15-Membered triolefinic macrocycles, their coordination chemistry with transition metals, and the catalytic properties of their palladium metal complexes. A review

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Dedicated to Professor Enrique Meléndez on occasion of his retirement

Abstract

(E,E,E)-1,6,11-Tris(arenesulfonyl)-1,6,11-triazacyclopentadeca-3,8,11-trienes, **1**, are prepared from arenesulfonamides and *trans*-1,4-dibromo-2-butene. Macrocycles **1** coordinate palladium(0), platinum(0), and silver(I), and the palladium complexes are useful and reutilizable catalysts or precatalysts in Suzuki cross-couplings, butadiene telomerizations, hydroarylation of alkynes, and in the Heck reaction. Structurally related macrocycles are also available by similar synthetic procedures.

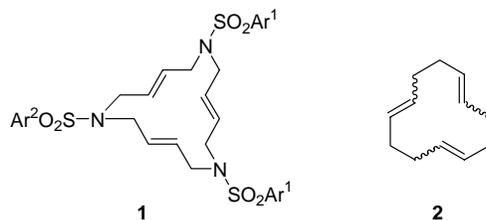**Keywords:** Alkene ligands, macrocycles, heterocycles, olefin complexes, catalysis

Contents

1. Introduction

Nitrogen-containing 15-membered macrocycles with endocyclic olefins are uncommon.[1] A few nitrogen-containing monoolefinic 15-membered rings have been prepared by metathesis.[2]

Figure 1. General Structure of macrocycles 1 and 2.

Macrocycles **1** (Figure 1) are structurally related to the 12-membered carbocyclic cyclododeca-1,5,9-trienes, **2**. Cyclotrienes **2** coordinate nickel(0) and are formed by trimerization of butadiene. The nickel complexes of **2** have played a fundamental role in catalysis and in organonickel chemistry.[3]

We discovered macrocycles **1** in a serendipitous manner when exploring the palladium-catalyzed reaction of arenesulfonamides with 2-butene-1,4-diol biscarbonate (Scheme 1).[4] 10-, 15-, and 20-membered cycles were isolated and identified. One part of the 15-membered rings appeared in the form of their palladium(0) complexes **4** (*vide infra*). Due to the similarity of IR and NMR data of 15- and 20-membered macrocycles, MALDI-TOF mass spectrometry was fundamental in the identification of the products.[5]
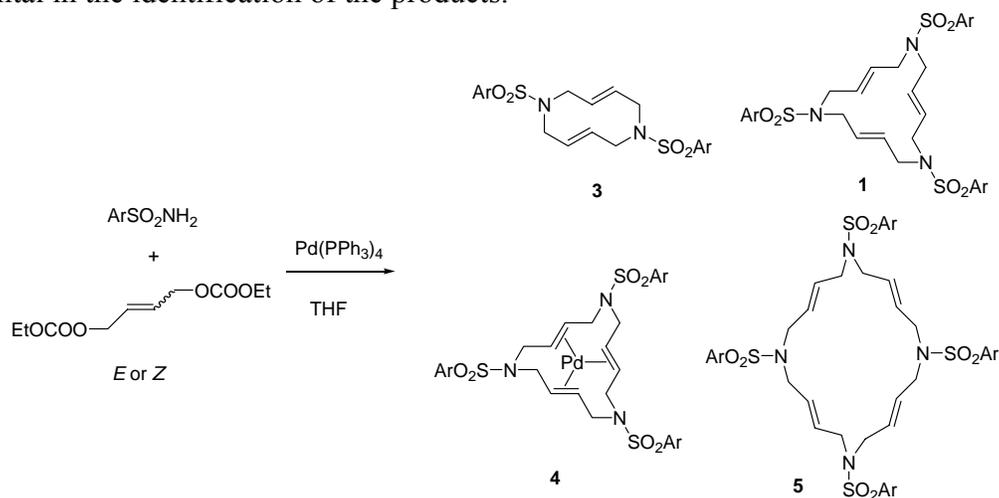
Scheme 1. Formation of medium and large cycles in a palladium catalyzed Tsuji-Trost reaction[4].

We soon noticed that we had a new chemistry in our hands. Indeed, the three olefinic double bonds are excellent coordinating centers for some transition metals. Moreover, the nitrogen atoms are devoid of coordinating ability due to lone pair conjugation with the SO_2 group, therefore leaving all coordination capacity to the three olefins.

Moreover, a broad array of arenesulfonamides or their immediate precursors arenesulfonyl chlorides are commercially available. Therefore, other properties of the macrocycles can be tuned by introducing arene or heteroarene groups that improve or impart solubility, crystallinity, electrochemical properties, polymerization ability, certain types of reactivity, etcetera. Since preparation of **1** involves the use of *trans*-1,4-dibromo-2-butene, different structurally related macrocycles can be built up by working with, for example, *cis*-1,4-dibromo-2-butene or 1,2-bis(bromomethyl)benzene.

2. Preparation of compounds

2.1 Preparation of 15-membered macrocycles

Our group described in 1998 the first 15-membered triolefinc macrocycles **1**.[4] Since then, a broad array of compounds **1** had been prepared (Table 1 and Figure 2).
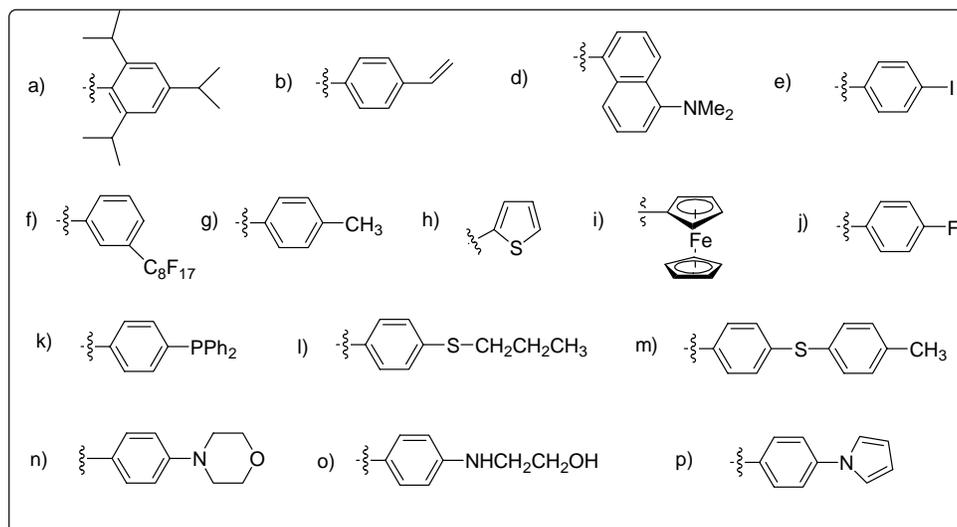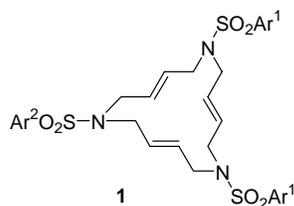
Figure 2. Substituents introduced in macrocycles 1.

