Preparation of Nitrogen-Containing 25-Membered Pentaolefinic Macrocycles: (*E*,*E*,*E*,*E*,*E*)-1,6,11,16,21-Penta(arylsulfonyl)-1,6,11,16,21-pentaazacyclopentacosa-3,8,13,18,23-pentaenes

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Dedicated to Prof. Marcial Moreno-Mañas on the occasion of his 63rd birthday.

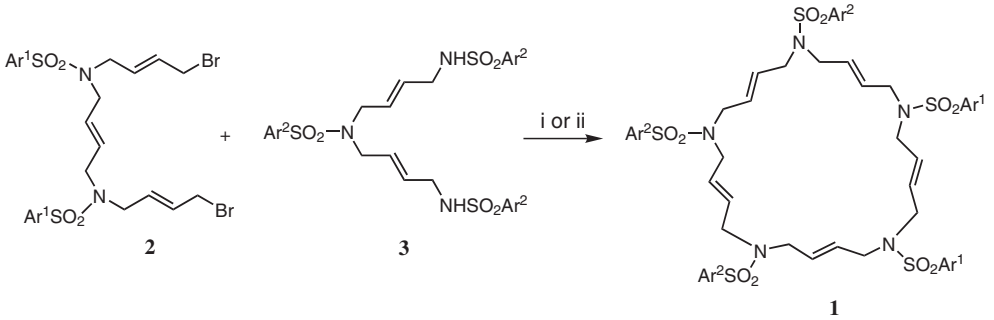
Abstract: A stepwise preparation of a series of nitrogen-containing 25-membered pentaolefinic macrocycles is presented. The corresponding arenesulfonamides and *trans*-1,4-dibromo-2-butene served as precursors for the synthesis.

Key words: alkenes, heterocycles, macrocycles, sulfonamides

Nitrogen-containing 25-membered macrocycles are relatively frequent.[1,2] However, nitrogen-containing macrocycles of this size with endocyclic olefinic double bonds are uncommon. 25-Membered macrocycles featuring five -N-C-C-C-C- units in any pattern of substitution or degree of unsaturation are even rarer. We have reported[3,4] the formation of complex mixtures of 10-, 15- and 20-membered macrocycles by non-selective Pd(0)-catalyzed allylation of arenesulfonamides with *cis*-2-butene-1,4-diol dicarbonate; minor amounts of 25-membered ring compounds being also detected in those mixtures. A bibliographic search showed that only the aforementioned 25-membered macrocycles have been reported[3,4] with olefinic bonds in these units, and that five of those endocyclic saturated units (1,6,11,16,21-pentaazacyclopentacosane moieties) are found in synthetic cyclopeptides and derivatives.[5]

We have described[6] the synthesis, coordination properties and catalytic activity [in the case of the Pd(0) complexes] of the nitrogen-containing triolefinic 15-membered macrocycles. As the intermediates required for the different final cyclisation steps leading to 15-membered rings are efficiently obtained in terms of yield and simplicity, we considered the possibility of preparing related 25-membered rings of type **1** (Scheme 1) by using the building blocks required for the lower-membered counterparts. Arenesulfonamides were chosen as to confer, enhance or modulate certain properties in the macrocycles.[6] The aim was to study the coordination properties of the pentaolefinic macrocycles with transition metals and to compare them with those found for the triolefinic macrocycles. Few complexes of transition metals with several types of triolefinic macrocycles are known.[7] To our knowledge, no metal complexes of tetra- and pentaolefinic macrocyles have been described.

25-Membered macrocycles **1** were prepared by reaction of dibrominated compounds **2** and intermediates **3** (Scheme 1 and Table 1) in the presence of K_2CO_3 in refluxing MeCN. In some cases, the use of sodium hydride in dimethylformamide gave better results. Variable yields of **1** were obtained after chromatographic purification. The yields can be considered moderate to good if compared with the reported cyclisation methods for the preparation of macrocycles of this size. Higher macrocycles



Scheme 1 Preparation of **1**. *Reagents and conditions*: i) K_2CO_3, refluxing CH_3CN; ii) NaH on **3** in DMF, then **2** in DMF, 90 °C.

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Table 1 Data of Pentaolefinic Macrocycles **1**

Compound	Ar^1	Ar^2	Yield (%) Method (i or ii)	Mp (°C)
1aaaaa	4-Me-C_6H_4-	4-Me-C_6H_4-	19 (i)	157–159
1bbbbb	ferrocenyl	ferrocenyl	28 (i)	93–94
1aabbb	4-Me-C_6H_4-	ferrocenyl	23 (i)	82–84
1ccccc	4-F-C_6H_4-	4-F-C_6H_4-	24 (ii)	168–171
1ddddd	2,4,6-triisopropylphenyl	2,4,6-triisopropylphenyl	48 (ii)	> 360
1aaeee	4-Me-C_6H_4-	4-Br-C_6H_4-	27 (i)	176–178

and lineal oligomers were also detected in the crude mixtures (MALDI–TOF MS).

