxed for 70 h. The suspension was then diluted with dichloromethane after which insoluble material was filtered off and washed with dichloromethane. The combined filtrate and washings were evaporated under reduced pressure and the residual oily residue was chromatographed on silica gel with hexane–ethyl acetate (3:1) to yield (R_f 0.24) **3b** (5.4 g, 29%), mp 94–98 °C (toluene) (Found: C, 58.15; H, 5.92. $C_{18}H_{22}Cl_2O_4$ requires C, 57.91; H, 5.95); δ_H($CDCl_3$–TMS) 7.86 (2 H, d, *J* 8.0), 7.36 (2 H, t, *J* 8.0), 6.85 (2 H, d, *J* 8.0), 4.30 (2 H, t, *J* 4.8), 4.02 (2 H, t, *J* 4.8), 3.91 (2 H, t, *J* 5.8) and 3.68 (2 H, t, *J* 5.8); δ_C($CDCl_3$–TMS) 154.3, 126.8, 125.1, 114.7, 105.8, 71.7, 69.9, 68.0 and 42.9; *m/z* (FAB) 372 (M^+, 100%. $C_{18}H_{27}O_4Cl_2$ requires 372) and 252 (30%).

1,4-Bis[6-(2-phenylindolizin-1-yl)-1,4-dioxahexyl]benzene 4a. To α-picoline (3.26 ml, 33 mmol) in diethyl ether (40 ml) (ice cooling, argon atmosphere) within 15 min was added butyllithium (1.6 M; 20.6 ml, 33 mmol). The dark red solution was stirred for an additional 45 min after which a solution of **3a** (4.85 g, 15 mmol) in THF (60 ml) was added to it. Stirring was continued at room temperature for 4 h after which the solution was kept overnight under argon. It was then treated with water (1 ml) and evaporated under reduced pressure. The oily residue was partitioned between toluene and water. After separation, the organic layer was dried ($MgSO_4$) and evaporated under reduced pressure; subsequently evaporation at 100 °C 17–20 mm for 1 h removed traces of unchanged α-picoline. The clear brown oil was dissolved in acetone (100 ml) to which KI was added. The solution was heated under reflux and whilst 2-bromoacetophenone (6 g, 30 mmol) in acetone (50 ml) was added to it over 90 min. Heating under reflux was continued for 10 h, after which the mixture was evaporated under reduced pressure. The solid residue was refluxed and vigorously stirred in a mixture of water (150 ml) containing $NaHCO_3$ (11 g) and toluene (80 ml) for 1 h. After cooling of the mixture, the organic phase was separated, washed with water (× 2), dried ($MgSO_4$) and evaporated under reduced pressure to afford a black oil. This was chromatographed on silica gel with hexane–ethyl acetate (3:1) to afford [R_f 0.44 (hexane–ethyl acetate, 2:1)] **2a** as yellow crystals (1.16 g, 14%), mp 60–67 °C (benzene) (Found: C, 78.79; H, 6.29; N, 4.94. $C_{42}H_{40}N_2O_4$ requires C, 79.21; H, 6.34; N, 4.40); δ_H([$^2H_6$]-DMSO–TMS) 8.12 (2 H, d, *J* 7.1), 7.58 (2 H, s), 7.47 (4 H, m), 7.41 (2 H, d, *J* 9.1), 7.36 (4 H, t, *J* 7.6), 7.25 (2 H, t, *J* 7.6), 6.76 (4 H, s), 6.58 (2 H, ddd, *J* 9.1, 6.4, 0.9), 6.45 (2 H, d of t, *J* 6.7, 1.2), 3.90 (2 H, t, *J* 4.6), 3.59 (2 H, t, *J* 4.6), 3.51 (2 H, t, *J* 7.3) and 3.02 (2 H, t, *J* 7.3); δ_C($CDCl_3$–HMDS) 153.1, 135.8, 131.3, 129.4, 128.9, 128.5, 126.5, 124.8, 117.7, 116.2, 115.5, 110.3, 106.5, 72.1, 69.3, 68.1 and 24.8; *m/z* (CI) 637 (M + H^+, 100%). $C_{42}H_{40}N_2O_4$ requires 636).

