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Preparation of nitrogen-containing 20-membered tetraolefinic macrocycles: (*E*,*E*,*E*,*E*)-1,6,11,16-tetra(arylsulfonyl)-1,6,11,16-tetraaza-cycloicosa-3,8,13,18-tetraenes

Belén Blanco, Silvia Cerezo, Marcial Moreno-Mañas,* Roser Pleixats and Jan Spengler

Department of Chemistry, Universitat Autònoma de Barcelona, Cerdanyola, 08193 Barcelona, Spain

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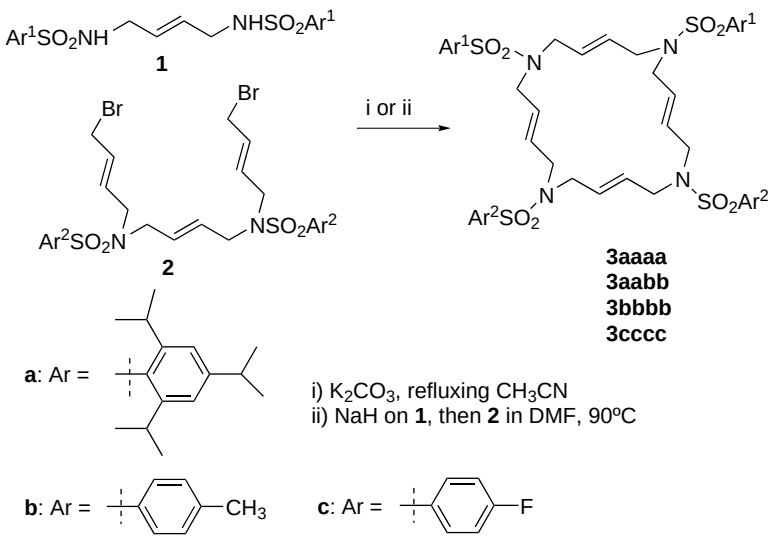
Abstract—Arenesulfonamides and *trans*-1,4-dibromobut-2-ene are the ultimate precursors for the stepwise preparation of the 20-membered macrocycles of the title. © 2001 Published by Elsevier Science Ltd.

Nitrogen-containing 20-membered macrocycles are relatively frequent.[1,2] However, nitrogen-containing 20-membered macrocycles featuring internal olefinic double bonds are rare. We have reported synthetic procedures for 15-membered rings featuring three (-N-C-C=C-C-) units in their structures, both in *E*,*E*,*E*[3] and *E*,*E*,*Z*[4] configurations. These 15-membered rings are excellent ligands for palladium(0), platinum(0), and silver(I).[3a,4,5]

20-Membered rings featuring four -N-C-C-C-C- units in any pattern of substitution or degree of unsaturation are even more rare. Thus, compounds of type -(N-C-C≡C-C-)$_n$ ($n=4$) have been reported as by-products in the preparation of 10-membered rings ($n=2$).[6] A good preparation for compounds -(NR-CH_2-CH_2-CH_2-CH_2-)$_4$ has been reported.[7] Enantiopure compounds of type (-NH-CH_2-CH(OEt)-CH(OEt)-CH_2-)$_4$ have been prepared from tartaric acid, albeit the cyclization steps



Scheme 1.

Keywords: alkene; macrocycle; nitrogen heterocycle.

* Corresponding author. Fax: 34-935811265; e-mail: marcial.moreno@uab.es

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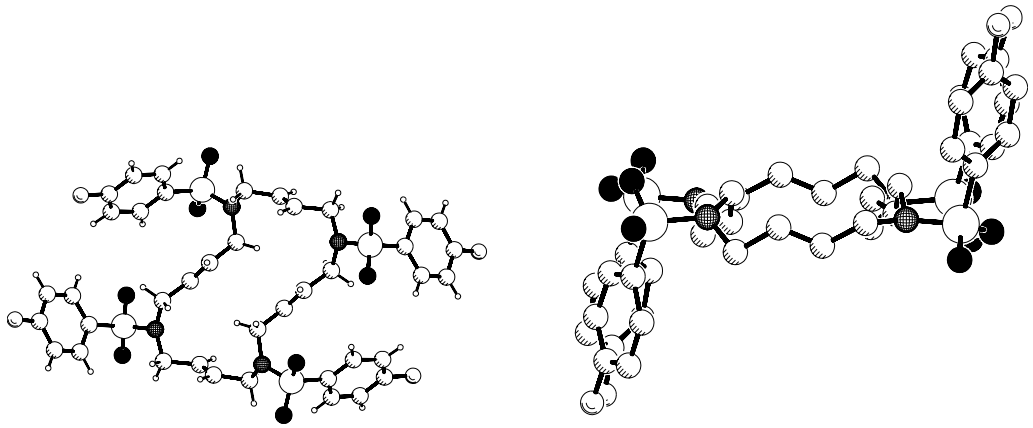