The molecular structure of **1aaaaa**, was confirmed by single crystal X-ray structure analysis. Figure 1 shows the Ortep-Plot diagram for the compound together with its labelling scheme. Compound **1aaaaa** is crystallizing free of solvents with a C_1 symmetry. Bond distances and angles are within expected values. The macrocyclic ring is highly folded with two of the aromatic rest orientated upwards and the other three orientated downwards. The planes of the double bonds at the macrocyclic ring are orientated randomly in different directions.[8]

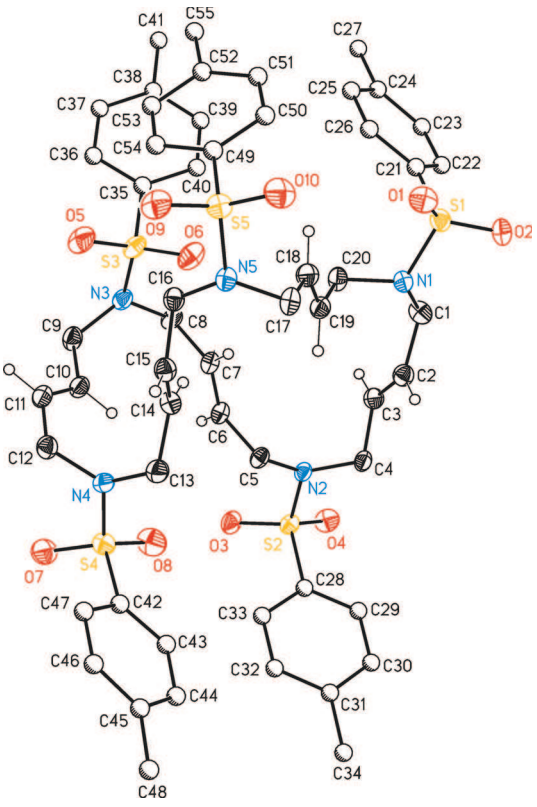
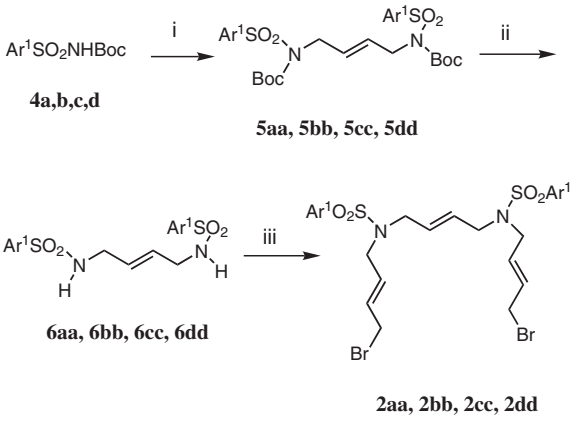


Figure 1 Ortep-Plot (50%) of compound **1aaaaa**. Hydrogen atoms, except the ones of the double bonds, are omitted to fully appreciate the geometry of the compound.

Dibromides **2** were obtained by the sequence outlined in Scheme 2 (see also Table 2). Protected sulfonamides **4**, prepared from the corresponding arenesulfonamides according to the general method described in the literature,[9] were treated with 0.5 equivalents of (*E*)-1,4-dibromo-2-butene in refluxing MeCN using K_2CO_3 as base. Compounds **5** were deprotected with trifluoroacetic acid, and the resulting intermediates **6** were dialkylated by treatment with excess of (*E*)-1,4-dibromo-2-butene in the presence of K_2CO_3 as base. This reaction gave variable yields depending on the aryl substitution.



Scheme 2 Preparation of **2**. *Reagents and conditions*: i) (*E*)-1,4-dibromo-2-butene (0.5 equiv), K_2CO_3, refluxing CH_3CN; ii) trifluoroacetic acid-CH_2Cl_2 1:1, r.t.; iii) (*E*)-1,4-dibromo-2-butene (*ca* 7 equiv), K_2CO_3, refluxing MeCN.

Compounds **3** were prepared by the sequence outlined in Scheme 3 (see also Table 3). Reaction of protected sulfonamides **4** with one equivalent of (*E*)-1,4-dibromo-2-butene in refluxing MeCN, in the presence of K_2CO_3, afforded the monoalkylated compounds **7**. These were treated with 0.5 equivalents of arenesulfonamides under analogous conditions to afford compounds **8**, which were deprotected by the usual procedure to afford the desired intermediates **3** in good yields.

In summary, we report an efficient stepwise preparation of 25-membered macrocycles featuring five all *trans* olefinic double bonds and five arylsulfonyl moieties. The

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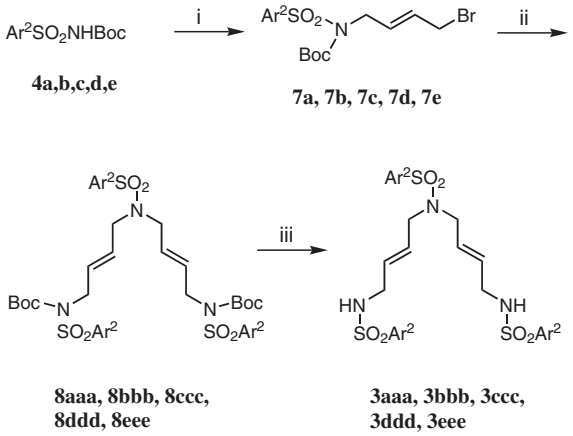
Table 2 Data of Compounds **5**, **6** and **2** (Scheme 2)

Compound	Ar[1]	Yield (%)	Mp (°C)	Lit. mp (°C)
5bb	ferrocenyl	70	160–161	–
6bb	ferrocenyl	50	200–202	–
6dd	2,4,6-triisopropylphenyl	84	183	183[10]
2aa	4-Me-C_6H_4-	31	112–113	112[11]
2bb	ferrocenyl	51	158–160	–
2cc	4-F-C_6H_4-	77	97–99	93–95[12]
2dd	2,4,6-triisopropylphenyl	67	123–125	123–125[10]



Scheme 3 Preparation of **3**. *Reagents and conditions*: i) (*E*)-1,4-dibromo-2-butene (1 equiv), K_2CO_3, refluxing CH_3CN; ii) Ar^2-SO_2NH_2 (0.5 equiv), K_2CO_3, refluxing CH_3CN; iii) CF_3CO_2H–CH_2Cl_2 1:1, r.t.

type of dielectrophilic and dinucleophilic compounds used in the cyclisation reaction are versatile intermediates that can also be used for the synthesis of 15-membered triolefinic macrocycles, arenesulfonamides and (*E*)-1,4-dibromo-2-butene being the ultimate precursors. Complexation experiments of macrocycles **1** with metals will be reported in due course.

