Total Synthesis of the Turrianes and Evaluation of Their DNA-Cleaving Properties

Alois Fürstner,* Frank Stelzer, Antonio Rumbo, and Helga Krause[a]

Abstract: The first total synthesis of three naturally occurring cyclophane derivatives belonging to the turriane family of natural products is described. Their sterically hindered biaryl entity is formed by reaction of the Grignard reagent derived from aryl bromide **10** with the oxazoline derivative **18**, and the macrocyclic tether of the targets is efficiently forged by ring closing metathesis. While conventional RCM catalyzed by the ruthenium-carbene complexes **33** or **34** invariably leads to the formation of mixtures of both stereoisomers with the undesirable (*E*)-alkene prevailing, ring closing alkyne metathesis (RCAM) followed by Lindlar reduction of the resulting cycloalkynes **37** and **38** opens a convenient and stereoselective entry into this class of compounds. RCAM can either be accomplished by using the tungsten alkylidyne complex $[(t\mathrm{BuO})_3\mathrm{W}{\equiv}\mathrm{CCMe}_3]$ or by means of a catalyst formed in situ from $[\mathrm{Mo(CO)}_6]$ and *para*-trifluoromethylphenol. The latter method is significantly accelerated when carried out under microwave heating. Furthermore, the judicious choice of the protecting groups for the phenolic -OH functions turned out to be crucial. PMB-ethers were found to be compatible with the diverse reaction conditions en route to **3**–**5**; their cleavage, however, had to be carried out under carefully optimized conditions to minimize competing O–C PMB migration. Turrianes **3**–**5** are shown to be potent DNA cleaving agents under oxidative conditions when administered in the presence of copper ions.

Keywords: alkynes · DNA · metathesis · molybdenum · natural products

Introduction

Many plants, particularly those belonging to the *Proteaceae*, *Anacardiaceae*, *Gingkoaceae* and *Graminae* families, are rich sources of 5-alkylresorcinol derivatives and related non-isoprenoid lipids.[1] Compounds of this type exhibit a variety of biological activities, including inhibitory effects on a number of enzymes and cytotoxicity against various tumor cell lines.[2] Therefore, it is particularly noteworthy that compounds as simple as **1** and its bola-formed analogue **2** isolated from the west Australian shrub *Hakea trifurcata* were recently shown to cleave DNA very efficiently under oxidative conditions. Studies by Hecht et al. shed light into their mechanism of action and have revealed a distinct correlation between the length of the aliphatic tether with the biological response to these antineoplastic agents.[3, 4]

Previous work from this laboratory has led to the development of an efficient and flexible methodology for the synthesis of such compounds,[5] thus enabling more detailed studies of their structure/activity profile. During this program we became aware of two additional types of naturally occurring resorcinols which seem to be close relatives of **2**. Thus, formal oxidative C–C coupling of the phenol rings of **2** as indicated in Scheme 1 leads to a cyclophane structure which is common to all members of the turriane family of natural products (**3**–**5**) isolated from the stem wood of the Australian tree *Grevillea striata* R. Br. (called "turraie" by the Aboriginees).[6] Similarly, oxidative C–O coupling entails the formation of the macrocyclic biaryl ether skeleton of robustol **6**, a secondary metabolite isolated from the leaves of *Grevillea robusta* A. Cunn.[7] Although the permethyl ether of **3** and **6** have previously been prepared,[8, 9] the natural products themselves have so far resisted total syntheses, not least because of prohibitively low yields during attempted formation of their core structures and because of problems in finding suitable protecting group patterns that allow the ultimate liberation of the very electron rich and hence rather sensitive biphenyl entities.[6]

No information is available on either the biological function of or the physiological response to the turrianes and robustol. In the light of the studies mentioned above,[3] however, one may speculate that these compounds share similar DNA-cleaving properties with the "parent" bola-resorcinol derivative **2**. The chemical challenges posed by these macrocycles and the hope to study some of their properties if samples can be made available prompted us to venture into the total

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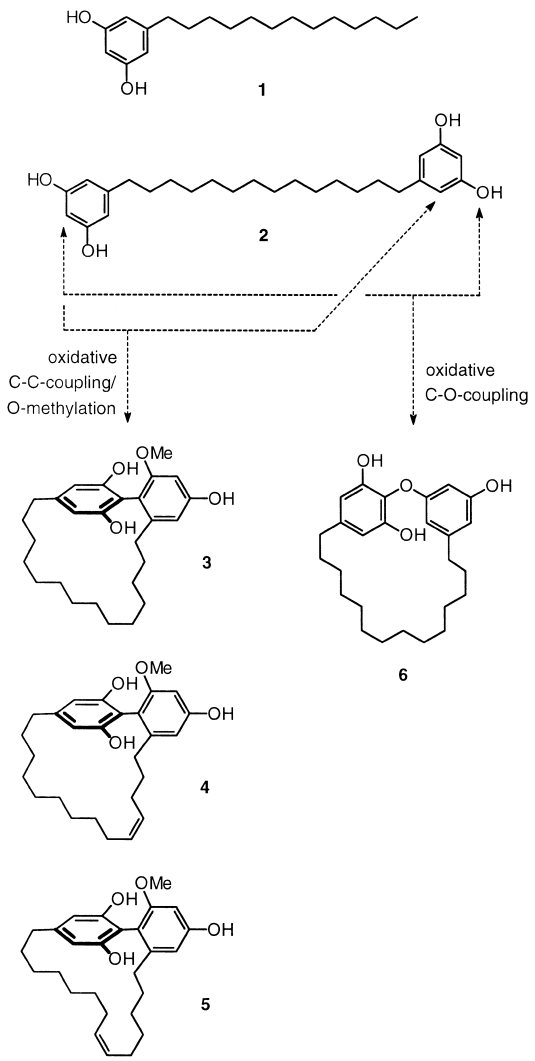