Arenesulfonamides were chosen, so as to confer, enhance or modulate certain properties of the macrocycles. The presence of three isopropyl groups in the benzenesulfonyl moiety improves

solubility of macrocycles in classical organic solvents (**1aaa**, **1aab**, and **1aad**).[4,6-8] Instead, methyl groups impart crystallinity and permitted a X-ray study of **1ggg**.[7] Perfluorinated long chains were envisaged to improve the solubility of **1aff** in perfluorinated solvents.[7] Complexes containing ferrocenyl (**1ggi**, **1gii**, **1iii**, **1iip**, and **1ipp**), thienyl (**1ggh**, **1ghh**) and 4-(pyrrol-1-yl)phenyl (**1iip**, **1ipp**, and **1ggp**) units have interest for electrochemical purposes.[9,11,12] From the point of view of applications of solid supports in catalysis, **1aab** has been used to prepare polymer **1aac** by copolymerization with styrene and divinylbenzene (*vide infra*).[6] We have also prepared macrocycle **1jjj**, featuring three fluorine atoms, that is a key intermediate for the synthesis of more elaborated macrocycles through aromatic nucleophilic substitution of the three fluorine atoms with phosphorus (**1kkk**), nitrogen (**1nnn**, **1ooo**), and sulphur (**1lll**, **1mmm**) nucleophiles.[10]

Table 1. Summary of all-*trans* 15-membered macrocycles **1** synthesized

| Entry	Macrocycle	Ar^1	Ar^2	References
1	**1aaa**	2,4,6-iPrC$_6$H$_2$-	2,4,6-iPrC$_6$H$_2$-	4, 6, 7, 8
2	**1aab**	2,4,6-iPrC$_6$H$_2$-	4-CH$_2$=CHC$_6$H$_4$-	6, 7
3	**1aac**	2,4,6-iPrC$_6$H$_2$-	4-Polymer-[a]	6
4	**1aad**	2,4,6-iPrC$_6$H$_2$-	5-Dimethylaminonaphthyl-	7
5	**1aee**	4-IC$_6$H$_4$-	2,4,6-iPrC$_6$H$_2$-	7
6	**1aff**	3-C$_8$F$_{17}$C$_6$H$_4$-	2,4,6-iPrC$_6$H$_2$-	7
7	**1ddd**	5-Dimethylaminonaphthyl-	5-Dimethylaminonaphthyl-	7
8	**1ggg**	4-CH$_3$C$_6$H$_4$-	4-CH$_3$C$_6$H$_4$-	7
9	**1ggh**	4-CH$_3$C$_6$H$_4$-	2-Thienyl-	7
10	**1ghh**	2-Thienyl-	4-CH$_3$C$_6$H$_4$-	7
11	**1ggi**	4-CH$_3$C$_6$H$_4$-	Ferrocenyl-	9, 11
12	**1gii**	Ferrocenyl-	4-CH$_3$C$_6$H$_4$-	9
13	**1iii**	Ferrocenyl-	Ferrocenyl-	9
14	**1jjj**	4-FC$_6$H$_4$-	4-FC$_6$H$_4$-	10
15	**1kkk**	4-Ph$_2$PC$_6$H$_4$-	4-Ph$_2$PC$_6$H$_4$-	10
16	**1lll**	4-CH$_3$CH$_2$CH$_2$SC$_6$H$_4$-	4-CH$_3$CH$_2$CH$_2$SC$_6$H$_4$-	10
17	**1mmm**	4-CH$_3$C$_6$H$_4$-S-C$_6$H$_4$-	4-CH$_3$C$_6$H$_4$-S-C$_6$H$_4$-	10
18	**1nnn**	4-(Morpholino)phenyl-	4-(Morpholino)phenyl-	10
19	**1ooo**	4-(HOCH$_2$CH$_2$NH)C$_6$H$_4$-	4-(HOCH$_2$CH$_2$NH)C$_6$H$_4$-	10
20	**1iip**	Ferrocenyl-	4-(Pyrrol-1-yl)phenyl-	12
21	**1ipp**	4-(Pyrrol-1-yl)phenyl-	Ferrocenyl-	12
22	**1ggp**	4-CH$_3$C$_6$H$_4$-	4-(Pyrrol-1-yl)phenyl-	12

[a] Polymer of **1aab** with styrene and divinylbenzene.

We have reported three different synthetic pathways "a", "b", and "c" for the synthesis of the triazatriolefinic macrocycles **1** based on three different disconnecting approaches for the final condensation step (Figure 3).[7]

In our initial synthesis corresponding to pathway "a" (Scheme 2), reaction of arenesulfonamides with *trans*-1,4-dibromo-2-butene gave a mixture of monosulfonamides **7** and bis-sulfonamides **6**. Condensation of **6** with different arenesulfonamides was straightforward and led to the formation of macrocycles **1aaa**, **1aab**, **1aad**, **1aee**, **1ddd**, **1ggh**, **1jjj**. The main problem of this synthesis is that bis-sulfonamides **6** are obtained as minor products. Optimization of this step has not been possible. However, compounds **6** can be obtained by reaction of bis-arenesulfonamides **8** with excess *trans*-1,4-dibromobutene (Scheme 2).[7]
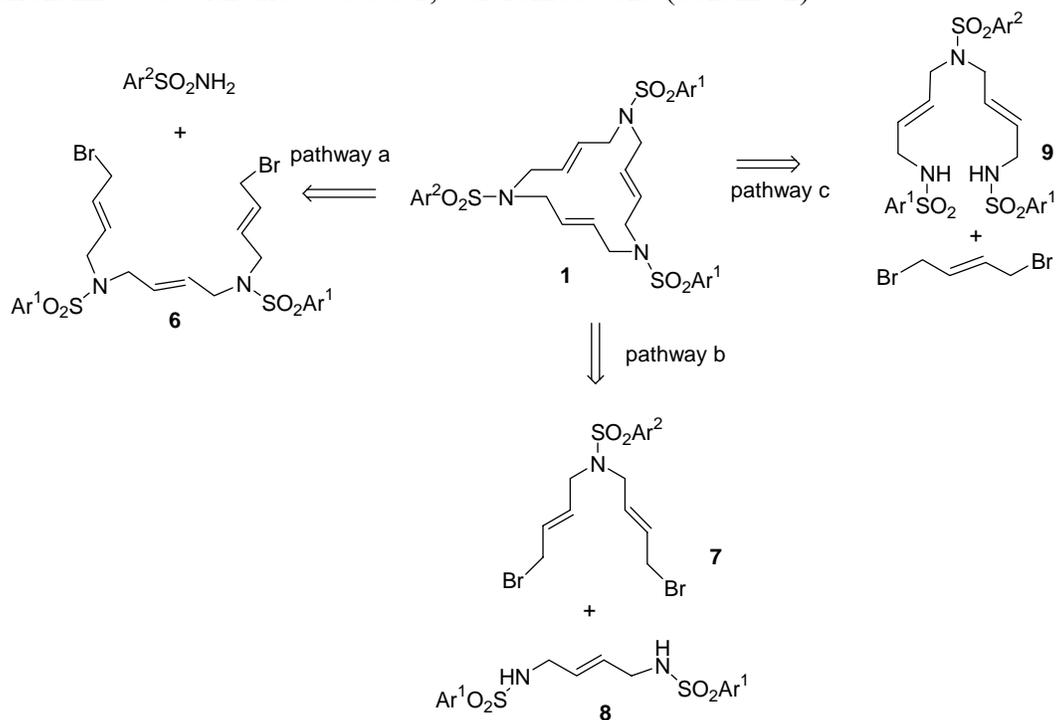

Figure 3. Retrosynthetic pathway for macrocycles **1**.
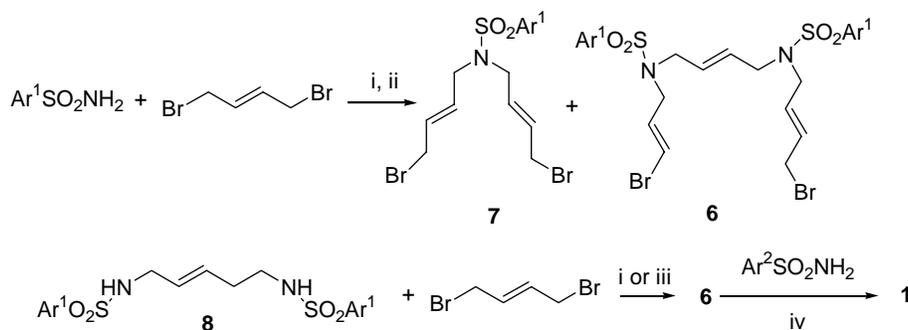
Scheme 2. Preparation according to pathway "a". Reagents and conditions: i.- NaH, DMF, then BrCH₂CH=CHCH₂Br, 90°C; ii.- column chromatography on silica gel; iii.- K₂CO3, refluxing

acetonitrile, then $BrCH_2CH=CHCH_2Br$ (8 equiv); iv.- NaH, DMF over arenesulfonamide, then **6**, 90ºC.