^1H (250 MHz or 200 MHz) and ^{13}C (62.5 MHz or 50 MHz) NMR chemical shifts are expressed relative to $CHCl_3$ (δ = 7.26 and δ = 77.0, respectively) and TMS (δ = 0.00). MALDI–TOF spectra were recorded on a system equipped with a pulsed nitrogen laser (337 nm), operating in positive-ion reflector mode, using 19 kV acceleration voltage and a matrix of α-cyano-4-hydroxycinnamic acid. ESI mass spectra were acquired using a Navigator quadrupole instrument; the instrument was operated in the positive ion mode (ES+) at a probe tip voltage of 3 kV. Ferrocenesulfonamide was prepared from ferrocene as previously reported.[14] *N*-(*tert*-Butyloxycarbonyl)arenesulfonamides **4a**,[9] **4b**,[15,16] **4c**,[12] **4d**,[11] and **4e**[17] were prepared according to a general method described in the literature.[9] Compounds **5aa**,[11] **5cc**,[12] **5dd**,[11] **6aa**,[11] **6cc**,[12] **7a**,[11] **7b**,[15,16] **8aaa**,[11] **3aaa**,[11] were prepared as previously reported by us.

Table 3 Data of Compounds **7**, **8** and **3** (Scheme 3)

Compound	Ar^2	Yield (%)	Mp (°C)	Lit. mp (°C)
7c	4-F-C_6H_4-	78	oil	oil[13]
7d	2,4,6-triisopropylphenyl	54	86–88	–
7e	4-Br-C_6H_4-	28	70–72	–
8bbb	ferrocenyl	100	85–88	–
8ccc	4-F-C_6H_4-	99	oil	oil[13]
8ddd	2,4,6-triisopropylphenyl	85	127–129	–
8eee	4-Br-C_6H_4-	38	90–92	–
3bbb	ferrocenyl	86	71–74	–
3ccc	4-F-C_6H_4-	86	174–176	174–176[13]
3ddd	2,4,6-triisopropylphenyl	91	145–147	–
3eee	4-Br-C_6H_4-	100	174–176	–

(*E,E,E,E,E*)-1,6,11,16,21-Pentakis[(4-methylphenyl)sulfonyl]-1,6,11,16,21-pentaazacyclopentacosa-3,8,13,18,23-pentaene (1aaaaa); General Procedure

A mixture of **3aaa**, (300 mg, 0.5 mmol), and anhyd K_2CO_3 (370 mg, 2.7 mmol) in MeCN (18 mL) was heated at 70 °C under stirring for 30 min. Then a solution of **2aa**, (320 mg, 0.5 mmol) in MeCN (30 mL) was added and the mixture was refluxed for 22 h (TLC monitoring). After cooling to r.t., the salts were filtered off and the filtrate was evaporated. The residue was purified by column chromatography through silica gel (230–400 mesh) with mixtures of hexane–EtOAc–CH_2Cl_2 of increasing polarity as eluent (9:1:0 → 16:3.5:0.5) to afford **1aaaaa**. Yield: 110 mg (19%); white solid; mp 157–159 °C.

IR (KBr): 2921, 1330, 1151 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 2.43 (s, 15 H), 3.62 (br s, 20 H), 5.44 (br s, 10 H), 7.31 (d, *J* = 8.2 Hz, 10 H), 7.64 (d, *J* = 8.2 Hz, 10 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.5, 49.0, 127.2, 129.3, 129.8, 136.3, 143.6.

MS (ESI): *m/z* = 1116 $[M + H]^+$.

Anal. Calcd for $C_{55}H_{65}N_5O_{10}S_5$: C, 59.17; N, 6.27; H, 5.87; S, 14.36. Found: C, 58.77; N, 6.21; H, 5.97; S, 14.17.

(*E,E,E,E,E*)-1,6,11,16,21-Pentakis(ferrocenylsulfonyl)-1,6,11,16,21-pentaazacyclopentacosa-3,8,13,18,23-pentaene (1bbbbb)

It was prepared from **2bb** and **3bbb** following the procedure employed for **1aaaaa** [silica gel chromatography, hexane–EtOAc–CH_2Cl_2, (7:1:2 → 4:3:3)]. Yield: 40 mg (28%); orange solid; mp 93–94 °C.

IR (KBr): 2919, 1332, 1132 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 3.47 (br s, 20 H), 4.40 (br s, 35 H), 4.54 (br s, 10 H), 5.32 (br s, 10 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 48.8, 68.6, 70.6, 70.8, 86.7, 129.1.

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MS (MALDI–TOF): *m/z* = 1585 $[M]^+$.

Anal. Calcd for $C_{70}H_{75}Fe_5N_5O_{10}S_5$: C, 53.01; N, 4.42; H, 4.77; S, 10.11. Found: C, 52.87; N, 4.11; H, 5.05; S, 9.81.

(*E,E,E,E,E*)-1,6,11-Tris(ferrocenylsulfonyl)-16,21-bis[(4-methylphenyl)sulfonyl]-1,6,11,16,21-pentaazacyclopentacosa-3,8,13,18,23-pentaene (1aabbb)

It was prepared from **2aa** and **3bbb** following the procedure employed for **1aaaaa** (silica gel chromatography, hexane–EtOAc, 9:1 → 6:4). Yield: 120 mg (23%); orange solid; mp 82–84 °C.