1,5-Bis[6-(2-phenylindolizin-1-yl)-1,4-dioxahexyl]naphthalene 4b. Starting from **3b** compound **4b** was synthesized following a similar procedure to that described above for **4a**: brownish crystals (1.60 g, 11%), mp 151–156 °C (toluene), R_f 0.29 (hexane–ethyl acetate, 3:1) (Found: C, 80.24; H, 6.04; N, 3.63. $C_{46}H_{42}N_2O_4$ requires C, 80.43; H, 6.18; N, 4.08); δ_H($CDCl_3$–TMS) 7.83 (4 H, m), 7.50 (4 H, m), 7.39 (6 H, m), 7.28 (6 H, m), 6.80 (2 H, d, *J* 7.6), 6.58 (2 H, m), 6.41 (2 H, d of t, *J* 6.7, 0.9), 4.22 (4 H, t, *J* 4.9), 3.88 (4 H, t, *J* 4.9), 3.73 (4 H, t, *J* 7.5) and 3.21 (4 H, t, *J* 7.5); δ_C($CDCl_3$–TMS) 154.4 (s), 135.9 (s), 131.4 (s), 129.5 (s), 128.9 (d), 128.5 (d), 126.9 (s), 126.5 (d), 125.0 (d), 124.8 (d), 117.7 (d), 116.2 (d), 114.7 (d), 110.4 (d), 110.3 (d), 106.7 (s), 105.8 (d), 72.3 (t), 69.3 (t), 67.9 (t) and 25.0 (t); *m/z* (MALDI) 688 (100%), 686 (M^+, 39%. $C_{46}H_{42}N_2O_4$ requires 686).

1,1′-[1,4-Bis(2-ethoxyethoxy)phenylene]-2,2′-diphenyl-3,3′-biindolizine 5a/6a and cyclobis{1,1′-[1,4-bis(2-ethoxyethoxy)-phenylene]-2,2′-diphenyl-3,3′-biindolizine} 7a. A mixture of ethanol (250 ml), 60% $HClO_4$ (6 ml), NEt_3 (9 ml) and K_3FeCN_6 (10 g) was stirred for 5 min, after which **4a** (408 mg, 0.64 mmol) and toluene (250 ml) were added to it. The resulting suspension was stirred for 7 days at room temperature after which it was evaporated under reduced pressure and the solid residue was dissolved in dichloromethane–water. After separation, the organic layer was dried ($MgSO_4$) and evaporated. Column chromatography of the residue on silica gel with hexane–ethyl acetate (6:1) to yield (R_f 0.25) **5a/6a** as an inseparable mixture (253 mg, 62%) of yellow crystals, mp 236–244 °C (toluene; after recrystallisation no change in diastereoisomeric composition). The column was further eluted with hexane–ethyl acetate (2:1) to give (R_f 0.08) **7a** (52 mg, 13%) as a white solid, mp 197–202 °C (toluene); **5a/6a** (diastereoisomeric mixture) (Found: C, 79.16, H, 5.94; N, 4.23. $C_{42}H_{38}N_2O_4$ requires C, 79.46; H, 6.05; N, 4.41); δ_H([$^2H_6$]-DMSO–HMDS, homodecoupling experiments) 7.70 (d, *J* 9.3, **6a**), 7.57 (d, *J* 9.3, **6a**), 7.34 (d, *J* 9.3, **6a**), 7.28 (d, *J* 6.8, **6a**), 7.04 (m, **5a/6a**), 6.97 (m, **5a/6a**), 6.91–6.71 (m, **5a/6a**), 6.66 (d of t, *J* 5.6, 1.1, **6a**), 6.49 (t, *J* 7.6, **6a**), 6.46 (s, **6a**), 6.42 (m, **5a**), 6.28 (d, *J* 8.8, **6a**), 6.23 (d, *J*

