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Preparation of 15-membered unsaturated N–H containing azamacrocycles and their differential coordination with Pd(0) and Pd(II)

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Abstract—The use of 2-(trimethylsilylethyl)sulfonamide (SES-NH_2) has permitted the selective and efficient synthesis of new triolefinic 15-membered azamacrocycles **3**. Differential coordination mode with palladium has been observed when macrocycle **3aab** [(*E*,*E*,*E*)-1,6-bis(*p*-tolylsulfonyl)-1,6,11-triazacyclopentadeca-3,8,13-triene] was treated with a palladium(0) or a palladium(II) source.

1. Introduction

In the last 5 years we have studied 15-membered triolefinic macrocycles of type **1** and their capacity to coordinate palladium(0) giving the air- and moisture stable Pd^0-complexes of type **2** (Fig. 1).[1,2] The three olefinic double bonds in **1** are the only coordinating centers for the palladium atom because the three nitrogen atoms are devoid of coordinating ability due to lone pair conjugation with the SO_2 group. Palladium(0) complexes **2** were obtained by interchange of ligand using either $Pd(PPh_3)_4$ or $Pd(dba)_2$ as metal source. The palladium atom perfectly fit inside of the macrocyclic cavity being the coordination mode with the three olefins planar trigonal.[3]

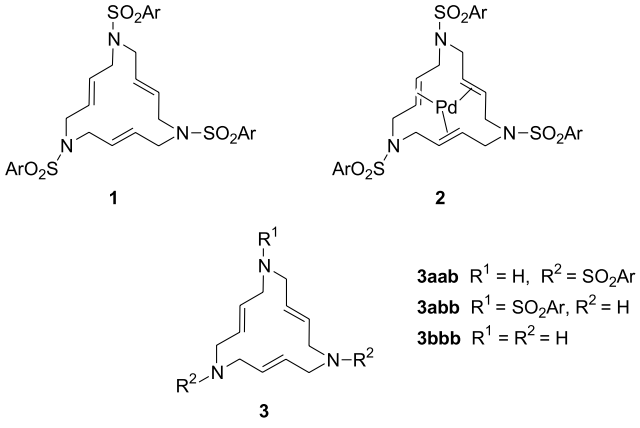

Figure 1.

On the other hand, azamacrocycles are important and powerful ligands in transition metal coordination chemistry.[4–7] Special attention has been paid to the coordination properties of cyclam[8] and porphyrin[9] derivatives. Since macrocycles **1** are structurally related to macrocyclic structures mentioned above, the preparation of N–H macrocycles **3** and the study of their coordinative properties was an interesting point of analysis. Unfortunately, the first attempts in our group to prepare unsaturated triolefinic azamacrocycles **3** by detosylation of **1** (Ar = *p*-tolyl) proved to be troublesome.

We present in this paper, the preparation of new unsaturated azamacrocycles **3** by selective removal of *N*-sulfonamide SE groups and their coordination with Pd^0 and Pd^{II}.

Moreover, introduction of two different metals—or the same metal in two different oxidation states—within the framework of an organic molecule in an ordered way at well-defined distances is a target that has interest in metal–metal interactions studies[10,11] and in metal deposition on solid supports for heterogeneous catalysis.[12–14] Our macrocycles **3** have the appropriate features for such an ordered distribution of metals.

Keywords: Macrocycles; Azamacrocycles; Sulfonamides; Protecting groups; Palladium.
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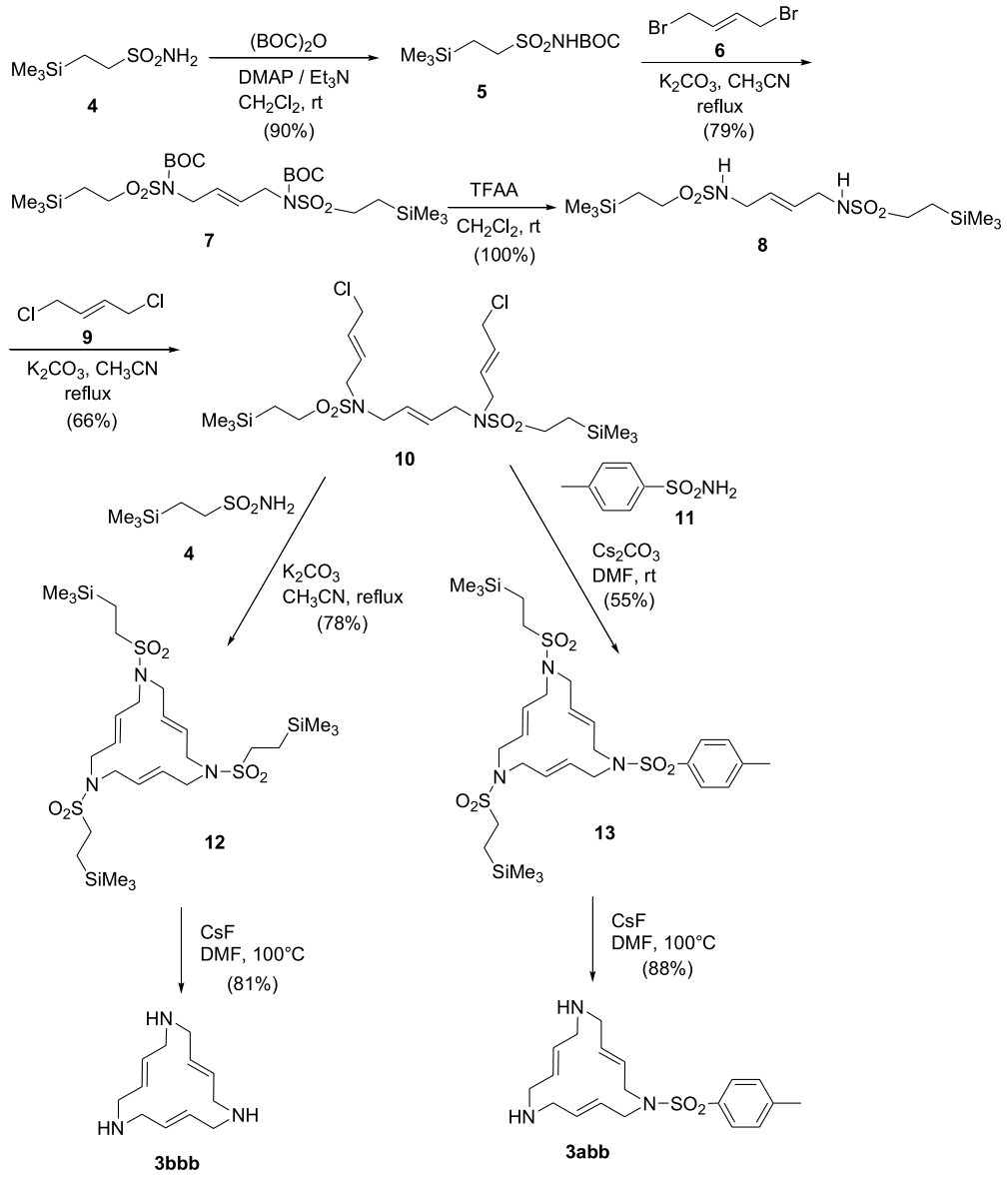


Scheme 1. Synthesis of 15-membered triolefinic azamacrocycles **3bbb** and **3abb**.