   Since in the first step of pathway "a" monosulfonamides **7** were obtained as major products, we soon envisaged another approach (Scheme 3). The preparation of macrocycles **1aaa**, **1ghh** and **1jjj** was achieved by reaction of the more abundant **7** with **8**.[7,10] Compound **8** was prepared by two different ways. One way is based in the diarenesulfonylation of 2-butene-1,4-diamine, which was prepared by a Gabriel reaction using *trans*-1,4-dibromo-2-butene.[6] Another way consists of a nucleophilic substitution reaction between two equivalents of **10** and *trans*-1,4-dibromo-2-butene to obtain **11**.[6] Deprotection of **11** gave quantitative yields of **8**.
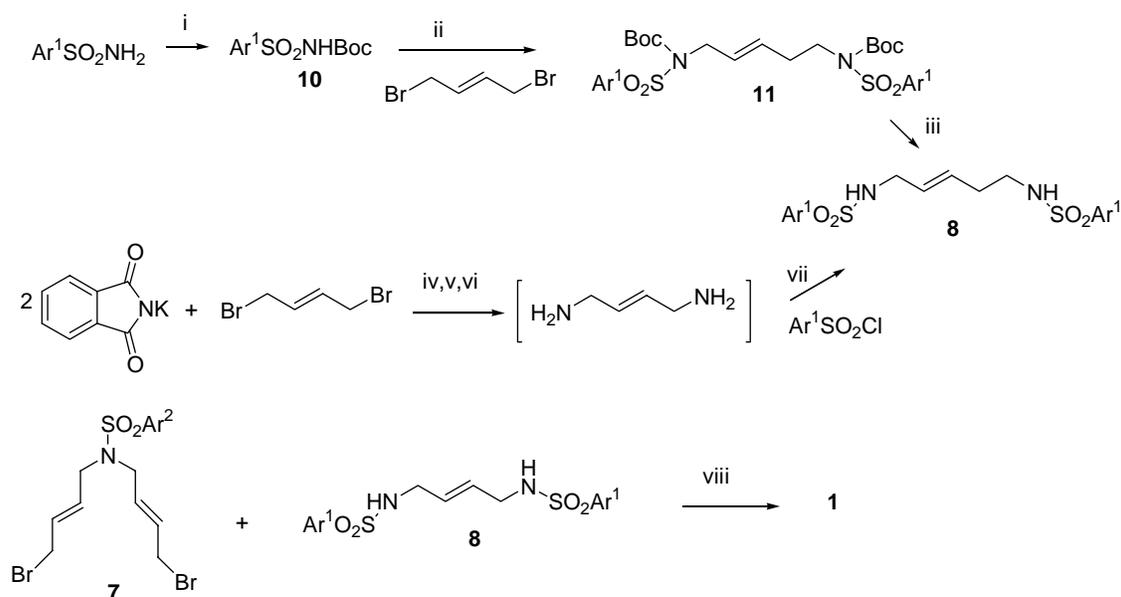
Scheme 3. Preparation according to pathway "b". Reagents and conditions: i.- (tert-BuOCO)$_2$O, Et$_3$N, DMAP (0.1 equiv), dichloromethane; ii.- K$_2$CO$_3$, acetonitrile, reflux or K$_2$CO$_3$, DMF, room temperature, then trans-1,4-dibromo-2-butene (0.5 equiv); iii.- TFAA, dichloromethane, room temperature; iv.- DMF, 80 ºC; v.- 80% hydrazine, ethanol, reflux; vi.- KOH, H2O; vii.- diethyl ether; viii.- NaH, DMF over 8, then 7, 90 ºC.

   Alternatively, macrocycles **1aff**, **1ggg**, **1ggi**, **1gii**, **1iii**, **1iip**, **1ipp,** and **1ggp** have been obtained in excellent yields by synthetic pathway "c" (Scheme 4). For the preparation of **9** the NH$_2$ groups must be protected in **10** and **12** to avoid *N*-dialkylation in step ii, and to obtain a successful reaction between **12** and the arenesulfonamide (step iii).
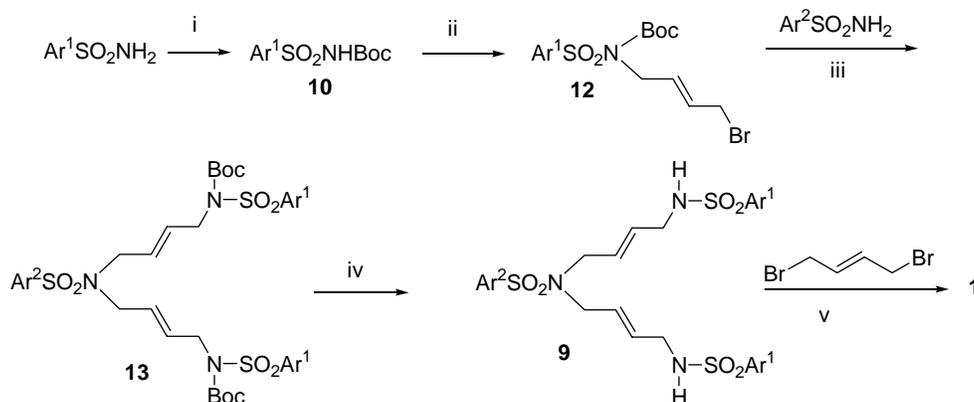
Scheme 4. Preparation according to pathway "c". Reagents and conditions: i.- (tert-BuOCO)$_2$O, Et$_3$N, DMAP (0.1 equiv), dichloromethane; ii.- K$_2$CO$_3$, acetonitrile, trans-1,4-dibromo-2-butene (4 equiv), reflux; iii.- K$_2$CO$_3$, acetonitrile, arenesulfonamide (0.5 equiv), reflux; iv.- TFAA, dichloromethane, room temperature; v.- K$_2$CO$_3$, refluxing acetonitrile, trans-1,4-dibromo-2-butene (4 equiv).

All three pathways "a", "b", and "c" are good enough. However, pathway "c" seems to be most convenient because of its versatility and it is the recommended one.

Moreover, further possibilities are offered by macrocycle **1jjj**, containing three fluorine atoms susceptible of substitution by nucleophiles. This pivotal compound has permitted us to increase the vast array of substituents possible (Scheme 5).
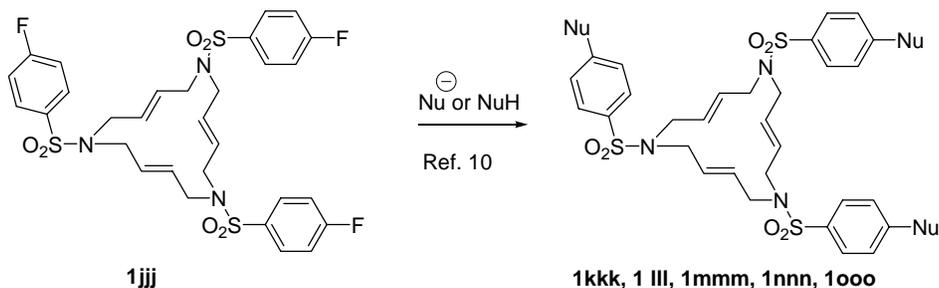
Scheme 5. Nucleophilic aromatic substitution on **1jjj**.