6.8, **6a**), 6.06 (m, **6a**), 5.90 (d of t, *J* 6.7, 1.2, **5a**), 5.58 (d, *J* 7.3, **6a**), 3.98 (m), 3.87 (t, *J* 6.8), 3.75 (t, *J* 4.9), 3.55 (m) and 3.44–2.80 (m); δ_C([$^2H_6$]-DMSO–HMDS) 152.4 (s), 151.7 (s), 151.2 (s), 135.0 (s), 134.7 (s), 134.4 (s), 132.3 (s), 130.7 (s), 130.5 (s), 129.5 (s), 129.0 (d), 128.9 (d), 128.4 (s), 128.2 (d), 128.1 (d), 127.1 (d), 127.0 (d), 126.0 (d), 125.3 (d), 124.8 (d), 123.6 (d), 123.3 (d), 122.2 (d), 119.1 (d), 117.8 (d), 116.8 (d), 116.3 (d), 116.2 (d), 116.0 (d), 115.8 (d), 115.6 (d), 114.3 (s), 114.2 (d), 113.4 (d), 113.3 (d), 112.6 (s), 111.4 (d), 111.1 (d), 110.7 (s), 110.5 (s), 109.3 (d), 109.0 (s), 108.7 (s), 108.3 (s), 72.3 (t), 70.9 (t), 69.3 (t), 68.8 (t), 68.1 (t), 68.0 (t), 67.9 (t), 67.3 (t), 65.5 (t), 25.1 (t), 24.9 (t) and 24.5 (t) [Found (HRMS/FAB): *m*/*z* 634.2825. Calc. for $C_{42}H_{38}N_2O_4$: 634.2832]. Compound **7a** (Found: C, 79.23, H, 5.97; N, 4.26 $C_{84}H_{76}N_4O_8$ requires C, 79.46; H, 6.05; N, 4.41); δ_H([$^2H_6$]-DMSO–TMS) 7.49 (4 H, d, *J* 9.2), 7.15 (4 H, m), 7.04 (12 H, br s), 6.93 (8 H, m), 6.71 (8 H, br s), 6.63 (4 H, m), 6.32 (4 H, m), 3.89 (8 H, t, *J* 4.2), 3.56 (16 H, m) and 2.95 (8 H, t, *J* 6.6); δ_C([$^2H_6$]-DMSO–TMS/50 °C) 152.6, 134.9, 131.1, 130.9, 128.9, 127.7, 126.2, 122.3, 117.6, 117.0, 115.6, 110.77, 110.5, 107.8, 70.9, 68.6, 68.0 and 24.7; *m*/*z* (FAB) 1269 ($M + H^+$, 100%) and 423 (14%) ($C_{84}H_{76}N_4O_8$ requires 1268).