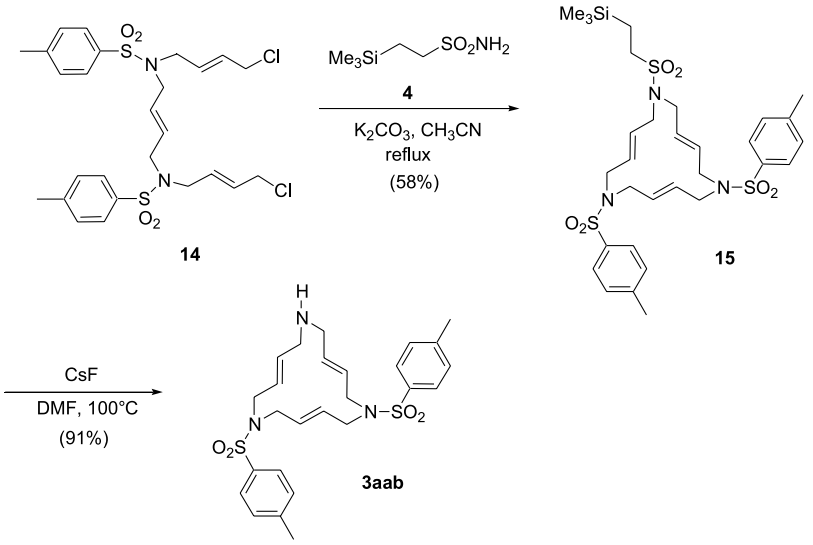
2. Results and discussion

The use of the 2-(tri-methylsilylethyl)sulfonyl (or SES) group as an amine protecting group has been reported in the literature.[15,16] SES-sulfonamides are easily deprotected under mild reaction conditions tolerating sensitive functionality in the compound and, in addition, the deprotection process leaves the free amine rather than the salt.[17,18] The selective and easy removal of the SES protecting group offers us the opportunity to prepare different types of unsaturated azamacrocycles **3** (Fig. 1). Preparation of macrocycles **3abb**, **3bbb** and **3aab** are outlined in Schemes 1 **and** 2.

2-(Trimethylsilylethyl)sulfonamide (SES-NH_2) **4** was prepared according to the procedure described in the literature.[18] Compound **4** was converted into its *N*-*tert*-butyloxycarbonyl (BOC) derivative **5**. Reaction of **5** with 0.5 equiv of *trans*-1,4-dibromo-2-butene (**6**) afforded the protected disulfonamide **7**. Treatment of **7** with trifluoroacetic acid selectively removed the BOC group to afford **8** in 100% yield. Conversion of **8** into **10** required an excess of dichloride **9** (8 equiv). After some optimizing work,[†] treatment of bis-sulfonamide **10** with one equiv of either SES-NH_2 **4** or *p*-tolylsulfonamide **11** gave, respectively, the two macrocycles **12** and **13**. The SES groups in macrocycles **12** and **13** were cleaved with cesium fluoride in anhydrous DMF at 100 °C affording azamacrocycles **3bbb** and **3abb** in 81 and 88% yield, respectively, (Scheme 1).

Macrocycle **3aab** was prepared as outlined in Scheme 2. Following the same pathway as for macrocycles **3bbb** and **3abb**, reaction of (*E*,*E*,*E*)-1,14-dichloro-*N*,*N*′-bis(*p*-tolylsulfonyl)-5,10-diazatetradeca-2,7,12-triene **14**[19] with SES-NH_2 **4** in the presence of potassium carbonate in refluxing

[†] The cyclisation step to **12** was also tried using Cs_2CO_3 as a base in DMF affording 45% yield when the reaction was run at room temperature and 58% yield when the reaction was run at 80 °C. The cyclisation step to **13** was also tried using K_2CO_3 in refluxing CH_3CN. Under these reaction conditions **13** was obtained in 45% yield.

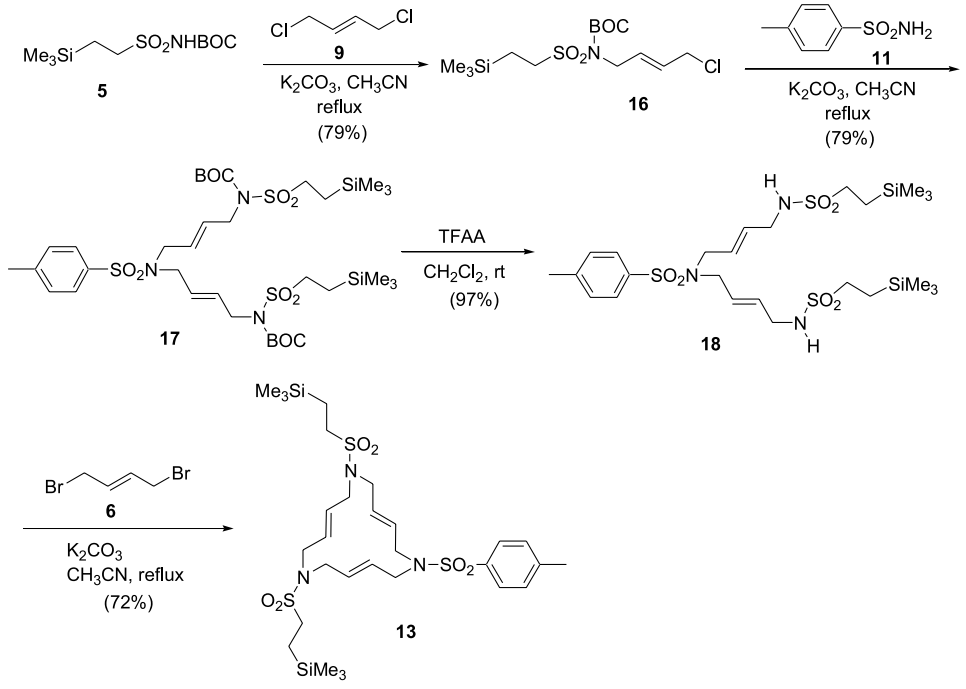


Scheme 2. Synthesis of 15-membered triolefinic azamacrocycle **3aab**.