IR (KBr): 2920, 1331, 1156, 1133 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 2.44 (s, 6 H), 3.45–3.61 (m, 20 H), 4.40 (br s, 21 H), 4.55 (br s, 6 H), 5.34–5.40 (m, 10 H), 7.32 (d, *J* = 8.2 Hz, 4 H), 7.64 (d, *J* = 8.2 Hz, 4 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.5, 48.7, 48.8, 68.6, 70.6, 70.7, 86.5, 127.2, 128.7, 129.0, 129.2, 129.6, 129.8, 136.6, 143.5.

MS (ESI): *m/z* = 1397 $[M]^+$.

Anal. Calcd for $C_{64}H_{71}Fe_3N_5O_{10}S_5$: C, 54.98; N, 5.01; H, 5.12; S, 11.47. Found: C, 55.09; N, 4.68; H, 5.47; S, 10.91.

(*E,E,E,E,E*)-1,6,11,16,21-Pentakis[(4-fluorophenyl)sulfonyl]-1,6,11,16,21-pentaazacyclopentacosa-3,8,13,18,23-pentaene (1ccccc)

A mixture of **3ccc** (50 mg, 0.08 mmol), NaH (60% dispersion in mineral oil, 12 mg, 0.29 mmol) in dimethylformamide (4 mL) was heated under stirring at 90 °C for 30 min. Then **2cc**, (42 mg, 0.06 mmol) was added and the mixture was heated at 90 °C for 20 h. After cooling to r.t. water (5 mL) was added and the solvent was evaporated under reduced pressure. The residue was dissolved in CH_2Cl_2 and washed three times with water. The organic phase was dried with anhyd Na_2SO_4 and the solvent was evaporated. The residue was purified by column chromatography under pressure through a reversed phase silica gel column (Bakerbond octadecyl C_{18}, 40 μm) with a mixture of MeOH–MeCN (5:1) as eluent, to afford **1ccccc**. Yield: 17 mg (24%); white solid; mp 168–171 °C.

IR (neat): 2919, 1591, 1492, 1335, 1152 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 3.65 (m, 20 H), 5.51 (m, 10 H), 7.19 (dd, *J* = 8.9, 8.3 Hz, 10 H), 7.79 (dd, *J* = 8.9, 5.0 Hz, 10 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 49.7, 116.9 (d, *J* = 21.9 Hz), 129.9, 130.25 (d, *J* = 8.6 Hz), 135.7 (d, *J* = 3.8 Hz), 165.5 (d, *J* = 253.7).

MS (MALDI–TOF): *m/z* = 1159 $[M + Na]^+$, 1175 $[M + K]^+$.

Anal. Calcd for $C_{50}H_{50}F_5N_5O_{10}S_5$: C, 52.85; N, 6.16; H, 4.44; S, 14.11. Found: C, 52.27; N, 5.97; H, 4.61; S, 13.70.

(*E,E,E,E,E*)-1,6,11,16,21-Pentakis[(2,4,6-triisopropylphenyl)sulfonyl]-1,6,11,16,21-pentaazacyclopentacosa-3,8,13,18,23-pentaene (1ddddd)

It was prepared from **2dd** and **3ddd** following the procedure employed for **1ccccc** [silica gel chromatography, hexane–EtOAc, (8:2)]. Yield: 169 mg (48%); white solid; mp > 360 °C.

IR (neat): 2958, 1600, 1461, 1363, 1310, 1148 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 1.20 (m, 90 H), 2.87 (septet, *J* = 7.1 Hz, 5 H), 3.74 (m, 20 H), 4.05 (septet, *J* = 7.1 Hz, 10 H), 5.67 (m, 10 H), 7.11 (s, 10 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 23.3, 24.55, 28.9, 33.9, 46.8, 123.6, 129.4, 130.8, 151.1, 152.9.

MS (MALDI–TOF): *m/z* = 1699 $[M + Na]^+$, 1715 $[M + K]^+$.

HRMS: *m/z* calcd for $C_{95}H_{145}N_5O_{10}S_5$ + Na: 1698.9487; found: 1698.9526.

(*E,E,E,E,E*)-1,6,11-Tris[4-bromophenyl)sulfonyl]-16,21-bis[(4-methylphenyl)sulfonyl]-1,6,11,16,21-pentaazacyclopentacosa-3,8,13,18,23-pentaene (1aaeee)

A solution of **2aa** (325 mg, 0.49 mmol) and **3eee** (400 mg, 0.49 mmol) in MeCN–THF (100 mL of each solvent) was slowly added to a refluxing and mechanically stirred mixture of anhyd K_2CO_3 (953 mg, 6.9 mmol) in MeCN–THF (150 mL of each solvent). The mixture was refluxed for 20 h; then it was filtered and evaporated. The residue was purified by column chromatography through silica gel under pressure with hexane–EtOAc (8:2) as eluent, to afford **1aaeee**. Yield: 177 mg (27%); white solid; mp 176–178 °C.

IR (neat): 2961, 1572, 1333, 1259, 1154 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 2.44 (s, 6 H), 3.64 (m, 20 H), 5.48 (m, 10 H), 7.32 (d, *J* = 8.0 Hz, 4 H), 7.63 (m, 16 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 20.7, 48.2, 48.4, 48.5, 48.6, 126.4, 126.8, 127.9, 128.0, 128.5, 128.6, 128.7, 129.0, 129.3, 131.7, 135.2, 137.6, 142.8.

MS (MALDI–TOF): *m/z* = 1330–1339 $[M + Na]^+$, 1346–1355 $[M + K]^+$.

HRMS: *m/z* calcd for $C_{52}H_{56}Br_3N_5O_{10}S_5$ + Na: 1330.0073; found: 1330.0101.