2.2 Preparation of metal complexes

The coordination ability of all-*trans* triazatriolefinic macrocycles with transition metals through the three double bonds, has been also studied. Thus, we have prepared a large amount of different transition metal macrocyclic complexes (Table 2). The palladium complexes **4** are obtained either by ligand-exchange using Pd(PPh$_3$)$_4$ or Pd(dba)$_2$ as sources of metal[4,6,8,11-15] or by in situ reduction of PdCl$_2$ with hydrazine in the presence of the macrocycle.[10] Excellent results

are obtained with Pt(PPh$_3$)$_4$ to prepare platinum complexes **14**, and less stable silver complexes **15** have been prepared from AgBF$_4$.
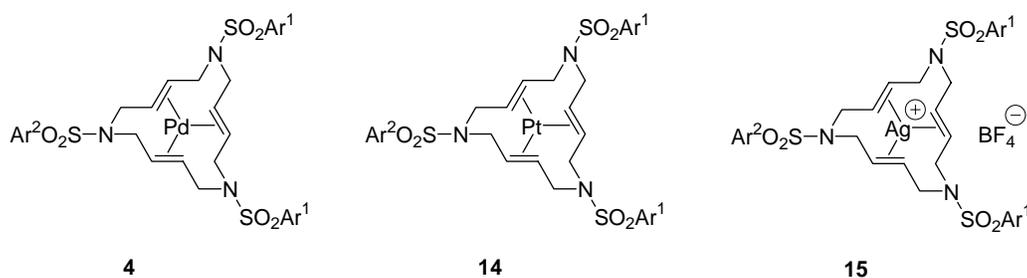
Figure 4. Palladium(0), platinum(0), and silver(I) complexes.

Table 2. Summary of transition metal complexes **4, 14** and **15** of all-*trans* 15-membered macrocycles **1**

Entry	Transition Metal Complexes	Applications in catalysis	References
1	**4aaa**	Cross-coupling type reactions, Butadiene telomerization	4, 6, 8, 14
2	**4aac**	Heterogeneous catalyst as above	6
3	**4aff**		13
4	**4ddd**		13
5	**4ggg**	Alkyne hydroarylation	13, 15
6	**4ggi**	Cross-coupling reaction, Heck reaction	9, 11
7	**4gii**		9
8	**4iii**		9
9	**4kkk**		10
10	**4iip**	Cross-coupling type reactions	12
11	**4ipp**	Cross-coupling type reactions	12
12	**4ggp**		12
13	**14aaa**		13
14	**14ggg**		13
15	**15aaa**		13
16	**15ggg**		13

3. Structure and spectroscopy

The structure of palladium complexes **4** has intrigued us since the moment of their discovery. As an example, significant ^{13}C and ^{1}H NMR data for compound **4aaa**, as well as for their uncomplexed macrocyclic ligand **1aaa** are summarized in Figure 5. The free ligand **1aaa** presented in its ^{1}H NMR spectrum only one signal at δ 3.77 for the twelve methylene protons, and in its ^{13}C NMR spectrum only one signal at δ 49.2 for the six methylene carbons; for the olefinic part, the ^{1}H NMR spectrum showed one olefinic signal at δ 5.79 for the six olefinic protons and the ^{13}C NMR spectrum presented only one signal at δ 123.9. All these data suggest that compound **1aaa** has an averaged C_3 axis of symmetry. In contrast, complex **4aaa** presented two magnetically equivalent olefinic systems with magnetically non-equivalent protons at δ 2.80 (H_a, apparent t, J = 12.4 Hz, 2H) and δ 4.10 (H_b, dd, J = 12.4 Hz and 11.1 Hz, 2H) plus a different olefinic system with magnetically equivalent protons at δ 3.85 (H_c, apparent d, J = 9.5 Hz, 2H). The strong upfield shift of olefinic signals as well as the *trans* coupling constant value of *ca.* 12 Hz are normal for olefin-Pd(0) complexes such as the palladium bis(dibenzylidene)acetone.[16] 2D NOESY experiments confirmed the *trans*-stereochemistry of the olefins. Clearly the third olefinic system in the ring is also coordinated to palladium but in a different way. ^{13}C NMR spectrum showed also three different olefinic carbon atoms (79.2, 79.3 and 83.7) shifted by $\Delta\delta_c$ = 40-44 ppm upfield as compared to the free ligand **1aaa**. These facts suggest that the presence of the palladium atom breaks the symmetry of the compound and the complexation of palladium by one olefin is different with respect to the other two.
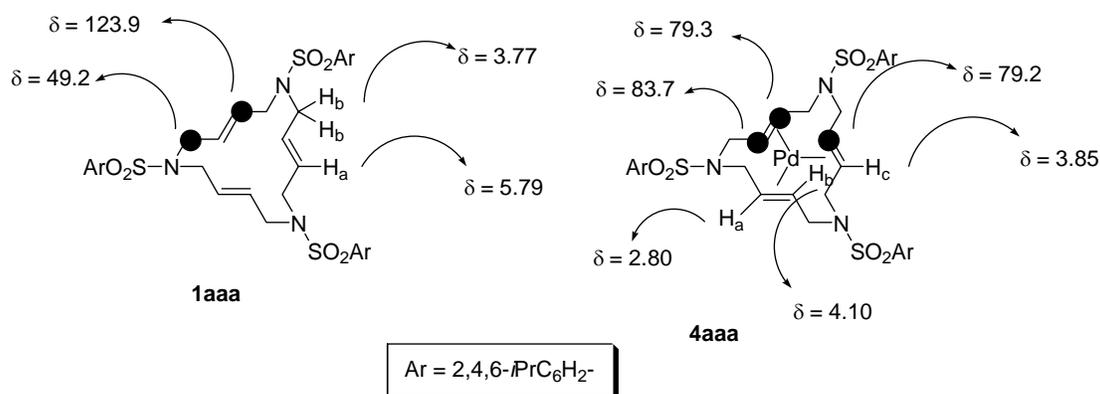
Figure 5. Significant ^{1}H and ^{13}C NMR signals for compound **1aaa** and their palladium(0) complex **4aaa**.

The same behavior is evident for other macrocycles containing three identical aryl groups on the basis of similar NMR spectra, and also for the corresponding platinum(0) complexes, **14**. Since the silver complexes **15** were not stable, they could not be studied in depth. Selected NMR data for complexes **4** and **14** are tabulated in Table 3.

Table 3. Selected NMR data[a] for complexes **4** and **14** bearing three identical aryl units

Metal Complexes	^{1}H NMR data		^{13}C NMR Data	
	Olefinic protons	Methylene protons	Olefinic carbons	Methylene carbons
4aaa	2.80 (t, *J* 12.4) 3.85 (d, *J* 9.5) 4.10 (dd, *J* 12.4, 11.1)	1.52 (dd, *J* 15.6, 11.1) 1.58 (dd, *J* 15.3, 9.5) 3.05 (dd, *J* 12.6, 12.4) 4.22 (dd, *J* 15.6, 3.2) 4.30 (d, *J* 15.3) 4.55 (d, *J* 12.6)	79.2, 79.3, 83.7	43.8, 46.5, 47.9
4ddd[b]	2.93-2.98 (m) 3.79-3.82 (m) 4.01-4.12 (m)	1.86-2.02 (m) 3.18 (dd, *J* 14.0, 10.7) 4.63 (t, *J* 13.5) 4.89 (d, *J* 13.5)	79.6, 79.8, 83.9	45.8, 48.0, 49.2
4ggg	2.79 (t, *J* 11.7) 3.75 (m) 3.93-4.03 (m)	1.50-1.80 (m) 1.63 (dd, *J* 14.3, 10.7) 3.07 (dd, *J* 14.2, 11.3) 4.62 (d, *J* 14.3) 4.64 (d, *J* 14.3) 4.78 (d, *J* 14.3)	78.5, 78.7, 82.8	45.1, 48.2, 49.5
4iii	2.64 (t, *J* 11) 3.47-3.73 (m) 3.74-3.88 (m)	1.42-1.59 (m) 2.90 (dd, *J* 14.0, 11.0) 4.24-4.47 (m)	78.5, 78.8, 83.0	45.6, 48.6, 49.8
4kkk[b]	2.84 (m) 3.72 (m) 3.95 (m)	1.80 (m) 3.10 (m) 4.64 (m) 4.78 (m)	not registered	not registered
14aaa[b]	2.49 (t, *J* 11.1) 3.38 (d, *J* 8.6) 4.36-4.40 (m)	1.84 (m) 3.14 (t, *J* 11.1) 3.58 (dt, *J* 12.5, 3.8) 4.45 (d, *J* 14.7) 4.82 (d, *J* 12.4)	62.9, 63.4, 69.7	43.1, 45.6, 47.0
14ggg	2.07 (td, *J* 13.3, 2.3) 3.22-3.25 (m) 3.41 (td, *J* 11.6, 3.8)	1.34 (dd, *J* 14.0, 10.9) 1.35-1.46 (m) 2.98 (dd, *J* 13.6, 11.5) 4.58 (dd, *J* 14.0, 3.8) 4.62 (d, *J* 12.0) 5.02 (d, *J* 12.7)	62.7, 63.2, 69.0	44.3, 47.2, 48.5

