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4-*exo-dig* and 5-*exo-dig* Cyclocarbopalladations: an expeditious solution toward molecular complexity?

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Abstract—The 4-*exo-dig* and 5-*exo-dig* cyclocarbopalladations have been efficiently used to produce molecular complexity in a straightforward manner. Strained 1,2-cyclobutanediols are rapidly obtained under microwave irradiation in high yields. In many cases, the cyclocarbopalladation cascade reaction is associated with a 6 or 8π electrocyclic reaction. During the process of the 5-*exo-dig* cyclocarbopalladation on benzosuberone derivatives, an aromatic C–H activation leads to vinylic substituted aromatics. Polycyclic skeletons of natural products of the family of Ophiobolin and Aleurodiscal can be prepared in few steps from simple starting material.
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1. Introduction

The potential of palladium-catalyzed process in organic synthesis has not yet been fully explored. The usefulness of strategies based on palladium cyclization cascades has been demonstrated in the past leading to polycyclic frameworks in regio- and stereoselective manner. One of the most efficient cyclization process that has been used in the literature concerns the intramolecular attack of an organopalladium activated species on a tethered triple bond. Most of the time, an initial 5-*exo-dig*, 6-*exo-dig*, or 7-*exo-dig* cyclocarbopalladation is involved followed by a terminating cross-coupling reaction with CO or various organometallic reagents.[1]

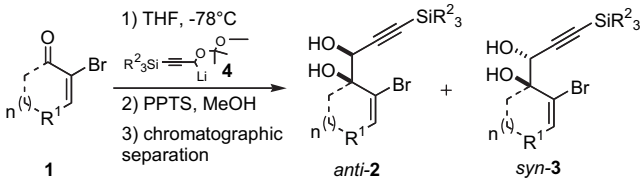
Significant recent studies in our laboratory are directed at the development of cyclocarbopalladation to design and elaborate complex molecules from simple starting material. In this context, we report herein our investigations in the study of cascade reactions involving 4-*exo-dig* and 5-*exo-dig* cyclocarbopalladations.

2. Results and discussion

2.1. An unprecedented 4-*exo-dig* cyclocarbopalladation

Our initial studies focused on a rare 4-*exo-dig* cyclocarbopalladation through a palladium catalysis using a vinyl or alkynylstannane as the terminating trapping species.[2] To the best of our knowledge, before our preliminary work in this field, there was no report on the preparation of related cyclobutanes by this process.

Diols *anti*-**2** and *syn*-**3** were selected as starting materials and prepared in large scale by addition of a properly protected metalated propargylic alcohol **4** onto bromoalkenones **1**, followed by deprotection and chromatographic separation of the two diastereomers *anti*-**2** and *syn*-**3** (Scheme 1).



Scheme 1.

With the diols in hands, we decided to explore the scope and the limitation of the 4-*exo-dig* cyclocarbopalladation. Two possible mechanistic pathways can be envisaged (Scheme 2):

- pathway A: favoring a direct Stille cross-coupling giving compounds of type **5**.
- pathway B: favoring a 4-*exo-dig* cyclocarbopalladation followed by a Stille cross-coupling giving compounds of type **6**.

The 4-*exo-dig* cyclizations are known to be disfavored process according to Baldwin's rules if one considers the organolithium or organomagnesium cyclizations.[3] Of course this

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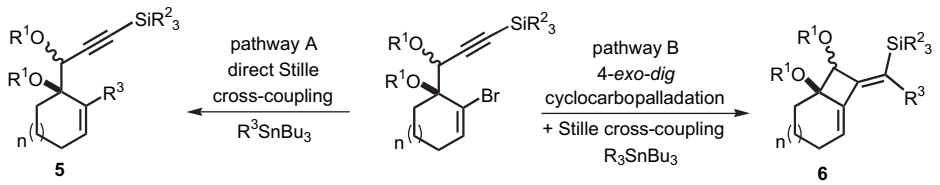


Scheme 2.

type of forbidden reaction can be revisited if in place of a lithium or magnesium intermediate species a transition metal activated route is used. In an effort to favor this process, we examined the effect of several different palladium catalysts, various inorganic and organic bases, and the phosphine ligands.[4] Palladium(II) catalysts such as $PdCl_2(PhCN)_2$, $PdCl_2(CH_3CN)_2$, and $PdCl_2(AsPh_3)_2$ were used, leading only to decomposition of the starting material. The catalytic system $Pd(OAc)_2/PPh_3$ is frequently used in carbopalladative processes. Applying these conditions to our substrates, we observed the exclusive formation of the Stille product **5**. With the same catalyst system, when additives such as Et_4NCl, silver salts,[5] or Et_3N[6] were used only the Stille product **5** was formed and with K_2CO_3 or Na_2CO_3 in benzene, black palladium precipitates rapidly and decomposition of the substrate occurred. When $Pd(PPh_3)_4$ was used, a single product **6** was formed resulting from a 4-*exo-dig* cyclocarbopalladation followed by a Stille cross-coupling. It is remarkable to note that, to this date, the only efficient catalyst for this process is $Pd(PPh_3)_4$. Any other Pd(0) sources gave a trace of the cyclobutane ring system. Different solvents were tested: THF, DMF, NMP, and CH_3CN cause the decomposition of the starting material. Benzene or toluene seems to give the best results for the 4-*exo-dig* cyclocarbopalladation.

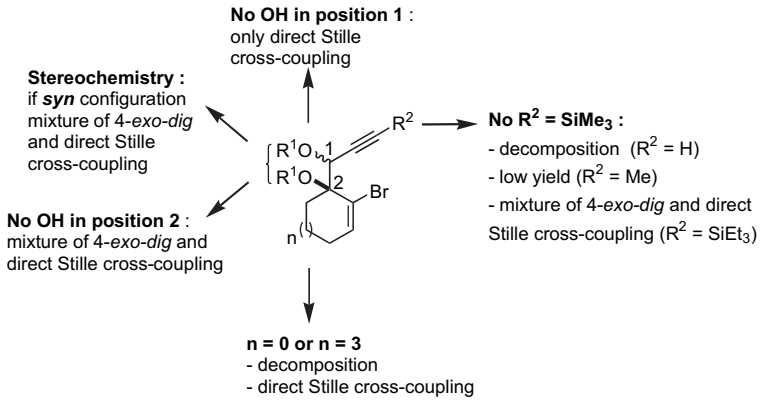
Eventually, this investigation led to the optimized reaction procedure: 10% mol $Pd(PPh_3)_4$ with 1.3 equiv of stannylated reagent in benzene or toluene.

Next, we explored this route to 1,2-cyclobutanediols by examining the influence of the different structural parameters of the substrate in order to favor the cyclocarbopalladation-Stille cross-coupling cascade (Scheme 3).

First the influence of the size of the ring bearing the vinyl bromide function was studied. We noticed that in the case of the five-membered ring the reaction proceeded only via an exclusive direct Stille cross-coupling, and decomposition lowered the yield. This result can be explained by the high ring strain induced by the presence of the cyclobutanediol connected to a smaller ring. Decomposition of the starting material occurred with the eight-membered ring, probably caused by transannular interactions in the cyclooctene. The six- and seven-membered rings led to compounds via a cyclocarbopalladation process followed by a Stille cross-coupling.

The presence of the diol functionality seems to be essential in the competition between the direct Stille cross-coupling and the cyclocarbopalladation-Stille cross-coupling cascades. We next turned our attention to examine the role of each of the hydroxyl groups at positions 1 and 2 (Scheme 3). Applying the same catalyst system described previously, it appeared that the propargylic hydroxyl group (position 1) controls the feasibility of the 4-*exo-dig* cyclocarbopalladation. Indeed, without this hydroxyl group in the propargylic position, the direct Stille cross-coupling was the only observed pathway. A mixture of the Stille product **5** and the cyclobutanediol **6** was isolated when the hydroxyl in the homopropargylic position (position 2) was removed. Therefore, to favor the exclusive 4-*exo-dig* cyclocarbopalladation, the presence of these two oxygen atoms is necessary.

Moreover, the stereochemistry of the diol is also important by directing the triple bond more or less into close proximity of the vinyl bromide. Thus, the experiments on the *syn*-propargylic diol **3** showed a versatile reactivity: a mixture of Stille product **5** and cyclobutanediol derivatives **6** was obtained unlike the reaction with the *anti* diol **2**, which gave only cyclobutanediol derivatives. As a consequence, the *anti* diol **2** was selected as a starting material, in all cases, for the rest of the studies.



Scheme 3.

To complete the studies on the different parameters related to the starting material, the substitution of the triple bond was varied. With the unprotected triple bond decomposition occurred, and even Sonogashira coupling was not observed. With a terminal methyl group, the substrate underwent a 4-*exo-dig* cyclocarbopalladation in moderate yields compared to the triple bond substituted by the trimethylsilyl group. In addition changing the terminal silyl group from trimethylsilyl to triethylsilyl group did not improve the reaction. The trimethylsilyl group turned out to be the most appropriate for protection of the triple bond, which may be due to an electronics effect.

In summary, the two oxygens in the γ-bromopropargylic diols in an *anti* configuration turned out to be essential for the reaction and the trimethylsilyl group is the most appropriate substituent on the triple bond for high reaction efficiency.

2.2. 4-*exo-dig* Cyclocarbopalladation followed by Stille cross-coupling

The previous study of different parameters of the reaction (catalyst, solvent, and temperature) and the starting materials allowed optimization of the conditions to favor the cyclocarbopalladation process.

Thus, different diols (cyclic **7**, **8**, and acyclic **9**) were treated according to the conditions described above in the presence of alkynes (entries 1, 4, and 6), heteroaromatics (entry 2), vinyl (entry 3), and allyltributylstannanes (Table 1, entry 5). Two methods of activation of the reaction were used: activation by heating the reaction mixture at 85 °C (method A) or by using microwave irradiation as a source of molecular activation for the catalytic process (method B).

In each case, the only product isolated resulted from a 4-*exo-dig* cyclocarbopalladation coupling following by a Stille termination coupling and not from a direct Stille cross-coupling reaction in keeping with the previous study. In majority of the cases, the isolated compounds are stable and were purified by chromatography on silica gel without any precaution.

The bicyclic and tricyclic cyclobutanediols **10**–**19** were obtained in moderate to good yields (12–84%) from cyclic diols **7** and **8**, and highly substituted cyclobutanedienynes **20**–**36** were prepared in high yields (46–86%) with acyclic diols **9**.[7] In the presence of stannylated aromatic heterocycles derived from thiophene and furan, it is possible to access the new heteroaromatic substrates (**12**, **13**, **18**, **26**, and **27**, entry 2).

2.3. The 6π electrocyclization process

In several examples, depending on the stannylated reagents, the original reaction of cyclocarbopalladation followed by Stille cross-coupling reaction is terminated by a 6π electrocyclization process.

Thermal conditions and microwave irradiation were also used with protected (**8**–**38**), unprotected (**7**, **9**, **37**), cyclic (**7**, **8**), and acyclic (**9**, **37**, **38**) diols (Table 2).

This process gave tricyclic or tetracyclic structures **39**–**45** bearing a strained cyclobutene ring fused to the two other rings and an anti-Bredt double bond is shared by three cycles (entries 1 and 2).

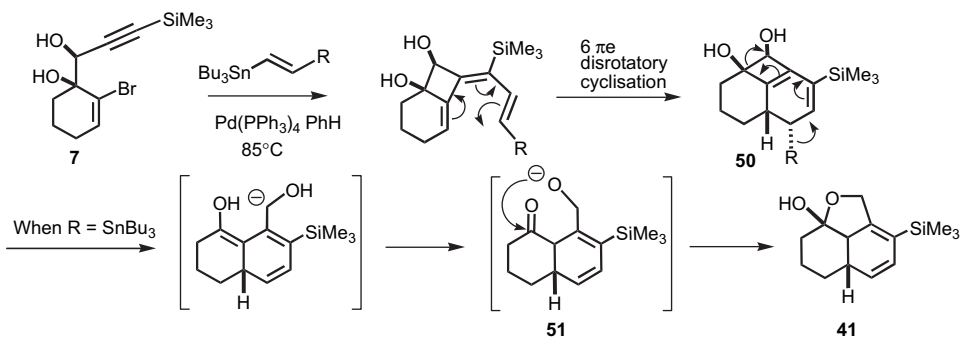
With acyclic diols, bicyclic compounds **46**–**49** were obtained, and the double bond in the bicycle system could be selectively oxidized to give functionalized cyclooctenes.