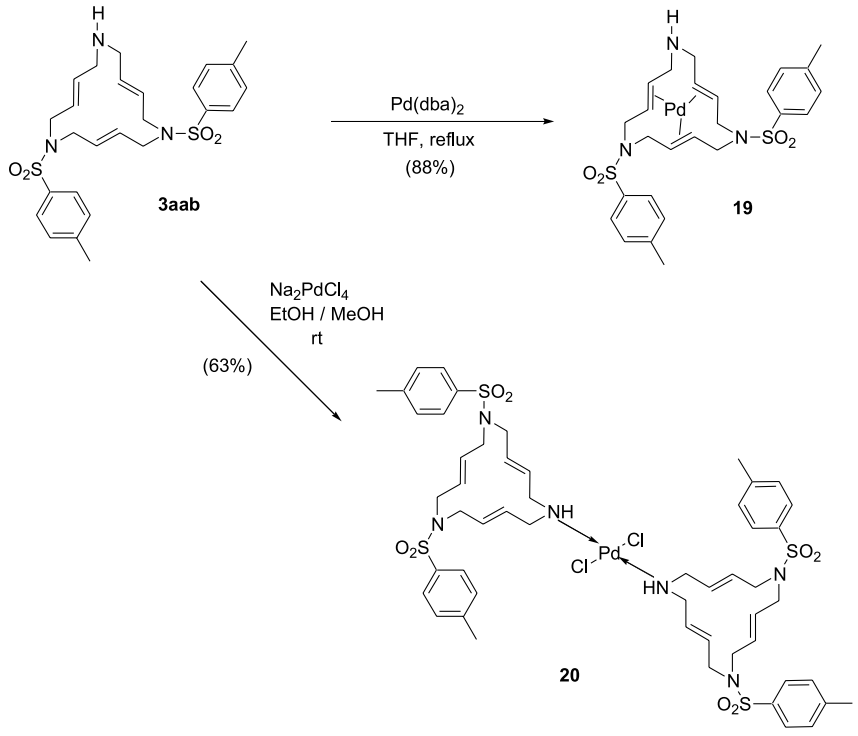
acetonitrile afforded macrocycle **15** in 58% yield. Deprotection of SES group using cesium fluoride in anhydrous DMF at 100 °C led to azamacrocycle **3aab** in 91% yield.

An alternative and more efficient way to prepare protected macrocycles, as for example **13**, is outlined in Scheme 3. The synthesis started with the BOC-protected SES-sulfonamide **5**, which was treated with an excess of dichloride **9** (4 equiv) to afford chlorosulfonamide **16** in 79% yield. Condensation of 2 equiv of **16** with 1 equiv of *p*-tolylsulfonamide **11** led to intermediate **17**. Again, treatment of **17** with trifluoroacetic acid removed selectively and efficiently (97% yield) the two BOC-protecting groups leaving the two SES-groups unaffected. Finally, cyclisation of **18** with 1 equiv of dibromobutene **6** in the presence of potassium carbonate in refluxing acetonitrile gave the macrocycle **13** in 72% yield. Comparing the two pathways for the synthesis of **13** the overall yield of five steps improves from 26% (Scheme 1) to 39% (Scheme 3).

Once we had azamacrocycles of type **3** in hand we decided to study their complexating ability towards palladium metal in its different oxidation states. Macrocycle **3aab** turned out to be the most soluble compound in classical organic solvents, therefore, it was the compound chosen for coordination studies. The results are summarized in Scheme 4. Owing to the high insolubility of macrocycles containing two or three NH groups (**3abb** and **3bbb**) no complexation studies with palladium could be done with them.



Scheme 3. Alternative pathway for the synthesis of protected macrocycle **13**.



Scheme 4. Complexation ability of azamacrocycle **3aab** in front of Pd^0 and Pd^{II} complexes.

Palladium(0) complex **19** was prepared in 88% yield by reaction of **3aab** with bis(dibenzylideneacetone)palladium(0) in refluxing THF. On the other hand, when **3aab** was treated with an alcoholic solution (EtOH–MeOH, 4:1) of sodium tetrachloropalladate(II) at room temperature, Pd^{II} complex **20** was obtained in 63% yield. Unfortunately, all attempts to obtain X-ray quality crystals of complexes **19** and **20** failed. However, the structure of Pd^0 complex **19** could be unequivocally assigned based on our previous structural analysis by means of NMR spectroscopy of Pd^0 complexes **2** (Fig. 1).[3] Upfield shift of the ^1H and ^{13}C NMR signals of the olefinic protons is an inequivocal proof of the triolefinic coordination mode of **19**.

Thus, the ^1H NMR spectrum of **3aab** showed a broad singlet at δ 5.69 ppm corresponding to the six olefinic protons and the ^{13}C NMR spectrum presented three signals at δ 129.4, 130.3 and 131.0 ppm for the olefinic carbon atoms. In contrast, the olefinic protons in Pd^0-complex **19**, compared to **3aab**, shifted strongly upfield ($\delta = 1.5$–4.8 ppm) following the normal behavior observed for complexes **2**,[3] as well as for other Pd^0-olefin complexes.[20–24] ^{13}C NMR spectrum of **19** showed the olefinic carbon atoms shifted by $\Delta\delta = 50$ ppm upfield as compared to the free ligand **3aab**. In contrast, this behavior is not observed for Pd^{II}-complex **20** (most probably *trans*-**20**). The ^1H NMR data for the olefins of Pd^{II}-complex **20** showed two broad signals at δ 5.5 and 5.8 ppm for the twelve olefinic protons and the ^{13}C NMR spectrum presented three signals in the same range (δ 128–132 ppm) as for the free ligand **3aab**. Furthermore, 2D heteronuclear (^1H–^{13}C HMQC) correlation spectrum has been done to confirm assignment of the ring protons (See Supplementary data)

In addition, complexes **19** and **20** presented correct elemental analysis and their molecular weight was confirmed by Electrospray Ionization Mass Spectrometry (ESI-MS). Compounds **19** and **20** were easily identified by the characteristic isotope distribution of the metal. Isotope abundance of clusters was compared with calculated values. The ESI mass spectra of **19** showed a cluster centered at *m*/*z* 622 assigned to the $[M+H]^+$ ion. The ESI mass spectra of **20** showed a cluster centered at *m*/*z* 1173 attributed to the cationic species $[M-Cl]^+$. Figure 2 shows the ESI-MS spectra of complexes **19** and **20**. The two insets show the isotope distribution pattern for the *m*/*z* 621 ion corresponding to $[M]^+$ of **19** and for the *m*/*z* 1173 ion corresponding to $[M-Cl]^+$ of **20**, respectively.