[a] Chemical shifts and coupling constants were determined by selective 1D TOCSY experiments.
[b] Assignment of chemical shifts for olefinic and methylenic protons has been done by similarity with compounds **4aaa**, **4ggg**, **4iii**, and **14ggg** that have undergone a full NMR analysis.

Strong evidence in support of these facts was secured by X-ray diffraction for **4ggg** and **14ggg**. In **4ggg** the middle point of the olefinic bonds and the metal center are all situated in the same plane and thus the coordination of the metal center is planar trigonal. The complex is not symmetrical, and, as it has been seen by NMR data, it lacks a C_3 symmetry axis. Two C=C bonds are longer than in the corresponding free ligand **1aaa**. However, the third C=C bond is shorter that the other two in the complex, suggesting that complexation with one olefin is weaker than complexation by the other two.

In complexes **4** possessing two different aryl units ($Ar^1 \neq Ar^2$) two isomers exist depending on which substituent occupies the position opposite to the singular olefin. The ^{13}C NMR spectra confirm the existence of isomers in solution: three carbon signals are found for a symmetrical isomers, but six more signals were found for isomer lacking symmetry elements. Selected ^{13}C NMR data for complexes **4** bearing two different aryl units are shown in Table 4. Further structural studies based on complexes **4** with three different aryl units are in progress.

Table 4. Selected ^{13}C NMR spectroscopic data for complexes **4** bearing two different aryl units

Complexes	Olefinic carbon atoms	Methylene carbon atoms
4aff	77.6, 77.9, 78.6, 78.8, 79.7, 79.9, 81.9, 82.8, 84.4	34.1, 43.7, 45.2, 45.4, 46.3, 47.6, 48.2, 49.3, 49.5
4ggi	78.1, 78.2, 78.3, 78.4, 78.6, 78.7, 82.5, 82.6, 82.9	45.1, 48.1, 48.2, 49.3, 49.4
4gii	78.0, 78.2, 78.3, 78.4, 78.7, 82.4, 82.7, 82.8	45.1, 48.1, 48.2, 49.4, 49.5
4iip	77.8, 78.1, 78.4, 78.6, 78.7, 78.9, 82.2, 82.9, 83.1	45.1, 45.2, 48.1, 48.2, 49.3, 49.4, 49.5
4ggp	78.1, 78.3, 78.5, 78.6, 78.7, 78.8, 82.4, 82.9, 83.0	45.0, 45.2, 48.2, 49.4

We chose Matrix-Assisted Laser Desorption/Ionization, time-of-flight (MALDI-TOF) and Electrospray Ionization Mass Spectrometry (ESI-MS) as analytical mass spectrometric techniques to identify complexes of type **4**, **14**, and **15**. Both techniques allow heavy molecules to be efficiently ionized and vaporized without degradation. Initially, MALDI-TOF mass spectrometry allowed the direct determination of the extent of macrocyclic and linear oligomer formation in the palladium(0)-catalyzed allylation of arenesulfonamides with 2-butene-1,4-diol biscarbonate[5] (Scheme 1). Later on, mass spectroscopic investigations were performed to elucidate the structure of all complexes. Compounds of type **4**, **14**, and **15** were easily identified by the characteristic isotope distribution of the metal. Isotopic abundance of clusters was compared with calculated values. Figure 6 displays a positive-ion electrospray mass spectrum of complex **14ggg** showing one peak at *m/z* 865 corresponding to [M + H]$^+$. The inset shows the isotope distribution pattern for the *m/z* 864 ion corresponding to [M]$^+$.
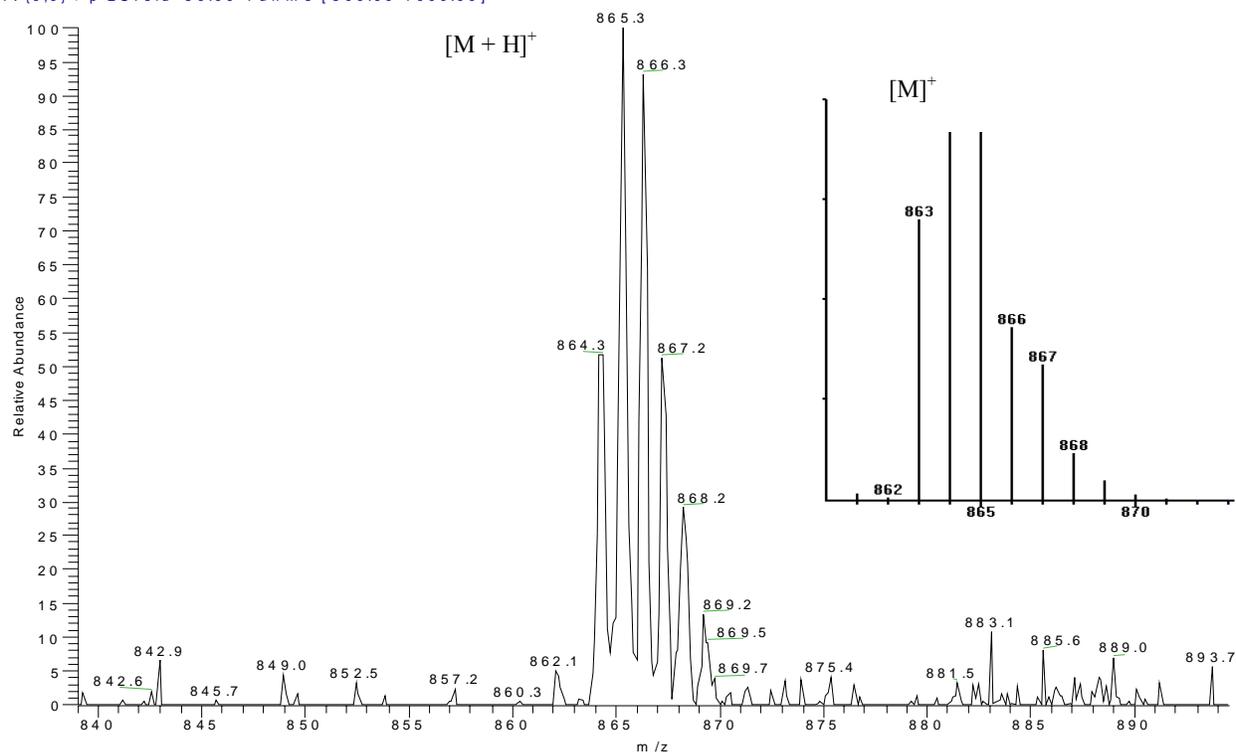
Figure 6. Positive-ion electrospray mass spectrum of complex **14ggg** in CH₃CN/H₂O (70/30) + 0.05% TFA. The inset shows the calculated isotope pattern for the [M]$^+$ ion (*m/z* 864).