To explain the formation of compounds **41** and **42**, in the case of use of bis-stannane **B** with unprotected diols **7**, the non-isolated strained tricyclic compounds **50** underwent a subsequent elimination of the three alkyl tin group followed by an opening of the 1,2-cyclobutendiol (Scheme 4, Table 2, entry 1). A final attack of the allylic oxygen on ketone **51** afforded the hemiketals **41**.

It is important to note that the absence of a tributylstannane group in molecule of type **50** completely prevents the opening of the cyclobutenediol through a 4π electron opening electrocyclic reaction. In the same manner, this elimination of the tin is not feasible with the protected diol because of the dioxolane protection that also prevents the opening of the cyclobutenediol. Thus, after the electrocyclization, a dehydrostannation event provides the unusual aromatic tetracyclic dioxolane **45** (Table 2, entry 2).

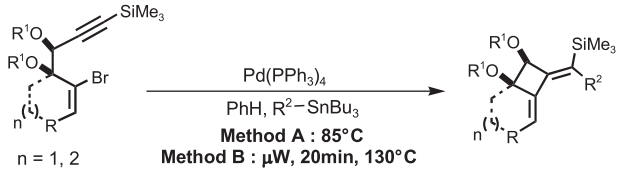
2.4. The 8π electrocyclization process

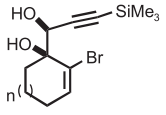
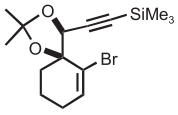
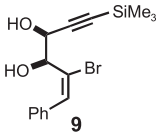
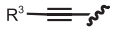
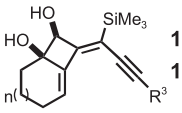
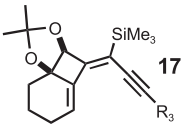
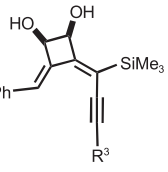
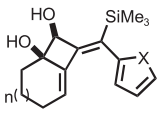
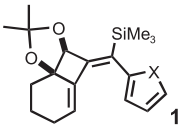
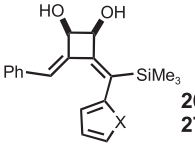
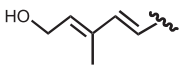
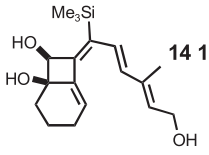
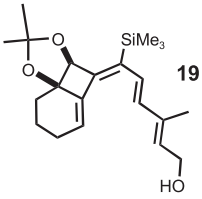
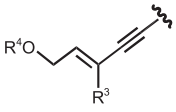
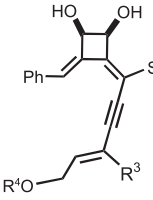
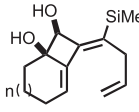
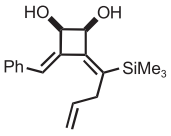
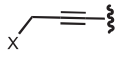
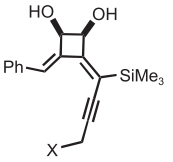
During the studies toward the extension of this new methodology to the synthesis of other polycyclic structures, we decided to examine the feasibility of a conrotatory 8π electrocyclization in the same reaction sequence. This cascade



Scheme 4.

Table 1. Cyclocarbopalladation followed by Stille cross-coupling

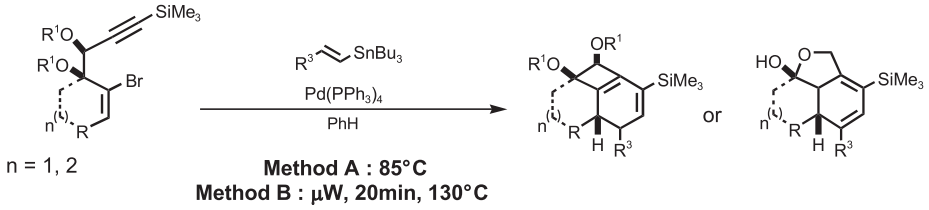


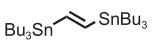
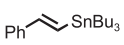
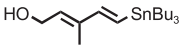
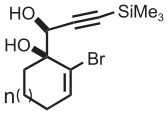
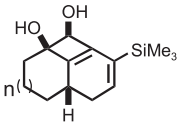
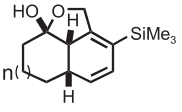
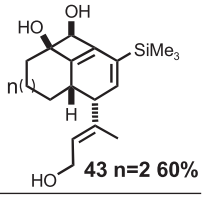
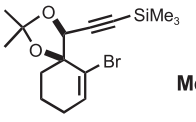
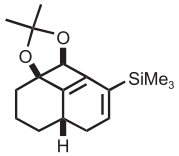
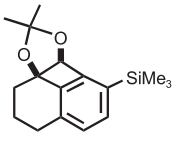
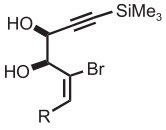
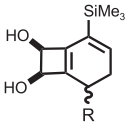
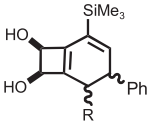
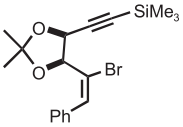
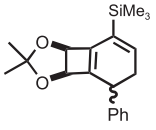
		Starting diol		
		 **7** **Method A**	 **8** **Method A**	 **9** **Method B**
Entries	R^2-SnBu_3	Products and yields		
1		 **10 n=1 R^3=Ph 69%** **11 n=2 R^3=Ph 61%**	 **17 R^3=Ph 53%**	 **20 R^3=Ph 85%** **21 R^3=TMS 80%** **22 R^3=$(CH_2)_2CH_3$ 86%** **23 R^3=$(CH_2)_3CH_3$ 85%** **24 R^3=$(CH_2)_4CH_3$ 80%** **25 R^3=$(CH_2)_7CH_3$ 80%**
2		 **12 n=1 X=O 84%** **13 n=2 X=O 70%**	 **18 X=O 83%**	 **26 X=O 63%** **27 X=S 46%**
3		 **14 12%**	 **19 40%**	
4			 **28 R^3=Me R^4=TMS 77%** **29 R^3=H R^4=TBDMS 75%** **30 R^3=Me R^4=TBDMS 71%**	
5		 **15 n=1 56%** **16 n=2 71%**	 **31 63%**	
6			 **32 X=OMe 84%** **33 X=OBn 72%** **34 X=CH_2OTBDMS 85%** **35 X=OTBDPS 80%** **36 X=N(Me)Ph 79%**	

sequence leads to an eight-membered ring, which is present in over hundred different natural products, many exhibiting exceptional and broad-ranging biological activity. For example, Ophiobolin A[8] have a broad spectrum of biological activity against nematodes, fungi, and bacteria[9] as well as potent antitumor activity.[10] Aleurodiscal[11] is an antifungal antibiotic and one of the most notable examples is the diterpene paclitaxel (taxol) (Scheme 5).

Due to high degree of ring strain, transannular interactions and unfavorable entropic and enthalpic factors, the synthesis of eight-membered ring compounds remains a difficult area.

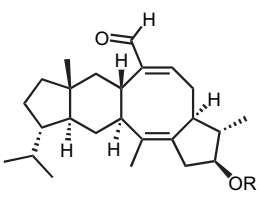
Table 2. Cyclocarbopalladation followed by Stille cross-coupling terminated by a 6π electrocyclization process

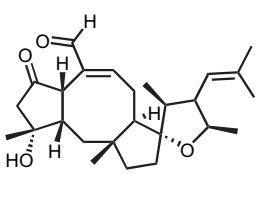


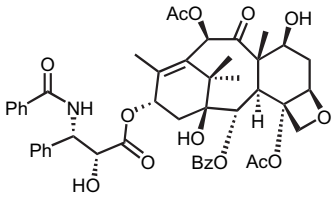
		Stannanes R^3–SnBu$_3$			
		 **A**	 **B**	 **C**	 **D**
Entries	Starting diol	Products and yields			
1	 **7** **Method A**	 **39 n=1 35%** **40 n=2 62%**	 **41 n=1 62%** **42 n=2 24%**		 **43 n=2 60%**
2	 **8** **Method A**	 **44 45%**	 **45 21%**		
3	 **37 R=H** **9 R=Ph** **Method B**	 **46 R=H 44%** **47 R=Ph 49%**		 **48 R=Ph 36%**	
4	 **38** **Method B**	 **49 91%**			

To solve this difficulty, several authors have presented, in the recent past, elegant approaches using transition metal catalysis.[12] The most recent approach implied the formation of a bicyclic structure using a rhodium catalyst in a one pot operation.[13] Extensive studies by several research groups[14] have been performed to reach analogues of Ophiobolin A and Aleurodiscal. The total synthesis of Ophiobolin C was completed by Kishi in 1989.[15] However, none of these approaches involved the direct formation of a 5-8-5 tricyclic skeleton.

Four types of diols were used for this study, unprotected (**7**, **9**, and **52**), protected (**38**), cyclic (**7** and **52**), and acyclic (**9** and **38**).[16] The stannanes were prepared by a straightforward method developed by Lautens et al.[17] The reaction cascade is based on three consecutive transformations starting from the

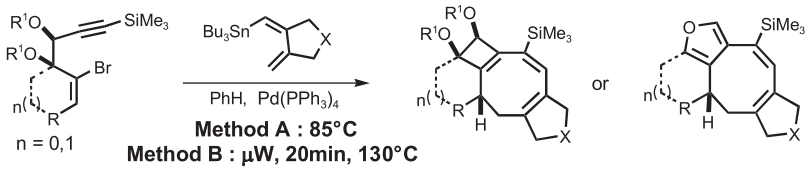

Aleurodiscal

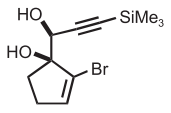
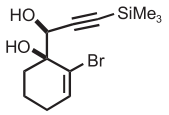
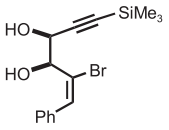
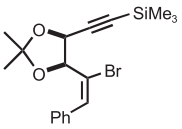
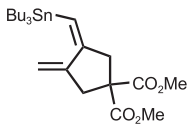
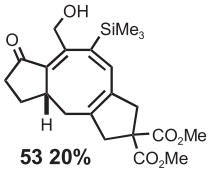
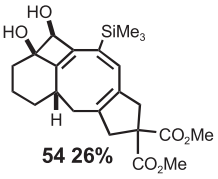
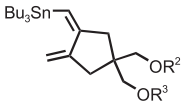
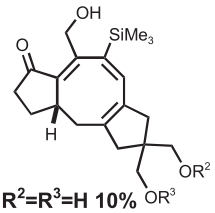
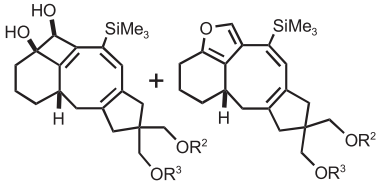
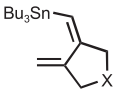
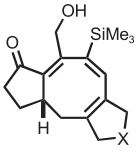
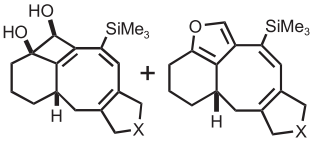
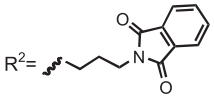
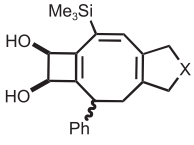
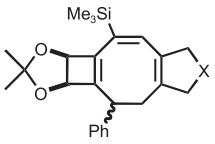

Ophiobolin A


Taxol

Scheme 5.