With all these data in hand, we can conclude that when macrocycle **3aab** is treated with a palladium(0) source, the metal atom is introduced into the macrocyclic cavity, being coordinated by the three olefins, whereas, when it is treated with palladium(II), the nitrogen donor atoms are responsible for the coordination.

Further studies on the complexation properties of this novel macrocycles are in progress in our laboratories.

3. Experimental

3.1. General remarks

2-(Trimethylsilylethyl)sulfonamide **4** was prepared according to the procedure of Robins et al.[18] (*E*,*E*,*E*)-1,14-dichloro-*N*,*N*′-bis(*p*-tolylsulfonyl)-5,10-diazatetradeca-2,7,12-triene **14** was prepared as previously reported by us for the 1,14-dibromo analogue.[19] 1,4-dibromo-2-butene, **6**,

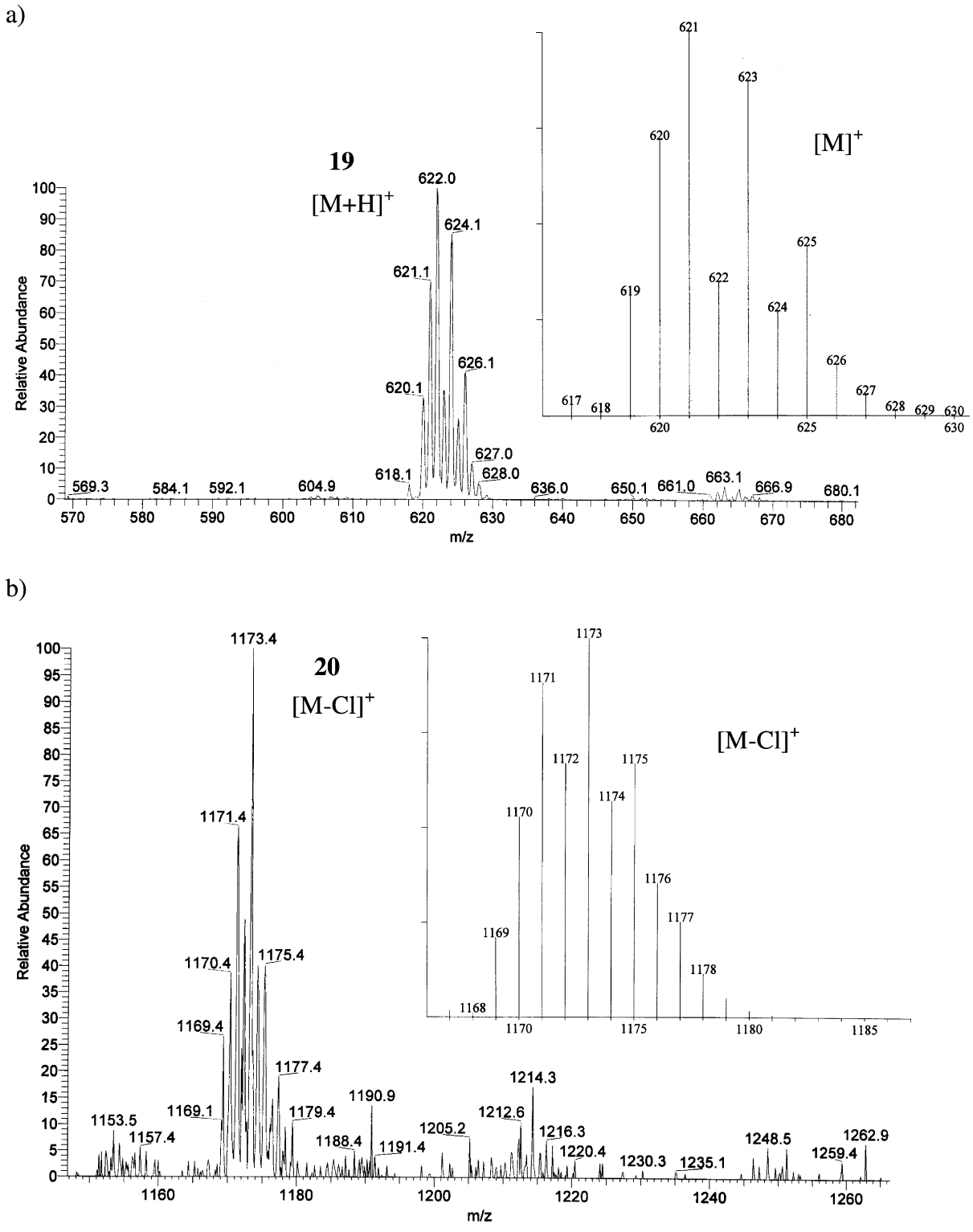


Figure 2. ESI(+) mass spectra of (a) complex **19** and (b) complex **20** compared with theoretical isotope distribution (the inset).

1,4-dichloro-2-butene, **9**, and *p*-tolylsulfonamide, **11**, are commercially available and were used as received.

^{1}H NMR (^{13}C NMR) spectra were recorded at 200 MHz (50 MHz) using Me_4Si as internal standard. Chemical shifts are given in δ units. ESI (electrospray ionization) mass spectra were acquired using a quadrupole mass spectrometer equipped with an electrospray ion source. The instrument was operated in the positive-ion mode (ESI+) at a probe tip voltage of 3 kV. Elemental analyses were determined at 'Servei d'Anàlisi de la Universitat de Girona'. TLC analyses were performed on silica gel 60 F 256 plates, and column chromatographies were performed on silica gel 60 (70–230 mesh).

3.1.1. *N*-(*tert*-Butyloxycarbonyl)(2-trimethylsilylethyl) sulfonamide (5). It was prepared according to the general method of ref.[25] Colorless solid. Mp 79–81 °C (*n*-hexane) (lit.[26] 82–82.5 °C). IR (ATR): ν 3258, 2984, 1710, 1432, 1341, 1245, 1130 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ 0.06 (s, 9H), 0.99–1.08 (m, 2H), 1.50 (s, 9H), 3.27–3.36 (m, 2H), 7.66 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): δ −1.5, 10.8, 28.4, 49.9, 84.6, 150.6. ESI-MS (*m/z*): 299 $[M+NH_4]^+$, 580 $[2M+NH_4]^+$.