Figure 1. Perspective views of the **3cccc** molecule.

give mixtures of different macrocycles.[8] We have reported the formation of (-N(SO_2Ar)-CH_2-CH=CH-CH_2-)$_n$ (n=2,3,4) by non-selective palladium(0)-catalyzed Tsuji–Trost allylation of arenesulfonamides with *(Z)*-2-butene-1,4-diol biscarbonate.[9]

Our syntheses of the 15-membered rings are very efficient in terms of yields and simplicity. We considered the possibility of preparing related 20-membered rings of type **3** (Scheme 1) by using the same building blocks required for the 15-membered counterparts.

Reactions of bisarenesulfonamides **1** with dibromides **2** were performed either in the presence of potassium carbonate in acetonitrile or by previous treatment of **1** with sodium hydride in DMF (Scheme 1).[10] Macrocycles **3** were obtained in excellent yields,[11] high dilution seems to be not a critical factor.

Additional evidence for structures was secured by X-ray diffraction for **3cccc** (Fig. 1).[12]

Acknowledgements

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10. Preparation of (*E*,*E*,*E*,*E*)-1,6-bis[(2,4,6-triisopropylphenyl)-sulfonyl]-11,16-bis[(4-methylphenyl)sulfonyl]-1,6,11,16-tetraazacycloicosa-3,8,13,18-tetraene (**3aabb**). Typical procedure. A mixture of (*E*)-*N*,*N*′-bis[(2,4,6-triisopropylphenyl)sulfonyl]-2-buten-1,4-diamine, **1aa**, (0.619 g, 1.00 mmol), anhydrous potassium carbonate (0.553 g, 4.00 mmol), and acetonitrile (50 mL) was heated at 70°C under mechanical stirring for 30 min. Then, (*E*,*E*,*E*)-*N*,*N*′-bis[(4-methylphenyl)sulfonyl]-1,14-dibromo-5,10-diazatetradeca-2,7,12-triene, (**2bb**), (0.660 g, 1.00 mmol) was added and the mixture refluxed for 15 h. After cooling to room temperature the salts were filtered off and the filtrate was evaporated. The residue was chomatographed through silica gel (230–400 mesh) with hexane–ethyl acetate (8:2) to afford **3aabb** (0.820 g, 73% yield).[11]
    The same procedure was followed for **3bbbb**, and for **3cccc**. For **3bbbb** the residue was not chromatographed but taken in chloroform. After addition of a minor amount of pentane, **3bbbb** precipitated out and was filtered off.

Preparation of (*E*,*E*,*E*,*E*)-1,6,11,16-tetrakis[(2,4,6-triisopropylphenyl)sulfonyl]-1,6,11,16-tetraazacycloicosa-3,8,13,18-tetraene (**3aaaa**). Typical procedure. A mixture of (*E*)-*N*,*N*′-bis[(2,4,6-triisopropylphenyl)sulfonyl]-2-buten-1,4-diamine, **1aa**, (0.42 g, 0.68 mmol), 60% suspension of sodium hydride (0.085 g, 2.04 mmol) and DMF (34 mL) was heated at 90°C under magnetic stirring for 30 min. Then,(*E*,*E*,*E*)-*N*,*N*′-bis[(2,4,6-triisopropylphenyl)sulfonyl]-1,14-dibromo-5,10-diazatetradeca-2,7,12-triene, (**2aa**), (0.60 g, 0.68 mmol) was added and the mixture was heated at 90°C for 24 h. After cooling at room temperature water was added and the solid formed was filtered and partitioned between chloroform and water. The organic layer was dried and evaporated and the residue was digested with diethyl ether and with pentane, to afford **3aaaa** (0.45 g, 50% yield).[11]