(*E*)-*N,N′*-Bis(*tert*-butyloxycarbonyl)-*N,N′*-bis(ferrocenylsulfonyl)-2-butene-1,4-diamine (5bb)

A mixture of **4b** (1.82 g, 5.0 mmol) and anhyd K_2CO_3 (2.15 g, 14.5 mmol) in MeCN (65 mL) was heated under stirring at 70 °C for 20 min, then a solution of (*E*)-1,4-dibromo-2-butene (570 mg, 2.7 mmol) in MeCN (25 mL) was added and the suspension was refluxed for 23 h (TLC monitoring). The mixture was filtered and evaporated. The residue was purified by column chromatography through silica gel under pressure with hexane–EtOAc (4:1) as eluent, affording **5bb**. Yield: 1.35 g (70%); orange solid; mp 160–161 °C.

IR (KBr): 2978, 1713, 1350, 1143 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.41 (s, 18 H), 4.26 (br abs, 4 H), 4.41 (s, 10 H), 4.39–4.43 (m, 4 H), 4.76 (app t, *J* = 2.0 Hz, 4 H), 5.61 (m, 2 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 28.0, 47.8, 70.2, 70.6, 70.9, 83.6, 87.0, 128.4, 150.9.

MS (ESI): *m/z* = 782 $[M]^+$, 800 $[M + NH_4]^+$, 805 $[M + Na]^+$.

Anal. Calcd for $C_{34}H_{42}Fe_2N_2O_8S_2$: C, 52.19; N, 3.58; H, 5.41; S, 8.19. Found: C, 52.41; N, 3.58; H, 5.45; S, 8.75.

(*E*)-*N,N′*-Bis(ferrocenylsulfonyl)-2-butene-1,4-diamine (6bb)

A solution of **5bb** (1.16 g, 1.5 mmol) in trifluoroacetic acid–CH_2Cl_2 (10 mL, 1:1) was stirred at r.t. for 2 h (TLC monitoring). Then, the solution was evaporated and the residue was taken in CH_2Cl_2 (25 mL), washed with water (2 × 20 mL) and a sat. aq solution of NaCl (25 mL). The organic layer was dried with anhyd Na_2SO_4 and the solvent was evaporated. The residue was purified by column chromatography through silica gel under pressure with CH_2Cl_2 as eluent, to afford **6bb**. Yield: 430 mg (50%); orange solid; mp 200–202 °C.

IR (KBr): 3267, 3096, 1322, 1135 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 3.45–3.48 (m, 4 H), 4.10 (t, *J* = 6.0 Hz, 2 H), 4.39 (s, 10 H), 4.37–4.40 (m, 4 H), 4.60 (app t, *J* = 1.8 Hz, 4 H), 5.40–5.44 (m, 2 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 44.4, 68.6, 70.5, 70.8, 87.4, 128.4.

MS (ESI): *m/z* = 582 $[M]^+$, 583 $[M + H]^+$.

Anal. Calcd for $C_{24}H_{26}Fe_2N_2O_4S_2$: C, 49.50; N, 4.81; H, 4.50; S, 11.01. Found: C, 49.52; N, 4.80; H, 4.50; S, 10.83.

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(*E*)-*N,N′*-Bis[(2,4,6-triisopropylphenyl)sulfonyl]-2-butene-1,4-diamine (6dd)

It was prepared by the general method described for **6bb** (84% yield, no chromatography was needed; mp 183 °C). This compound had been previously synthesized by us by another method.[10]

(*E,E,E*)-1,14-Dibromo-*N,N′*-bis[(4-methylphenyl)sulfonyl]-5,10-diazatetradeca-2,7,12-triene (2aa)

A stirred mixture of **6aa** (1.00 g, 2.5 mmol), (*E*)-1,4-dibromo-2-butene (5.53 g, 21.2 mmol) and anhyd K_2CO_3 (1.55 g, 11.2 mmol) in MeCN (10 mL) was heated under reflux for 24 h. Then, the mixture was filtered and evaporated. The residue was purified by column chromatography through silica gel under pressure with hexane–EtOAc (5:3) as eluent, to afford **2aa**. Yield: 520 mg (31%); white solid; mp 112–113 ºC; lit.[11] mp 112 °C.

(*E,E,E*)-1,14-Dibromo-*N,N′*-bis(ferrocenylsulfonyl)-5,10-diazatetradeca-2,7,12-triene (2bb)

It was prepared in 51% yield by the general method described for **2aa** [mixtures of hexane–EtOAc (7:3 → 1:1) as eluent]; mp 158–160 °C.

IR (KBr) 2905, 1335, 1132 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 3.56–3.65 (m, 8 H), 3.86 (d, *J* = 7.2 Hz, 4 H), 4.38–4.41 (m, 4 H), 4.40 (s, 10 H), 4.57 (app t, *J* = 1.8 Hz, 4 H), 5.37–5.81 (m, 6 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 31.5, 48.0, 48.4, 68.5, 70.6, 70.8, 87.2, 129.0, 129.9, 130.0.

MS (ESI): *m/z* = 848 $[M]^+$, 849 $[M + H]^+$.

Anal. Calcd for $C_{32}H_{36}Br_2Fe_2N_2O_4S_2$: C, 45.31; N, 3.30; H, 4.28; found: C, 45.62; N, 3.25; H, 4.20.

(*E,E,E*)-1,14-Dibromo-*N,N′*-bis[(4-fluorophenyl)sulfonyl]-5,10-diazatetradeca-2,7,12-triene (2cc)

It was prepared in 77% yield by the general method described for **2aa** [hexane–EtOAc, (4:1) as eluent]; mp 97–99 °C; lit.[12] mp 93–95 °C.

(*E,E,E*)-1,14-Dibromo-*N,N′*-bis[(2,4,6-triisopropylphenyl)sulfonyl]-5,10-diazatetradeca-2,7,12-triene (2dd)

It was prepared in 67% yield by the general method described for **2aa.** The crude mixture was not chromatographed, the remaining (*E*)-1,4-dibromo-2-butene being eliminated by sublimation (50 °C, 0.3–0.5 mbar) and subsequent washing of the residue with pentane; mp 123–125 °C; lit.[10] mp 123–125 °C.