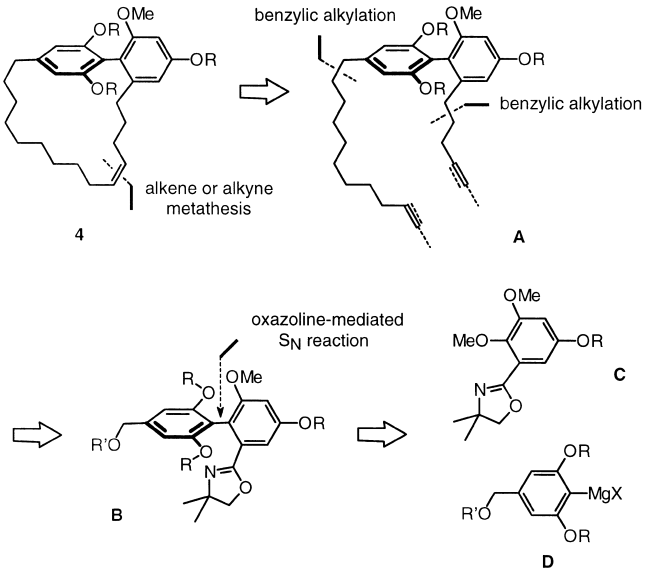
Scheme 1. Proposed biosynthetic pathway for the formation of the turrianes **3**–**5** and robustol **6**.

synthesis of these targets. Summarized below is our metathesis approach to the turriane family together with an interim report on the effects of these compounds on supercoiled DNA.

Results and Discussion

Retrosynthetic analysis: Despite the tantalizing possibility of converting the now readily available bola-resorcinol **2**[5] and unsaturated congeners thereof into **3**–**5** via a biomimetic route (Scheme 1), this option was dismissed for the following reasons: Previous attempts to reduce the desired oxidative C–C coupling to practice were extremely low yielding and the expected product could never be isolated in pure form.[6] Although it might be possible to improve on that prior art, we actually suppose that a *non-enzymatic* oxidative C–C coupling of **2** leads to an unwanted isomer. There is strong evidence in the literature that the normal reactivity mode of for example orcinol under oxidative conditions involves only the 4- rather than the 2-position;[10] as the same likely applies to **2**, an isomeric product would ensue.

Therefore the purely "chemical" analysis spelled out in Scheme 2 for cyclophane **4** seemed to be more rewarding and was preferred over the biomimetic approach. Our excellent



Scheme 2. Retrosynthetic analysis of turriane **4**.

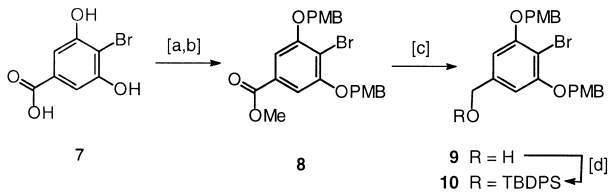
experiences with metathesis strongly recommended this transformation as a means to form the macrocyclic ring.[11] Thereby, alkyne metathesis followed by Lindlar reduction may be preferable over the more conventional alkene metathesis en route to **4** and **5** containing a (*Z*)-configured double bond.[12] We were well aware, however, that the 2,2′,6,6′-tetrasubstituted biaryl entity of the required metathesis substrate **A** constitutes a formidable challenge. Transition metal catalyzed cross coupling reactions allowing the formation of biphenyl linkages are known to be quite sensitive to steric hindrance and have hardly been successful when applied to such encumbered motifs.[13, 14] The previous synthesis of the per-O-methyl ether of **3**,[8] however, nicely illustrates that Meyers oxazoline chemistry[15] represents a viable alternative although it has to be adapted for our purposes such that it allows to attach two different lateral chains to the individual arene rings in **A**.

A major concern in the planning (and the execution, see below) of the turriane synthesis is the choice of the protecting groups R for the phenolic -OH functions. The presence of double bonds in two of the final targets precludes hydrogenolytically labile ones, while the electron rich arenes are incompatible with groups that are cleaved off under oxidative conditions. Moreover, one has to keep in mind that the original publication reporting the isolation of the turrianes explicitly mentions the pronounced sensitivity of these compounds to basic media.[6] Furthermore, the protecting groups R must be orthogonal to the residual methyl ether, should not increase the steric hindrance at the biphenyl linkage any further, and have to be stable towards organometallic reagents if the oxazoline route is chosen for the construction

of the biphenyl unit. Taken together, these stringent criteria severely limit the possible choices. *p*-Methoxybenzyl (PMB) or methoxymethyl (MOM) ethers seemed to be suitable candidates, although we were somewhat apprehensive that the acidic conditions for their cleavage in the final stages might be far from ideal.[16]

Preparation of the biphenyl core: After model studies had soon revealed substantial problems upon attempted formation of the *ortho*-tetrasubstituted biphenyl unit **B** by transition metal catalyzed cross coupling,[17] recourse was taken to the oxazoline chemistry referred to above as it has previously been successfully employed in a number of syntheses of sterically hindered biaryls.[8, 15, 18]

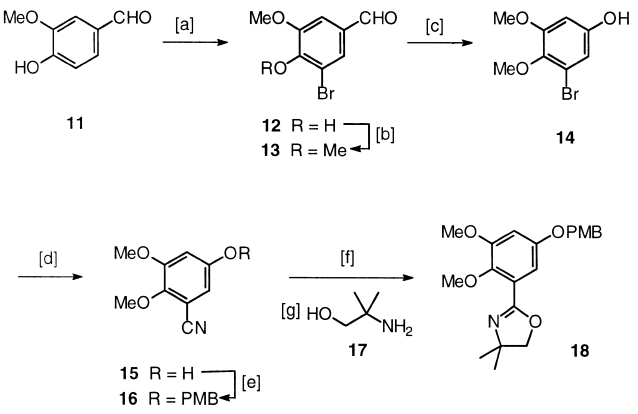
Commercially available 4-bromo-3,5-dihydroxybenzoic acid (**7**) serves as a convenient and cheap starting material (Scheme 3), which is reduced with $LiBH_4$ after esterification