1,1′-[1,5-Bis(2-ethoxyethoxy)naphthylene]-2,2′-diphenyl-3,3′-biindolizine 5b/6b and cyclobis{1,1′-[1,5-bis(2-ethoxyethoxy)-naphthylene]-2,2′-diphenyl-3,3′-biindolizine} 7b. A mixture of ethanol (200 ml), 60% $HClO_4$ (10 ml) and NEt_3 (14 ml) was stirred for 5 min after which K_3FeCN_6 (12 g) was suspended in it. After the mixture has been stirred for a further 5 min, toluene (150 ml), **4b** (510 mg, 0.74 mmol) dissolved in toluene (100 ml) and toluene (50 ml) were added to it. Stirring was continued for 5 days. After a similar work-up to that described above for **5a/6a** and **7a** column chromatography on silica gel with heptane–ethyl acetate (3 : 1) yielded an inseparable mixture of **5b/6b** (363 mg, 72%), mp 225–231 °C (toluene; after recrystallisation no change in diastereoisomeric composition); R_f 0.67, (hexane–ethyl acetate, 1 : 1) and **7b** (30 mg, 6%); mp 227–231 °C (benzene); R_f 0.53 (hexane–ethyl acetate, 1 : 1); **5b/6b** (diastereoisomeric mixture) (Found: C, 80.63; H, 5.77; N, 3.82. $C_{46}H_{40}N_2O_4$ requires C, 80.66; H, 5.90; N, 4.09); δ_H([$^2H_6$]-DMSO–TMS) 7.76 (d, *J* 8.8), 7.59 (d, *J* 8.8), 7.50–6.38 (m), 6.20 (d, *J* 7.8), 5.91 (t, *J* 7.1), 5.86 (t, *J* 6.6), 5.62 (t, *J* 6.6), 5.06 (d, *J* 7.3), 4.33 (m), 4.13–3.95 (m) and 3.65–2.83 (m); δ_C([$^2H_6$]-DMSO–TMS) 154.37, 154.34, 154.29, 136.0, 135.8, 133.8, 131.9, 130.3, 130.1, 129.9, 129.3, 129.1, 128.8, 128.2, 127.8, 127.4, 126.7, 126.1, 125.3, 124.6, 123.5, 120.1, 118.7, 117.7, 117.5, 117.3, 115.3, 112.5, 112.3, 110.3, 108.7, 108.0, 73.9, 72.4, 72.3, 71.2, 70.8, 70.0, 69.9, 69.5, 67.9, 26.2, 26.0 and 25.5 [Found (HRMS/FAB): *m*/*z* 684.3001. Calc. for $C_{46}H_{42}N_2O_4$: 684.2988].

Compound **7b** (Found: C, 80.27; H, 5.89; N, 3.94. $C_{92}H_{80}N_4O_8$ requires C, 80.66; H, 5.90; N, 4.09); δ_H([$^2H_6$]-DMSO–TMS) 7.62 (4 H, d, *J* 8.3), 7.47 (4 H, m), 7.24 (4 H, t, *J* 8.0), 7.10 (4 H, m), 6.93 (24 H, m), 6.57 (4 H, m), 6.25 (4 H, m), 4.13 (8 H, m), 3.75 (8 H, m), 3.65 (8 H, t, *J* 6.9) and 2.97 (8 H, m); δ_C([$^2H_6$]-DMSO–TMS) 153.7, 134.7, 131.0, 130.7, 128.8, 127.7, 126.1, 126.0, 125.1, 122.2, 117.5, 116.9, 113.7, 110.6, 110.2, 107.6, 106.0, 71.0, 68.5, 67.9 and 24.7; *m*/*z* (FAB) 1368 (M^+, 100%) and 1058 (8%) ($C_{92}H_{80}N_4O_8$ requires 1368).

1,1′-Dimethyl-2,2′-di-2-pyridyl-3,3′-biindolizine 8. A mixture of 2-ethylpyridine (4.6 ml, 40 mmol), 2-acetylpyridine (2.29 ml, 20 mmol) and iodine (5.08 g, 20 mmol) was vigorously stirred at 100 °C for 8 h. After cooling the mixture was treated with water (100 ml), $NaHCO_3$ (10 g) and toluene (50 ml) and then refluxed for 2 h. After this, the organic layer was separated, washed with water, dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed on silica gel with toluene–ethyl acetate (2 : 1) to yield (R_f 0.58) a clear greenish oil (1 g), of 1-methyl-2-(2-pyridyl)indolizine. This oil dissolved in toluene (100 ml) was added to a vigorously stirred suspension of K_3FeCN_6 (12 g) in ethanol (250 ml), 60% $HClO_4$ (10 ml) and NEt_3 (14 ml). Stirring was continued for 2 days after which the mixture was evaporated under reduced pressure. The resulting residue was partitioned between CH_2Cl_2 and water. The organic layer was separated, washed with water, dried and evaporated. Column chromatography of the residue on silica gel with toluene–ethyl acetate (2 : 1) yielded (R_f 0.37) yellow–green crystals (384 mg, 18%), mp 221–223 °C (toluene) (Found: C, 81.61; H, 5.41; N, 13.12. $C_{28}H_{22}N_4$ requires C, 81.12; H, 5.36; N, 13.52); δ_H($CDCl_3$–TMS) 8.59 (2 H, t of d, *J* 4.6 and 0.9), 7.35 (6 H, m), 7.00 (2 H, dd, *J* 7.0 and 5.3), 6.23 (2 H, t, *J* 6.7) and 2.58 (6 H, br s); δ_C($CDCl_3$–TMS) 155.1 (s), 149.2 (d), 136.0 (d), 131.8 (s), 128.9 (s), 123.2 (d), 122.8 (d), 120.7 (d), 117.6 (d), 116.7 (d), 111.5 (s), 110.6 (d), 108.2 (s) and 9.9 (q); *m*/*z* (FAB) 415 ($M + H^+$, 100%), 336 (12%) and 207 (23%) ($C_{28}H_{22}N_4$ requires 414).

