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Organometallic chemistry of 15-membered tri-olefinic macrocycles: catalysis by palladium(0) complexes in carbon–carbon bond-forming reactions

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Abstract

15-Membered macrocycles (*E*,*E*,*E*)-1,6,11-tris(arenesulfonyl)-1,6,11-triazacyclopentadeca-3,8,13-trienes (**1**) are prepared from arenesulfonamides and *trans*-1,4-dibromo-2-butene. Macrocycles **1** coordinate palladium(0), platinum(0), and silver(I). 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

1. Introduction

Nitrogen-containing 15-membered macrocycles featuring endocyclic double bonds are not common [1]. A few monoolefinic compounds of this type have been prepared by metathesis [2].

Macrocycles **1** (Fig. 1) are reminiscent of the 12-membered carbocyclic cyclododeca-1,5,9-trienes (**2**). Cyclotrienes **2** are trimers of butadiene and coordinate nickel(0). These nickel complexes have played a fundamental role in organonickel chemistry [3].

We serendipitously discovered macrocycles **1** when studying the palladium-catalyzed reaction of arenesulfonamides with 2-butene-1,4-diol biscarbonate (Scheme 1) [4]. Then, 10-, 15-, and 20-membered cycles were isolated. Part of the 15-membered cycles were isolated as their palladium(0) complexes **4** (vide infra). Since IR and NMR data of 15- and 20-membered macrocycles were very similar, MALDI-TOF mass spectrometry was of paramount importance in the identification of the products [5].

We soon noticed that the three double bonds were excellent coordinating centers for some transition metals. Moreover, the nitrogen atoms are not coordinating due to lone pair conjugation with the SO_2 group. Thus, all coordination capacity is due to the three olefins.

A broad array of arenesulfonamides and arenesulfonyl chlorides are commercially available. Therefore, many properties of the macrocycles can be tuned by incorporating arene or heteroarene groups appropriate to improve or impart solubility, crystallinity, electrochemical properties, polymerization ability, and certain types of reactivity. Similar to the preparation of **1** from *trans*-1,4-dibromo-2-butene, preparation of structurally

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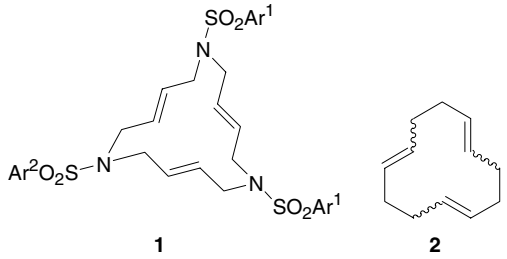


Fig. 1. General structure of macrocycles **1** and **2**.

related macrocycles can be performed by working with *cis*-1,4-dibromo-2-butene, 1,2-bis(bromomethyl)benzene, or 1,4-dibromo-2-butyne.

2. Preparation of 15-membered (*E*,*E*,*E*)-1,6,11-tris(arenesulfonyl)-1,6,11-triazacyclopentadeca-3,8,13-trienes (1) and their metal complexes 4, 14, and 15

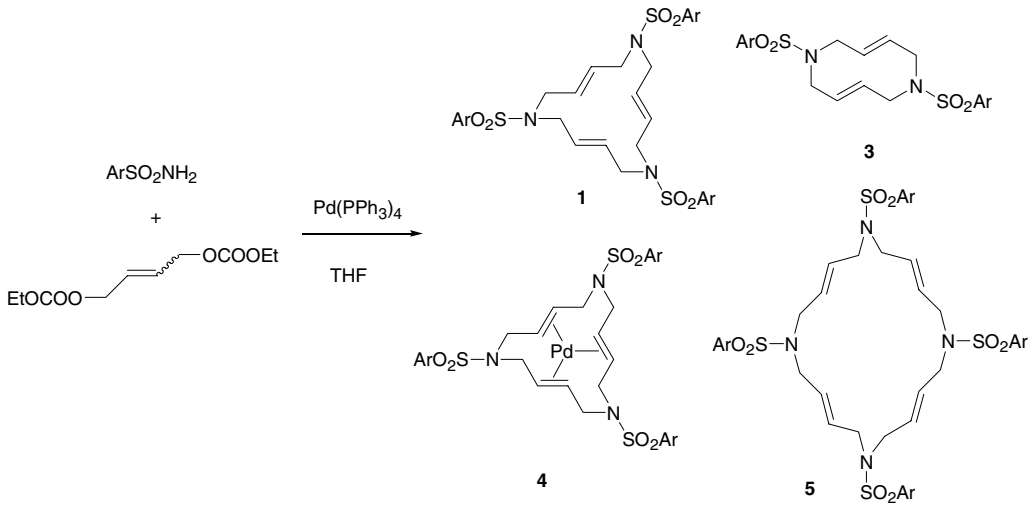
*2.1. Preparation of 15-membered (E,E,E)-1,6,11-tris(arenesulfonyl)-1,6,11-triazacyclopentadeca-3,8,13-trienes (**1**)*

Since when we described in 1998 the first 15-membered triolefinc macrocycles **1** [4], a broad selection has been prepared (Table 1 and Fig. 2). Arenesulfonamides were chosen to confer, enhance, or modulate certain properties of the macrocycles. Thus, three isopropyl groups in the benzenesulfonyl moiety improve solubility in classical organic solvents (**1aaa**, **1aab**, and **1aad**) [4,6–8]. Methyl groups impart crystallinity and have permitted a X-ray diffraction study of **1ggg** [7]. Perfluorinated long chains were introduced to confer solubility of **1aff** in perfluorinated solvents [7]. Complexes featuring 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 studies [9,11,12]. Vinyl-substituted **1aab** has been copolymerized with styrene and divinylbenzene to afford polymer **1aac** (vide infra) [6]. We have also prepared macrocycle **1jjj**, a key intermediate for the synthesis of more elaborated macrocycles by aromatic nucleophilic substitution of the three fluorine atoms with phosphorus (**1kkk**), nitrogen (**1nnn**, **1ooo**), and sulphur (**1lll**, **1mmm**) nucleophiles [10].

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

Our initial synthesis corresponds to pathway "a" (Scheme 2). Thus, reaction of arenesulfonamides with *trans*-1,4-dibromo-2-butene gave easily separable mixtures of monosulfonamides **7** and bis-sulfonamides **6**. Condensation of **6** with different arenesulfonamides was straightforward affording macrocycles **1aaa**, **1aab**, **1aad**, **1aee**, **1ddd**, **1ggh**, **1jjj**, and **1ggj**. The main problem of this synthesis is that bis-sulfonamides **6** are always the 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].

Since monosulfonamides **7** were the major products in the first step of pathway "a", we envisaged another approach (Scheme 3). Thus, 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, previously prepared from *trans*-1,4-dibromo-2-butene by a Gabriel reaction [6]. Another way consists of a nucleophilic sub-



Scheme 1. Formation of cycles in a palladium-catalyzed Tsuji–Trost reaction [4].