Scheme 3. [a] i) $SOCl_2$, MeOH, 0 °C; ii) reflux, 2 h, 96 %. [b] *p*$MeOC_6H_4CH_2Cl$, K_2CO_3, Bu_4NI cat., DMF, 80 °C, 12 h, 84 %. [c] $LiBH_4$, MeOH, THF, reflux, 3 h, 98 %. [d] *t*$BuPh_2SiCl$ (TBDPS-Cl), imidazole, DMF, RT, 12 h, 82 %.

and PMB protection. The resulting benzylic alcohol **9** is transformed into *tert*-butyldiphenylsilyl (TBDPS) ether **10** because this group promises excellent stability upon conversion of **10** into the corresponding Grignard reagent in the coupling step.[16]

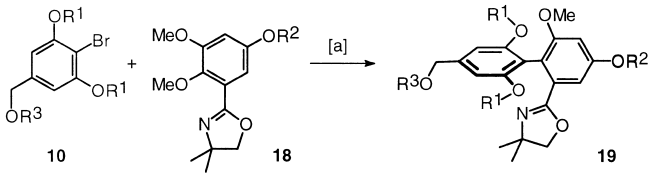
Vanilline **11** as the source for the second building block (Scheme 4) is regioselectively brominated at the 5-position to give compound **12**.[19] Subsequent O-methylation[20] followed by Baeyer–Villiger oxidation of the resulting product **13** readily provides phenol **14**[21] which undergoes smooth -CN



Scheme 4. [a] Br_2, MeOH, 0 °C (2.5 h), then RT (1 h), 95 %. [b] MeI, K_2CO_3, DMF, RT, 24 h, 97 %. [c] i) 3-Chloroperbenzoic acid, CH_2Cl_2, reflux, 16 h; ii) aq. HCl, aq. MeOH, RT, 30 min, 70 %. [d] CuCN, DMF, reflux, 12 h, 89 %. [e] *p*$MeOC_6H_4CH_2Cl$, K_2CO_3, Bu_4NI cat., DMF, 80 °C, 12 h, 82 %. [f] LiOH, $MeOH/H_2O$, reflux, 3 d, 98 %. [g] Aminoalcohol **17**, PPh_3, CCl_4, $(iPr)_2NEt$, pyridine, MeCN, 80 °C, 16 h, 80 %.

for -Br exchange on treatment with CuCN in refluxing DMF.[22] After conversion of the -OH group of **15** into a PMB-ether, the nitrile in **16** is saponified to afford the corresponding carboxylic acid. Not unexpectedly, this transformation is rather slow but very high yielding. Subsequent exposure to amino alcohol **17** in the presence of an excess of PPh_3, CCl_4, and $(iPr)_2NEt$ in pyridine/MeCN delivers oxazoline **18** required for the crucial biaryl formation. This sequence of reactions gives an excellent overall yield and can be carried out on a multigram scale without difficulties.

We were pleased to find that the coupling of bromide **10** with oxazoline **18** to the desired product **19** proceeds in 84 % yield if a 2:1 mixture of these compounds is refluxed in the presence of an excess of Mg activated by 1,2-dibromoethane (Scheme 5, Table 1, entry 1). Surprisingly though, this chem-



Scheme 5. [a] Mg, 1,2-dibromoethane, THF, reflux, 2 d, see Table 1.

Table 1. Effect of the protecting groups on the outcome of the biaryl formation depicted in Scheme 5.

Entry	R^1	R^2	R^3	Yield [%]
1	PMB	PMB	TBDPS	84
2	PMB	PMB	TBS	80
3	PMB	MOM	TBS	61
4	MOM	PMB	TBS	8
5	MOM	MOM	TBS	0

istry turned out to be very responsive to the chosen protecting group pattern. Replacement of only one PMB-ether by a MOM group renders the coupling process significantly less productive (entry 3). Even more deleterious is the use of MOM groups in the Grignard reagent derived from **10** (entry 4), and the attempted coupling of substrates bearing only MOM-groups failed to afford any of the expected biaryl (entry 5). Hence, these results exclude one of the protecting groups initially considered as possible candidate for the turriane total synthesis.

Preparation of the metathesis precursors: Further elaboration of **19** into a set of substrates suitable for macrocyclization starts with N-alkylation of the oxazoline group with methyl triflate, reduction of the resulting salt with $NaBH_4$ followed by acid-catalyzed hydrolysis to afford aldehyde **20** (Scheme 6).[23] Reduction of the latter provides the corresponding alcohol **21**. It is noteworthy that all attempts to convert oxazoline **19** directly into **21** according to a literature protocol[24] met with failure.