Table 3. Cyclocarbopalladation followed by a Stille cross-coupling terminating by a 8π electrocyclization process



		Starting diol			
					
		52	**7**	**9**	**38**
		Method A	**Method A**	**Method B**	**Method B**
Entries	Stannanes	Products and yields			
1		 **53 20%**	 **54 26%**		
2		 **55 R^2=R^3=H 10%** **56 R^2,R^3=$C(CH_3)_2$ 16%**	 **57-58 R^2=R^3=H 61% ratio 59:41** **59-60 R^2,R^3=$C(CH_3)_2$ 15% ratio 100:0**	Decomposition **R^2,R^3=$C(CH_3)_2$**	Decomposition **R^2,R^3=$C(CH_3)_2$**
3		 **61 X=NTs 16%** **62 X=O 24%**	 **63-64 X=NTs 56% ratio 48:52** **65-66 X=O 11% ratio 100:0** **67-68 X=CH-CH_2-OH 41% ratio 100:0** **69-70 X=NR^2 58% ratio 40:60** 	 **71 X=NTs 27%** **2 dias**	 **72 X=NTs 62%** **2 dias**

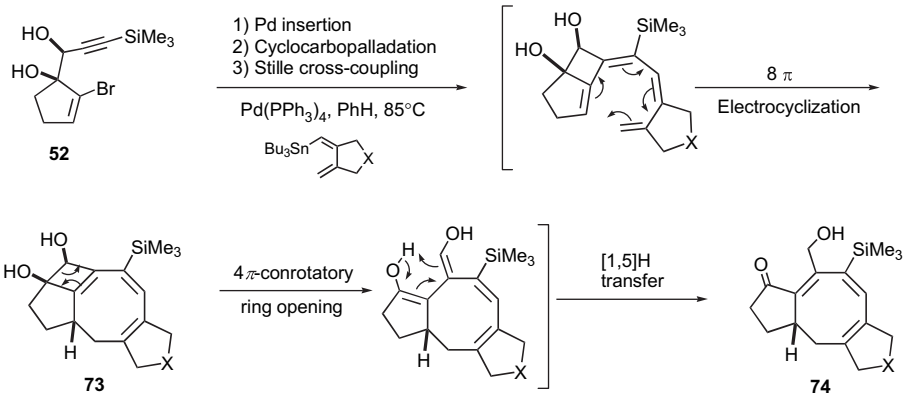
diol: an initial 4-*exo-dig* cyclocarbopalladation followed by a Stille cross-coupling and eventually a concerted conrotatory 8π electrocyclization. The results are summarized in Table 3.

Different types of products were obtained with this cascade depending on the ring size of the starting substrate. The first product type (**53**, **55**, **56**, **61**, and **62**) was generated from cyclopentene diol **52** in a sequence of six steps (Scheme 6). After the palladium insertion, the cyclocarbopalladation, the Stille cross-coupling, and the 8π electrocyclization, the strained cyclobutene **73** underwent a 4π conrotatory ring opening and a [1,5]-hydrogen shift to give the compound of type **74**.

When the cyclohexene diol **7** were used, the reaction to obtain the corresponding cyclobutenediol was limited by the formation of furyl derivatives (**58**, **64**, and **70**), which probably result from a final rearrangement (ring opening, cyclization, and elimination). The yields observed ranging up to 58% were modest to acceptable if one consider the complexity of the new products formed in formally just one step from the readily available diols.

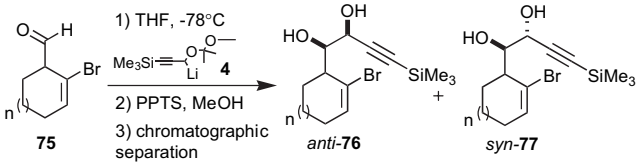
2.5. 5-*exo-dig* Cyclocarbopalladation

Considering the results obtained with the 4-*exo-dig* cyclocarbopalladation, our attention next focused on the use of



Scheme 6.

another type of reaction: the 5-*exo-dig* cyclization, a favored process according to Baldwin's rules,[8] starting from a substrate containing a propargylic diol function and the vinyl bromide included in an aliphatic ring. The starting diols *anti*-**76** and *syn*-**77** were again easily prepared in good yields by addition of the protected metalated propargylic alcohol **4** on bromo-aldehydes **75** followed by deprotection and chromatographic separation of the two *anti*- and *syn*-diastereomers (Scheme 7).[18]



Scheme 7.

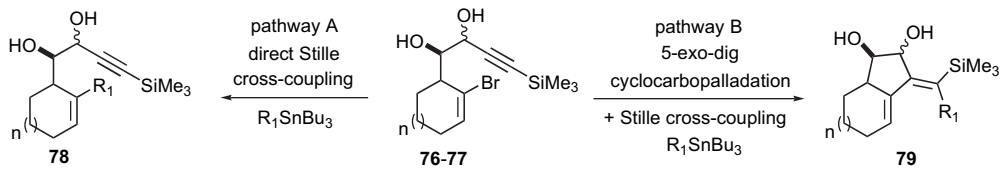
The impact of the stereochemistry of the starting diol and the size of the ring bearing the vinyl bromide function was examined with the same conditions and catalytic system described before for the 4-*exo-dig* cyclocarbopalladation: at 85 °C in benzene in the presence of a catalytic amount of $Pd(PPh_3)_4$ (10 mol %). The *trans*-bis(tributylstannyl)-ethylene was used to explore the competition between the two reactions: a direct Stille reaction (pathway A, compound **78**) or cyclocarbopalladation followed by a Stille termination (pathway B, compound **79**) (Scheme 8).

It turns out that the diols *anti*-**76** and *syn*-**77**, irrespective of cycle size, afforded only the products resulting from a 5-*exo-dig* cyclocarbopalladation, **82** and **83** (Table 4, entries 1 and 2), generally with acceptable to good yields. However, when the diols are protected (entries 3 and 4, **80** and **81**) as a dioxolane, the direct Stille cross-coupling competes significantly. Independent of considerations of the size of the ring, we distinguished the *cis*-dioxolane **80** that proceeded via a cyclocarbopalladation process to obtain compound **84**, from the *trans* dioxolane **81** that led exclusively to the direct Stille cross-coupling product **85**. In the later case, the cyclocarbopalladation did not proceed at all due to the highly strained tricyclic derivatives that should be obtained in theory.

2.6. 5-*exo-dig* Cyclocarbopalladation and CH activation

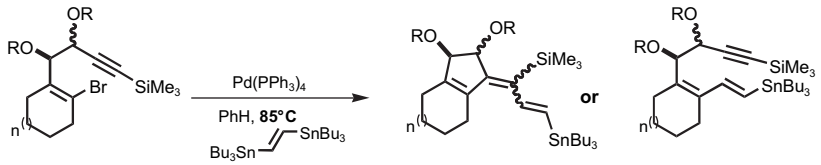
Considering the results obtained from the 5-*exo-dig* cyclocarbopalladation, our attention focused on the use of new, original *anti*-propargylic-1,2-diols **86**, **87**, **88**, **89** derived, respectively, from acetophenone, indole, tetralone, or benzosuberone (Table 5).[19] In the presence of vinylic (entry 1), allylic, or heteroaromatic stannane derivatives (entry 2), 5-*exo-dig* cyclocarbopalladation under classical conditions (85 °C, PhH, 10% mol $Pd(PPh_3)_4$) is efficient and products were isolated ranging up to 70% yields. The use of diol **88** gave the expected products **93** and **94** after the 5-*exo-dig* cyclocarbopalladation and the Stille cross-coupling. The five-membered ring diol **87**, under the same reaction conditions, led to the decomposition of starting materials. However, when acyclic diol **86** and benzosuberone derivative diol **89** are employed under these conditions, none of the expected products were obtained but only the styrene derivatives **90**, **95**–**103** were observed. The formation of these products resulted from a C–H palladative activation. Some recent papers describe a new C–H activation process of nonactivated aromatic derivatives using metal catalysis.[20] In the case of the diol **87**, this C–H activation was not observed probably because of the low flexibility of the ring. Thus, the regioselectivity of the final vinylic stannane partner is totally dependent of the substrate.

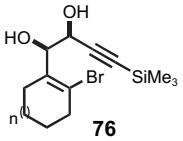
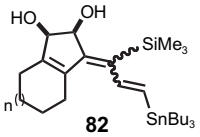
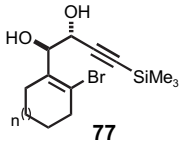
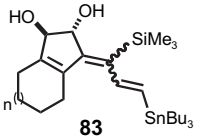
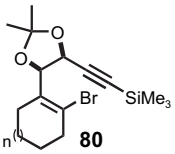
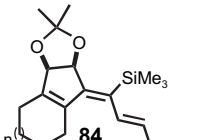
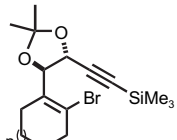
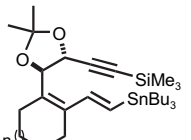
On the other hand, when alkynylstannanes were used, only the Stille cross-coupling product was observed with yields



Scheme 8.

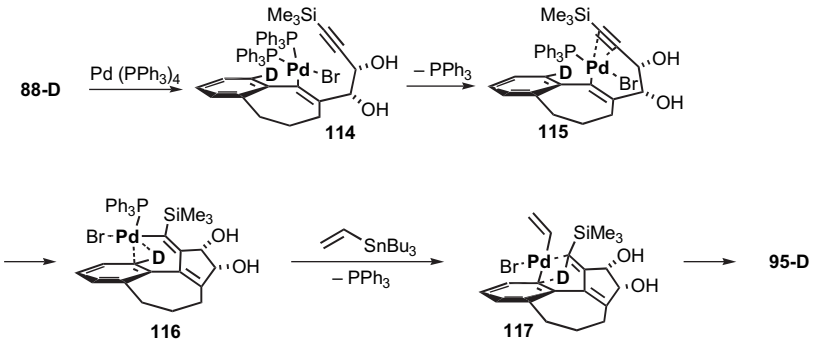
Table 4. Effect of the ring size and the protection of the hydroxyl functions



Entries	Starting diol	Products	*n*	Time (h)	Yield (%)	Ratio (*E*/*Z*)
1	 **76**	 **82**	0	14	75	78/22
			1	27	71	66/34
			2	16	45	100/0
			3	23	27	100/0
2	 **77**	 **83**	0	14	54	70/30
			1	27	52	100/0
			2	16	31	100/0
			3	23	—	100/0
3	 **80**	 **84**	0	17	54	—
			1	18	64	—
			2	14	48	—
4	 **81**	 **85**	0	17	38	—
			1	20	56	—
			2	17	52	—

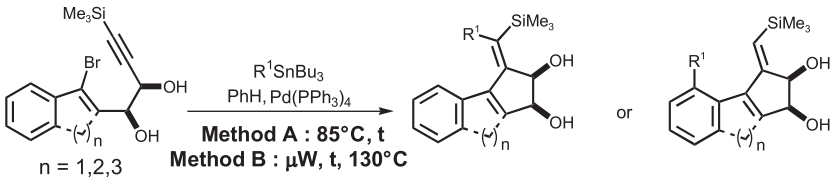
ranging up to 75% after cyclocarbopalladation on the silylated exocyclic double bond (**104**–**113**, Table 5, entry 3).