4. Catalysis

Phosphine-free triolefinic palladium complexes **4**, being air and moisture stable, were considered good candidates as recoverable Pd(0) catalysts. We first tested[6] complex **4aaa** as catalyst in the Suzuki-type cross-coupling.[17] Thus, cinnamyl bromide, **16,** reacts with arene boronic acids, **17a-e**, affording diarylpropenes **18a-e** in good yields (Scheme 6). The reactions were performed with unoptimized 4-5% molar of catalyst in toluene at 80-90º in the presence of potassium carbonate as base. In all cases the complex **4aaa** was quantitatively recovered by column chromatography on silica gel.
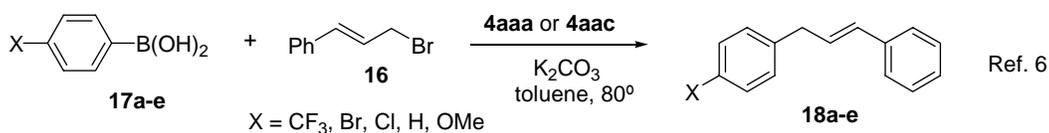
75-99% yield with **4aaa**, recovery of **4aaa** by chromatography
5 runs for each X-Ph-B(OH)$_2$ with **4aac**, similar yields, recovery of **4aac** by filtration
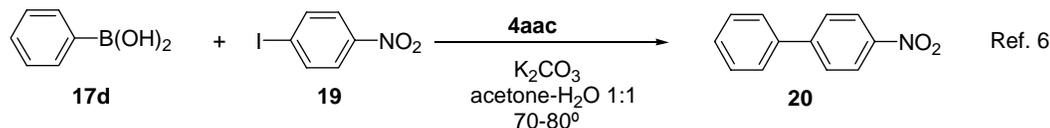
5 runs with the same batch of **4aac**: 82, 91, 94, 96, 89%. Quantitative recovery of **4aac** by filtration

Scheme 6. Macrocyclic complexes **4** as catalysts in Suzuki-type couplings.
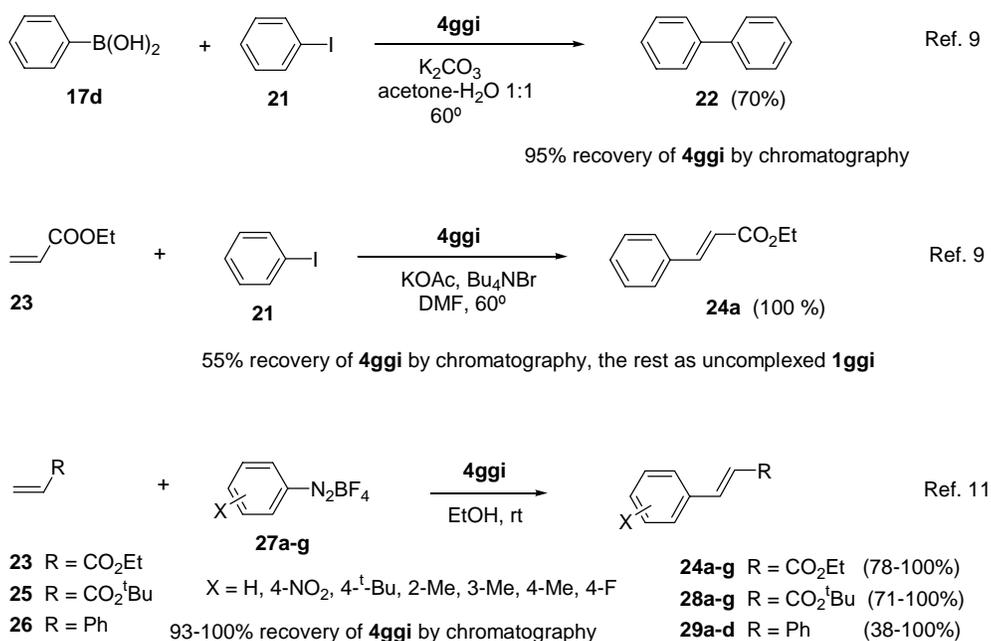
Anchoring the homogeneous catalyst to an insoluble organic polymer allows easy complex recovery by simple filtration. Thus, the macrocycle-containing cross-linked polystyrene catalyst **4aac** was tested[6] in the same reaction (Scheme 6). Five consecutive runs for each areneboronic acid were performed with the same batch of catalyst, which was quantitatively recovered by filtration and reused in the next run without decrease of activity. Polymer **4aac** was also an efective catalyst[6] in the Suzuki cross-coupling between 4-iodonitrobenzene **19** and phenylboronic acid **17d** to afford nitrobiphenyl **20** (scheme 6). The reaction was performed in acetone-water (1:1) at 70-80º in the presence of potassium carbonate, with recovery and reuse as mentioned before.

The pyrrole groups of complexes containing ferrocenyl and pyrrole groups, **4iip** and **4ipp**, were electropolymerized upon exposure to sufficiently positive potentials, in order to generate highly stable modified electrodes. Ferrocenyl groups were attached for electrochemical monitoring of the polymerization process. These polypyrrole modified electrodes are efficient heterogeneous catalysts for the same cross-coupling reactions of Scheme 6.[12]

Catalytic activity does not depend on the aryl substitution on the macrocycle. Thus, complex **4ggi** is also a good catalyst[9] for the Suzuki-type reaction between iodobenzene **21** and phenylboronic acid **17d** (K$_2$CO$_3$, acetone-water 1:1, 60º) and for the Heck reaction[18] of ethyl acrylate **23** with iodobenzene **21** (KOAc, Bu$_4$NBr, DMF, 60º) (Scheme 7). In both cases complex **4ggi** was recovered by column chromatography on silica gel in 95 and 55% yield, respectively. For the Heck reaction the rest of the macrocyclic catalyst was recovered as uncomplexed **1ggi**.

The above mentioned partial decomplexation in the Heck reaction led us to consider arenediazonium salts as substrates for that reaction, as they present some advantages, such as superior reactivity of the nucleofuge (N$_2$) over bromide and iodide, short reaction times, and mild reaction conditions without added base. Indeed, complex **4ggi** efficiently catalyzed[11] the arylation of acrylates and styrene with different arenediazonium tetrafluoroborates **27a-g** in ethanol at room temperature (Scheme 7). Recovery of **4ggi** by column chromatography was

practically quantitative. ESI-MS studies[19] provided evidence for oxidative addition species formed in the catalytic cycle immediately before the rate-limiting step.[11]


95% recovery of **4ggi** by chromatography

55% recovery of **4ggi** by chromatography, the rest as uncomplexed **1ggi**

23 R = CO$_2$Et

25 R = CO$_2$^{t}Bu

26 R = Ph

X = H, 4-NO$_2$, 4-^{t}-Bu, 2-Me, 3-Me, 4-Me, 4-F

93-100% recovery of **4ggi** by chromatography

24a-g R = CO$_2$Et   (78-100%)

28a-g R = CO$_2$^{t}Bu   (71-100%)

29a-d R = Ph   (38-100%)

Scheme 7. Macrocyclic complexes 4 as catalysts in Suzuki-type couplings and in Heck reactions.

X = 4-MeO, 3-MeO, 4-F, 4-MeCO, 4-EtO$_2$C, 3-EtO$_2$C, 2-NO$_2$-4-Me

32a-g (35-89%)

The ionic solvent containing the catalytic species is recycled and reused up to six times without noticeable lose of activity
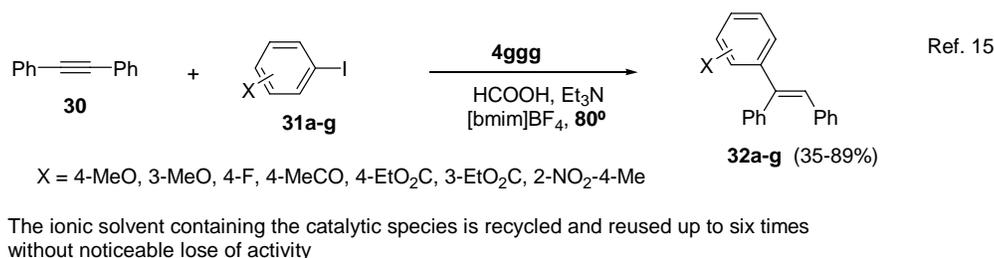
Scheme 8. Macrocyclic complexes 4 as catalyst in hydroarylation reactions in ionic solvents.