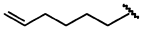
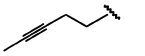
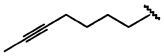
The severe steric crowding at the biaryl junction was experienced in our attempts to perform substitution reactions at the benzylic position of the corresponding iodide **22a**, bromide **22b**, or mesylate **22c**. Due to the orthogonal arrangement of the phenyl units, the benzylic site is held

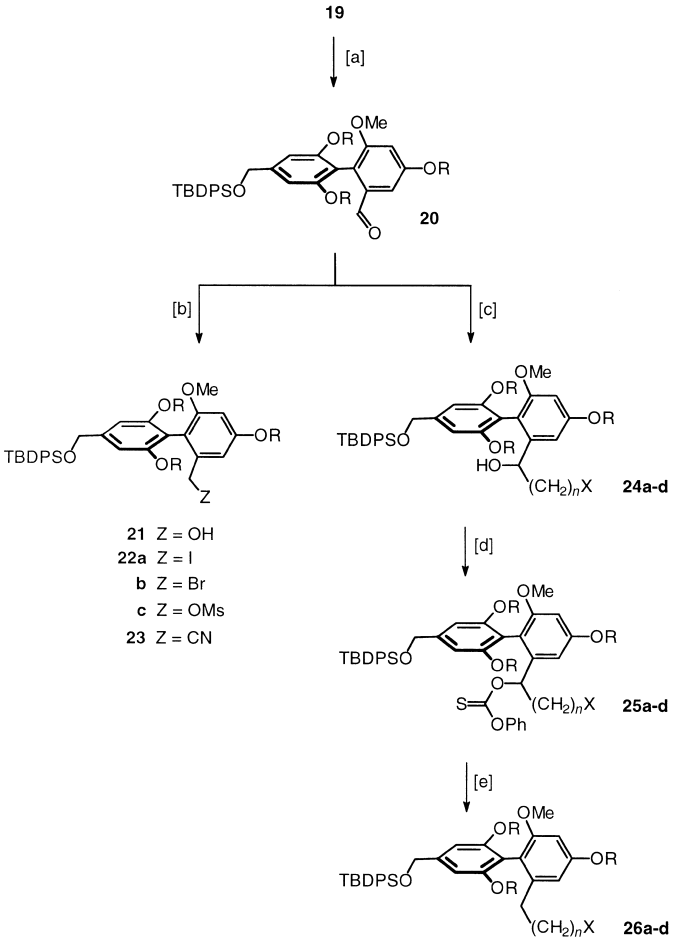
0947-6539/02/0808-1858 $ 20.00+.50/0 *Chem. Eur. J.* **2002**, *8*, No. 8

under the A-ring and hence hardly accessible for external nucleophiles (cf. Scheme 6). Although various organometallic reagents were tried, all attempts to attach the lateral chain in such a way were unsuccessful. The only carbon nucleophile that could be introduced was cyanide to give **23** which is, however, of little furtherance to the total synthesis.

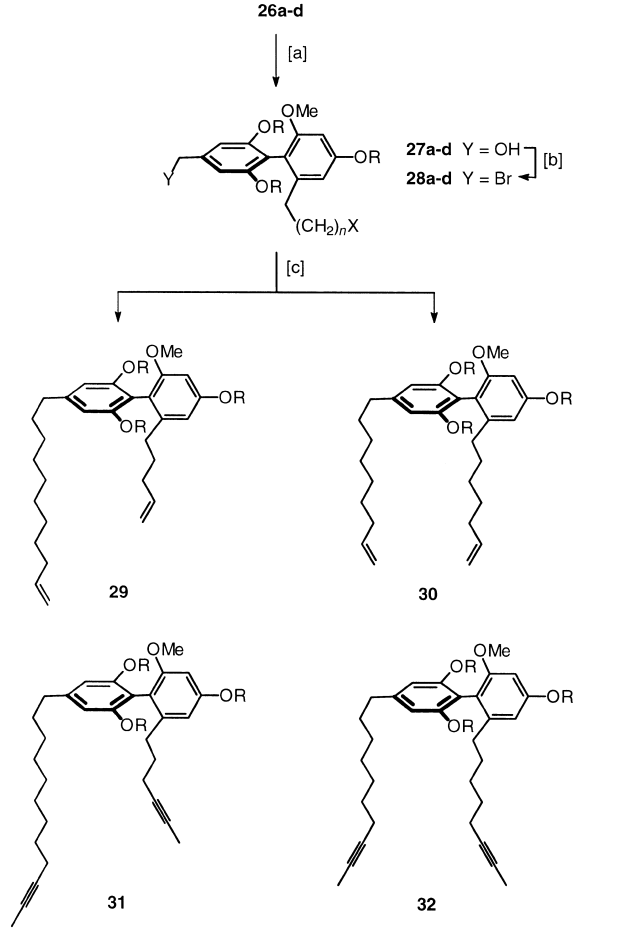
Therefore we focused our attention on the elaboration of aldehyde **20**. Its treatment with different alkyl Grignard reagents affords the corresponding alcohols **24a–d** in good to excellent yields (Scheme 6, Table 2). These compounds are

Table 2. Preparation of the metathesis substrates as shown in Schemes 6 and 7.

X-$(CH_2)_n$-	Series	**24** [%]	**25** [%]	**26** [%]	**27** [%]	**28** [%]
	**a**	82	94	97	99	73
	**b**	79	78	82	95	77
	**c**	87	94	83	99	76
	**d**	66	90	76	96	81



Scheme 6. [a] i) F_3CSO_3Me, CH_2Cl_2, $-10\rightarrow 0\,^{\circ}C$, 2 h; ii) $NaBH_4$, MeOH/THF 4:1, $0\,^{\circ}C\rightarrow$ RT, 3 h; iii) oxalic acid, THF/H_2O (4:1), 12 h, 61–70%. [b] See text. [c] X-$(CH_2)_n$MgBr, THF, $0\,^{\circ}C$, 1 h, see Table 2. [d] PhOC(S)Cl, pyridine, CH_2Cl_2, $-20\,^{\circ}C$ (1 h), then RT (12 h), see Table 2. [e] $n$$Bu_3SnH$, AIBN, toluene, $75\,^{\circ}C$, 12 h, see Table 2. R = PMB.