***N*-[(*E*)-4-Bromo-2-butenyl]-*N*-(*tert*-butyloxycarbonyl)-(4-fluorophenyl)sulfonamide (7c)**

A stirred mixture of **4c** (6.73 g, 24.5 mmol), (*E*)-1,4-dibromo-2-butene (25.57 g, 119.5 mmol), anhyd K_2CO_3 (7.01 g, 50.1 mmol), and MeCN (90 mL) was refluxed for 20 h. After cooling at r.t., the mixture was filtered off and the filtrate was evaporated. The residue was sublimed at 50 °C (0.3–0.5 mbar) to eliminate most of the excess of (*E*)-1,4-dibromo-2-butene. The residue of sublimation was purified by column chromatography through silica gel with a mixture of hexane–EtOAc (9:1) as eluent to afford **7c**. Yield: 7.74 g (78%); oil.

IR (neat): 2979, 1729, 1591, 1494, 1361, 1152 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 1.39 (s, 9 H), 3.99 (d, *J* = 7.2 Hz, 2 H), 4.46 (d, *J* = 5.6 Hz, 2 H), 5.87 (dt, *J* = 15.2, 5.7 Hz, 1 H), 6.02 (dt, *J* = 15.2, 7.2 Hz, 1 H), 7.20 (dd, *J* = 9.1, 8.2 Hz, 2 H), 7.97 (dd, *J* = 9.1, 5.0 Hz, 2 H).[13]

***N*-[(*E*)-4-Bromo-2-butenyl]-*N*-(*tert*-butyloxycarbonyl)-(2,4,6-triisopropylphenyl)sulfonamide (7d)**

It was prepared from **4d** following the procedure employed for **7c**. The crude mixture was purified by column chromatography through silica gel with hexane–EtOAc (10:1) as eluent to afford **7d**. Yield: 5.68 g (54%); white solid; mp 86–88 °C.

IR (KBr): 2959, 2934, 1719, 1598, 1367, 1337,1165, 1143 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 1.21 (m, 27 H), 2.89 (septet, *J* = 6.9 Hz, 1 H), 3.87 (septet, *J* = 6.9 Hz, 2 H), 3.95 (d, *J* = 7.2 Hz, 2 H), 4.40 (d, *J* = 5.2 Hz, 2 H), 5.85–6.06 (m, 2 H), 7.12 (s, 2 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 24.0, 24.9, 28.1, 29.7, 32.05, 34.6, 46.35, 84.25, 123.85, 130.2, 134.1, 150.6, 151.2, 153.6.

Anal. Calcd for $C_{24}H_{38}BrNO_4S$: C, 55.81; N, 2.71; H, 7.41; S, 6.21. Found: C, 56.06; N, 2.82; H, 7.56; S, 6.00.

***N*-[(*E*)-4-Bromo-2-butenyl]-*N*-(*tert*-butyloxycarbonyl)-(4-bromophenyl)sulfonamide (7e)**

It was prepared from **4e** following the procedure employed for **7c**. The crude mixture was purified by column chromatography through silica gel with hexane–EtOAc (8:2) as eluent. Compound **7e** eluted from the column was washed with Et_2O and petroleum ether to afford **7e**. Yield: 1.45 g (28%); white solid; mp 70–72 °C.

IR (neat): 2983, 1719, 1572, 1360, 1145 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 1.38 (s, 9 H), 3.97 (d, *J* = 7.2 Hz, 2 H), 4.44 (d, *J* = 5.9 Hz, 2 H), 5.83 (dt, *J* = 15.2, 5.9 Hz, 1 H), 5.99 (dt, *J* = 15.2, 7.3 Hz, 1 H), 7.66 (d, *J* = 8.9 Hz, 2 H), 7.80 (d, *J* = 8.9 Hz, 2 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 28.3, 31.8, 47.6, 85.4, 128.8, 130.1, 130.2, 130.8, 132.4, 139.2, 150.7.

Anal. Calcd for $C_{15}H_{19}Br_2NO_4S$: C, 38.40; N, 2.99; H, 4.08; S, 6.83. Found: C, 38.75; N, 2.84; H, 4.32; S, 6.70.

(*E,E*)-1,11-Bis(*tert*-butyloxycarbonyl)-1,6,11-tris(ferrocenylsulfonyl)-1,6,11-triazaundeca-3,8-diene (8bbb)

A stirred mixture of ferrocenylsulfonamide (260 mg, 1.0 mmol), **7b** (1.00 g, 2.0 mmol), anhyd K_2CO_3 (830 mg, 6.0 mmol), and MeCN (15 mL) was refluxed for 18 h (TLC monitoring). After cooling to r.t., the mixture was filtered off and the filtrate was evaporated. The residue was redissolved in EtOAc (15 mL), washed with water (3 × 10 mL) and a sat. solution of NaCl. The organic phase was dried with anhyd Na_2SO_4 and the solvent was evaporated to afford **8bbb** as an oil (1.10 g, 100%), which crystallized upon addition of hexane; mp 85–88 °C (hexane).

IR (KBr): 2973, 2922, 1720, 1359, 1130 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.42 (s, 18 H), 3.62 (app d, *J* = 5.0 Hz, 4 H), 4.19 (app d, *J* = 4.6 Hz, 4 H), 4.41 (s, 15 H), 4.35–4.42 (m, 6 H), 4.56 (app t, *J* = 1.9 Hz, 2 H), 4.74 (app t, *J* = 2.0 Hz, 4 H), 5.38–5.57 (m, 4 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 28.1, 47.7, 47.8, 68.6, 70.1, 70.5, 70.6, 70.7, 71.0, 83.7, 87.3, 87.8, 127.5, 129.7, 151.0.