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

	1	Ar^1	Ar^2	References
1	**1aaa**	2,4,6-*i*PrC_6H_2-	2,4,6-*i*PrC_6H_2-	[4,6–8]
2	**1aab**	2,4,6-*i*PrC_6H_2-	4-CH_2=CHC_6H_4-	[6,7]
3	**1aac**	2,4,6-*i*PrC_6H_2-	4-Polymer-[a]	[6]
4	**1aad**	2,4,6-*i*PrC_6H_2-	5-Dimethylaminonaphthyl-	[7]
5	**1aee**	4-IC_6H_4-	2,4,6-*i*PrC_6H_2-	[7]
6	**1aff**	3-$C_8F_{17}C_6H_4$-	2,4,6-*i*PrC_6H_2-	[7]
7	**1ddd**	5-Dimethylaminonaphthyl-	5-Dimethylaminonaphthyl-	[7]
8	**1ggg**	4-$CH_3C_6H_4$-	4-$CH_3C_6H_4$-	[7]
9	**1ggh**	4-$CH_3C_6H_4$-	2-Thienyl-	[7]
10	**1ghh**	2-Thienyl-	4-$CH_3C_6H_4$-	[7]
11	**1ggi**	4-$CH_3C_6H_4$-	Ferrocenyl-	[9,11]
12	**1gii**	Ferrocenyl-	4-$CH_3C_6H_4$-	[9]
13	**1iii**	Ferrocenyl-	Ferrocenyl-	[9]
14	**1jjj**	4-FC_6H_4-	4-FC_6H_4-	[10]
15	**1kkk**	4-$Ph_2PC_6H_4$-	4-$Ph_2PC_6H_4$-	[10]
16	**1lll**	4-$CH_3CH_2CH_2SC_6H_4$-	4-$CH_3CH_2CH_2SC_6H_4$-	[10]
17	**1mmm**	4-$CH_3C_6H_4$-S-C_6H_4-	4-$CH_3C_6H_4$-S-C_6H_4-	[10]
18	**1nnn**	4-(Morpholino)phenyl-	4-(Morpholino)phenyl-	[10]
19	**1ooo**	4-($HOCH_2CH_2NH$)C_6H_4-	4-($HOCH_2CH_2NH$)C_6H_4-	[10]
20	**1iip**	Ferrocenyl-	4-(Pyrrol-1-yl)phenyl-	[12]
21	**1ipp**	4-(Pyrrol-1-yl)phenyl-	Ferrocenyl-	[12]
22	**1ggp**	4-$CH_3C_6H_4$-	4-(Pyrrol-1-yl)phenyl-	[12]
23	**1ggj**	4-$CH_3C_6H_4$-	4-FC_6H_4-	[24]
24	**1ggq**	4-$CH_3C_6H_4$-	4-($H_2NCH_2CH_2NH$)C_6H_4-	[24]
25	**1ggr**	4-$CH_3C_6H_4$-	See Scheme 15	[24]

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

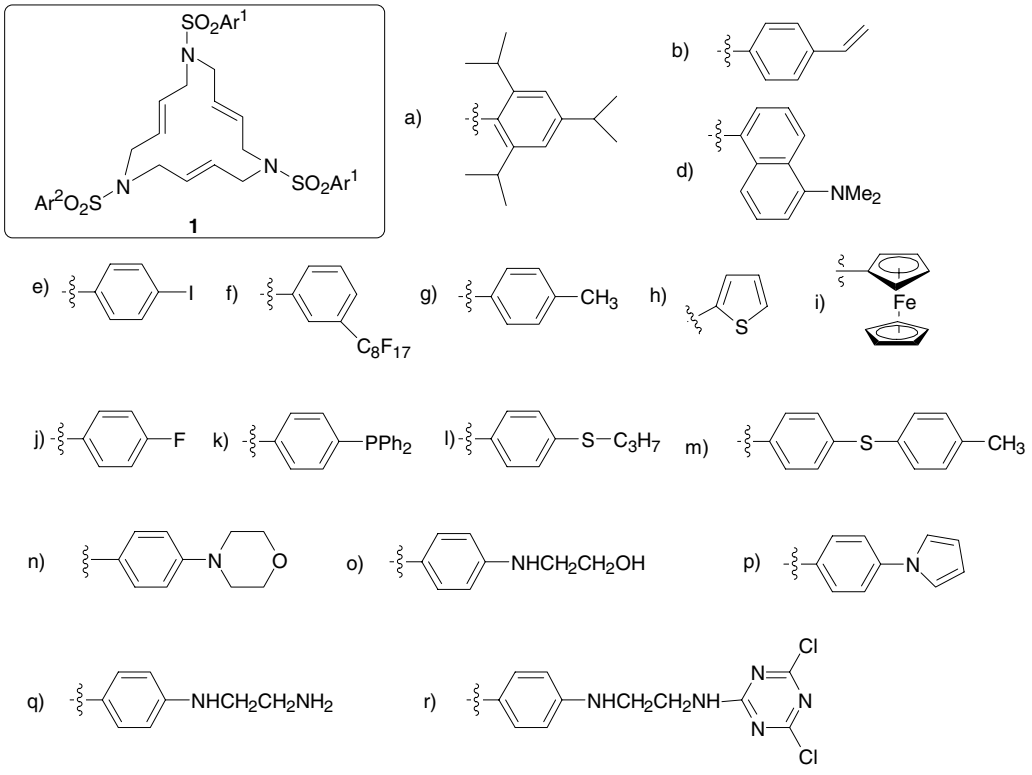


Fig. 2. Substitute introduced in macrocycles **1**.

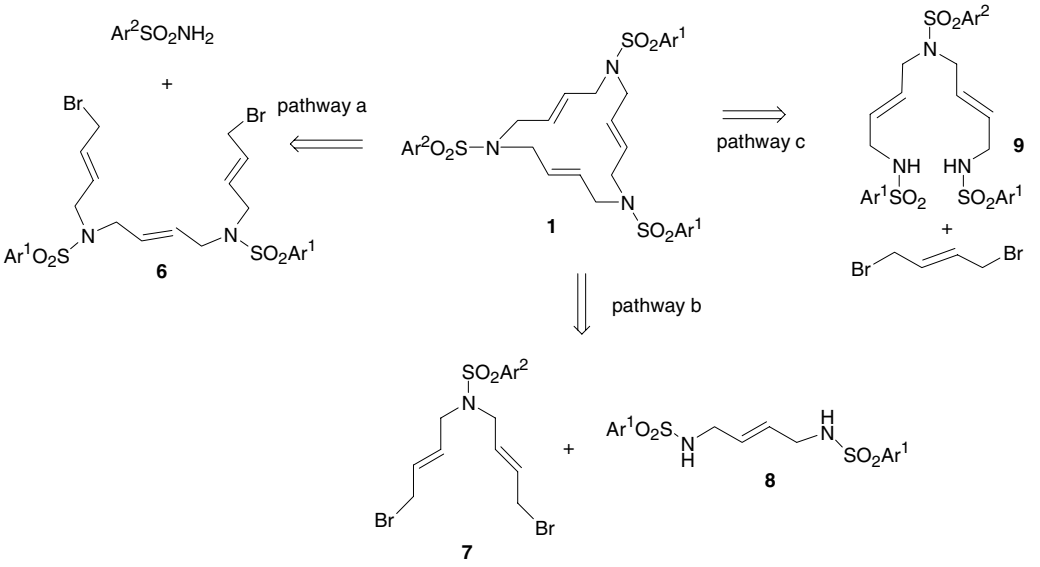
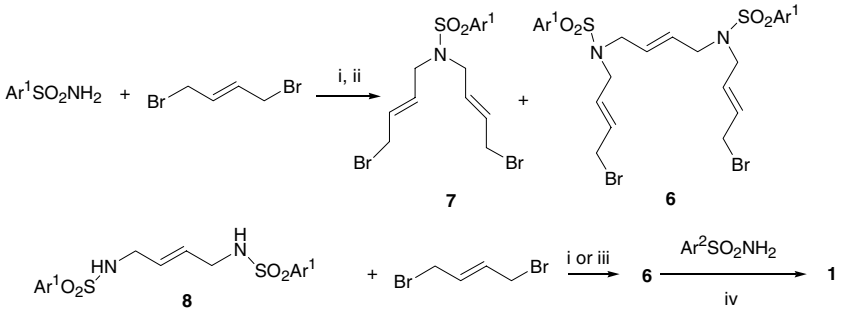
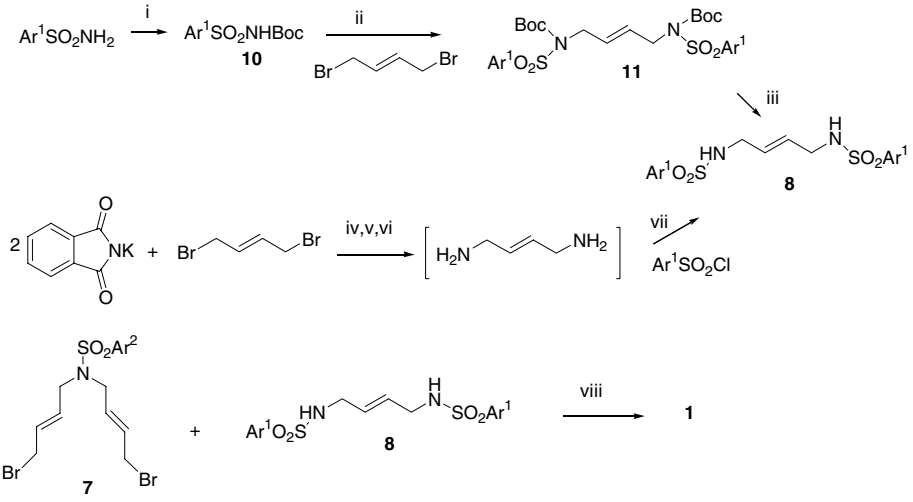