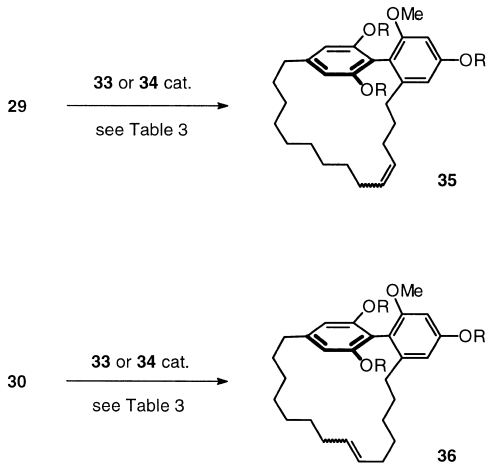
Scheme 7. [a] $n$$Bu_4NF\cdot 3H_2O$, THF, RT, 2 h, see Table 2. [b] i) Methanesulfonic anhydride, Et_3N, CH_2Cl_2, $0\,^{\circ}C$, 30 min; ii) LiBr, THF, $60\,^{\circ}C$, 2 h, see Table 2. [c] For **29**: $H_2C{=}CH(CH_2)_8MgBr$, Li_2CuCl_4 cat., THF, $-20\,^{\circ}C$, 1 h, 65%; for **30**: $H_2C{=}CH(CH_2)_6MgBr$, Li_2CuCl_4 cat., THF, $-20\,^{\circ}C$, 1 h, 66%; for **31**: $H_3CC{\equiv}C(CH_2)_8MgBr$, Li_2CuCl_4 cat., THF, $-20\,^{\circ}C$, 1 h, 80%; for **32**: $H_3CC{\equiv}C(CH_2)_6MgBr$, Li_2CuCl_4 cat., THF, $-20\,^{\circ}C$, 1 h, 73%. R = PMB.

converted into the thiocarbonates **25a–d** which readily reduce to the corresponding products **26a–d** on exposure to $n$$Bu_3SnH$/AIBN in toluene at $75\,^{\circ}C$ (Table 2). In no case does the intermediate benzyl radical interfere with the alkene or alkyne moieties in its vicinity.

The attachment of the lateral chain to the other arene moiety turned out to be more facile. Fluoride mediated cleavage of the O-TBDPS ether in **26a–d** followed by conversion of the resulting alcohols **27a–d** into the corresponding bromides **28a–d** proceeds well if carried out under the conditions shown in Scheme 7 and Table 2.[25] Since this benzylic position is sterically much more accessible, the nucleophilic displacement of the bromides by Grignard reagents in the presence of catalytic amounts of Li_2CuCl_4 in THF at $-20\,^{\circ}C$ delivers the desired products in high yields. Dienes **29** and **30** as well as diynes **31** and **32** thus obtained serve as substrates for the envisaged metathetic ring closure.

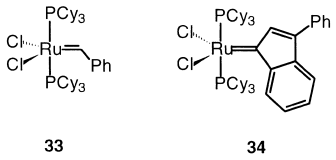
Macrocyclization by ring closing olefin metathesis: Despite some early scepticism about the suitability of ring closing metathesis (RCM) of dienes for the formation of macro-

cycles,[26] this reaction turned out to be a powerful, flexible, and convenient entry into carbo- and heterocyclic rings of any ring size ≥ 5.[11, 27] Many previous applications from our laboratory have encouraged us to pursue RCM en route to turriane as well.[28] As expected, dienes **29** and **30** smoothly cyclize to the corresponding 20-membered rings **35** and **36**, respectively, when exposed to catalytic amounts of the classical Grubbs catalyst **33**[29] in refluxing CH_2Cl_2 (Scheme 8,



Scheme 8. Formation of the cyclophane core of the turrianes by RCM.

Table 3). The use of the phenylindenylidene analogue **34**,[30, 31] which was recently introduced as a particularly well accessible alternative to **33**, gave similar results.



The data compiled in Table 3, however, also illustrate one of the present limitations of RCM. While cycloalkenes **35** and **36** are formed in acceptable chemical yields, the stereochemical outcome of the reaction remains beyond control. In line with most examples reported in the literature,[11] the (*E*)-isomer also predominates in the present cases. It is, however, instructive to see how a change of the site of ring closure within the target has a quite significant impact on the stereochemical course (compare entries 1/3 and 2/4). Although this result is certainly not unexpected, our present understanding of the reaction does not allow us to predict these changes with reasonable accuracy.[32]

Apart from these more heuristic aspects, the prevalence of the (*E*)-isomer in compounds **35** and **36** makes clear that conventional RCM is useful only for the synthesis of the turriane **3** having a *saturated* tether. Obviously, this method is inadequate for the preparation of turrianes **4** and **5** containing a (*Z*)-alkene, in particular since it is most difficult to separate the geometrical isomers of **35** and **36** even by preparative HPLC.

Table 3. Formation of the cyclophane core by RCM. All reactions have been carried out in refluxing CH_2Cl_2 using 5 mol% of the catalyst.

Entry	Substrate	Catalyst	Product	Yield [%]	*E*:*Z*
1	**29**	**33**	**35**	78	1.2:1
2	**29**	**34**	**35**	76	1:1.1
3	**30**	**33**	**36**	73	5.8:1
4	**30**	**34**	**36**	84	6.9:1

The ring closing alkyne metathesis (RCAM)/Lindlar reduction manifold: This difficulty can be circumvented by taking recourse to ring closing alkyne metathesis (RCAM) as previously outlined by our laboratory.[12, 33] The cycloalkynes initially formed serve as relays for the stereoselective formation of alkenes by a subsequent semi-reduction process (e.g. Lindlar hydrogenation). As this concept has already been successfully applied to a number of total syntheses,[34–40] it deserves consideration in the present context as well.