The mechanism of the C–H activation could be as follows. The sequence is initiated by the insertion of palladium(0) into the vinylic C–Br bond giving **114** by an oxidative addition (Scheme 9). After elimination of the first PPh_3 and cyclocarbopalladation of the triple bond (compound **116**), one can postulate a strong agostic interaction of the palladium atom with the closest aromatic C–H bond as shown in compound **117**. This intermediate is determinant for the C–H activation. Theoretical studies have been performed and corroborated with our postulation.[21] The intimate mechanism of the 1,5-vinyl to aryl palladium shift best corresponds to a proton transfer between the two formally negatively charged carbon atoms of the vinyl and the phenyl groups that are bound to the palladium atom in the transition state. As a consequence, the palladium center retains its +II oxidation state throughout the tandem reaction.[22] Deuterium labeled diol confirms that the H is transferred to the terminal vinyl silane through the coordination sphere of palladium.[24]

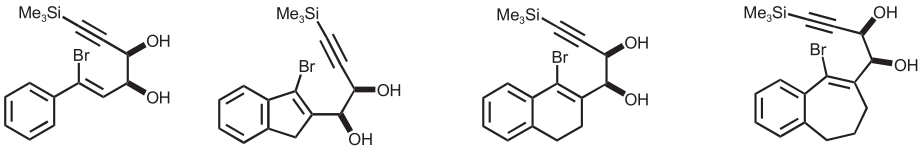


Scheme 9.

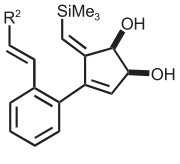
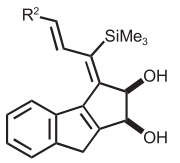
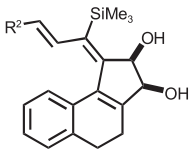
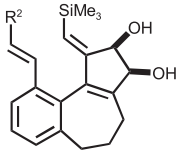
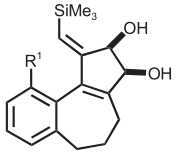
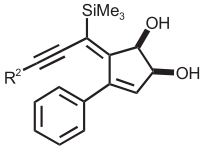
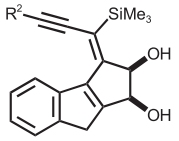
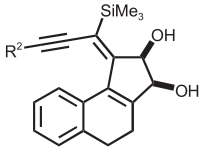
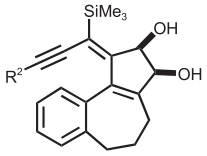
Table 5. Synthesis of Polycycles via palladium CH activation



Starting diol



86 **87** **88** **89**

Entries	R^1SnBu_3	Products
1		 **90 R^2=H, 30 min, 43%, B**  **91 R^2=H, 20 min, 0%, B** **92 R^2=$SnBu_3$, 20 min, 0%, B**  **93 R^2=H, 20 min, 59%, B** **94 R^2=$SnBu_3$, 20 min, 55%, B**  **95 R^2=H, 8h, 70%, A** **96 R^2=$SnBu_3$, 5h, 58%, A** **97 R^2=Ph, 10 min, 45%, B** **98 R^2=$SiMe_3$, 18 min, 70%, B** **99 R^2=(3-hydroxymethyl)phenyl, 18h, 61%, A**
2	R^1—$SnBu_3$	 **100 R^1=pyr, 20h, 53%, A** **101 R^1=thio, 54h, 48%, A** **102 R^1=allyl, 20h, 52%, A** **103 R^1=fur, 30 min, 53%, B**
3	R^2—≡—$SnBu_3$	 **104 R^2=$SiMe_3$, 38 min, 63%, B**  **105 R^2=Ph, 20 min, 0%, B** **106 R^2=$SiMe_3$, 20 min, 0%, B**  **107 R^2=Ph, 20 min, 49%, B** **108 R^2=$SiMe_3$, 20 min, 56%, B**  **109 R^2=Ph, 12h, 58%, A** **110 R^2=$SiMe_3$, 5h, 45%, A** **111 R^2=Pr, 18h, 75%, A** **112 R^2=TBSO$(CH_2)_3$, 8h, 54%, A** **113 R^2=TBSO$(CH_2)_2$, 8h, 48%, A**

3. Conclusion

In conclusion, we have shown that different sequences including a 4-*exo-dig* cyclization can be realized from γ-bromopropargylic diols under palladium catalysis. We first summarized the study of different parameters of the reaction (catalyst, solvent, and temperature) and the starting materials giving the optimal conditions to favor the cyclocarbopalladation process. These conditions were applied to realize different cascades: 4-*exo-dig* cyclocarbopalladation followed by a Stille cross-coupling and a 6π or 8π electrocyclizations.

The same kind of cascades has been realized including a 5-*exo-dig* cyclocarbopalladation and Stille cross-coupling. In some cases, with acetophenone and benzosuberone diols, a C–H palladative activation after the Stille cross-coupling was observed and styrene derivatives were isolated.

We have shown a major advancement in the field of cyclocarbopalladation cascades for the consecutive formation of several new carbon–carbon bonds in a single-step process. These approaches have already allowed impressive and economical constructions of polycyclic compounds with high molecular complexity. Some applications to the synthesis

of analogues of natural compounds are already in progress in the laboratory. These results will be disclosed in the future.

4. Experimental

4.1. General

Reactions were run under an atmosphere of argon in oven-dried glassware using a standard syringe, cannula, and septa apparatus. Et_2O and THF were distilled from sodium benzophenone. Benzene and DMF were distilled from CaH_2, and CH_2Cl_2 was distilled from P_2O_5. EtN_3 and *i*-Pr_2NH were distilled from KOH. Crude products were purified by flash column chromatography on Merck 230–400 mesh silica gel. For some compounds, 5% Et_3N treated silica gel was used to avoid decomposition. Analytical TLC was carried out on Merck (Kieselgel $60F_{254}$) silica gel plates. ^1H NMR spectra were recorded at 200 or 300 MHz using the residual solvent signal as internal reference ($CDCl_3$, 7.26, C_6D_6, 7.16 ppm). Chemical shifts are quoted in parts per million, coupling constants (*J*) are given in hertz. The following abbreviations are used to describe peak patterns when appropriate: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), m (multiplet), ap (apparent), br (broad). ^{13}C NMR spectra were recorded at 50 or 75 MHz at ambient temperature in $CDCl_3$ at 77.0 as internal reference. Multiplicities were determined in some cases by Jmod pulse sequence. Melting points were determined with a glass capillary apparatus and were uncorrected. IR were determined with a Perkin–Elmer 2000 apparatus. Mass spectra were obtained from the *Service de spectrométrie de Masse* of the Chemistry Institute of Strasbourg (France). High-Resolution Mass Spectral Analysis (HRMS) was performed using a Mariner ESI-Tof instrument from Applied Bio-System Perkin–Elmer. *n*-BuLi was titrated using pivaloyl *o*-toluidine following the Suffert method.[23] Microwave irradiations have been performed using BIOTAGE Smith Creator. Stannanes derivatives were prepared according to the literature methods[24] or commercially available.

4.2. Method A: general procedure: 4-*exo-dig* or 5-*exo-dig* cyclocarbopalladation under classical conditions

The reaction was carried out in an oven-dried 25 mL two-necked flask, equipped with a reflux condenser, under argon atmosphere. To a solution of the diol (1 equiv) in dried benzene was added $Pd(PPh_3)_4$ (0.1 equiv) followed by the stannylated reagent (1.3 equiv). The reaction mixture was stirred for 1–17 h in a preheated 85 °C oil bath. The reaction is followed by TLC. Then, the reaction mixture was concentrated in vacuo and immediately purified by flash chromatography.

4.3. Method B: general procedure: 4-*exo-dig* or 5-*exo-dig* cyclocarbopalladation under microwave irradiation (BIOTAGE system initiator)

The reaction was carried out in a special BIOTAGE flask, under argon atmosphere. To a solution of the diol (1 equiv) in dried benzene (2 mL) was added $Pd(PPh_3)_4$ (0.1 equiv) followed by the stannylated reagent (1.3 equiv). The mixture was purged 20 min with argon and heated at 130 °C under microwave irradiation. The reaction was followed by TLC. After the reaction time, the mixture was cooled, diluted with Et_2O (10 mL), treated with active charcoal, filtrated over Celite, and concentrated to dryness. The reaction mixture was purified by flash chromatography (in the majority of the cases two chromatographies are necessary).

4.3.1. Cyclocarbopalladation 4-*exo-dig* following by a Stille cross-coupling. Compounds **10**–**19** are already described in Ref. 2b.

4.3.2. (1*S*,2*R*,3*Z*,4*Z*)-3-Benzylidene-4-(3-phenyl-1-(trimethylsilyl)prop-2-ynylidene)cyclobutane-1,2-diol (20). Preparation by method B on 0.295 mmol scale with a reaction time of 20 min. Purification by flash chromatography eluting with Et_2O/Hept (20/80) afforded the product (90 mg, 85%) as a yellow solid. R_f: 0.36 (Et_2O/Hept: 30/70). ^1H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, 1H, *J*=1.5 Hz, Ar*H*), 7.63 (d, 2H, *J*=7.1 Hz, Ar*H*), 7.48 (d, 1H, *J*=1.5 Hz, Ar*H*), 7.45 (d, 1H, *J*=1.5 Hz, Ar*H*), 7.38-7.31 (m, 6H, Ar*H*, Ph-C*H*), 4.99 (t, 1H, *J*=5.6 Hz, HO-C*H*-CH-OH), 4.81 (t, 1H, *J*=6 Hz, HO-CH-C*H*-OH), 3.74 (br s, 1H, OH), 3.61 (br s, 1H, OH), 0.32 (s, 9H, $SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.8, 142.8, 135.8, 131.2, 129.7, 129.5, 128.6, 128.5, 128.3, 128.1, 124.2, 121.0, 103.4, 91.9, 72.4, 71.3, −1.0. HRMS (ESI, positive ion 180 eV) calcd for $(C_{23}H_{24}O_2SiNa)^+$: 383.1441; found: 383.1502. IR (FTIR, film): ν=3400 (br), 2118, 1646, 1485, 1249, 1047, 976, 844, 756 cm^{-1}.

4.3.3. (1*S*,2*R*,3*Z*,4*Z*)-3-Benzylidene-4-[1,3-bis(trimethylsilyl)prop-2-ynylidene]cyclobutane-1,2-diol (21). Preparation by method B on 0.295 mmol scale with a reaction time of 20 min. Purification by flash chromatography eluting with Et_2O/Hept (20/80) afforded the product (108 mg, 80%) as a yellow solid. R_f: 0.30 (Et_2O/Hept: 30/70). ^1H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, 1H, *J*=1.5 Hz, Ar*H*), 7.57 (d, 2H, *J*=6.8 Hz, Ar*H*), 7.35–7.29 (m, 3H, Ar*H*, Ph-C*H*), 4.89 (br t, 1H, HO-C*H*-CH-OH), 4.68 (t, 1H, *J*=6.2 Hz, HO-CH-C*H*-OH), 4.40 (br s, 1H, OH), 4.22 (br s, 1H, OH), 0.24 (s, 9H, $SiMe_3$), 0.22 (s, 9H, $SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.1, 142.6, 135.8, 129.9, 129.5, 128.7, 128.3, 121.3, 109.35, 106.9, 72.3, 71.3, 0.1, −1.0. HRMS (ESI, positive ion 180 eV) calcd for $(C_{20}H_{28}O_2Si_2Na)^+$: 379.1526; found: 379.1519. IR (FTIR, film): ν=3410 (br), 2116, 1639, 1487, 1245, 1045, 975, 842, 752 cm^{-1}.

4.3.4. (1*S*,2*R*,3*Z*,4*Z*)-3-Benzylidene-4-[1-(trimethylsilyl)-hex-2-ynylidene]cyclobutane-1,2-diol (22). Preparation by method B on 0.295 mmol scale with a reaction time of 20 min. Purification by flash chromatography eluting with Et_2O/Hept (20/80) afforded the product (83 mg, 86%) as a yellow powder. R_f: 0.30 (Et_2O/Hept: 30/70). ^1H NMR (300 MHz, $CDCl_3$) δ 7.70 (s, 1H, Ar*H*), 7.58 (d, 2H, *J*=7.8 Hz, Ar*H*), 7.35–7.25 (m, 3H, Ar*H*, Ph-C*H*), 4.90 (t, 1H, *J*=5.9 Hz, HO-C*H*-CH-OH), 4.72 (t, 1H, *J*=5.9 Hz, HO-CH-C*H*-OH), 3.89 (br s, 1H, O*H*), 3.69 (br s, 1H, O*H*), 2.50 (t, 2H, *J*=6.8 Hz, CH_2), 1.65 (q, 2H, *J*=7.2 Hz, CH_2), 1.05 (t, 3H, *J*=7.2 Hz, CH_3), 0.23 (s, 9H, $SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.7, 142.8, 136.0, 129.3, 128.6, 128.3, 128.0, 122.6, 105.4, 82.7, 72.2, 71.1, 22.5, 13.7, −1.1. HRMS (ESI, positive ion 180 eV) calcd for $(C_{20}H_{26}O_2SiNa)^+$: 349.1600; found: 349.1595.