Fig. 3. Retrosynthetic pathways for macrocycles **1**.



Scheme 2. Preparation of **1** (pathway "a"). Reagents and conditions: i: NaH, DMF, then $BrCH_2CH{=}CHCH_2Br$, 90 °C; ii: column chromatography on silica gel. iii: K_2CO_3, refluxing acetonitrite, then $BrCH_2CH{=}CHCH_2Br$ (8 equiv.); iv: NaH DMF, over arenesulfonamide, then **6**, 90 °C.



Scheme 3. Preparation of **1** (pathway "b"). Reagents and conditions: i: (*tert*-BuOCO)$_2$O, Et_3N, DMAP (0.1 equiv.), CH_2Cl_2; ii: K_2CO_3, CH_3CN, reflux or K_2CO_3, DMF, room temperature, then *trans*-1,4-dibromo-2-butene (0.5 equiv.); iii: TFAA, CH_2Cl_2, room temperature; iv: DMF, 80 °C; v: 80% hydrazine, ethanol, reflux; vi: KOH, H_2O, vii: diethyl ether, viii: NaH, DMF over **8**, then **7**, 90 °C.

stitution reaction between two equivalents of **10** and *trans*-1,4-dibromo-2-butene to afford **11** [6]. Deprotection of **11** gave quantitative yields of **8**.

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 amino groups must be protected in **10** and **12**.

We believe that pathway "c" is to be most convenient because of its versatility and selectivity in each step, and we recommend it. Yields for all steps before cyclization are in the range from 74% to >90%. Cyclizations are not particularly sensitive to concentration as usually happens for most preparation of macrocycles. A study of the influence of concentration on the cyclization to **1jjj** has been published [10]. We have found yields in the range 50–80% for all cyclizations in the three different pathways. However, impurities have similar polarity to macrocycles **1**. Therefore, in general chromatography is frequently required to obtain pure compounds. We make attempts to avoid chromatographic procedures.

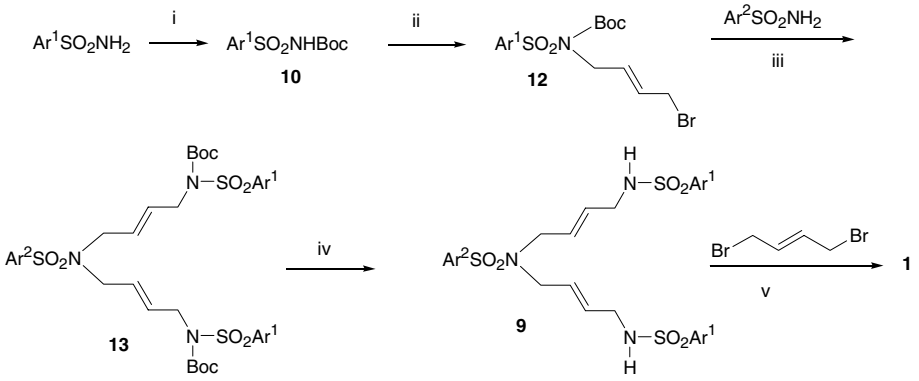
Moreover, further modifications are possible on macrocycle **1jjj**, containing three fluorine atoms that are susceptible of substitution by nucleophiles. This pivotal compound has permitted to increase the array of substituents (Scheme 5).

2.2. Preparation of metal complexes *4*, *14*, and *15*

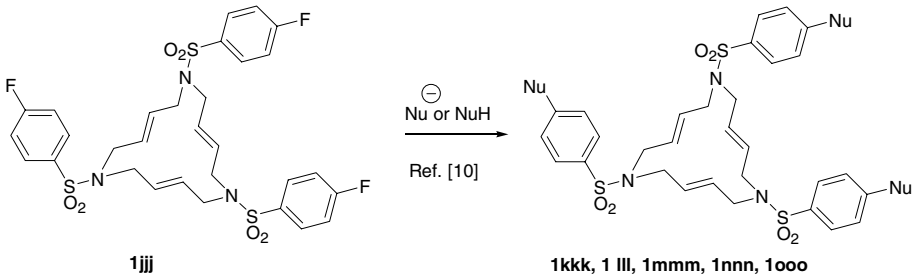
All-*trans* triazatriolefinic macrocycles coordinate transition metals through the double bonds. Thus, we have prepared many transition metal complexes (Fig. 4 and Table 2). Palladium complexes **4** are obtained either by ligand-exchange using $Pd(PPh_3)_4$ or $Pd(dba)_2$ as sources of metal [4,6,8,9,11–15] 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 $AgBF_4$. For palladium and platinum we obtain regularly yields in the 50–90% range. The election between $Pd(PPh_3)_4$ or $Pd(dba)_2$ depends on the facility of separation of either dba or the mixture $PPh_3 + PPh_3{=}O$ from the final complex (see Fig. 4).

3. Structure and spectroscopy

The structure of palladium complexes **4** intrigued us since the moment of their discovery. As an example, significant ^{13}C and ^{1}H NMR data for **4aaa**, as well as for their ligand **1aaa** are summarized in Fig. 5. The ligand **1aaa** presented in its ^{1}H NMR spectrum signals at δ



Scheme 4. Preparation of **1** (pathway "c"). Reagents and conditions: i: (*tert*-BuOCO)$_2$O, Et_3N, DMAP (0.1 equiv.), CH_2Cl_2; ii: K_2CO_3, CH_3CN, *trans*-1,4-dibromo-2-butene (4 equiv.), reflux; iii: K_2CO_3, CH_3CN, arenesulfonamide (0.5 equiv.), reflux; iv: TFAA, CH_2Cl_2, room temperature; v: K_2CO_3, refluxing CH_3CN, *trans*-1,4-dibromo-2-butene (1 equiv.).



Scheme 5. Nucleophilic aromatic substitution on **1jjj**.