3.1.2. (*E*)-*N*,*N*′-Bis(*tert*-butyloxycarbonyl)-*N*,*N*′-bis[(2-trimethylsilylethyl)sulfonyl]-2-butene-1,4-diamine (7). A stirred mixture of **5** (0.74 g, 2.63 mmol), (*E*)-1,4-dibromo-2-butene (**6**) (0.28 g, 1.31 mmol), potassium carbonate (0.66 g, 4.77 mmol), and acetonitrile (10 mL) was refluxed for 27 h (TLC monitoring). The salts were filtered off and the filtrate was evaporated to afford a residue, which was purified by column chromatograpy on silica gel (*n*-hexane–EtOAc, 9:1) to afford **7** (0.64 g, 79%) as a colorless solid. A sample specially purified for elemental analysis was obtained by digestion with *n*-hexane. Mp 120–121 °C (*n*-hexane). IR (ATR): ν 2954, 1723, 1346, 1137 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ 0.07 (s, 18H), 0.93–1.02 (m, 4H), 1.52 (s, 18H), 3.35–3.44 (m, 4H), 4.24 (br abs, 4H), 5.78 (s, 2H). ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): δ −1.4, 10.9, 28.6, 48.0, 51.5, 85.0, 129.5, 152.0. ESI-MS (*m/z*): 632 $[M+NH_4]^+$. Anal. Calcd for $C_{24}H_{50}N_2O_8S_2Si_2$ (614.96): C, 46.87; H, 8.20; N, 4.56. Found: C, 47.03 and 47.02; H, 8.53 and 8.33; N, 4.51 and 4.50.

3.1.3. (*E*)-*N*,*N*′-Bis[(2-trimethylsilylethyl)sulfonyl]-2-butene-1,4-diamine (8). A mixture of **7** (0.41 g, 0.67 mmol), trifluoroacetic acid (0.31 mL, 4.02 mmol), and dichloromethane (6 mL) was stirred at room temperature for 24 h. Then, a second portion of trifluoroacetic acid (0.47 mL, 6.10 mmol) was added and the mixture was stirred 24 h more until completion of the reaction (TLC monitoring). The solution was washed with aqueous $NaHCO_3$ (2×10 mL), water (2×10 mL), dried over anhydrous sodium sulfate and evaporated. Compound **8** (0.28 g, 100%) was obtained as a colorless solid. A sample specially purified for elemental analysis was obtained by crystallization from CH_2Cl_2–*n*-hexane. Mp 119.5–120.5 °C (CH_2Cl_2–*n*-hexane). IR (ATR): ν 3283, 2954, 1310, 1248, 1134 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ 0.06 (s, 18H), 0.97–1.06 (m, 4H), 2.90–2.99 (m, 4H), 3.72 (br abs, 4H), 4.98 (br s, 2H), 5.78 (s, 2H). ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): δ −1.3, 11.2, 45.3, 49.9, 129.8. ESI-MS (*m/z*): 415 $[M+H]^+$, 432 $[M+NH_4]^+$. Anal. Calcd for $C_{14}H_{34}N_2O_4S_2Si_2$ (414.73): C, 40.54; H, 8.26; N, 6.75. Found: C, 40.56 and 40.84; H, 8.34 and 8.53; N, 6.73 and 6.72.

3.1.4. (*E*,*E*,*E*)-*N*,*N*′-Bis[(2-trimethylsilylethyl)sulfonyl]-1,14-dichloro-5,10-diazatetradeca-2,7,12-triene (10). A stirred mixture of **8** (2.43 g, 5.86 mmol) and potassium carbonate (3.64 g, 26.34 mmol) was heated at 70 °C in acetonitrile (25 mL) for 10 min. Then, (*E*)-1,4-dichloro-2-butene (**9**) (5.43 mL, 49.72 mmol) was added. The mixture was refluxed for 18 h (TLC monitoring). The salts were filtered off and the solvent was evaporated under vacuum. The residue was crystallized from CH_2Cl_2–EtOAc–*n*-hexane to afford **10** (2.28 g, 66%) as a colorless solid. Mp 79.5–80.5 °C (*n*-hexane). IR (ATR): ν 2951, 1321, 1247, 1142 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ 0.09 (s, 18H), 0.98–1.07 (m, 4H), 2.88–2.97 (m, 4H), 3.87 (d, J=4.2 Hz, 8H), 4.09 (d, J=5.6 Hz, 4H), 5.60–5.95 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): δ −1.4, 11.0, 44.4, 48.6, 49.1, 50.0, 130.0, 130.3, 131.0. ESI-MS (*m/z*): 591–593 $[M+H]^+$, 608–610 $[M+NH_4]^+$. Anal. Calcd for $C_{22}H_{44}Cl_2N_2O_4S_2Si_2$ (591.80): C, 44.65; H, 7.49; N, 4.73. Found: C, 44.34 and 44.33; H, 7.85 and 7.88; N, 4.68 and 4.66.

3.1.5. (*E*,*E*,*E*)-1-6,11-Bis[(2-trimethylsilylethyl)sulfonyl]-1,6,11-triazacyclopentadeca-3,8,13-triene (12). A stirred mixture of **10** (0.63 g, 1.06 mmol), **4** (0.24 g, 1.32 mmol), potassium carbonate (0.59 g, 4.27 mmol), and acetonitrile (50 mL) was refluxed for 24 h (TLC monitoring). The salts were filtered off and the filtrated was evaporated. The residue was purified by column chromatography on silica gel (*n*-hexane–EtOAc, polarity from 9:1 to 8:2) to afford **12** (0.58 g, 78%) as a colorless solid. A sample specially purified for elemental analysis was obtained by digestion with *n*-hexane. Mp 150.5–151.5 °C (*n*-hexane). IR (ATR): ν 2955, 1328, 1249, 1134 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ 0.06 (s, 27H), 0.95–1.04 (m, 6H), 2.86–2.95 (m, 6H), 3.88 (br s, 12H), 5.76 (br s, 6H). ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): δ −1.3, 11.0, 48.7, 51.3, 130.9. ESI-MS (*m/z*): 717 $[M+NH_4]^+$. Anal. Calcd for $C_{27}H_{57}N_3O_6S_3Si_3$ (700.21): C, 46.31; H, 8.21; N, 6.00. Found: C, 46.44 and 46.60; H, 8.49 and 8.50; N, 5.92 and 5.91.