S. Cacchi's group has found[15] that the hydroarylation of alkynes in ionic liquids can be efficiently conducted with our macrocyclic catalysts. Thus, diphenylacetylene **30** reacts with aryl iodides **31a-g** and triethylamine/formic acid under catalyst by **4ggg,** in 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim]BF$_4$) (Scheme 8). The ionic solution containing the catalyst can be recycled and reused in six runs without loss of activity. Other classical palladium sources gave poorer results with respect to yields and recovery. The procedure has been applied[15] to the preparation of 3-arylquinolines through a domino hydroarylation/cyclization process.

Macrocyclic palladium complexes **4** were not catalytically active in telomerization and in Tsuji-Trost allylation reactions in the absence of added phosphine.[8,14] However, J. Muzart, F. Henin and coworkers showed[8,14] that the telomerization of butadiene with methanol can be performed with **4aaa** and monodentate phosphines, the catalytic species being recycled up to four times by adding fresh phosphine each time (Scheme 9).
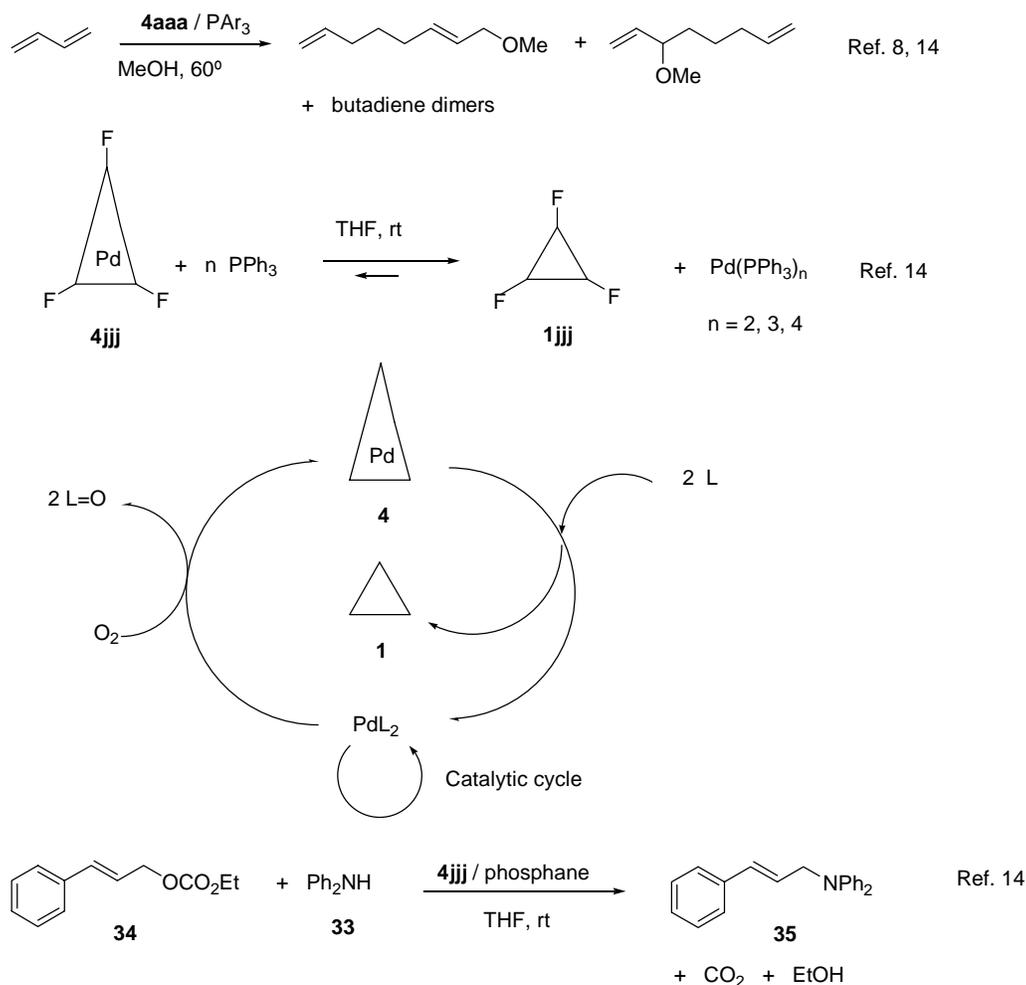

Scheme 9. Role of macrocyclic complexes 4 in telomerization and Tsuji-Trost reactions.

Moreover, the addition of free macrocycle **1aaa** to the catalytic systems formed *in situ* from palladium sources (Pd(dba)$_2$, Pd(OAc)$_2$) associated with phosphines has a stabilizing effect on palladium and allowed the recovery and reuse of the catalyst after addition of fresh phosphine each time. This was not possible without added **1aaa**. To get information about the real catalytic species in the telomerization reaction in the presence of macrocycle, we undertook mechanistic studies[14] by ^{19}F-NMR and ^{31}P-NMR with macrocycle **1jjj** and complex **4jjj**. The three fluorine atoms show one signal in the ligand **1jjj**, whereas the complex **4jjj** shows two fluorine signals of relative intensity 1:2. The conclusions are in Scheme 9. Complex **4jjj** reacts with two moles of

phosphine (or one mole of bidentate phosphine) to afford directly the highly active 14-electron PdL_2 species. After catalysis ends up, if the phosphine is oxidized, palladium(0) reverts to the free macrocycle **1jjj**, to be stored as complex **4jjj**, thus preventing agglomeration and remaining available for a new reaction, that requires addition of fresh phosphine but not of fresh palladium.

The allylation of diphenylamine **33** with cinnamyl carbonate **34** (Scheme 9) in the presence of **4jjj** and phosphine in THF at room temperature to give **35** was also monitored[14] by ^{19}F and ^{31}P-NMR, the results being consistent with the same mechanistic proposal. Further evidence of the formation of intermediate species PdL_n when macrocycles **4** react with phosphines was gained by an ESI-MS study[14] of the reactions between complex **4ggi** and several phosphines in THF.

5. Related macrocycles
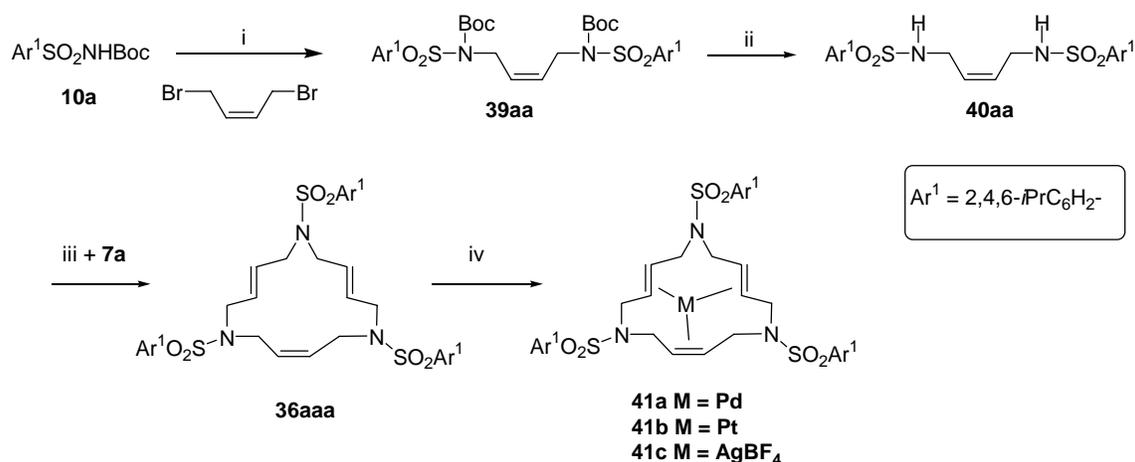
Scheme 10. Preparation of macrocycle **36**. Reagents and conditions: i.- K_2CO_3, acetonitrile, reflux, then cis-1,4-dibromobutene (0.5 equiv); ii.- TFAA, dichloromethane, room temperature; iii.- K_2CO_3, refluxing acetonitrile; iv.- $Pd(PPh_3)_4$, refluxing THF, or $Pt(PPh_3)_4$, DMF, 130ºC, or $AgBF_4$, refluxing acetone.