4.3.5. (1*S*,2*R*,3*Z*,4*Z*)-3-Benzylidene-4-[1-(trimethylsilyl)-hept-2-ynylidene]cyclobutane-1,2-diol (23). Preparation by method B on 0.295 mmol scale with a reaction time of 20 min. Purification by flash chromatography eluting with Et_2O/Hept (20/80) afforded the product (85 mg, 85%) as a yellow powder. R_f: 0.32 (Et_2O/Hept: 30/70). ^1H NMR (300 MHz, $CDCl_3$) δ 7.70 (s, 1H, Ar*H*), 7.58 (d, 2H, *J*=7.8 Hz, Ar*H*), 7.36–7.26 (m, 3H, Ar*H*, Ph-C*H*), 4.92 (t, 1H, *J*=5.3 Hz, HO-C*H*-CH-OH), 4.74 (t, 1H, *J*=6.24 Hz, HO-CH-C*H*-OH), 3.62 (d, 1H, *J*=6.8 Hz, O*H*), 3.44 (d, 1H, *J*=7.5 Hz, O*H*), 2.53 (t, 2H, *J*=6.8 Hz, CH_2), 1.64–1.27 (m, 4H, 2×CH_2), 0.94 (t, 3H, *J*=7.2 Hz, CH_3), 0.24 (s, 9H, $SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.6, 142.7, 136.0, 129.3, 128.6, 128.3, 128.0, 122.7, 105.6, 82.6, 72.1, 71.1, 31.1, 22.1, 20.1, 13.6, −1.1. HRMS (ESI, positive ion 180 eV) calcd for $(C_{21}H_{28}O_2SiNa)^+$: 363.1756; found: 363.1760.

4.3.6. (1*S*,2*R*,3*Z*,4*Z*)-3-Benzylidene-4-[1-(trimethylsilyl)-oct-2-ynylidene]cyclobutane-1,2-diol (24). Preparation by method B on 0.295 mmol scale with a reaction time of 20 min. Purification by flash chromatography eluting with Et_2O/Hept (20/80) afforded the product (83 mg, 80%) as a yellow powder. R_f: 0.33 (Et_2O/Hept: 30/70). ^1H NMR (300 MHz, $CDCl_3$) δ 7.71 (s, 1H, Ar*H*), 7.56 (d, 2H, *J*=6.8 Hz, Ar*H*), 7.33–7.24 (m, 3H, Ar*H*, Ph-C*H*), 4.85 (br d, 1H, *J*=5.2 Hz, HO-C*H*-CH-OH), 4.68 (br m, 1H, HO-CH-C*H*-OH, O*H*), 2.51 (t, 2H, *J*=7.2 Hz, CH_2), 1.68–1.57 (m, 2H, CH_2), 1.46–1.27 (m, 4H, 2×CH_2), 0.94 (t, 3H, *J*=7.2 Hz, CH_3), 0.19 (s, 9H, $SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.6, 142.8, 136.0, 129.3, 128.6, 128.3, 128.0, 122.7, 105.7, 82.6, 72.2, 71.1, 31.2, 28.7, 22.2, 20.4, 13.9, 13.6, −1.1. HRMS (ESI, positive ion 180 eV) calcd for $(C_{22}H_{30}O_2SiNa)^+$: 377.1913; found: 377.1829.

4.3.7. (1*S*,2*R*,3*Z*,4*Z*)-3-Benzylidene-4-[1-(trimethylsilyl)-undec-2-ynylidene]cyclobutane-1,2-diol (25). Preparation by method B on 0.295 mmol scale with a reaction time of 20 min. Purification by flash chromatography eluting with Et_2O/Hept (20/80) afforded the product (84 mg, 80%) as a yellow oil. R_f: 0.39 (Et_2O/Hept: 30/70). ^1H NMR (300 MHz, $CDCl_3$) δ 7.70 (s, 1H, Ar*H*), 7.59 (d, 2H, *J*=7.1 Hz, Ar*H*), 7.35–7.25 (m, 3H, Ar*H*, Ph-C*H*), 4.92 (t, 1H, *J*=7.2 Hz, HO-C*H*-CH-OH), 4.73 (t, 1H, *J*=7.2 Hz, HO-CH-C*H*-OH), 3.63 (d, 1H, *J*=6.2 Hz, O*H*), 3.45 (d, 1H, *J*=7.2 Hz, O*H*), 2.52 (t, 2H, *J*=6.9 Hz, CH_2), 1.68–1.58 (m, 2H, CH_2), 1.48–1.27 (m, 10H, 5×CH_2) 0.93 (t, 3H, *J*=7.2 Hz, CH_3), 0.24 (s, 9H, $SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.6, 143.0, 136.0, 129.4, 128.5, 128.2, 127.9, 122.5, 105.6, 82.7, 72.2, 71.2, 31.8, 29.1, 29.0, 22.6, 20.4, 17.3, 14.1, 13.6, −1.1. HRMS (ESI, positive ion 180 eV) calcd for $(C_{25}H_{36}O_2SiNa)^+$: 419.2382; found: 419.2377.

4.3.8. (1*S*,2*R*,3*Z*,4*Z*)-3-Benzylidene-4-[2-furyl(trimethylsilyl)methylene]cyclobutane-1,2-diol (26). Preparation by method B on 0.295 mmol scale with a reaction time of 20 min. Purification by flash chromatography eluting with AcOEt/Hept (20/80) afforded the product (61 mg, 63%) as a yellow oil. R_f: 0.40 (AcOEt/Hept: 30/70). ^1H NMR (300 MHz, $CDCl_3$) δ 7.49 (d, 2H, *J*=7.2 Hz, Ar*H*), 7.44 (s, 1H, Ar*H*), 7.33–7.24 (m, 3H, Ar*H*, Ph-C*H*), 6.48 (br s, 1H, furyl-*H*), 6.46 (t, 1H, *J*=3.2 Hz, furyl-*H*), 6.24 (d, 1H, *J*=3.2 Hz, furyl-*H*), 4.93 (d, 1H, *J*=5.6 Hz, HO-C*H*-CH-OH), 5.82 (d, 1H, *J*=5.6 Hz, HO-CH-C*H*-OH), 3.29 (br s, 2H, O*H*), 0.24 (s, 9H, $SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.3, 153.9, 141.5, 140.9, 135.9, 130.8, 129.3, 129.2, 128.6, 128.1, 111.3, 107.9, 71.8, 70.5, −0.3. MS (ESI, positive ion 180 eV) calcd for $(C_{19}H_{22}O_3SiNa)^+$: 349.12; found: 349.13.

4.3.9. (1*S*,2*R*,3*Z*,4*Z*)-3-Benzylidene-4-[thien-2-yl(trimethylsilyl)methylene]cyclobutane-1,2-diol (27). Preparation by method B on 0.295 mmol scale with a reaction time of 30 min. Purification by flash chromatography eluting with AcOEt/Hept (20/80) afforded the product (47 mg, 46%) as a yellow oil. R_f: 0.31 (AcOEt/Hept: 30/70). ^1H NMR (300 MHz, $CDCl_3$) δ 7.39-7.21 (m, 6H, Ar*H*, Ph-C*H*), 7.05 (dd, 1H, *J*=3.1, 1.5 Hz, thionyl-*H*), 6.66 (d, 1H, *J*=3.1 Hz, thionyl-*H*), 5.98 (d, 1H, *J*=1.5 Hz, thionyl-*H*), 4.95 (d, 1H, *J*=5.3 Hz, HO-C*H*-CH-OH), 4.84 (d, 1H, *J*=6.5 Hz, HO-CH-C*H*-OH), 2.90 (br s, 2H, O*H*), 0.21 (s, 9H, $SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.2, 153.5, 141.0, 140.9, 135.8, 130.2, 129.1, 129.0, 127.9, 127.6, 110.9, 107.5, 71.6, 70.1, −0.2. MS (ESI, positive ion 180 eV) calcd for $(C_{19}H_{22}O_2SSiNa)^+$: 365.10; found: 365.12.

4.3.10. (1*S*,2*R*,3*Z*,4*Z*)-3-Benzylidene-4-{(4*E*)-4-methyl-1-(trimethylsilyl)-6-[(trimethylsilyl)oxy]hex-4-en-2-ynylidene}cyclobutane-1,2-diol (28). Preparation by method B on 0.295 mmol scale with a reaction time of 20 min. Purification by flash chromatography eluting with Et_2O/Hept (20/80) afforded the product (97 mg, 77%) as a yellow powder. R_f: 0.36 (Et_2O/Hept: 30/70). ^1H NMR (300 MHz, $CDCl_3$) δ 7.67 (s, 1H, Ph-C*H*), 7.59 (d, 2H, *J*=7.8 Hz, Ar*H*), 7.38–7.19 (m, 3H, Ar*H*), 5.98 (t, 1H, *J*=6.3 Hz, CH_2-C*H*), 4.93 (dd, 1H, *J*=7.8, 6.8 Hz HO-C*H*-CH-OH), 4.77 (dd, 1H, *J*=7.1, 6.8 Hz, HO-C*H*-CH-OH), 4.28 (d, 2H, *J*=6.3 Hz, O-CH_2), 3.35 (d, 1H, *J*=7.1 Hz, O*H*), 3.23 (d, 1H, *J*=7.1 Hz, O*H*), 1.92 (s, 3H, CH_3), 0.27 (s, 9H, O-$SiMe_3$), 0.15 (s, 9H, $SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.0, 142.5, 141.5, 134.8, 129.3, 128.6, 128.1, 121.5, 109.8, 102.0, 92.1, 73.2, 72.6, 65.5, 57.3, 17.7, 0.2, −1.3. MS (ESI, positive ion 180 eV) calcd for $(C_{24}H_{34}O_3SiNa)^+$: 449.19; found: 449.23.

4.3.11. (1*S*,2*R*,3*Z*,4*Z*)-3-Benzylidene-4-[(4*E*)-6-{[*tert*-butyl(dimethyl)silyl]oxy}-1-(trimethylsilyl)hex-4-en-2-ynylidene]cyclobutane-1,2-diol (29). Preparation by method B on 0.295 mmol scale with a reaction time of 20 min. Purification by flash chromatography eluting with Et_2O/Hept (20/80) afforded the product (98 mg, 75%) as a yellow oil. R_f: 0.40 (Et_2O/Hept: 30/70). ^1H NMR (200 MHz, $CDCl_3$) δ 7.69 (s, 1H, Ph-C*H*), 7.60 (d, 2H, *J*=6.8 Hz, Ar*H*), 7.35–7.29 (m, 3H, Ar*H*), 6.21 (dt, 1H, *J*=15, 4.4 Hz, O-CH_2-C*H*=CH), 6.06 (d, 1H, *J*=15 Hz, O-CH_2-CH=C*H*), 4.91 (t, 1H, *J*=5.9 Hz, HO-C*H*-CH-OH), 4.72 (t, 1H, *J*=5.9 Hz, HO-CH-C*H*-OH), 4.30 (d, 2H, *J*=4.4 Hz, O-CH_2), 4.05 (br s, 1H, O*H*), 3.88 (br s, 1H, O*H*), 0.94 (s, 9H, O-Si-*t*Butyl), 0.24 (s, 9H, $SiMe_3$), 0.10 (s, 6H, O-$SiMe_2$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.5, 142.7, 141.6, 135.9, 129.4, 128.7, 128.2, 121.5, 109.9, 102.0, 92.1, 72.2, 71.2, 63.2, 25.9, 18.4, −1.1, −5.3. MS (ESI, positive ion 180 eV) calcd for $(C_{23}H_{38}O_3Si_2Na)^+$: 477.23; found: 477.22.