3.1.6. (*E*,*E*,*E*)-1-(*p*-Tolylsulfonyl)-6,11-bis[(2-trimethylsilylethyl)sulfonyl]-1,6,11-triazacyclopentadeca-3,8,13-triene (13). A mixture of **10** (0.77 g, 1.30 mmol), **11** (0.22 g, 1.28 mmol), cesium carbonate (1.70 g, 5.20 mmol), and DMF (50 mL) was stirred at room temperature for 24 h (TLC monitoring). The solvent was evaporated and CH_2Cl_2 (50 mL) was added. The salts were filtered of through Celite and the organic layer was dried and evaporated. The residue was purified by column chromatography on silica gel (*n*-hexane–EtOAc, polarity from 9:1 to 8:2) to afford **13** (0.49 g, 55%) as a colorless solid. A sample specially purified for elemental analysis was obtained by digestion with *n*-hexane. Mp 113–114 °C (*n*-hexane). IR (ATR): ν 2954, 1330, 1250, 1136 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ 0.06 (s, 18H), 0.95–1.04 (m, 4H), 2.43 (s, 3H), 2.85–2.94 (m, 4H), 3.75 (br s, 4H), 3.84 (br s, 8H), 5.70 (br s, 6H), 7.32 (d, J=8 Hz, 2H), 7.68 (d, J=8 Hz, 2H). ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): δ −1.4, 10.9, 22.1, 48.5, 51.0, 51.5, 127.7, 130.4, 130.5, 130.6, 130.7, 136.8, 144.1. ESI-MS (*m/z*): 690 $[M+H]^+$, 707 $[M+NH_4]^+$. Anal. Calcd for $C_{29}H_{51}N_3O_6S_3Si_2 \cdot CH_3OH$ (722.14): C, 50.47; H, 7.45; N, 6.09. Found: C, 49.84 and 49.63; H, 7.92 and 8.09; N, 5.91 and 5.92. HRMS Calcd *m/z* for (M+Na) 712.2370. Found: 712.2387.

3.1.7. (*E*,*E*,*E*)-1,6-Bis(*p*-tolylsulfonyl)-11-[(2-trimethylsilylethyl)sulfonyl]-1,6,11-triazacyclopentadeca-3,8,13-triene (15). This was obtained as for **12**. Colorless solid. Mp 118–120 °C (*n*-hexane–diethyl ether). IR (ATR): ν 2923, 1328, 1155, 1090 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ 0.06 (s, 9H), 0.95–1.04 (m, 2H), 2.43 (s,

6H), 2.83–2.95 (m, 2H), 3.72 (br s, 8H), 3.81 (br s, 4H), 5.64 (br s, 6H), 7.32 (d, $J=7.6$ Hz, 4H), 7.67 (d, $J=7.6$ Hz, 4H). ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): δ −1.4, 10.8, 22.0, 48.5, 50.8, 51.3, 51.4, 127.7, 130.1, 130.2, 130.4, 136.7, 144.1. ESI-MS (*m/z*): 680 $[M+H]^+$, 697 $[M+NH_4]^+$. Anal. Calcd for $C_{31}H_{45}N_3O_6S_3Si.Et_2O$ (754.10): C, 55.74; H, 7.35; N, 5.57; S, 12.76. Found: C, 55.71 and 55.63; H, 7.42 and 7.38; N, 5.76 and 5.75; S, 12.64 and 13.06.

3.1.8. General procedure for deprotection of macrocycles 12, 13, and 15. Preparation of (*E*,*E*,*E*)-1,6,11-triazacyclopentadeca-3,8,13-triene (3bbb). A stirred mixture of macrocycle **12** (0.53 g, 0.76 mmol), anhydrous cesium fluoride (1.15 g, 7.57 mmol), and anhydrous DMF (15 mL) was heated at 100 °C for 19 h (TLC and RMN monitoring). Methanol (1 mL) was added and the solvents were evaporated under vacuum. The oily residue was purified by bulb-to-bulb distillation affording **3bbb** (0.13 g, 81%) as a colorless oil. Bp 175–185 °C/3 mmHg. IR (ATR): ν 3293, 2907 cm^{-1}. ^{1}H NMR (200 MHz, CD_3OD, 25 °C, TMS): δ 3.20–3.27 (m, 12H), 5.55–5.70 (m, 6H). ^{13}C NMR (50 MHz, CD_3OD, 25 °C, TMS): δ 51.7, 132.7. ESI-MS (*m/z*): 208 $[M+H]^+$, 249 $[M+CH_3CN+H]^+$. HRMS Calcd *m/z* for (M+H) 208.1810. Found: 208.1803.

3.1.9. (*E*,*E*,*E*)-1-(*p*-Tolylsulfonyl)-1,6,11-triazacyclopentadeca-3,8,13-triene (3abb). Colorless solid. Mp 91.5–92.5 °C (*n*-hexane). IR (ATR): ν 3251, 2890, 1323, 1150, 1088 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ 2.43 (s, 3H), 3.25–3.34 (m, 8H), 3.74 (d, $J=5$ Hz, 4H), 5.50–5.75 (m, 6H), 7.30 (d, $J=8.2$ Hz, 2H), 7.70 (d, $J=8.2$ Hz, 2H). ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): δ 22.1, 51.0, 51.5, 51.8, 127.6, 127.8, 130.4, 131.6, 134.4, 137.2, 143.9. ESI-MS (*m/z*): 362 $[M+H]^+$. HRMS Calcd *m/z* for (M+H) 362.1900. Found: 362.1892.

3.1.10. (*E*,*E*,*E*)-1,6-Bis(*p*-tolylsulfonyl)-1,6,11-triazacyclopentadeca-3,8,13-triene (3aab). Colorless solid. Mp 144–145 °C (*n*-hexane). IR (ATR): ν 1331, 1154 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ 2.43 (s, 6H), 3.42 (br s, 4H), 3.73 (br s, 8H), 4.87 (br s, 1H), 5.69 (br s, 6H), 7.31 (d, $J=8$ Hz, 4H), 7.67 (d, $J=8$ Hz, 4H). ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): δ 22.1, 49.1, 51.4, 51.9, 127.8, 129.4, 130.3, 130.4, 131.1, 136.8, 144.1. ESI-MS (*m/z*): 516 $[M+H]^+$. Anal. Calcd for $C_{26}H_{33}N_3O_4S_2\cdot{}^1/_2$MeOH (531.70): C, 59.86; H, 6.63; N, 7.90; S, 12.06. Found: C, 59.99 and 59.80; H, 6.71 and 6.83; N, 8.00 and 8.01; S, 12.00 and 11.87.