We have increased the family of our 15-membered macrocycles modifying the olefin precursors with the aim of studying the complexating ability of the new members of the family. Thus, we have prepared (*E,E,Z*)-1,6,11-tris[(2,4,6-triisopropylphenyl)sulfonyl]-1,6,11-triazacyclopentadeca-3,8,13-triene, **36**, (Scheme 10),[20] (*E,E*)-1,6,11-tris(arenesulfonyl)-3,4-benzo-1,6,11-triazacyclopentadeca-8,13-dienes, **37** (Scheme 11),[21] and 1,6,11-tris(arenesulfonyl)-3,4;8,9;13,14-tribenzo-1,6,11-triazacyclopentadecanes, **38** (Scheme 12).[21]

Macrocycle **36** featuring one cis double bond was synthesized through pathway "b" as indicated in Scheme 10.[20] It forms palladium(0), platinum(0), and silver(I) complexes **41**, the same as its all-*trans* counterpart **1aaa**. However, preparation of **36** has the disadvantage that *cis*-1,4-dibromo-2-butene has to be prepared whereas its trans isomer is commercially available.

Scheme 11. Preparation of macrocycles 37. Reagents and conditions: i.- K_2CO_3, refluxing acetonitrile; ii.- TFAA, dichloromethane, room temperature; iii.- 42 (one equiv), K_2CO_3, refluxing acetonitrile.

Scheme 12. Preparation of macrocyles 38. Reagents and conditions: i.- 42 (four equiv), K_2CO_3, refluxing acetonitrile; ii.- $Ar^2SO_2NH_2$ (0.5 equiv), K_2CO_3, refluxing acetonitrile; iii.- TFAA, dichloromethane, room temperature; iv.- 42 (1 equiv), K_2CO_3, refluxing acetonitrile.

Pathway "c" was followed for the synthesis of macrocycles **37** and **38**.[21] In these cases *trans*-1,4-dibromo-2-butene was substituted by 1,2-bis(bromomethyl)benzene in the required steps (Schemes 11 and 12). This type of synthesis is versatile, and it permits once more one to combine different aryl groups at different synthetic steps. Moreover, the cyclization step is excellent, the formation of higher cycles and/or polymers not being a problem.

Macrocycles **37** and **38** exhibit only weak coordinating ability towards silver tetrafluoroborate but none towards silver triflate or palladium(0). When macrocycles **37aaa, 37ggg, 38aaa**, and **38aag** were treated with $Cr(CO)_6$ in refluxing di-*n*-butylether under inert atmosphere, extremely insoluble complexes were formed. Each of them showed two strong infrared peaks in the 1898 ± 6 and 1972 ± 4 cm^{-1} regions, as required for trigonal-pyramidal complexes of the $L_3Cr(CO)_3$ type. Evidence for structures **37ggg-Cr(CO)₃** and **38aag- Cr(CO)₃** was obtained by HRMS.

Finally we have taken advantage of the availability of intermediates **6** and **8**, required for the formation of 15-membered macrocycles **1** through routes "a" and "b", for the preparation of 20-membered macrocycles **46** (Scheme 13).[22]
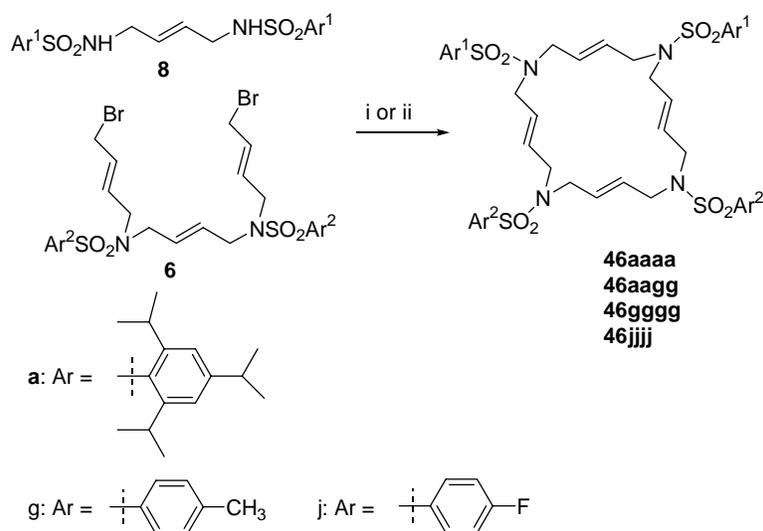
Scheme 13. Preparation of macrocycles **46**. Reagents and conditions:
i.- K_2CO_3, refluxing CH_3CN; ii.- NaH on **8**, then **6** in DMF, 90ºC.

6. Concluding remarks

We have discovered a new family of 15-membered macrocycles easily made from commercially available *trans*-1,4-dibromo-2-butene and arenesulfonamides. The cyclization step is performed in good yield without special difficulties due to the formation of polymers or higher rings, although in certain cases both polymers and 30-membered rings have been detected or isolated.[10] Macrocycles of this family coordinate certain transition metals. Thus, palladium(0), platinum(0),

and silver(I) complexes have been prepared and analyzed. The palladium and platinum complexes are planar trigonal. Little is known on complexes with other transition metals.

The palladium complexes **4** are excellent catalysts or precatalysts in certain organic reactions traditionally catalyzed by palladium species. Thus, compounds **4** catalyze Suzuki-type cross couplings,[6] Heck reactions,[11] hydroarylation of alkynes,[15] and telomerization of butadiene.[8,14] The mechanisms of catalysis are different, and in some cases are far from clear. For telomerizations we have shown that complexes **4** play the role of palladium source before catalysis and harbor for palladium after catalysis, preventing agglomeration and precipitation.[14] Recovery and reuse of our catalysts is possible in all the cases above referred, and even a polymeric version, amenable to recovery by simple filtration, has been successfully used.[6] These facts permits us to believe that our palladium complexes of 15-membered macrocycles can be excellent substitutes for the more classical sources of palladium such as $Pd_2(dba)_3$ and $Pd(PPh_3)_4$. The traditional and broadly spread phosphine ligands have a serious drawback: they are strong reducing agents and, more frequently than not, they are converted into their phosphine oxides, thus permitting palladium to agglomerate and to precipitate in an inactive form.

Furthermore, the preparation of our ligands **1** is versatile. Only the olefinic double bonds are active as coordinating centers, the nitrogen atoms being non-coordinating. This permits to play with the sulfonamide moieties for different purposes. Thus, different substituents in the benzene ring, or other non-benzenic groups in the sulfonamide permit to enhance and improve certain properties to the macrocycles. This has been explained along the text of this review. Furthermore, we have opened a new axis of research in which we try to convert our macrocycles into molecular materials.

Finally, by varying the open-chain precursors, the synthesis of structurally related macrocycles is possible. Thus, preparations of its geometrical isomers, of compounds possessing benzene rings in the place of isolated double bonds, and of larger macrocycles such as 20-membered rings have been performed.

Acknowledgements

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