4.3.12. (1*S*,2*R*,3*Z*,4*Z*)-3-Benzylidene-4-[(4*E*)-6-{[*tert*-butyl(dimethyl)silyl]oxy}-4-methyl-1-(trimethylsilyl)hex-4-en-2-ynylidene]cyclobutane-1,2-diol (30). Preparation by method B on 0.295 mmol scale with a reaction time of 20 min. Purification by flash chromatography eluting with Et_2O/Hept (20/80) afforded the product (98 mg, 71%) as a yellow powder. R_f: 0.41 (Et_2O/Hept: 30/70). ^1H NMR (300 MHz, $CDCl_3$) δ 7.62 (s, 1H, Ph-C*H*), 7.58 (d, 2H, J=7.7 Hz, Ar*H*) 7.39–7.20 (m, 3H, Ar*H*), 6.01 (t, 1H, J=6.2 Hz, CH_2-C*H*), 4.98 (dd, 1H, J=7.3, 6.8 Hz, HO-C*H*-CH-OH), 4.77 (dd, 1H, J=7.3, 6.8 Hz, HO-CH-C*H*-OH), 4.19 (d, 2H, J=6.2 Hz, O-CH_2), 3.60 (d, 1H, J=7.3 Hz, O*H*), 3.46 (d, 1H, J=7.3 Hz, O*H*), 1.92 (s, 3H, CH_3), 0.96 (s, 9H, O-Si-*t*Butyl), 0.23 (s, 9H, $SiMe_3$), 0.12 (s, 6H, O-$SiMe_2$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.4, 142.4, 141.2, 137.0, 136.0, 129.2, 128.7, 128.3, 121.5, 119.7, 106.3, 102.0, 89.1, 72.0, 71.1, 60.2, 26.8, 18.3, −1.0, −5.1. MS (ESI, positive ion 180 eV) calcd for $(C_{27}H_{40}O_3Si_2Na)^+$: 491.24; found: 491.20.

4.3.13. (1*S*,2*R*,3*Z*,4*Z*)-3-Benzylidene-4-[1-(trimethylsilyl)but-3-enylidene]cyclobutane-1,2-diol (31). Preparation by method B on 0.295 mmol scale with a reaction time of 30 min. Purification by flash chromatography eluting with Et_2O/Hept (20/80) afforded the product (60 mg, 63%) as a yellow oil. R_f: 0.30 (Et_2O/Hept: 30/70). ^1H NMR (200 MHz, $CDCl_3$) δ 7.58 (d, 2H, J=7.6 Hz, Ar*H*), 7.38–7.25 (m, 3H, Ar*H*), 6.75 (s, 1H, Ph-C*H*), 5.97–5.78 (m, 1H, CH_2=C*H*), 5.15–5.05 (m, 2H, CH_2=CH), 4.87 (ap t, 1H, J=7.3 Hz, HO-C*H*-CH-OH), 4.73 (ap t, 1H, J=6.8 Hz, HO-C*H*-CH-OH), 3.17 (d, 2H, J=5.6 Hz, CH_2), 2.97 (d, 1H, J=6.6 Hz, O*H*), 2.72 (d, 1H, J=7.3 Hz, O*H*), 0.22 (s, 9H, $SiMe_3$). ^{13}C NMR (50 MHz, $CDCl_3$) δ 151.9, 142.3, 141.1, 136.2, 135.3, 128.8, 128.6, 127.9, 115.7, 71.5, 70.4, 36.4, −0.6. HRMS (ESI, positive ion 180 eV) calcd for $(C_{18}H_{24}OSiNa)^+$: 323.1438; found: 323.1421.

4.3.14. (1*S*,2*R*,3*Z*,4*Z*)-3-Benzylidene-4-[4-methoxy-1-(trimethylsilyl)but-2-ynylidene]cyclobutane-1,2-diol (32). Preparation by method B on 0.295 mmol scale with a reaction time of 20 min. Purification by flash chromatography eluting with Et_2O/Hept (20/80) afforded the product (86 mg, 84%) as a yellow oil. R_f: 0.39 (Et_2O/Hept: 30/70). ^1H NMR (300 MHz, $CDCl_3$) δ 7.70 (s, 1H, Ar*H*), 7.57 (d, 2H, J=7.5 Hz, Ar*H*), 7.33–7.26 (m, 3H, Ar*H*, Ph-C*H*), 4.87 (d, 1H, J=6.5 Hz, HO-C*H*-CH-OH), 4.68 (d, 1H, J=6.5 Hz, HO-CH-C*H*-OH), 4.40 (s, 2H, CH_2-OMe), 3.43 (s, 3H, O*Me*), 0.21 (s, 9H, $SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.5, 142.1, 135.8, 129.5, 129.3, 128.7, 128.4, 120.5, 98.8, 88.1, 72.0, 71.1, 61.0, 57.6, −1.0. MS (ESI, positive ion 180 eV) calcd for $(C_{19}H_{24}O_3SiNa)^+$: 351.56; found: 351.56.

4.3.15. (1*S*,2*R*,3*Z*,4*Z*)-3-Benzylidene-4-[4-benzyloxy-1-(trimethylsilyl)but-2-ynylidene]cyclobutane-1,2-diol (33). Preparation by method B on 0.295 mmol scale with a reaction time of 20 min. Purification by flash chromatography eluting with Et_2O/Hept (20/80) afforded the product (90 mg, 72%) as a yellow oil. R_f: 0.45 (Et_2O/Hept: 30/70). ^1H NMR (200 MHz, $CDCl_3$) δ 7.56–7.34 (m, 11H, Ar*H*, Ph-C*H*), 5.31 (s, 2H, HO-C*H*-C*H*-OH), 4.53 (s, 2H, Ph-CH_2-O), 4.49 (s, 2H, Ph-CH_2-O-CH_2), 0.39 (s, 9H, $SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.8, 149.0, 142.3, 135.7, 130.9, 129.5, 129.2, 129.1, 128.5, 128.1, 127.3, 120.8, 118.1, 114.1, 99.3, 85.7, 72.0, 71.1, 43.7, 38.7, −1.2. MS (ESI, positive ion 180 eV) calcd for $(C_{25}H_{28}O_3SiNa)^+$: 427.17; found: 427.18.

4.3.16. (1*S*,2*R*,3*Z*,4*Z*)-3-Benzylidene-4-[5-{[*tert*-butyl(dimethyl)silyl]oxy}-1-(trimethylsilyl)pent-2-ynylidene]-cyclobutane-1,2-diol (34). Preparation by method B on 0.295 mmol scale with a reaction time of 20 min. Purification by flash chromatography eluting with Et_2O/Hept (20/80 → 30/70) afforded the product (111 mg, 85%) as a yellow powder. R_f: 0.29 (Et_2O/Hept: 30/70). ^1H NMR (300 MHz, $CDCl_3$) δ 7.69 (s, 1H, Ar*H*), 7.57 (d, 2H, J=7.2 Hz, Ar*H*), 7.33–7.26 (m, 3H, Ar*H*, Ph-C*H*), 4.84 (br s, 2H, HO-CH-C*H*-OH, O*H*), 4.66 (br s, 2H, HO-C*H*-CH-OH, O*H*), 3.82 (t, 2H, J=7.6 Hz, O-CH_2), 2.74 (t, 2H, J=7.6 Hz, O-CH_2-CH_2), 0.90 (s, 9H, Si-*t*Butyl), 0.19 (s, 9H, $SiMe_3$), 0.08 (s, 6H, $SiMe_2$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.1, 142.8, 129.5, 128.6, 128.0, 122.0, 101.4, 83.7, 72.2, 71.1, 62.2, 25.8, 24.8, 18.2, −1.1, −5.3. MS (ESI, positive ion 180 eV) calcd for $(C_{25}H_{38}O_3Si_2Na)^+$: 475.22; found: 475.18.

4.3.17. (1*S*,2*R*,3*Z*,4*Z*)-3-Benzylidene-4-[4-{[*tert*-butyl(diphenyl)silyl]oxy}-1-(trimethylsilyl)but-2-ynylidene]-cyclobutane-1,2-diol (35). Preparation by method B on 0.295 mmol scale with a reaction time of 20 min. Purification by flash chromatography eluting with Et_2O/Hept (20/80) afforded the product (101 mg, 80%) as a yellow powder. R_f: 0.33 (Et_2O/Hept: 30/70). ^1H NMR (300 MHz, $CDCl_3$) δ 7.61–7.30 (m, 16H, Ar*H*, Ph-C*H*), 4.86–4.81 (m, 2H, HO-C*H*-C*H*-OH), 4.62 (s, 2H, O-CH_2), 0.91 (s, 9H, Si-*t*Butyl), 0.31 (s, 9H, $SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.6, 144.5, 138.2, 137.8, 136.7, 136.5, 136.1, 135.6, 135.5, 134.7, 134.6, 133.5, 129.7, 129.6, 129.4, 128.8, 128.5, 128.4, 128.1, 127.6, 127.4, 73.5, 72.9, 63.8, 26.7, 19.2, −0.9. MS (ESI, positive ion 180 eV) calcd for $(C_{34}H_{40}O_3SiNa)^+$: 575.25; found: 575.32.

4.3.18. (1*S*,2*R*,3*Z*,4*Z*)-3-Benzylidene-4-[4-[methyl(phenyl)-amino]-1-(trimethylsilyl)but-2-ynylidene]cyclobutane-1,2-diol (36). Preparation by method B on 0.295 mmol scale with a reaction time of 20 min. Purification by flash chromatography eluting with Et_2O/Hept (20/80) afforded the product (94 mg, 79%) as a yellow powder. R_f: 0.18 (Et_2O/Hept: 30/70). ^1H NMR (200 MHz, $CDCl_3$) δ 7.56–7.11 (m, 11H, Ar*H*, Ph-C*H*), 5.11 (d, 1H, J=6.8 Hz, HO-C*H*-CH-OH), 4.86 (d, 1H, J=6.8 Hz, HO-CH-C*H*-OH), 3.89 (s, 2H, N-CH_2), 3.05 (s, 3H, N-CH_3), 0.22 (s, 9H, $SiMe_3$). ^{13}C NMR (50 MHz, $CDCl_3$) δ 151.6, 148.9, 147.0, 139.5, 138.9, 137.8, 128.7, 128.4, 127.5, 127.3, 127.0, 117.3, 95.1, 88.6, 72.2, 69.8, 51.0, 38.9, −1.3. MS (ESI, positive ion 180 eV) calcd for $(C_{25}H_{29}O_2SiNa)^+$: 403.19; found: 403.22.

4.3.19. The 6π electrocyclization process. Compounds **39**–**45** are already reported in Ref. 2b.

4.3.20. (7*R*,8*S*)-2-(Trimethylsilyl)bicyclo[4.2.0]octa-1(6),2-diene-7,8-diol (46). Preparation by method B on 0.758 mmol scale with a reaction time of 30 min. Purification by flash chromatography eluting with Et_2O/Hept (30/70) afforded the product (65 mg, 44%) as a white solid. R_f: 0.28 (Et_2O/Hept: 30/70). ^1H NMR (200 MHz, $CDCl_3$)

δ 6.06 (t, 1H, J=4.9 Hz, C*H*-CH_2), 4.69 (d, 1H, J=4.4 Hz, HO-C*H*-CH-OH), 4.28 (d, 1H, J=4.4 Hz, HO-CH-C*H*-OH), 2.25–1.98 (m, 6H, 2×CH_2, 2×O*H*), 0.18 (s, 9H, $SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.8, 146.2, 138.4, 132.2, 74.4, 73.6, 24.2, 19.4, −1.5. MS (ESI, positive ion 180 eV) calcd for $(C_{11}H_{18}O_2SiNa)^+$: 233.09; found: 233.13.