3.1.11. *N*-[(*E*)-4-Chloro-2-butenyl]-*N*-(*tert*-butyloxycarbonyl)(2-trimethylsilylethyl)sulfonamide (16). A stirred mixture of **5** (3.32 g, 11.80 mmol), dichlorobutene **9** (5.15 mL, 47.16 mmol), potassium carbonate (8.14 g, 58.90 mmol), and acetonitrile (80 mL) was refluxed for 6 h (TLC monitoring). The salts were filtered off and the filtrated was evaporated. The oily residue was purified by column chromatography on silica gel (*n*-hexane–EtOAc, 15:1) to afford **16** (3.44 g, 79%) as a colorless oil. IR (ATR): ν 2955, 1727, 1355 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ 0.09 (s, 9H), 0.95–1.04 (m, 2H), 1.57 (s, 9H), 3.38–3.47 (m, 2H), 4.08 (d, $J=4.5$ Hz, 2H), 4.30 (d, $J=4.5$ Hz, 2H), 5.85–5.92 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): δ −1.4, 11.2, 28.7, 44.7, 47.7, 51.5, 85.2, 130.3, 130.4, 152.0. ESI-MS (*m/z*): 370 $[M+H]^+$, 387 $[M+NH_4]^+$.

3.1.12. (*E*,*E*)-1,11-Bis(*tert*-butyloxycarbonyl)-1,11-bis[(2-trimethylsilylethyl)sulfonyl]-6-(*p*-tolylsulfonyl)-1,6,11-triazaundeca-3,8-diene (17). A stirred mixture of **16** (2.29 g, 6.19 mmol), **11** (0.54 g, 3.15 mmol), potassium carbonate (2.62 g, 18.96 mmol), and acetonitrile (60 mL) was refluxed for 19 h (TLC monitoring). The salts were filtered off and the filtrated was evaporated. The residue was purified by column chromatography on silica gel (*n*-hexane–EtOAc, 9:1) to afford **17** (2.06 g, 79%) as a colorless oil. IR (ATR): ν 2953, 1723, 1349, 1133 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ 0.06 (s, 18H), 0.90–0.99 (m, 4H), 1.51 (s, 18H), 2.42 (s, 3H), 3.33–3.45 (m, 4H), 3.77 (d, $J=6$ Hz, 4H), 4.17 (d, $J=6$ Hz, 4H), 5.45–5.70 (m, 4H), 7.29 (d, $J=8.2$ Hz, 2H), 7.67 (d, $J=8.2$ Hz, 2H). ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): δ −1.4, 11.0, 22.2, 28.6, 48.1, 48.5, 51.5, 85.0, 127.8, 128.5, 130.4, 130.7, 137.8, 143.9, 152.0. ESI-MS (*m/z*): 855 $[M+NH_4]^+$. Anal. Calcd for $C_{35}H_{63}N_3O_{10}S_3Si_2\cdot 2Et_2O$ (986.49): C, 52.35; H, 8.48; N, 4.26. Found: C, 52.50 and 51.58; H, 8.62 and 8.82; N, 4.63 and 4.83.

3.1.13. (*E*,*E*)-1,11-Bis[(2-trimethylsilylethyl)sulfonyl]-6-(*p*-tolylsulfonyl)-1,6,11-triazaundeca-3,8-diene (18). A mixture of **17** (1.97 g, 2.35 mmol), trifluoroacetic acid (1.08 mL, 14.02 mmol), and dichloromethane (30 mL) was stirred at room temperature for 24 h. Then, a second portion of trifluoroacetic acid (1.63 mL, 21.16 mmol) was added and the mixture was stirred 24 h more until completion of the reaction (TLC monitoring). The crude solution was washed with aqueous $NaHCO_3$ (2×30 mL), water (2×30 mL), dried over anhydrous sodium sulfate and evaporated. Compound **18** (1.45 g, 97%) was obtained as a colorless solid. A sample specially purified for elemental analysis was obtained by digestion with *n*-hexane. Mp 123–124 °C (*n*-hexane). IR (ATR): ν 3280, 2954, 1314, 1134 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ 0.09 (s, 18H), 0.99–1.08 (m, 4H), 2.47 (s, 3H), 2.92–3.01 (m, 4H), 3.68–3.79 (m, 8H), 4.73 (t, $J=6.2$ Hz, 2H), 5.64–5.72 (m, 4H), 7.35 (d, $J=8.0$ Hz, 2H), 7.71 (d, $J=8.0$ Hz, 2H). ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): δ −1.4, 10.9, 22.0, 44.9, 49.7, 49.8, 127.7, 128.3, 130.4, 131.1, 137.1, 144.4. ESI-MS (*m/z*): 638 $[M+H]^+$, 655 $[M+NH_4]^+$. Anal. Calcd for $C_{25}H_{47}N_3O_6S_3Si_2$ (638.02): C, 47.06; H, 7.42; N, 6.59. Found: C, 46.78; H, 7.85; N, 6.33.

3.1.14. (*E*,*E*,*E*)-1-(*p*-Tolylsulfonyl)-6,11-bis(2-trimethylsilylethyl)sulfonyl-1,6,11-triazacyclopentadeca-3,8,13-triene (13). A stirred mixture of **18** (1.39 g, 2.18 mmol), dibromobutene **6** (0.48 g, 2.24 mmol), potassium carbonate (1.51 g, 10.92 mmol), and acetonitrile (180 mL) was refluxed for 22 h (TLC monitoring). The salts were filtered off and the filtrated was evaporated. The residue was purified by column chromatography on silica gel (*n*-hexane–EtOAc, 8:2) to afford **13** (1.08 g, 72%) as a colorless solid.

3.1.15. (*E*,*E*,*E*)-1,6-Bis(*p*-tolylsulfonyl)-1,6,11-triazacyclopentadeca-3,8,13-trienepalladium(0) (19). A magnetically stirred solution of macrocycle **3aab** (0.14 g,

0.27 mmol) and bis(dibenzylideneacetone)palladium(0) (0.16 g, 0.28 mmol) in THF (14 mL) was refluxed for 3.5 h (TLC monitoring). The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel (EtOAc–CH_2Cl_2–methanol, 8:1:1) to afford **19** as a colorless solid (0.15 g, 88%). Mp 150–152 °C (dec). IR (ATR): ν 2918, 1329, 1156 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ 1.55–1.95 (m, 4H), 2.39 (s, 6H), 2.80 (q, $J=11.6$ Hz, 2H), 3.13 (dt, $J=13.0$, 2.8 Hz, 2H), 3.53–4.10 (m, 6H), 4.55–4.87 (m, 4H), 7.25–7.32 (m, 4H), 7.60–7.75 (m, 4H). ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): δ 22.0, 45.8, 46.0, 48.8, 49.1, 50.2, 50.3, 77.6, 77.7, 78.4, 81.3, 81.7, 82.5, 127.5, 127.6, 130.3, 130.4, 135.9, 136.6, 143.8, 143.9. ESI-MS (*m/z*): 622 $[M+H]^+$. Anal. Calcd for $C_{26}H_{33}N_3O_4S_2Pd\cdot\frac{1}{2}CHCl_3$ (681.78): C, 46.68; H, 4.95; N, 6.16; S, 9.40. Found: C, 46.63 and 46.76; H, 5.21 and 5.26; N, 5.93 and 5.93; S, 9.17 and 9.32.