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

Entry	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	**4ggr**		[24]
14	**14aaa**		[13]
15	**14ggg**		[13]
16	**14ggj**		[24]
17	**14ggq**		[24]
18	**15aaa**		[13]
19	**15ggg**		[13]

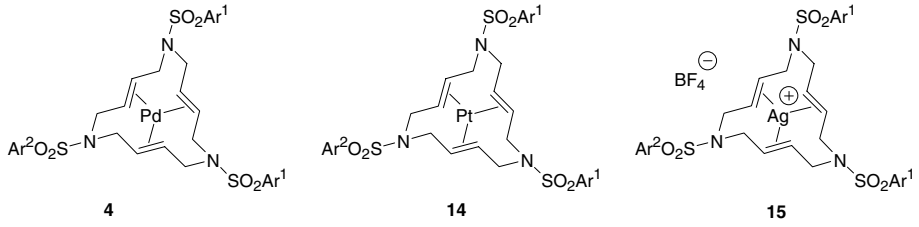


Fig. 4. Palladium(0), platinum(0), and silver(I) complexes.

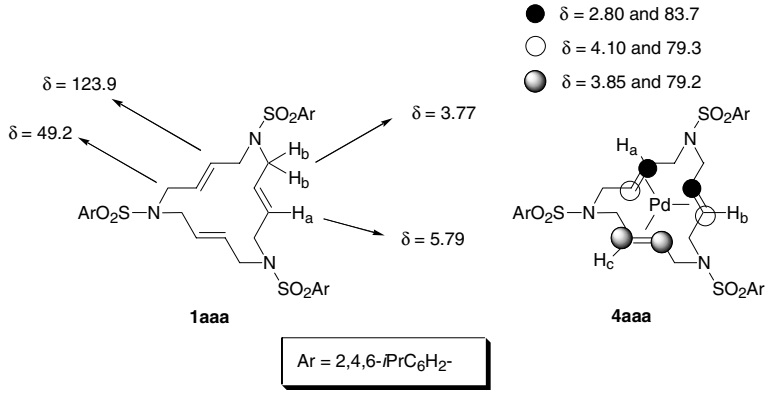


Fig. 5. Significant ^{1}H and ^{13}C NMR signals for **1aaa** and **4aaa**.

3.77 (CH_2, 12H) and 5.79 (olefinic CH, 6H), and in its ^{13}C NMR spectrum signals at δ 49.2 (CH_2) and 123.9 (olefinic CH). These data suggest that compound **1aaa** has an averaged C_3 axis of symmetry. Complex **4aaa** presented in the olefinic region signals as indicated in Fig. 5. Two olefins are magnetically equivalent but, in each of them, the two CH groups are magnetically non-equivalent with signals for protons at δ 2.80 (H_a, apparent t, $J = 12.4$ Hz, 2H) and 4.10 (H_b, dd, $J = 12.4$ and 11.1 Hz, 2H) and for carbon atoms at δ 83.7 and 79.3. The third olefin is different from the other two and both CH of this third olefin are magnetically equivalent, presenting signals for both protons at δ 3.85 (H_c, apparent d, $J = 9.5$ Hz, 2H) and for both carbon atoms at δ 79.2. 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. These facts suggest that the presence of the palladium atom breaks the C_3 symmetry and that the complexation of palladium with one olefin is different with respect to the other two.

Other palladium(0) and platinum(0) complexes **4** and **14**, containing three identical aryl groups exhibit the same behavior. 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.

Strong evidence in support of these facts was secured by X-ray diffraction analysis of **4ggg** and **14ggg**. 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 is planar trigonal. The complexes are not symmetrical, and, as it has been seen by NMR data, they lack a C_3 symmetry axis. The C═C bonds are longer than in the corresponding free ligand **1aaa**. However, one C═C bond is shorter than the other two in the

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

4, **14**	^{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 analogy with compounds **4aaa**, **4ggg**, **4iii**, and **14ggg** that have undergone a full NMR analysis.

complex, suggesting that complexation with one olefin is weaker than complexation with the other two.

In complexes **4** and **14** having two different aryl units ($Ar^1 \neq Ar^2$) two isomers exist depending on which aryl unit 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 symmetrical isomers, but six more signals are found for isomers lacking symmetry elements. Selected ^{13}C NMR data for complexes **4** and **14** bearing two different aryl units are in Table 4. Further structural studies on complexes **4** with three different aryl units are in progress.

Matrix-assisted laser desorption/ionization, time-of-flight MS (MALDI-TOF) and electrospray ionization mass spectrometry (ESI-MS) are convenient analytical techniques to identify complexes **4**, **14**, and **15**. Both techniques allow heavy molecules to be ionized and vaporized without degradation. Initially, MALDI-TOF mass spectrometry allowed direct determination of the size of macrocycles and linear oligomers formed in the palladium(0)-catalyzed allylation of arenesulfonamides with 2-butene-1,4-diol biscarbonate [4,5] (Scheme 1). Later on, mass spectroscopic investigations were performed to elucidate the structure of all complexes. Compounds **4**, **14**, and **15** were easily identified thanks to the characteristic isotope distribution of the metal. Isotopic abundance of clusters was compared with calculated values. Fig. 6 displays a positive-ion electrospray mass spectrum of **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 $[M]^+$.

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

4	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
4ggr	78.9, 79.0, 79.2, 79.4, 83.2, 83.3, 83.8	45.8, 48.9, 50.1
14ggj	63.0, 63.4, 63.5, 63.7, 63.9, 64.2, 69.3, 69.8, 70.0	45.0, 47.8, 49.2
14ggq	63.0, 63.3, 63.5, 63.8, 64.3, 69.4, 69.6, 70.2	45.0, 47.9, 49.2

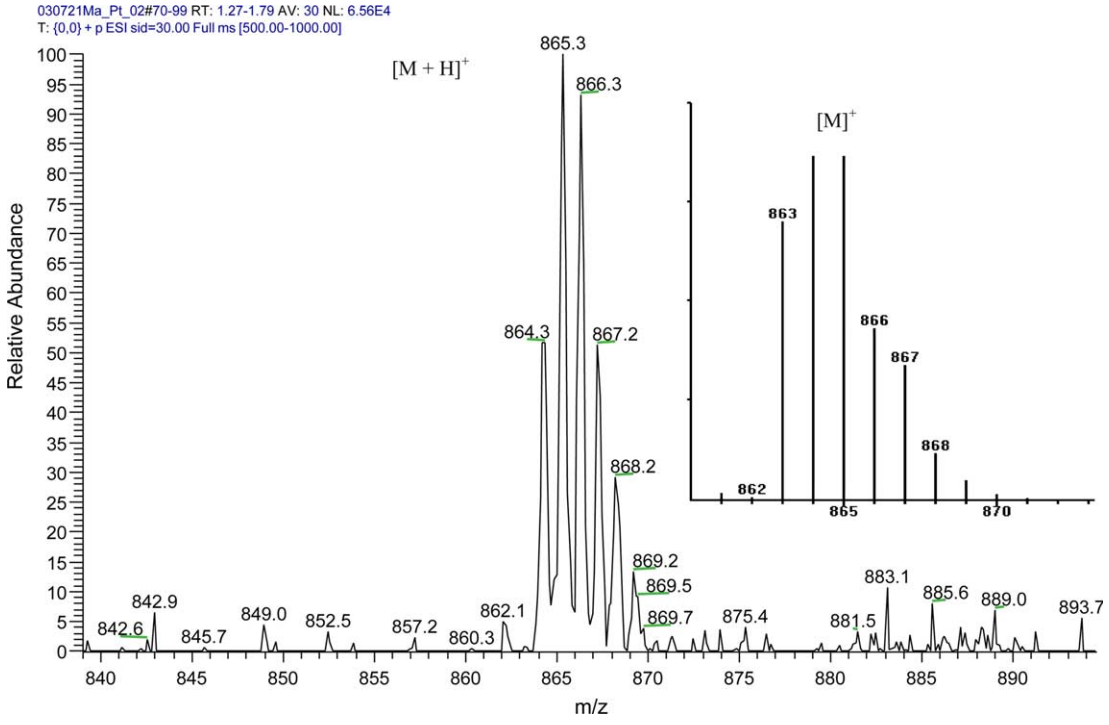
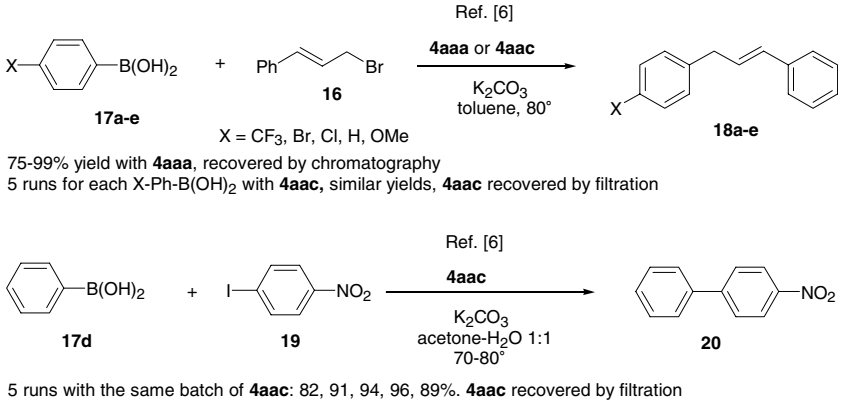