Three different types of alkyne metathesis catalysts are known to date. These comprise:

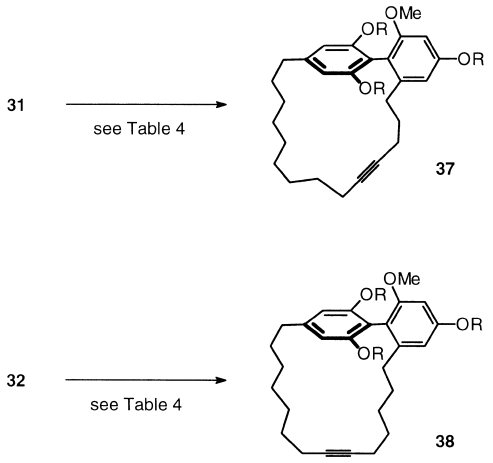
i) the mechanistically well understood tungsten alkylidyne complex $[(t\mathrm{BuO})_3\mathrm{W}{\equiv}\mathrm{CCMe}_3]$,[41]

ii) the very powerful molybdenum amido complex $[\{(t\mathrm{Bu})(\mathrm{Ar})\mathrm{N}\}_3\mathrm{Mo}]$ activated with CH_2Cl_2,[42, 43] and

iii) an "instant protocol" in which a structurally unknown catalyst is generated in situ from $[\mathrm{Mo(CO)_6}]$ and phenol additives.[44]

The latter system is very user-friendly but requires rather harsh conditions ($\geq 130\,^{\circ}\mathrm{C}$ in chlorobenzene).[45, 46] We reasoned, however, that it might be applicable in the present case as the turrianes should be thermally robust enough to withstand high temperatures.

The results displayed in Scheme 9 and Table 4 show that this is indeed the case. While the tungsten alkylidyne complex $[(t\mathrm{BuO})_3\mathrm{W}{\equiv}\mathrm{CCMe}_3]$ converts diynes **31** and **32** into the



Scheme 9. Formation of the cyclophane core of the turrianes by ring closing alkyne metathesis (RCAM).

desired cycloalkynes **37** and **38** in reasonable yields (method **A**), the use of $[\mathrm{Mo(CO)_6}]$ activated with 4-trifluoromethylphenol in chlorobenzene at $135\,^{\circ}\mathrm{C}$ (method **B**) provides even better results. The fact that the application of microwave technology (method **C**)[47] instead of conventional heating allows to reduce the reaction time from 4–6 hours to five

0947-6539/02/0808-1860 $ 20.00+.50/0 *Chem. Eur. J.* **2002**, *8*, No. 8

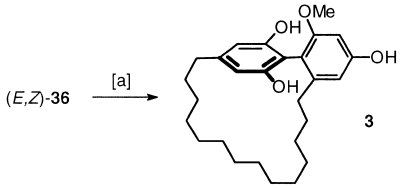
Table 4. Formation of the cyclophane core by RCAM using 10 mol% of the catalyst.

Entry	Substr.	Catalyst	Conditions[a]	*t*	Prod.	Yield [%]
1	**31**	$[(t\text{BuO})_3\text{W}{\equiv}\text{CCMe}_3]$	A	16 h	**37**	64
2	**31**	$[\text{Mo(CO)}_6]$, $F_3CC_6H_4OH$	B	4 h	**37**	83
3	**31**	$[\text{Mo(CO)}_6]$, $F_3CC_6H_4OH$	C	5 min	**37**	69
4	**32**	$[(t\text{BuO})_3\text{W}{\equiv}\text{CCMe}_3]$	A	16 h	**38**	61
5	**32**	$[\text{Mo(CO)}_6]$, $F_3CC_6H_4OH$	B	6 h	**38**	76
6	**32**	$[\text{Mo(CO)}_6]$, $F_3CC_6H_4OH$	C	5 min	**38**	71

[a] A: toluene, 80 °C; B: chlorobenzene, 135 °C; C: chlorobenzene, 150 °C, microwave heating.

minutes constitutes a particularly appealing facet of this chemistry. We are presently studying the generality of this finding.

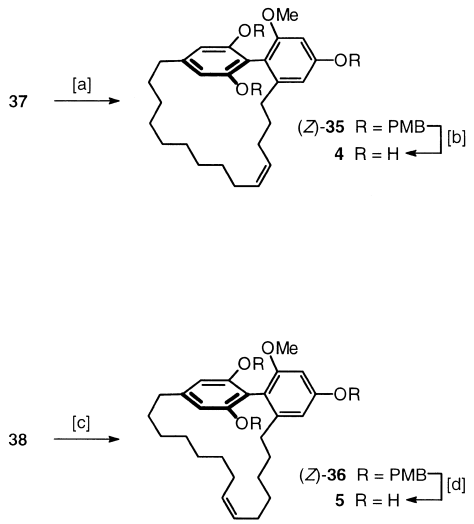
Completion of the total syntheses: Turriane **3** having a saturated tether was the first target reached (Scheme 10). Hydrogenation (1 atm) of the RCM product mixture (*E*,*Z*)-**36** over palladium on charcoal saturates the ring and leads to the concurrent cleavage of the O-PMB ethers, thus providing the desired product in 87% isolated yield.



Scheme 10. [a] H_2 (1 atm), Pd/C, EtOAc/EtOH/H_2O, 24 h, 87%.

To complete the syntheses of the other members of this series, the cycloalkynes **37** and **38** were subjected to Lindlar hydrogenation delivering (*Z*)-alkenes (*Z*)-**35** and (*Z*)-**36** in virtually quantitative yield and excellent stereochemical integrity (Scheme 11). With these materials in hand, the stage was set for the final deprotection step which turned out to be significantly more delicate than anticipated.