3.1.16. *trans*-(*E*,*E*,*E*)-Dichlorobis[1,6-bis(*p*-tolylsulfonyl)-1,6,11-triazacyclopentadeca-3,8,13-triene]palladium(II) (20). Macrocycle **3aab** (0.10 g, 0.19 mmol) was stirred in a mixture of EtOH–MeOH (20–5 mL) until complete dissolution. Then, a solution of sodium tetrachloropalladate (II) (0.058 g, 0.20 mmol) in MeOH (3 mL) was added slowly to the previous one and the mixture was stirred 10 min until precipitation of a yellow solid. The reaction mixture was stored in the freeze overnight to assure the complete precipitation of the complex. Then, the solid residue was filtered, washed with cold methanol to give Pd(II) complex **20** (0.074 g, 63%) as a yellow solid. A sample specially purified for elemental analysis was obtained by crystallization from *n*-hexane–$CHCl_3$. Mp 137–139 °C (dec). IR (ATR): ν 1332, 1155 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ 2.45 (s, 12H), 3.15–3.45 (m, 4H), 3.50–3.90 (m, 20H), 5.40–5.95 (m, 12H), 7.33 (d, $J=8$ Hz, 8H), 7.68 (d, $J=8$ Hz, 8H). ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): δ 22.2, 51.4, 51.9, 54.7, 127.9, 128.3, 130.4, 130.6, 132.3, 136.7, 144.4. ESI-MS (*m/z*): 1173 $[M-Cl]^+$. Anal. Calcd for $C_{52}H_{66}N_6O_8S_4Cl_2Pd\cdot CHCl_3$ (1328.06): C, 47.93; H, 5.08; N, 6.33; S, 9.66. Found: C, 47.87 and 47.76; H, 5.49 and 5.46; N, 6.23 and 6.20; S, 9.36 and 9.34.

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Supplementary data

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NMR spectroscopic data for macrocycle **3aab** Palladium(0) complex **19** and Palladium(II) complex **20**.

References and notes

1. Moreno-Mañas, M.; Pleixats, R.; Roglans, A.; Sebastián, R. M.; Vallribera, A. *Arkivoc* **2004**, 109–129 available from http//www.arkat-usa.org.
2. Moreno-Mañas, M.; Pleixats, R.; Sebastián, R. M.; Vallribera, A.; Roglans, A. *J. Organomet. Chem.* **2004**, *689*, 3669–3684.
3. Pla-Quintana, A.; Roglans, A.; Vicente de Julián-Ortiz, J.; Moreno-Mañas, M.; Parella, T.; Benet-Buchholz, J.; Solans, X. *Chem. Eur. J.* **2005**, *11*, 2689–2697.
4. Dietrich, B.; Viout, P.; Lehn, J.-M. *Aspects de la Chimie des Composés Macrocycliques*; InterEditions/CNRS: Paris, 1991.
5. *Macrocycle Synthesis. A Practical Approach.* Parker, D. Ed.; Oxford University: Oxford, 1996.
6. Constable, E. C. *Coordination Chemistry of Macrocyclic Compounds*; Oxford University Press: Oxford, 1999.
7. Melson, G. A. *Coordination Chemistry of Macrocyclic Compounds*; Plenum: New York, 1979.
8. Hubin, T. J. *Coord. Chem. Rev.* **2003**, *241*, 27–46 and references cited therein.
9. *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academia: San Diego, CA, 2000.
10. Giuffrida, G.; Campagna, S. *Coord. Chem. Rev.* **1994**, *135/136*, 517–531.
11. Braunstein, P. *New J. Chem.* **1994**, *18*, 51–60.
12. Thomas, J. M.; Raja, R. *J. Organomet. Chem.* **2004**, *689*, 4110–4124.
13. Thomas, J. M.; Raja, R. *Chem. Rec.* **2001**, *1*, 448–466.
14. Absihalabi, M.; Stanislaus, A.; Qabazard, H. *Hydrocarbon Process., Int. Ed.* **1997**, *76*, 45–50 pp 53–55.
15. Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 3rd ed.; Wiley: New York, 1999; p 612.
16. Kocienski, P. J. In *Protecting Groups*; Enders, D., Noyori, R., Trost, B. M., Eds.; Thieme: New York, 2000; pp 554–558.
17. Hoye, R. C.; Richman, J. E.; Dantas, G. A.; Lightbourne, M. F.; Shinneman, L. S. *J. Org. Chem.* **2001**, *66*, 2722–2725.
18. Parker, L. L.; Gowans, N. D.; Jones, S. W.; Robins, D. J. *Tetrahedron* **2003**, *59*, 10165–10171.
19. The related 1,14-dibromo compounds has been described: Cerezo, S.; Cortès, J.; Galvan, D.; Lago, E.; Marchi, C.; Molins, E.; Moreno-Mañas, M.; Pleixats, R.; Torrejón, J.; Vallribera, A. *Eur. J. Org. Chem.* **2001**, 329–337.
20. Keasey, A.; Mann, B. E.; Yates, A.; Maitlis, P. M. *J. Organomet. Chem.* **1978**, *152*, 117–123.
21. Itoh, K.; Ueda, F.; Hirai, K.; Ishii, Y. *Chem. Lett.* **1977**, 877–880.
22. Krause, J.; Cestaric, G.; Haack, K.-J.; Seevogel, K.; Storm, W.; Pörschke, K.-R. *J. Am. Chem. Soc.* **1999**, *121*, 9807–9823.
23. Porth, S.; Bats, J. W.; Trauner, D.; Giester, G.; Mulzer, J. *Angew. Chem., Int. Ed.* **1999**, *38*, 2015–2016.
24. Kluwer, A. M.; Elsevier, C. J.; Bühl, M.; Lutz, M.; Spek, A. L. *Angew. Chem., Int. Ed.* **2003**, *42*, 3501–3504.
25. Neustadt, B. R. *Tetrahedron Lett.* **1994**, *35*, 379–380.
26. Campbell, J. A.; Hart, D. J. *J. Org. Chem.* **1993**, *58*, 2900–2990.