Fig. 6. Positive-ion electrospray mass spectrum of complex **14ggg** in CH_3CN/H_2O (70/30) + 0.05% TFA. The inset shows the calculated isotope pattern for the $[M]^+$ ion (*m/z* 864).



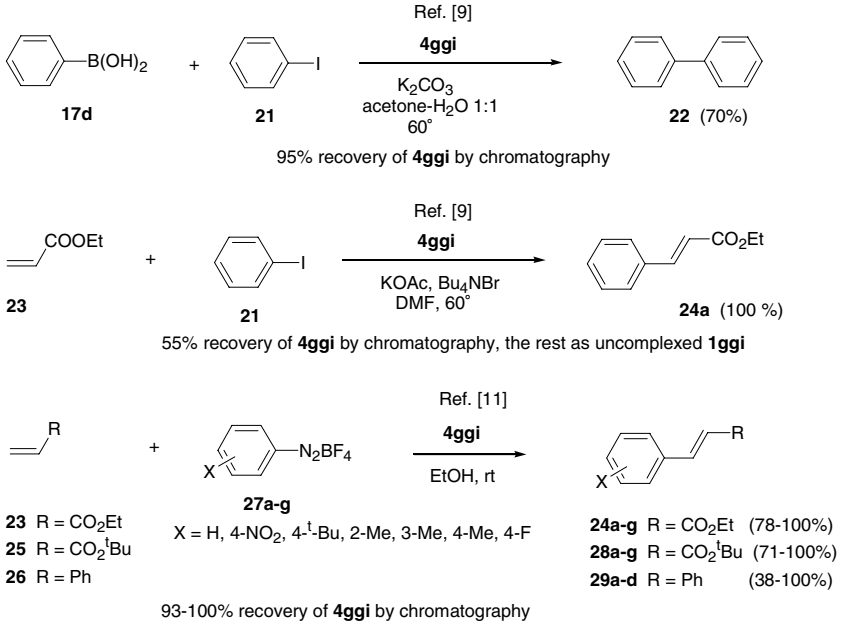
Scheme 6. Macrocyclic complexes **4** as catalysts in Suzuki-type couplings.

4. Catalysis

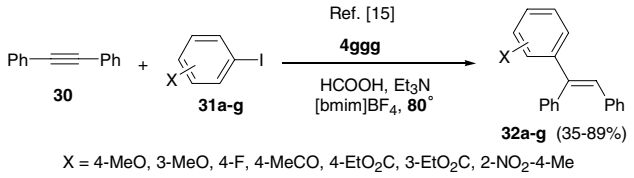
Since phosphine-free palladium complexes **4** are air and moisture stable, they were considered good candidates as recoverable Pd(0) catalysts. We tested [6] complex **4aaa** as catalyst in Suzuki-type cross-couplings [17]. Thus, cinnamyl bromide (**16**) reacted with areneboronic acids (**17a**–**e**), affording diarylpropenes (**18a**–**e**) in good yields (Scheme 6). All reactions were performed with unoptimized 4–5% molar of catalyst in toluene at 80–90 °C in the presence of potassium carbonate as base. In all cases complex **4aaa** was quantitatively recovered by column chromatography on silica gel.

By anchoring the homogeneous catalyst to an insoluble organic polymer the catalytic material is recovered by simple filtration. Thus, the cross-linked polystyrene-based catalyst **4aac** was tested [6] in the same reaction (Scheme 6). For each areneboronic acid, five consecutive runs were performed with the same batch of catalyst, which was recovered by filtration and reused in the next run without noticeable decrease of activity. Catalytic polymer **4aac** was also effective in the Suzuki cross-coupling between 4-iodonitrobenzene **19** and phenylboronic acid **17d** to afford nitrobiphenyl **20** (Scheme 6) [6]. This reaction was performed in acetone–water (1:1) at 70–80 °C with potassium carbonate as a base. Again, the catalytic material was recovered and reused.

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



Scheme 7. Complexes **4** catalyze Suzuki-type coupling and Heck reactions.

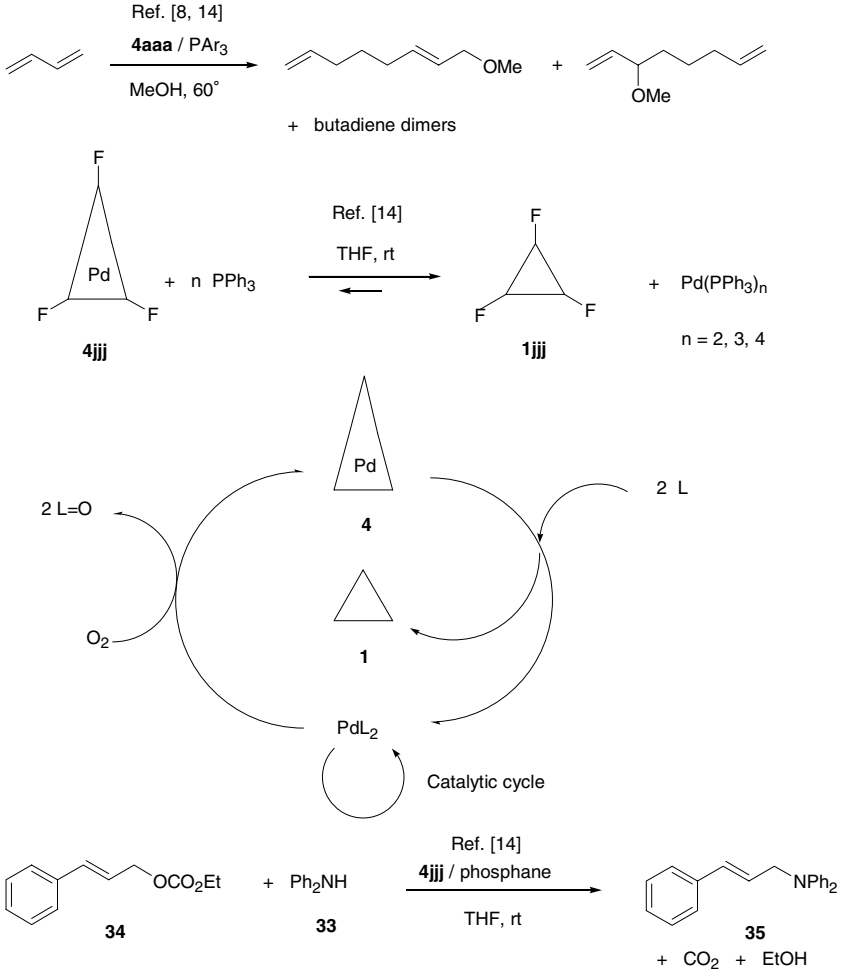


Scheme 8. Macrocyclic complexes **4** catalyze hydroarylations in ionic solvents.