1,1′-Dimethyl-2,2′-di-2-thienyl-3,3′-biindolizine 9. A mixture of 2-acetylthiophene (2.15 ml, 20 mmol), 2-ethylpyridine (4.6 ml, 40 mmol) and iodine (5.08 g, 20 mmol) was refluxed for 9 h. After cooling, the mixture was treated with water (100 ml), $NaHCO_3$ (10 g) and toluene (50 ml) and then was refluxed for 2 h. The dark aqueous phase was then separated and extracted with toluene (3 × 50 ml). The combined organic phases were washed with water, dried ($MgSO_4$) and added to a vigorously stirred suspension of K_3FeCN_6 (10 g) in ethanol (250 ml), 60% $HClO_4$ (10 ml) and NEt_3 (14 ml). Stirring was continued for 3 days at room temperature after which the mixture was evaporated under reduced pressure. The resulting residue was partitioned between CH_2Cl_2 and water. The organic layer was separated, washed with water, dried and evaporated. Column chromatography of the residue on silica gel with toluene yielded (R_f 0.9) yellow crystals (150 mg, 2%), mp 178–188 °C (methanol) (Found: C, 73.17; H, 4.70; N, 6.37. $C_{26}H_{20}N_2S_2$ requires C, 73.54; H, 4.76; N, 6.60); δ_H($CDCl_3$–TMS) 7.42 (2 H, t of d, *J* 9.1 and 1.0), 7.25 (2 H, m), 7.05 (2 H, dd, *J* 4.8 and 1.2), 6.80 (4 H, m), 6.68 (2 H, ddd, *J* 9.0, 6.4 and 1.0), 6.28 (2 H, d of t, *J* 6.8 and 1.2) and 2.60 (6 H, s); δ_C($CDCl_3$–TMS) 136.8, 131.9, 126.8, 124.8, 124.7, 124.2, 122.8, 117.1, 117.0, 110.4, 109.7, 106.5 and 10.5 [Found (HRMS/FAB): *m*/*z* 424.1065. Calc. for $C_{26}H_{20}N_2S_2$: 424.1068].

Crystal data for 6a

$C_{42}H_{38}N_2O_4$, $M = 634.77$, monoclinic, $a = 17.850(4)$, $b = 9.697(4)$, $c = 19.522(4)$ Å, $\beta = 99.76(2)°$, $V = 3330.0(2)$ Å^3 (by least squares refinement on diffractometer angles of 25 automatically centered reflections), $\lambda = 0.710\ 73$ Å, $T = 295$ K, space group $P2_1/n$, $Z = 4$, $D_x = 1.266$ g cm^{-3}, colourless plate-like crystals, 0.30 × 0.20 × 0.10 mm, μ(Mo-Kα) = 0.081 mm^{-1}.

Data collection and processing. CAD4 diffractometer, ω–2θ scans, graphite monochromated Mo-Kα X-radiation; 3226 reflections measured ($2\theta_{max} = 40°$), 3094 unique (merging $R = 0.0266$), 1692 with $F \geqslant 4\sigma(F)$, and all 3094 were retained in all calculations. No crystal decay was observed. Data were corrected for Lorentz and polarization effects, but not for absorption.