4.3.21. (7*R*,8*S*)-5-Phenyl-2-(trimethylsilyl)bicyclo[4.2.0]-octa-1(6),2-diene-7,8-diol (47). Preparation by method B on 0.295 mmol scale with a reaction time of 30 min. Purification by flash chromatography eluting with AcOEt/Hept (20/80) afforded the product (65 mg, 49%) as a white solid. R_f: 0.36 (Et_2O/Hept: 30/70). ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.34–7.21 (m, 3H, Ar*H*), 7.17–7.12 (m, 2H, Ar*H*, Ph-C*H*), 6.10 (t, 1H, J=4.9 Hz, Ar*H*), 4.85 (d, 1H, J=3 Hz, HO-C*H*-CH-OH), 4.73 (d, 1H, J=3 Hz, HO-CH-C*H*-OH), 3.70 (dd, 1H, J=11, 5 Hz, C*H*-CH_2), 2.94–2.45 (m, 4H, CH_2, 2×O*H*), 0.18 (s, 9H, $SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.2, 147.2, 137.8, 132.1, 128.6, 127.3, 126.6, 73.0, 73.0, 36.2, 35.4, −1.5. HRMS (ESI, positive ion 180 eV) calcd for $(C_{17}H_{22}O_2SiNa)^+$: 309.1287; found: 309.1253. IR (FTIR, film): ν=3410 (br), 2924, 2845, 1652, 1490, 1448, 1250, 1107, 1062, 893, 749 cm^{-1}.

4.3.22. [(3a*S*,7b*R*)-2,2-Dimethyl-7-phenyl-3a,6,7,7b-tetrahydrobenzo[3,4]cyclobuta[1,2-*d*][1,3]dioxol-4-yl](trimethyl)silane (49). Preparation by method B on 0.78 mmol scale with a reaction time of 20 min. Purification by flash chromatography eluting with Et_2O/Hept (5/95→40/60) afforded product (232 mg, 91%) as a white solid. R_f: 0.38 (Et_2O/Hept: 40/60). ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.36-7.20 (m, 5H, Ar*H*), 6.16 (t, 1H, J=4.4 Hz, =C*H*-CH_2), 5.36 (d, 1H, J=3 Hz, HO-C*H*-CH-OH), 5.26 (d, 1H, J=3 Hz, HO-CH-C*H*-OH), 3.74 (t, 1H, J=12 Hz, C*H*-CH_2), 2.84–2.67 (m, 1H, CH_{2a}), 2.54–2.37 (m, 1H, CH_{2b}), 1.53 (s, 3H), 1.43 (s, 3H), 0.19 (s, 9H, $SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.6, 146.8, 142.7, 138.1, 132.3, 128.6, 127.5, 126.5, 115.2, 81.7, 81.4, 37.4, 33.7, 29.4, 28.9, −1.5. HRMS (ESI, positive ion 180 eV) calcd for $(C_{20}H_{26}O_2SiNa)^+$: 346.1600; found: 346.1595.

4.3.23. The 8π electrocyclization process. Compounds **53–54** and **56–65** are already described in Ref. 16.

4.3.24. (10a*S*)-4,8,8-Tris(hydroxymethyl)-5-(trimethylsilyl)-1,7,8,9,10,10a-hexahydrodicyclopenta[*a,d*][8]annulen-3(2*H*)-one (55). Preparation by method A on 0.265 mmol scale with a reaction time of 9 h. Purification by flash chromatography eluting with Et_2O/Hept (20/80) afforded product (19 mg, 10%) as yellow oil. R_f: 0.13 (AcOEt/Hept: 30/70). ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.00 (s, 1H, =C*H*), 4.48 (d, 1H, J=13.3 Hz, CH_{2a}-OH), 4.07 (d, 1H, J=13.3 Hz, CH_{2b}-OH), 3.63 (s, 2H, CH_2-OH), 3.58 (s, 2H, CH_2-OH), 3.40–3.21 (m, 1H, C*H*), 3.01–2.71 (br s, 2H, 2×O*H*), 2.62–1.89 (m, 7H), 0.15 (s, 9H, $SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.4, 156.3, 144.0, 138.8, 136.7, 136.1, 131.6, 69.8, 69.7, 62.3, 45.5, 45.0, 44.6, 40.0, 37.5, 37.0, 26.7, −0.5. HRMS (ESI, positive ion 175 eV) calcd for $(C_{20}H_{36}O_4Si)^+$: 363.1992; found: 363.1999.

4.3.25. (7*R*,12*S*)-2-(Hydroxymethyl)-5-(trimethylsilyl)-1,2,3,8,9,10,10a,11-octahydro-7*H*-6,7-methanobenzo[*a*]-cyclopenta[*d*][8]annulene-7,12-diol (67). Preparation by method B on 0.33 mmol scale with a reaction time of 38 min. Purification by flash chromatography eluting with AcOEt/Hept (5/95→40/60) afforded two diastereoisomers (47 mg, ratio 1/1, 41%) as yellow oils. R_f: 0.30, 0.35 (AcOEt/Hept: 40/60). Diastereoisomer **A**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.05 (s, 1H, =C*H*), 4.52 (s, 1H, C*H*-OH), 3.56 (d, 1H, J=6.4 Hz, CH_2-OH), 2.57–2.44 (m, 12H, 4×CH_2, C*H*, 3×O*H*), 2.31–1.64 (m, 6H), 0.21 ($SiMe_3$).^{13}C NMR (75 MHz, $CDCl_3$) δ 154.2, 144.3, 140.5, 136.7, 135.6, 134.9, 133.1, 79.6, 75.5, 67.10, 41.3, 40.0, 38.6, 36.8, 34.8, 33.4, 26.7, 22.4, −0.29 ($SiMe_3$). HRMS (ESI, positive ion 180 eV) calcd for $(C_{20}H_{30}O_3SiNa)^+$: 369.1862; found: 369.2182. Diastereoisomer **B**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.0 (s, 1H, =C*H*), 4.4 (s, 1H, C*H*-OH), 3.5 (d, 1H, J=4.9 Hz, CH_2-OH), 2.8 (br s, 3H, 3×O*H*), 2.7–1.6 (m, 15H), 0.20 ($SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.3, 144.2, 139.6, 136.3, 135.6, 134.8, 133.1, 80.7, 75.9, 67.3, 41.2, 39.8, 38.4, 36.8, 34.9, 33.5, 26.7, 22.4, −0.3. HRMS (ESI, positive ion 180 eV) calcd for $(C_{20}H_{30}O_3SiNa)^+$: 369.1862; found: 369.1934.

Preparation by method B on1.64 mmol scale with a reaction time of 32 min. Purification by flash chromatography eluting with AcOEt/Hept (20/80→80/20) afforded two products: furan derivative **69** (28 mg, 34%) as yellow oil, R_f: 0.30 (AcOEt/Hept: 40/60) and diol derivative **70** (20 mg, 24%) as yellow oil, R_f: 0.05 (AcOEt/Hept: 40/60); 58% as global yield.

4.3.26. 2-{3-[(7*S*,10a*S*,12*S*)-7,12-Dihydroxy-10a-methyl-5-(trimethylsilyl)-1,3,7,8,9,10,10a,11-octahydro-2*H*-6,7-methanobenzo[4,5]cycloocta[1,2-*c*]pyrrol-9(1*H*)-yl]propyl}-1*H*-isoindole-1,3(2*H*)-dione (69). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86–7.83 (m, 2H, Ar*H*), 7.73–7.71 (m, 2H, Ar*H*), 5.96 (s, 1H, =C*H*), 4.48 (s, 1H, C*H*-OH), 3.81–3.72 (ap t, 2H, J=7.2 Hz, N-CH_2), 3.64–3.43 (m, 4H), 2.74 (m, 3H), 2.53–2.46 (m, 1H), 2.04–1.83 (m, 10H), 1.63 (m, 1H), 0.21 ($SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.0, 143.4, 139.1, 135.6, 134.3, 133.9, 131.0, 123.2, 79.5, 75.1, 65.8, 64.5, 53.4, 35.9, 34.7, 30.3, 29.7, 29.4, 27.0, 22.3, 21.5, −0.5. MS (ESI, positive ion 180 eV) calcd for $(C_{29}H_{36}N_2O_4SiNa)^+$: 527.23; found: 527.22.

4.3.27. 2-{3-[(11a*S*)-11a-Methyl-6-(trimethylsilyl)-2,3,8,10,11,11a-hexahydro[1]benzofuro[3′,4′:5,6,7]cycloocta[1,2-*c*]pyrrol-9(1*H*)-yl]propyl}-1*H*-isoindole-1,3(2*H*)-dione (70). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82–7.80 (m, 2H, Ar*H*), 7.72–7.68 (m, 2H, Ar*H*), 7.05 (s, 1H, furyl-*H*), 6.05 (s, 1H, =C*H*), 3.81–3.72 (ap t, 4H, J=7.2 Hz, 2×N-CH_2), 3.51–3,43 (m, 2H), 2.83–2.70 (m, 2H), 2.60–2.54 (m, 4H), 2.48–2.38 (m, 1H), 2.21–2.17 (m, 1H), 2.04–1.83 (m, 4H), 1.82 (m, 1H), 0.11 (s, 9H, $SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.1, 149.1, 136.5, 135.6, 135.4, 133.9, 132.1, 125.2, 123.2, 120.7, 65.7, 64.5, 53.4, 36.0, 34.8, 30.3, 29.7, 29.3, 27.0, 23.0, 19.3, −1.2. MS (ESI, positive ion 180 eV) calcd for $(C_{29}H_{34}N_2O_3SiNa)^+$: 509.22; found: 509.22.

4.3.28. (6*R*,7*S*)-2[(4-Methylphenyl)sulfonyl]-5-phenyl-8-(trimethylsilyl)-2,3,4,5,6,7-octahexahydro-1*H*-cyclobuta[5,6]cycloocta[1,2-*c*]pyrrole-6,7-diol (71). Preparation by method B on 0.59 mmol scale with a reaction time of 38 min. Purification by flash chromatography eluting

with AcOEt/Hept (5/95→40/60) afforded two diastereoisomers (36 mg, 1/1, 27%) as yellow oil. R_f: 0.30, 0.35 (AcOEt/Hept: 40/60). ^{1}H NMR (200 MHz, $CDCl_3$). Diastereoisomer **A**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.68 (d, 2H, J=8.1 Hz, Ar*H*), 7.40–7.17 (m, 7H, Ar*H*), 6.00 (s, 1H, =C*H*), 4.53 (d, 1H, J=6.2 Hz, C*H*-OH), 4.47 (d, 1H, J=5.3 Hz, C*H*-OH), 4.15 (s, 2H, CH_2-N), 4.05-4.00 (br s, 2H, 2×O*H*), 3.63–3.50 (br s, 2H, CH_2-N), 2.58 (d, 1H, J=7.2 Hz, CH_a), 2.45 (s, 3H, Ar-CH_3), 2.34 (d, 1H, J=7.2 Hz, CH_b), 1.66 (s, 1H, C*H*-Ar), 0.21 ($SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.0, 147.5, 143.7, 143.4, 142.7, 136.6, 133.1, 129.7, 128.9, 127.8, 127.5, 127.2, 73.0, 71.9, 58.4, 57.1, 44.0, 33.4, 26.8, −0.59. HRMS (ESI, positive ion 180 eV) calcd for $(C_{28}H_{33}NO_4Si_2Na)^+$: 507.19; found: 507.19. Diastereoisomer **B**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.76–7.71 (m, 2H, Ar*H*), 7.40–7.23 (m, 7H, Ar*H*), 6.02 (s, 1H, =C*H*), 4.71 (br s, 1H, O*H*), 4.30–4.15 (m, 5H), 4.05–4.00 (d, 2H, J=7.1 Hz), 3.52–3.47 (m, 2H, CH_2-N), 2.43 (s, 3H, Ar-CH_3), 1.62 (s, 1H, C*H*-Ar), 0.26 ($SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.9, 147.4, 143.4, 142.9, 142.7, 135.6, 133.1, 130.1, 128.8, 127.6, 127.5, 127.2, 73.1, 71.9, 58.4, 57.1, 44.0, 33.4, 26.8, −0.7. MS (ESI, positive ion 180 eV) calcd for $(C_{28}H_{33}NO_4Si_2Na)^+$: 507.19; found: 507.21.