As discussed in the introductory section, PMB-ethers seemed to match all stringent criteria imposed on the choice of the protecting groups. Importantly, they can be cleaved under a variety of conditions, some of which are described to be particularly mild.[16, 48] Unfortunately, however, all of these methods invariably led to the formation of very complex reaction mixtures. Although traces of the desired products could be detected by LC/MS and NMR, a plethora of compounds had formed which *still contained up to three PMB-groups* in addition to free -OH functions. Obviously, the electron rich phenol rings are subject to *extensive C-alkylation* under the chosen reaction conditions. Hence, a competitive scavenger for the intermediate *para*-methoxybenzyl cations had to be administered to avoid this undesirable intramolecular Friedel–Crafts pathway. Attempts to do so by adding a large excess of $NaBH_3CN$[49] were equally unsuccessful as those employing admixed EtSH, $MeSC_6H_4OMe$, anisole or trimethoxybenzene (10 equiv each).[50] Only if the cleavage is performed with $SnCl_2$ (1 equiv) and TMSCl (10 equiv) in



Scheme 11. [a] H_2 (1 atm), Lindlar catalyst, quinoline cat., EtOAc, 6 h, 96%. [b] $BF_3 \cdot Et_2O$, EtSH, $-20\,^\circ\text{C} \rightarrow$ RT, 16 h, 50%. [c] H_2 (1 atm), Lindlar catalyst, quinoline cat., EtOAc/MeOH, 2 h, 96%. [d] $BF_3 \cdot Et_2O$, EtSH, $-20\,^\circ\text{C} \rightarrow$ RT, 16 h, 54%.

molten, *neat* trimethoxybenzene at 70 °C, the HPLC of the crude mixture indicates that the desired turrianes **4** and **5** are formed as the major products which are isolated in 39 and 46% yield. Somewhat better results are obtained with an excess of $BF_3 \cdot Et_2O$ (20 equiv) in *neat* EtSH as the reaction medium.[51] In this case, preparative HPLC allowed the isolation of the desired products **4** and **5** in 50 and 54% yield, respectively. The spectroscopic data of the analytically pure samples thus obtained are in excellent agreement with the proposed structures.

The turrianes as effective DNA-cleaving agents: As discussed in the Introduction, the turrianes might be biogenetically related to the bola-form resorcinol derivative **2** which is known to mediate the cleavage of DNA in the presence of Cu^{II} under oxidative conditions.[3] Therefore a study was called for to see if products **3**–**5** exert similar functions.

It is well established in the literature that phenols are regioselectively oxygenated by O_2 in the presence of copper-amine complexes as catalysts.[52] The resulting catechols are further oxidized to *ortho*-quinones and derivatives thereof. During this autooxidation process, H_2O_2 is produced which is concomitantly cleaved by the copper catalyst to form diffusible oxygen radicals (most likely HO•) that constitute severe DNA-damaging agents.[52, 3]

It has also been mentioned earlier that the catalytic action of copper in this overall process is remarkably specific, as this metal cation cannot be replaced by other ones known to effect the decomposition of H_2O_2.[52] In line with this notion, the agarose gel depicted in Figure 1 shows that turriane **3** in the presence of *n*-butylamine is able to relax purified double-stranded plasmid DNA (form I) of the bacteriophage ΦX174 only in the presence of $Cu(OAc)_2$ (lane 11), whereas all other transition metal salts assayed turned out to be more or less inactive (some weak activity is detected for Mn^{II}, cf. lane 6).

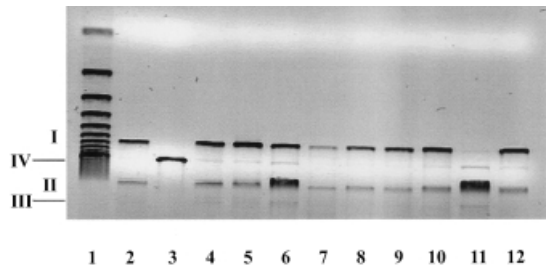


Figure 1. Result of an agarose gel electrophoresis showing the extent of DNA cleavage produced by turriane **3** in the presence of *n*-butylamine and various metal salts as indicated after 1.5 h incubation time at 37 °C. Lane 1: DNA marker (500 base pairs); lane 2: DNA only; lane 3: linear DNA formed from scDNA by using the restriction endonuclease Xho I; lane 4: DNA + **3** + nBuNH$_2$; lane 5: DNA + **3** + nBuNH$_2$ + Cr^{III}; lane 6: DNA + **3** + nBuNH$_2$ + Mn^{II}; lane 7: DNA + **3** + nBuNH$_2$ + Fe^{III}; lane 8: DNA + **3** + nBuNH$_2$ + Fe^{II}; lane 9: DNA + **3** + nBuNH$_2$ + Co^{II}; lane 10: DNA + **3** + nBuNH$_2$ + Ni^{II}; lane 11: DNA + **3** + nBuNH$_2$ + Cu^{II}; lane 12: DNA + **3** + nBuNH$_2$ + Zn^{II}.

The influence of Cu^{II} was then investigated in more detail. The agarose gel depicted in Figure 2 makes clear that neither Cu(OAc)$_2$+*n*-butylamine alone (lane 4), nor turriane **3** itself (lane 5), nor **3**+Cu(OAc)$_2$ in the absence of base (lane 6) were able to cleave supercoiled DNA (scDNA) to any noticeable extent after 90 min incubation time. In contrast, a combination of **3**, Cu(OAc)$_2$ and *n*-butylamine was very effective.

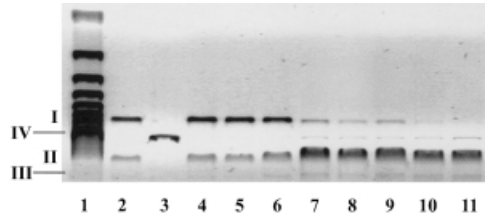


Figure 2. Result of an agarose gel electrophoresis showing the extent of DNA cleavage produced by turriane **3** in the presence of *n*-butylamine and Cu(OAc)$_2$ with increasing incubation time at 37 °C. Lane 1: DNA marker (500 base pairs); lane 2: DNA alone; lane 3: linear DNA formed from scDNA by using the restriction endonuclease Xho I; lane 4: DNA + Cu^{II} + nBuNH$_2$; lane 5: DNA + **3** + nBuNH$_2$; lane 6: DNA + **3** + Cu^{II}; lanes 7–11: DNA + **3** + nBuNH$_2$ + Cu^{II} after the following incubation times: 10 min (7), 30 min (8), 60 min (9), 90 min (10), 120 min (11).