Structure solution and refinement. Solution with direct methods using SHELXS-86.[17] Refinement by full-matrix least squares on F^2 using SHELXL-93[18] with all non-H atoms anisotropic, all hydrogen atoms were located geometrically and refined using a riding model $w = 1/[\sigma^2(F_o^2) + (0.0942P)^2]$, $P = (F_o^2 + 2F_c^2)/3$, final R_1 [$F \geqslant 4\sigma(F)$] = 0.0649, $wR_2 = 0.1890$. Goodness-of-fit parameter = 1.146 for 436 parameters, extinction correction refined to 0.0007, residual electron densities +0.33/−0.20 e A^{-3}. Fig. 1 was produced using program CELLGRAPH.[19]

Crystal data for 6b

$C_{46}H_{40}N_2O_4 \cdot 2CH_3OH$, $M = 748.88$, triclinic, $a = 12.268(2)$, $b = 12.586(3)$, $c = 14.059(3)$ Å, $\alpha = 112.28(3)$, $\beta = 102.92(3)$, $\gamma = 91.87(3)°$, $V = 1941.2(7)$ Å^3 (by least squares refinement on

diffractometer angles of 25 automatically centered reflections), $\lambda = 0.710\ 73$ Å, $T = 295$ K, space group $P\bar{1}$, $Z = 2$, $D_x = 1.281$ g cm^{-3}, colourless plate-like crystals, $0.25 \times 0.40 \times 0.15$ mm, μ(Mo-Kα) = 0.084 mm^{-1}.

Data collection and processing. CAD4 diffractometer, ω–2θ scans, graphite monochromated Mo-Kα X-radiation; 3855 reflections measured ($2\theta_{max} = 40°$), 3625 unique (merging $R = 0.0976$), giving 1891 with $F \geqslant 4\sigma(F)$, and all 3625 were retained in all calculations. No crystal decay was observed. Data were corrected for Lorentz and polarization effects, but not for absorption.

Structure solution and refinement. Solution with direct methods using SHELXS-86.[17] Refinement by full-matrix least squares on F^2 using SHELXL-93[18] with all non-H atoms anisotropic, all hydrogen atoms (except those of the disordered CH_3OH molecules) were located geometrically and refined using riding model $w = 1/[\sigma^2(F_o^2) + (0.1061P)^2]$, $P = (F_o^2 + 2F_c^2)/3$, final R_1 [$F \geqslant 4\sigma(F)$] = 0.055, $wR_2 = 0.1955$. Goodness-of-fit parameter 1.035 for 508 parameters, extinction correction refined 0.010, residual electron densities +0.23/−0.22 e A^{-3}.

Full crystallographic details for **6a** and **6b**, excluding structure factor tables, have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc.*, *Perkin Trans. 1*, available *via* the RSC Web pages (http://chemistry.rsc.org/rsc/p1pifa.htm). Any request to the CCDC for this material should quote the full literature citation and the reference number 207/163.

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15 In another experiment, **8** (195 mg, 0.47 mmol) dissolved in methanol (50 ml) was treated with tetrakis(acetonitrile)copper(I) hexafluorophosphate (93 mg, 0.25 mmol). After storage overnight, the mixture provided a dark yellow precipitate which was filtered off and washed several times with boiling methanol. The solid had mp ⩽ 360 °C. The cyclic voltammogram of this compound in dichloromethane was similar to that obtained as mentioned in the text [addition of tetrakis(acetonitrile)copper(I) hexafluorophosphate to a solution of **8**].
16 Compound **8** (50 mg) was refluxed in methyl iodide (1 ml) for 3 h after which diethyl ether was added to the mixture. The solid was filtered off and washed several times with diethyl ether. The yield was almost quantitative: red–orange crystals, mp 265–275 °C (decomp.) (Found C, 49.1; H, 4.0; N, 7.6. $C_{30}H_{28}N_4I_2$ requires C, 51.6; H, 4.0; N, 8.0%).
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