4.3.29. (3a*R*,10b*S*)-2,2-Dimethyl-7-[(4-methylphenyl)sulfonyl]-4-phenyl-10-(trimethylsilyl)-4,5,6,7,10b-hexahydro-3a*H*-[1,3]dioxolo[3′,4′]cycloocta[1′,2′:5,6]cycloocta-[1,2*c*]pyrrole (72). Preparation by method B on 0.264 mmol scale with a reaction time of 30 min. Purification by flash chromatography eluting with AcOEt/Hept (20/80→40/60) afforded two nonseparable diastereoisomers (91 mg, 1/1, 62%) as yellow solid. R_f: 0.33, 0.35 (AcOEt/Hept: 40/60). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (d, 2H, Ar*H*), 7.67–7.20 (m, 5H, Ar*H*), 7.07 (m, 2H, Ar*H*), 6.04 (s, 1H, =C*H*), 5.18 (d, 1H, J=3.4 Hz, C*H*-OH), 4.65 (d, 1H, J=3.4 Hz, C*H*-OH), 4.30–4.06, (m, 4H, 2×CH_2-N), 3.47 (dd, 1H, J=8.7, 3.1 Hz, C*H*-Ar), 2.58–2.49 (m, 2H, CH_2), 2.43 (s, 3H, Ar-CH_3), 1.27 (br s, 6H, 2×CH_3), 0.25 (s, 9H, $SiMe_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.8, 147.1, 143.4, 141.2, 140.1, 132.9, 131.0, 129.8, 129.7, 128.8, 128.4, 128.3, 127.4, 127.0, 114.8, 81.5, 78.2, 58.0, 57.2, 41.2, 32.9, 29.2, 28.3, 21.4, −0.7. MS (ESI, positive ion 180 eV) calcd for $(C_{31}H_{37}NO_4SiNa)^+$: 570.21; found: 570.20.

4.3.30. 5-*exo*-*dig* Cyclocarbopalladation. Compounds **74**–**84** and **85**–**112** are already described in Refs. 18 and 19.

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References and notes

1. (a) Mizoroki, T.; Mori, K.; Ozaki, A. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 581; (b) Heck, R. F.; Nolley, J. P. *J. Org. Chem.* **1972**, *37*, 2320; (c) Burns, B.; Grigg, R.; Sridharan, V.; Worakun, T. *Tetrahedron Lett.* **1988**, *29*, 4325; (d) Burns, B.; Grigg, R.; Ratananukul, P.; Sridharan, V.; Stevenson, P.; Sukirthalingam, S.; Worakun, T. *Tetrahedron Lett.* **1988**, *29*, 5565; (e) Burns, B.; Grigg, R.; Sridharan, V.; Stevenson, P. *Tetrahedron Lett.* **1989**, *30*, 1135; (f) Zhang, Y.; Negishi, E. *J. Am. Chem. Soc.* **1989**, *111*, 3454; (g) Negishi, E.; Noda, Y.; Lamaty, F.; Vawter, E. *Tetrahedron Lett.* **1990**, *31*, 4393; (h) von Zezschwitz, P.; Petry, F.; de Meijere, A. *Chem.—Eur. J.* **2001**, *7*, 4035; (i) de Meijere, A.; Meyer, F. E. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2379; (j) Malacria, M. *Chem. Rev.* **1996**, *96*, 289; (k) Yu, H.; Richey, R. N.; Carson, M. W.; Coghlan, M. J. *Org. Lett.* **2006**, *8*, 1685.
2. (a) Suffert, J.; Salem, B.; Klotz, P. *J. Am. Chem. Soc.* **2001**, *123*, 12107; (b) Salem, B.; Klotz, P.; Suffert, J. *Org. Lett.* **2003**, *5*, 845.
3. (a) Bogen, S.; Fernstenbanck, L.; Malacria, M. *J. Am. Chem. Soc.* **1997**, *119*, 5037; (b) Bailey, W. H.; Ovaska, T. V. *J. Am. Chem. Soc.* **1993**, *115*, 3080.
4. Salem, B.; Klotz, P.; Suffert, J. *Synthesis* **2004**, *2*, 298.
5. Grigg, R.; Loganathan, V.; Sukirthalingam, S.; Sridharan, V. *Tetrahedron Lett.* **1990**, *31*, 6573.
6. Bräse, S. *Synlett* **1999**, 1654.
7. Bour, C.; Suffert, J. *Eur. J. Org. Chem.*, in press.
8. Lauer, U.; Anke, T.; Sheldrick, W. S. *J. Antibiot.* **1989**, *42*, 875.
9. (a) Sugawara, F.; Stroble, G.; Strage, R. N.; Siedow, J. N.; Van Duyne, G. D.; Clardy, J. *Proc. Natl. Acad. Sci. U.S.A.* **1987**, *84*, 3081; (b) Au, T. K.; Chick, W. S. H.; Leung, P. C. *Life Sci.* **2000**, *67*, 733; (c) Hanson, J. R. *Nat. Prod. Rep.* **1986**, *3*, 123 and **1992**, *9*, 481.
10. Shen, X.; Krasnoff, S. B.; Lu, S.-W.; Dunbar, C. D.; O'Neal, J.; Turgeon, B. G.; Yoder, O. C.; Gibson, D. M.; Hamann, M. T. *J. Nat. Prod.* **1999**, *62*, 895.
11. (a) Nozoe, S.; Morisaki, M.; Tsuda, K.; Iitaka, Y.; Takahashi, N.; Tamura, S.; Ishibashi, K.; Shirasaka, M. *J. Am. Chem. Soc.* **1965**, *87*, 4968; (b) Erguang, L.; Clark, A. M.; Rotella, D. P.; Hufford, C. D. *J. Nat. Prod.* **1995**, *58*, 74.
12. (a) Wender, P. A.; Ihle, N. C. *J. Am. Chem. Soc.* **1986**, *108*, 4678; (b) Wender, P. A.; Snapper, M. L. *Tetrahedron Lett.* **1987**, *28*, 2451; (c) Wender, P. A.; Tebbe, M. J. *Synthesis* **1991**, 1089; (d) Jorand-Lebrun, C.; Fensterbank, L.; Malacria, M. *Tetrahedron Lett.* **1995**, *36*, 6447; (e) Wender, P. A.; Nuss, J. M.; Smith, D. B.; Suarez-Sobrino, A.; Vågberg, J.; Decosta, D.; Bordner, J. *J. Org. Chem.* **1997**, *62*, 4908; (f) Snapper, M. L.; Tallarico, J. A.; Randall, M. L. *J. Am. Chem. Soc.* **1997**, *119*, 1478; (g) Wender, P. A.; Correa, A. G.; Sato, Y.; Sun, R. *J. Am. Chem. Soc.* **2000**, *122*, 7815; (h) Evans, P. A.; Robinson, J. E.; Baum, E. W.; Fazal, A. N. *J. Am. Chem. Soc.* **2002**, *124*, 8782.
13. (a) Wender, P. A.; Gamber, G. G.; Hubbard, R. D.; Zhang, L. *J. Am. Chem. Soc.* **2002**, *124*, 2876; (b) Gilbertson, S. R.; DeBoef, B. *J. Am. Chem. Soc.* **2002**, *124*, 8734.
14. (a) Coates, R. M.; Muskopf, J. W.; Senter, P. A. *J. Org. Chem.* **1985**, *50*, 3541; (b) Rowley, M.; Kishi, Y. *Tetrahedron Lett.* **1988**, *29*, 4909; (c) Paquette, L. A.; Liang, S.; Galatsis, P. *Synlett* **1990**, 663; (d) Snider, B. M.; Yang, K. *J. Org. Chem.* **1992**, *57*, 3615; (e) Lo, P. C.-K.; Snapper, M. L. *Org. Lett.* **2001**, *3*, 2819; (f) Ruprah, P. K.; Cros, J.-P.; Pease, J. E.; Whittingham, W. G.; Williams, J. M. J. *Eur. J. Org. Chem.* **2002**, 3145.
15. Rowley, M.; Tsukamoto, M.; Kishi, Y. *J. Am. Chem. Soc.* **1989**, *111*, 2735.
16. Salem, B.; Suffert, J. *Angew. Chem., Int. Ed.* **2004**, *43*, 2826.
17. Lautens, M.; Smith, N. D.; Ostrovsky, D. *J. Org. Chem.* **1997**, *62*, 8970.

18. Salem, B.; Delort, E.; Klotz, P.; Suffert, J. *Org. Lett.* **2003**, *5*, 2307.
19. Bour, C.; Suffert, J. *Org. Lett.* **2005**, *7*, 653.
20. For a few recent examples of 1,4-Pd shift, see for instance: (a) Wang, L.; Pan, Y.; Jiang, X.; Hu, H. *Tetrahedron Lett.* **2000**, *41*, 725; (b) Karig, G.; Moon, M.-T.; Thasana, N.; Gallagher, T. *Org. Lett.* **2002**, *4*, 3115; (c) Campo, M. A.; Larock, R. C. *J. Am. Chem. Soc.* **2002**, *124*, 14326; (d) Campo, M. A.; Huang, Q.; Yao, T.; Tian, Q.; Larock, R. C. *J. Am. Chem. Soc.* **2003**, *125*, 11506; (e) Huang, Q.; Fazio, A.; Dai, G.; Campo, M. A.; Larock, R. C. *J. Am. Chem. Soc.* **2004**, *126*, 7460; (f) Zhao, J.; Larock, R. C. *Org. Lett.* **2005**, *7*, 701.
21. Mota, A. J.; Dedieu, A.; Bour, C.; Suffert, J. *J. Am. Chem. Soc.* **2005**, *127*, 7171.
22. For a few recent examples of tandem or cascade reactions that may involve Pd(IV) palladacycles, see for instance: (a) Catallani, M.; Frignani, F.; Rangoni, A. *Angew. Chem., Int. Ed.* **1997**, *36*, 119; (b) Catellani, M. *Pure Appl. Chem.* **2002**, *74*, 63; (c) Catellani, M. *Synlett* **2003**, 298; (d) Motti, E.; Mignozzi, A.; Catellani, M. *J. Am. Chem. Soc.* **2004**, *126*, 78; (e) Motti, E.; Rossetti, M.; Bocelli, G.; Catellani, M. *J. Organomet. Chem.* **2004**, *689*, 3741; (f) Grigg, R.; Loganathan, V.; Stevenson, P.; Sukirthalingam, S.; Worakun, T. *Tetrahedron* **1996**, *52*, 11479; (g) Dyker, G. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1023; (h) Dyker, G. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 103; (i) Dyker, G. *Angew. Chem., Int. Ed.* **1999**, *38*, 1699; (j) Albrecht, K.; Reiser, O.; Weber, M.; Knieriem, B.; de Meijere, A. *Tetrahedron* **1994**, *50*, 383; (k) de Meijere, A.; Meyer, F. E. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2379; (l) Huang, Q.; Campo, M. A.; Yao, T.; Tian, Q.; Larock, R. C. *J. Org. Chem.* **2004**, *69*, 8251.
23. Suffert, J. *J. Org. Chem.* **1989**, *54*, 509.
24. (a) Brakta, M.; Doyle Daves, G., Jr. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1883; (b) Betzer, J. F.; Ardisson, J.; Lallemand, J. Y.; Pancrazi, A. *Tetrahedron Lett.* **1997**, *38*, 2279; (c) Betzer, J. F.; Delaloge, F.; Muller, B.; Pancrazi, A.; Prunet, J. *J. Org. Chem.* **1997**, *62*, 7768; (d) Rim, C.; Son, D. Y. *Org. Lett.* **2003**, *5*, 3443.