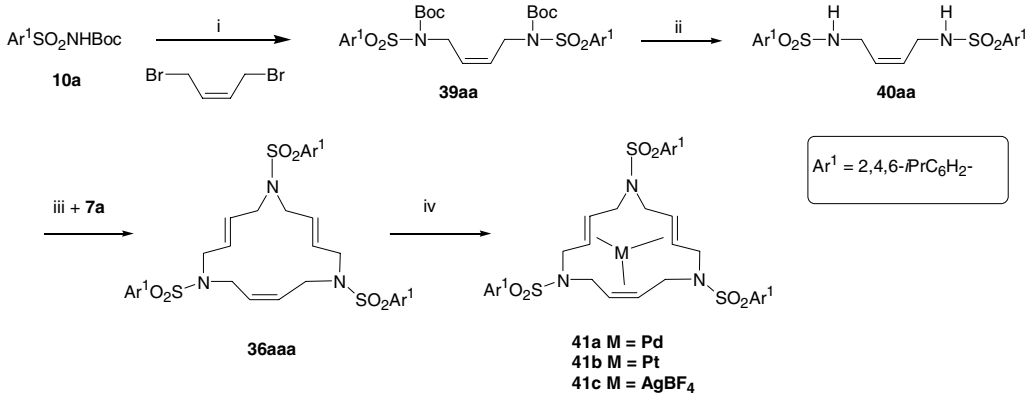
Catalytic activity does not depend on the aryl substitution on the macrocycle. Thus, complex **4ggi** catalyzes also the Suzuki coupling between iodobenzene **21** and phenylboronic acid **17d** (K_2CO_3, acetone–water 1:1, 60 °C) [9] and the Heck reaction of ethyl acrylate **23** with iodobenzene **21** (KOAc, Bu_4NBr, DMF, 60 °C) (Scheme 7) [18]. 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 macrocycle was recovered as uncomplexed **1ggi**.

The partial decomplexation in the Heck reaction commented in the precedent paragraph led us to test arenediazonium salts as substrates, since they offer some advantages, such as superior activity of the nucleofuge (N_2) over bromide and iodide, shorter reaction times, and milder reaction conditions without adding base. Indeed, **4ggi** efficiently catalyzed the arylation of acrylates and styrene with arenediazonium tetrafluoroborates **27a–g** in ethanol at room temperature (Scheme 7) [11]. Recovery of **4ggi** by column chromatography was practically quantitative. ESI-MS studies [19] provided evidence for accumulation of oxidative addition species ($[\mathbf{4ggi}/C_6H_4X]^+$) formed in the catalytic cycle immediately before the rate-limiting step that is located at the transmetallation level [11].

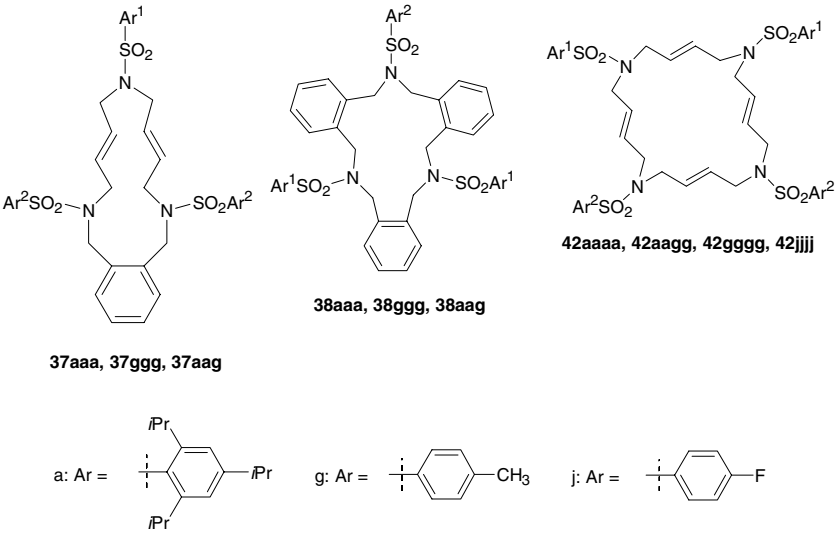
Cacchi et al. [15] have found that hydroarylation of alkynes in ionic liquids can be efficiently catalyzed by our macrocyclic catalysts. Thus, diphenylacetylene **30** reacts with aryl iodides **31a–g** and triethylamine/formic acid under catalyst by **4ggg**, in 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim]BF_4) (Scheme 8). The ionic solution containing the catalyst could be recycled and reused in six runs without loss of activity. Other classical palladium sources gave poorer results in terms



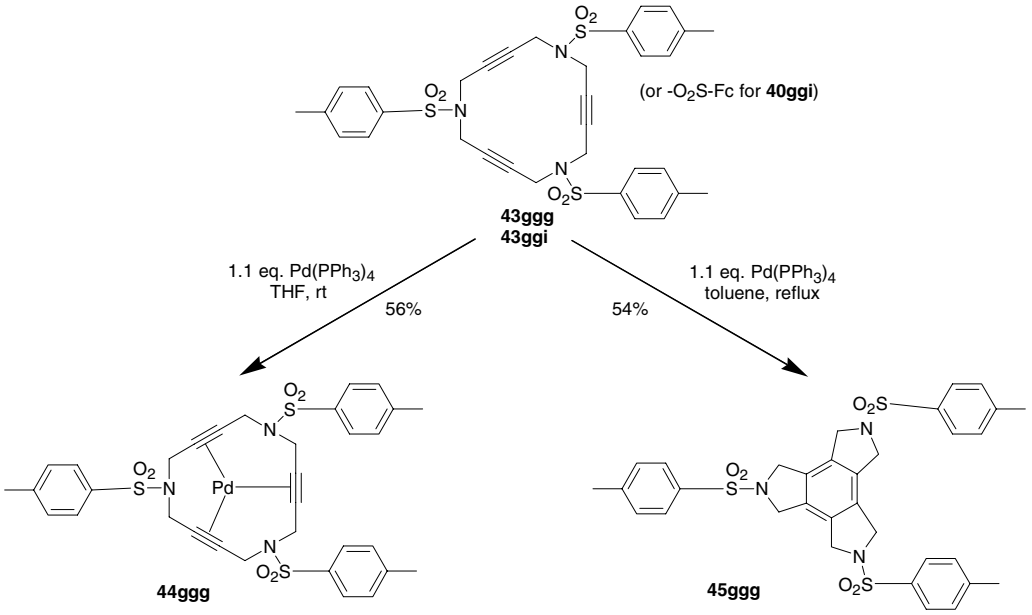
Scheme 9. Role of macrocyclic complex **4** in telomerization and Tsuji–Trost reations.



Scheme 10. Preparation of macrocycle **36**. Reagents and conditions: i: K_2CO_3, CH_3CN, reflux, then *cis*-1,4-dibromobutene (0.5 equiv.); ii: TFAA, CH_2Cl_2e, room temperature; iii: K_2CO_3, refluxing CH_3CN; iv: $Pd(PPh_3)_4$, refluxing THF, or $Pt(PPh_3)_4$, DMF, 130 °C, or $AgBF_4$, refluxing acetone.