Anal. Calcd for $C_{48}H_{57}Fe_3N_3O_{10}S_3$: C, 52.43; N, 3.82; H, 5.22; S, 8.75. Found: C, 52.10; N, 3.48; H, 5.40; S, 8.35.

(*E,E*)-1,11-Bis(*tert*-butyloxycarbonyl)-1,6,11-tris[(4-fluorophenyl)sulfonyl]-1,6,11-triazaundeca-3,8-diene (8ccc)

It was prepared following the procedure employed for **8bbb**, from **7c** and 4-fluorophenylsulfonamide. Yield: 7.79 g (99%); oil.

IR (neat): 2981, 1726, 1591, 1494, 1353, 1151 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 1.36 (s, 18 H), 3.67 (d, *J* = 6.1 Hz, 4 H), 4.40 (d, *J* = 5.5 Hz, 4 H), 5.60 (dt, *J* = 15.5, 5.7 Hz, 2 H), 5.78 (dt, *J* = 15.4, 6.0 Hz, 2 H), 7.20 (dd, *J* = 9.1, 8.3 Hz, 6 H), 7.87 (dd, *J* = 8.8, 5.0 Hz, 2 H), 7.92 (dd, *J* = 8.8, 5.0 Hz, 4 H).[13]

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(*E,E*)-1,11-Bis(*tert*-butyloxycarbonyl)-1,6,11-tris[(2,4,6-triisopropylphenyl)sulfonyl]-1,6,11-triazaundeca-3,8-diene (8ddd)
It was prepared following the procedure employed for **8bbb**, from **7d** and (2,4,6-triisopropylphenyl)sulfonamide. Yield: 3.16 g (85%) (after recrystallization of the crude mixture in MeOH); white solid; mp 127–129 °C.

IR (KBr): 2958, 2870, 1732, 1601, 1368, 1339, 1259, 1149 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 1.21 (m, 72 H), 2.88 (septet, *J* = 6.9 Hz, 3 H), 3.80 (d, *J* = 5.3 Hz, 4 H), 3.86 (septet, *J* = 6.9 Hz, 4 H), 4.14 (septet, *J* = 6.9 Hz, 2 H), 4.37 (d, *J* = 4.7 Hz, 4 H), 5.77 (m, 4 H), 7.10 (s, 4 H), 7.14 (s, 2 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 23.91, 23.94, 24.8, 25.2, 28.1, 29.6, 34.51, 34.55, 46.68, 46.75, 83.9, 123.7, 124.2, 128.4, 130.7, 131.6, 134.6, 159.5, 151.2, 151.9, 153.27, 153.35.

Anal. Calcd for $C_{63}H_{99}N_3O_{10}S_3$: C, 65.53; N, 3.64; H, 8.64; S, 8.33: Found: C, 65.37; N, 3.62; H, 8.81; S, 8.01.

(*E,E*)-1,11-Bis(*tert*-butyloxycarbonyl)-1,6,11-tris[(4-bromophenyl)sulfonyl]-1,6,11-triazaundeca-3,8-diene (8eee)
It was prepared following the procedure employed for **8bbb**, from **7e** and (4-bromophenyl)sulfonamide [chromatography on silica gel with hexane–EtOAc (7:3), then washing with petroleum ether]. Yield: 910 mg (38%); white solid; mp 90–92 °C.

IR (neat): 2982, 1725, 1574, 1349, 1323, 1148 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 1.34 (s, 18 H), 3.84 (d, *J* = 6.2 Hz, 4 H), 4.37 (d, *J* = 5.5 Hz, 4 H), 5.59 (dt, *J* = 15.4, 6.1 Hz, 2 H), 5.77 (dt, *J* = 15.4, 5.6 Hz, 2 H), 7.66 (d, *J* = 8.8 Hz, 6 H), 7.76 (d, *J* = 8.8 Hz, 6 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 28.2, 48.0, 48.4, 85.3, 127.9, 128.4, 128.7, 129.0, 130.3, 132.4, 132.9, 139.4, 139.7, 150.7.

Anal. Calcd for $C_{36}H_{42}Br_3N_3O_{10}S_3$: C, 42.70; N, 4.15; H, 4.18; S, 9.50. Found: C, 42.89; N, 4.05; H, 4.28; S, 9.18.

Partial deprotection of nitrogen was observed, as a second fraction eluted from the column was unpurified with (*E,E*)-1-(*tert*-butyloxycarbonyl)-1,6,11-tris[4-bromophenyl)sulfonyl]-1,6,11-triazaundeca-3,8-diene.

(*E,E*)-1,6,11-Tris(ferrocenylsulfonyl)-1,6,11-triazaundeca-3,8-diene (3bbb); General Procedure
A solution of **8bbb**, (910 mg, 1.0 mmol) in trifluoroacetic acid–CH_2Cl_2 (20 mL, 1:1) was stirred at r.t. for 2 h (TLC monitoring). Then, the solution was evaporated, the residue taken in EtOAc (15 mL), and washed with water (3 × 10 mL). The organic layer was dried with anhyd Na_2SO_4 and the solvent evaporated to afford **3bbb** as an orange foam (650 mg, 86%). An orange solid was obtained upon digestion with hexane; mp 71–74 °C.

IR (KBr): 3268, 3099, 2919, 2850, 1320, 1185, 1132 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 3.46–3.57 (m, 8 H), 4.42 (br abs, 2 H), 4.43 (s, 15 H), 4.38–4.47 (m, 6 H), 4.57 (app t, *J* = 1.9 Hz, 2 H), 4.66 (app t, *J* = 1.9 Hz, 4 H), 5.42–5.48 (m, 4 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 44.4, 48.5, 68.6, 70.5, 70.6, 70.7, 87.2, 87.5, 127.9, 129.4.