11. Selected data for all new compounds: Compounds **1aa**,[3b] **1bb**,[3b] **2aa**,[3a] and **2bb**[3b] have been already described.
Compound **1cc** mp 174–177°C. It was prepared as for **1aa** and **1bb**.[3b]
Compound **2cc** mp 93–95°C. It was prepared as for **2aa**.[3a]
Compound **3aaaa** (50% yield), mp 249–251°C; IR (KBr) 2960, 1601, 1460, 1364, 1313, 1151 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) $\delta=1.72$ (t, $J=$ca 7 Hz, 72H), 2.87 (septet, $J=7.0$ Hz, 4H), 3.74 (br s, 16H), 4.05 (septet, $J=6.5$ Hz, 8H), 5.71 (br s, 8H), 7.12 (s, 8H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) $\delta=23.5$, 24.8, 29.2, 34.1, 47.5, 123.9, 130.1, 131.0, 151.5, 153.2; MALDI-TOF MS m/z 1363.8 $[M+Na]^+$.
Compound **3aabb** (73% yield), mp 68–70°C; IR (KBr) 2959, 1600, 1463, 1339, 1161 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) $\delta=1.26$ (t, $J=7.4$ Hz, 36H), 2.46 (s, 6H), 2.92 (septet, $J=7.0$ Hz, 2H), 3.73 (m, 16H), 4.08 (septet, $J=6.6$ Hz, 4H), 5.50–5.72 (m, 8H), 7.17 (s, 4H), 7.33 (d, $J=8.4$ Hz, 4H), 7.68 (d, $J=8.3$ Hz, 4H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) $\delta=21.3$, 23.3, 24.5, 29.0, 33.9, 47.3, 48.8, 49.0, 123.7, 126.9, 129.6, 129.7, 130.6, 136.1; MALDI-TOF MS m/z 1156.5 $[M+K]^+$, 1140.4 $[M+Na]^+$.
Compound **3bbbb** (47% yield), mp 219–220°C; IR (KBr) 2922, 1597, 1340, 1160, 1091 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) $\delta=2.47$ (s, 12H), 3.65 (br s, 16H), 5.47 (br s, 8H), 7.35 (d, $J=8.5$ Hz, 8H), 7.66 (d, $J=8.4$ Hz, 8H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) $\delta=21.6$, 49.2, 127.2, 129.7, 129.9, 136.4, 143.7; MALDI-TOF MS m/z 932.1 $[M+K]^+$, 916.1 $[M+Na]^+$.
Compound **3cccc** was prepared as for **3aaaa**, inorganic salts being removed by washing with water. It was difficult to obtain in pure form due to low solubility. MALDI-TOF mass spectrum of crude **3cccc** indicated the presence of minor amounts of the 40-membered ring (m/z 1839.1 $[M+Na]^+$). A pure sample of **3cccc** (0.34 g from 0.91 g of crude material) was obtained after two column chromatographies on silica gel with chloroform containing 2–4% (v/v) of trifluoroacetic acid (TFA) and final recrystallization from trifluoroethanol/trifluoroacetic acid/water. Physical data are: mp 235–241°C; IR (KBr) 1594, 1495, 1337, 1241, 1166, 1155, 1091, 840, 549 cm^{-1}; ^1H NMR ($CDCl_3$+20% TFA, 250 MHz) $\delta=3.76$ (br s, 16H), 5.60 (br s, 8H), 7.27 (m, 8H), 7.82 (m, 8H); ^{13}C NMR ($CDCl_3$+20% TFA, 62.9 MHz) $\delta=49.4$, 117.0 (d, $J=22.9$ Hz), 129.7, 129.9 (d, $J=9.5$ Hz), 133.8 (d, $J=2.9$ Hz), 165.8 (d, $J=255.6$ Hz); ^{19}F NMR ($CDCl_3$+20% TFA, 235 MHz) $\delta=-103.93$ (s, with respect to trifluoroacetic acid); MALDI-TOF MS m/z 947.1 $[M+K]^+$, 931.2 $[M+Na]^+$; ESIMS m/z 925.1 $[M+NH_4]^+$, 908.2 $[M]^+$.
Correct elemental analyses were secured for products **1cc**, **2cc**, **3aabb** and **3cccc**.

12. Crystallographic data (excluding structure factors) for the structure in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication number CCDC172445. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0) 1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].