Scheme 11. Structures of related macrocycles.

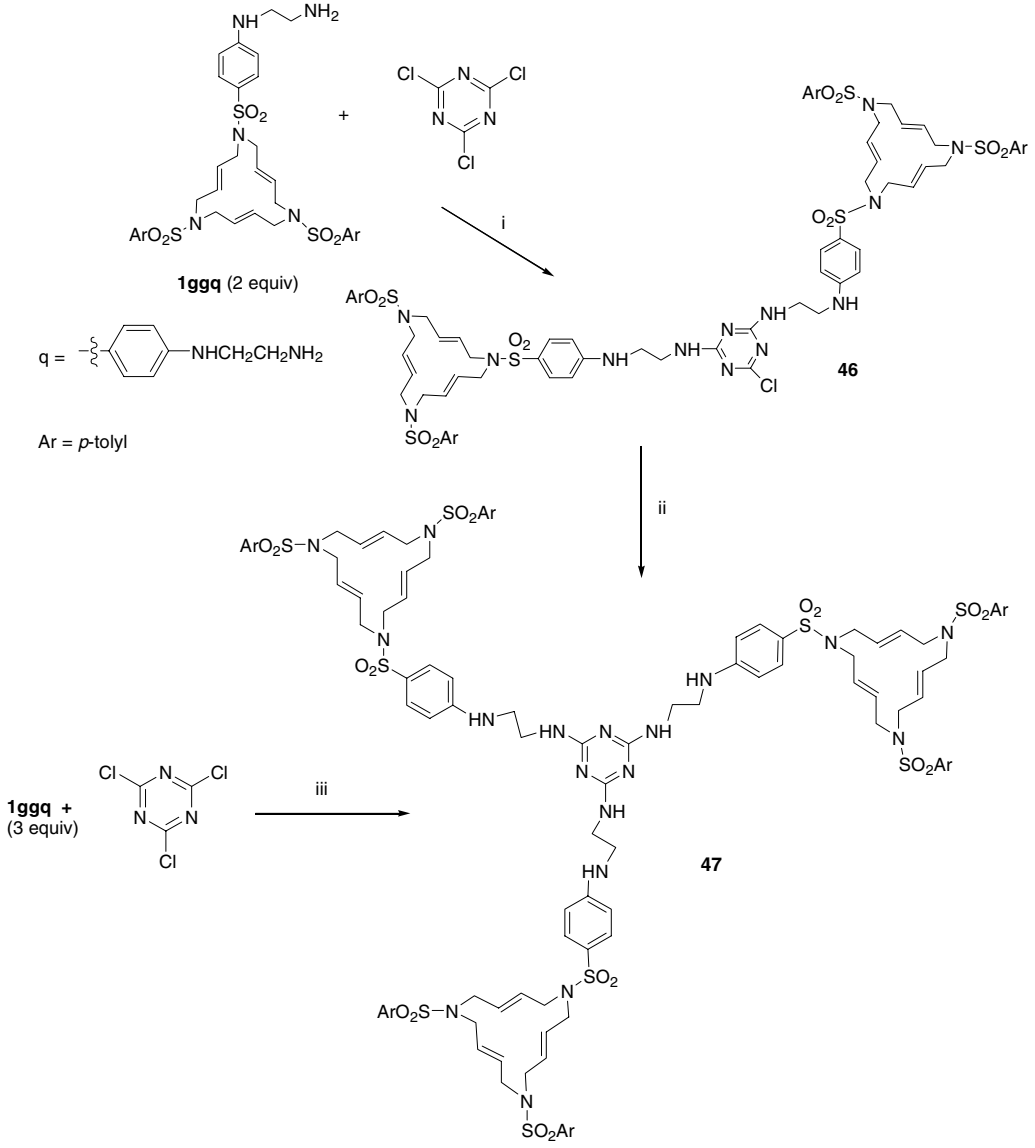


Scheme 12. Reactivity of triacetylenic macrocycle **43ggg**.

of yield and recovery. The procedure has been applied to the synthesis of 3-arylquinolines in a domino hydroarylation/cyclization process [15].

Palladium complexes **4** were not catalytically active in telomerization and in Tsuji–Trost allylation in the absence of added phosphine [8,14]. However, Muzart co-workers [8,14] showed that the telomerization of butadiene with methanol occurs with **4aaa** and monodentate phosphines, the catalytic species being recycled up to four times by adding fresh phosphine each time (Scheme 9).

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 catalytic species after addition of fresh phosphine each time. This was not possible without added **1aaa**. To get information on the nature of the actual catalytic species in the telomerization when macrocycle was present, we undertook mechanistic studies by ^{19}F and ^{31}P NMR with macrocycle **1jjj** and complex **4jjj** [14]. The three fluorine atoms show one signal for ligand **1jjj**, whereas 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 species, PdL_2. After catalysis came to an end, if the phosphine was oxidized, palladium(0) reverted to the free ligand **1jjj**, to be stored as complex **4jjj**, thus preventing agglomeration and therefore, remaining available for a new reaction, that requires addition of fresh phosphine but not of fresh palladium.



Scheme 13. Preparation of **46** and **47**. Reagent and conditions: i: Et_3N, CH_3CN, r.t., 2.5 h; ii: **1ggq** (1 equiv.), Et_3N, CH_3CN, 120 °C, 48 h.; iii: Et_3N, CH_3CN, 120 °C, 29 h.

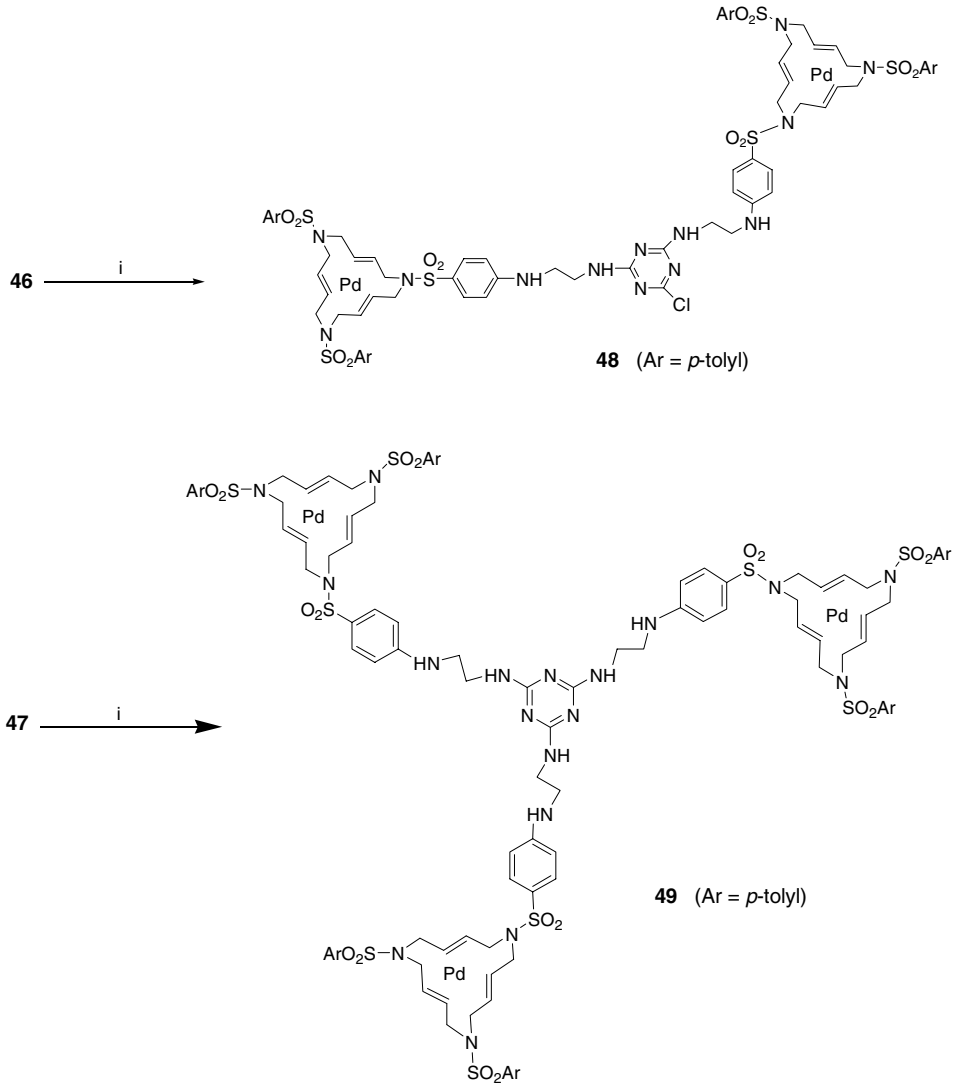
The allylation of diphenylamine **33** with cinnamyl carbonate **34** (Scheme 9) in the presence of **4jjj** and phosphine in THF at room temperature gives **35**. This reaction was also monitored by ^{19}F and ^{31}P NMR [14], the results being consistent with the same mechanistic proposal. Further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