MS (ESI): *m/z* = 900 $[M + H]^+$, 917 $[M + NH_4]^+$.

HRMS: *m/z* calcd for $C_{38}H_{41}Fe_3N_3O_6S_3$ 899.0209; found: 899.0205.

(*E,E*)-1,6,11-Tris[(4-fluorophenyl)sulfonyl]-1,6,11-triazaundeca-3,8-diene (3ccc)
It was prepared following the procedure employed for **3bbb**, from **8ccc**; (5.09 g, 86%, white solid precipitating upon addition of more CH_2Cl_2 to the reaction mixture); mp 174–176 °C.

IR (neat): 3276, 1591, 1430, 1327, 1154 cm^{-1}.

^1H NMR (250 MHz, CD_3SOCD_3): δ = 3.38 (m, 4 H), 3.61 (d, *J* = 5.9 Hz, 4 H), 5.33 (dt, *J* = 15.5, 5.7 Hz, 2 H), 5.45 (dt, *J* = 15.5, 5.2 Hz, 2 H), 7.46 (dd, *J* = 12.5, 8.7 Hz, 6 H), 7.86 (dd, *J* = 8.7, 5.2 Hz, 6 H).[13]

(*E,E*)-1,6,11-Tris[(2,4,6-triisopropylphenyl)sulfonyl]-1,6,11-triazaundeca-3,8-diene (3ddd)
It was prepared following the procedure employed for **3bbb**, from **8ddd**; (more CH_2Cl_2 was added to the reaction mixture and it was washed with a sat. aq solution of Na_2CO_3, the organic phase being dried and evaporated). Yield: 780 mg (91%); mp 145–147 °C (Et_2O).

IR (neat): 3294, 1600, 1461, 1424, 1363, 1149 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 1.22 (m, 54 H), 2.87 (septet, *J* = 6.8 Hz, 3 H), 3.51 (app t, *J* = 5.3 Hz, 4 H), 3.80 (d, *J* = 7.0 Hz, 4 H), 4.10 (m, 6 H), 4.55 (t, *J* = 6.2 Hz, 2 H), 5.58 (m, 4 H), 7.12 (s, 2 H), 7.14 (s, 4 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 23.9, 25.2, 29.6, 29.9, 34.5, 44.5, 46.9, 124.2, 128.2, 131.15, 131.8, 132.5, 150.7, 151.8, 153.2, 153.6.

Anal. Calcd for $C_{53}H_{83}N_3O_6S_3$: C, 66.70; N, 4.40; H, 8.76; S, 10.08. Found: C, 66.13; N, 4.41; H, 8.73; S, 9.56.

(*E,E*)-1,6,11-Tris[(4-bromophenyl)sulfonyl]-1,6,11-triazaundeca-3,8-diene (3eee)
It was prepared following the procedure employed for **3bbb**, from **8eee** (the oily crude mixture crystallized upon addition of Et_2O). Yield: 1.13 g (ca. 100%); white solid; mp 174–176 °C.

IR (neat): 3301, 3271, 1575, 1328, 1158 cm^{-1}.

^1H NMR (250 MHz, CD_3SOCD_3): δ = 3.37 (masked d, 4 H), 3.58 (d, *J* = 5.9 Hz, 4 H), 5.40 (m, 4 H), 7.72 (d, *J* = 8.4 Hz, 6 H), 7.83 (d, *J* = 8.4 Hz, 6 H), 7.92 (m, 2 H).

^{13}C NMR (62.5 MHz, CD_3SOCD_3): δ = 44.5, 48.4, 127.0, 127.1, 127.6, 129.4, 129.8, 131.2, 133.2, 133.3, 139.9, 140.8.

Anal. Calcd for $C_{26}H_{26}Br_3N_3O_6S_3$: C, 38.44; N, 5.17; H, 3.23; S, 11.84. Found: C, 38.14; N, 4.89; H, 3.14; S, 11.49.

X-ray Crystallographic Study
Suitable crystals of **1aaaaa** were grown by slow evaporation of a *n*-hexane–EtOAc–CH_2Cl_2 solution at r.t. The measured crystal (700 × 40 × 20 μm^3) was prepared routinely under inert conditions immersed in perfluoropolyether as protecting oil for manipulation, even if macrocycles **1** are very stable compounds. The measurement was made on a Siemens P4 diffractometer equipped with a SMART-CCD-1000 area detector, a MACScience Co rotating anode with $Mo_{K\alpha}$ radiation, a graphite monochromator and a Siemens low temperature device LT2 (T = –120 °C). The measurements were made in the range 1.40°–31.49°. Fullsphere data collection was done with ω and φ scans. Following programs were used: Data collection Smart 5.625 (Bruker-AXS 2001), data reduction Saint Plus Version 1.6 (Bruker-Nonius 2002), absorption correction SADABS V. 2.03 (2002) and structure solution and refinement SHELXTL Version 6.12 (Sheldrick, 2000).

Compound **1aaaaa**

$C_{55}H_{65}N_5O_{10}S_5$, M_r = 1116.42; monoclinic; space group $P2_1/c$, a = 16.4897 (7) Å, b = 11.4315 (6) Å, c = 29.2425 (14) Å, β = 94.841 (2)°, V = 5492.6 (5) Å3, Z = 4, ρ_{cal} = 1.350 Mg/m3, μ = 0.274 mm^{-1}, 82074 reflections were collected of which 17675 are unique (R_{int} = 0.0819), 12673 Fo > 4 σ (Fo), 681 refined parameters, R_1 [I > 2 σ (I)] = 0.0484, *wR*2 [I > 2 σ (I)] = 0.1214. Goodness of fit on F^2 = 1.032, maximum residual electron density 0.369 (–0.550) e Å3.

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