5. Related macrocycles

The macrocyclic family was augmented by modifying the olefin precursors with the aim of studying the complexating ability of the new members. 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 11) [21].

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

Pathway "c" was followed for the synthesis of macrocycles **37** and **38** [21]. Now, 1,2-bis(bromomethyl)benzene was used in the required steps (Scheme 11).



Scheme 14. Preparation of Pd(0) homopolymetallic complexes **48** and **49**. Reagent and conditions: i: $Pd(dba)_2$, THF, reflux.

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

Moreover, we have taken advantage of the availability of intermediates **6** and **8**, required for the formation of macrocycles **1** through routes "a" and "b", for the preparation of 20-membered macrocycles **42** (Scheme 11) [22].

6. Preparation of 15-membered 1,6,11-tris(arenesulfonyl)-1,6,11-triazacyclopentadeca-3,8,13-triynes (43) and their metal complexes 44

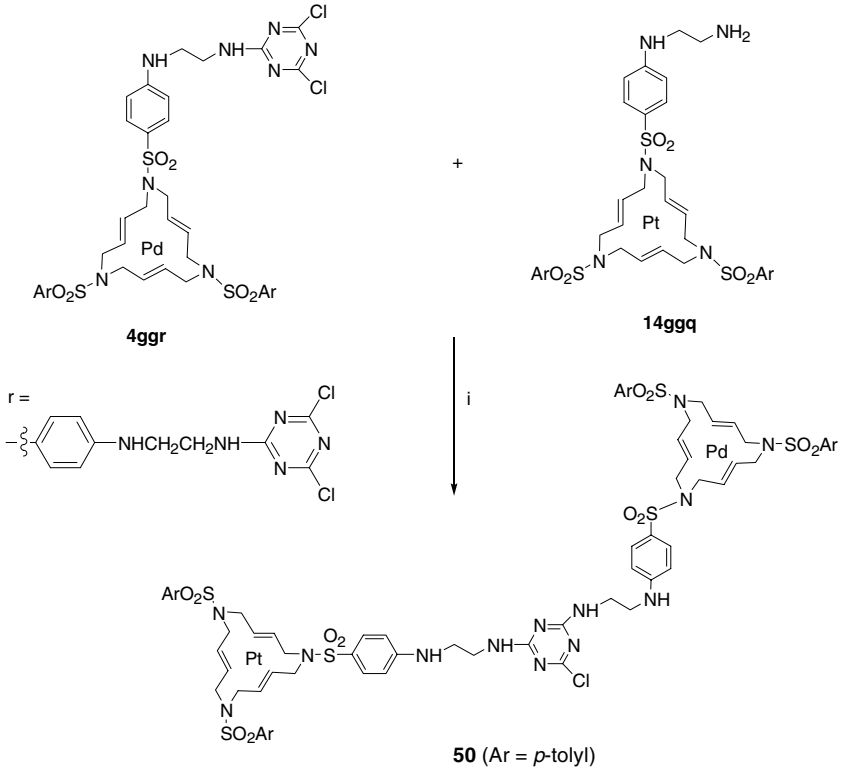
Macrocycles **43** were prepared by pathway "c" using either 1,4-dibromobutyne or the bismethanesulfonate of 1,4-butynediol [23]. Reactivity of **43ggg** was studied (Scheme 12). It formed the stable complex with palladium(0) **44ggg** at room temperature. However, under harsher conditions cycloisomerization to the triazatridane **45ggg** was achieved. These preliminary results opened a new line of exploration that we pursue at present.

7. Preparation of homo- and heterobimetallic complexes 48, 49, and 50

Finally, we speculated [24] with the possibility of preparing molecular architectures featuring two macrocycles of type **1** connected by a triazine core as in **46** and **47** (Scheme 13). These superstructures have been constructed thanks to the differential reactivity of the three chlorine atoms of 2,4,6-trichlorotriazine (Scheme 13). The triazine acts as a linker, around which 15-membered macrocycles are placed.

Then, bis- and tris-macrocyclic ligands **46** and **47** were loaded with palladium to afford homobi- and homotrimetallic complexes **48** and **49**, respectively (Scheme 14).

Moreover, when each macrocycle was loaded with palladium or platinum in an ordered manner, heterobimetallic complex **50** was obtained in good yield (Scheme 15). These complexes have potential in bimetallic catalysis. Several mass spectrometry techniques such as MALDI-TOF, ESI-MS and LSI-MS were fundamental in the identification of all these products [24].



Scheme 15. Preparation of Pd(0),Pt(0) heterobimetallic complexes **50**. Reagent and conditions: i: Et_3N, CH_3CN, reflux.

8. Concluding remarks

A new family of 15-membered macrocycles is easily prepared from commercially available *trans*-1,4-dibromo-2-butene and arenesulfonamides. The cyclization step is performed in good yield without special difficulties arising from the formation of polymers or higher rings. However, in certain cases both polymers and 30-membered rings have been detected or isolated [10]. Macrocycles of this family coordinate certain transition metals, such as palladium(0), platinum(0), and silver(I). The palladium and platinum complexes are planar trigonal. Little is known on complexes with other transition metals.

Palladium complexes **4** are excellent catalysts or precatalysts in carbon–carbon bond forming reactions: 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 even far from clear. For telomerizations, 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 the catalysts is possible in all the cases above mentioned, and even a polymeric version, recoverable by simple filtration, has been described [6]. These facts permit us to believe that our phosphine-free palladium complexes of 15-membered macrocycles can be excellent substitutes for the more classical sources of palladium such as $Pd_2(dba)_3$ and $Pd(PPh_3)_4$.

Furthermore, the preparation of 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. Furthermore, we have opened a new axis of research in which we try to convert our macrocycles into molecular materials.

By varying the open-chain precursors, the synthesis of structurally related macrocycles is possible. Thus, preparations of a geometrical isomer of **1**, of compounds possessing benzene rings in the place of isolated double bonds, and of larger macrocycles such as 20-membered rings have been performed.

15-Membered macrocycles featuring three triple bonds have been prepared. They are excellent ligands for palladium(0), but upon forcing the experimental conditions they cycloisomerize to hexa-substituted benzenes.

More complicated architectures featuring two and even three macrocycles organized around a central linker have been prepared. Two or three equal metal atoms or two different metal atoms can be incorporated at will in these superstructures.

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