Even after 10 min incubation time considerable single strand cleavage has taken place as can be seen from the gain in intensity of band II corresponding to the nicked form of the DNA (lane 7). After 90 min, the supercoiled plasmid DNA (band I) has almost completely disappeared and only the nicked (band II), concatemere (band III) and even the linear form of DNA (band IV) are detectable (lane 10).

Figure 3 proves that all three turrianes available by our preparative studies behave similarly, with double strand cleavage being slightly more pronounced in case of the unsaturated compounds **4** and **5** (lanes 5 and 6). These data nicely corroborate those reported by Hecht et al. for simple 5-alkylresorcinol derivatives such as **1** or **2**.[3] More generally speaking, they suggest that the ability to damage DNA might be a rather generic property of electron rich phenols occurring in nature. Ongoing investigations in this laboratory are meant to study this hypothesis in more detail.[53]

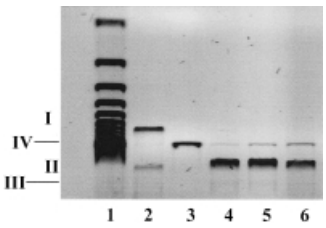


Figure 3. Result of an agarose gel electrophoresis showing the extent of DNA cleavage produced by turrianes **3**–**5** in the presence of *n*-butylamine and Cu(OAc)$_2$ after 1.5 h incubation time at 37 °C. Lane 1: DNA marker (500 base pairs); lane 2: DNA alone; lane 3: linear DNA formed from scDNA by using the restriction endonuclease Xho I; lane 4: DNA + **3** + Cu^{II} + nBuNH$_2$; lane 5: DNA + **4** + Cu^{II} + nBuNH$_2$; lane 6: DNA + **5** + Cu^{II} + nBuNH$_2$.

Conclusion

The first total synthesis of three members of the turriane family of natural products has been achieved. Key steps are the oxazoline-based formation of the sterically hindered 2,2′,6,6′-tetrasubstituted biphenyl axis as well as ring closing metathesis reactions to form the cyclophane rings. Thereby, conventional olefin metathesis mediated by the ruthenium carbene complexes **33** or **34**, though chemically very productive, invariably affords mixtures of the diastereomeric cycloalkenes with the undesired (*E*)-isomer prevailing. In contrast, alkyne metathesis followed by Lindlar reduction opens a stereoselective entry into the (*Z*)-configured macrocycles **4** and **5**. This notion has potentially broader ramifications in synthesis as it suggests that this transformation constitutes a valuable tool for advanced organic synthesis. The reaction can be catalyzed either by the alkylidyne complex [(*t*BuO)$_3$-W≡CCMe$_3$] or by [Mo(CO)$_6$] in the presence or 4-trifluoromethylphenol. The latter method benefits tremendously from microwave heating. Finally, it has been shown that the turrianes **3**–**5** are effective DNA cleaving agents when administered in the presence of Cu^{II}. If seen in the context of previous studies, this finding suggests that many structurally different phenol derivatives might exert a similar physiological function.

Experimental Section

General: All reactions were carried out under Ar. The solvents used were purified by distillation over the drying agents indicated and were transferred under Ar: THF, Et$_2$O (Mg/anthracene), CH$_2$Cl$_2$ (P$_4$O$_{10}$), MeCN, Et$_3$N, pyridine, DMF (CaH$_2$), MeOH (Mg), hexane, toluene (Na/K). Microwave heating was carried out in sealed vessels using a Smith Creator reactor (Personal Chemistry, Konstanz, Germany). Flash chromatography: Merck silica gel 60 (230–400 mesh). NMR: Spectra were recorded on a DPX 300, AV 400 or DMX 600 spectrometer (Bruker) in the solvents indicated; chemical shifts (δ) are given in ppm relative to TMS, coupling constants (J) in Hz. IR: Nicolet FT-7199 spectrometer, wavenumbers in cm^{-1}. MS (EI): Finnigan MAT 8200 (70 eV), HRMS: Finnigan MAT 95. Melting points: Büchi melting point apparatus (uncorrected). Elemental analyses: Kolbe, Mülheim/Ruhr. All commercially available compounds (Lancaster, Fluka, Aldrich) were used as received.

4-Bromo-3,5-bis-(4-methoxybenzyloxy)-benzoic methyl ester (8): SOCl$_2$ (63.83 g, 39 mL, 0.536 mol) was added dropwise over a period of 1 h to a solution of 4-bromo-3,5-dihydroxy-benzoic acid (**7**; 25 g, 0.107 mol) in methanol (500 mL) at 0 °C. After the resulting mixture had been refluxed

  0947-6539/02/0808-1862 $ 20.00+.50/0 *Chem. Eur. J.* **2002**, *8*, No. 8

for 2 h, the solvent and excess $SOCl_2$ were distilled off, the remaining solid was triturated with hexanes/diethyl ether (1:1) and was dried in vacuo affording 4-bromo-3,5-dihydroxy-benzoic acid methyl ester as a colorless solid (25.4 g, 96 %). ^{1}H NMR (300.1 MHz, [D$_6$]acetone): $\delta = 7.15$ (s, 2H), 3.82 (s, 3H); ^{13}C NMR (75.5 MHz, [D$_6$]acetone): $\delta = 166.6$, 156.1, 131.1, 108.6, 104.3, 52.4; IR: $\nu = 3427$, 3342, 3095, 3067, 3037, 2962, 2899, 1704, 1601, 1528, 1424, 1374, 1274, 1251, 1122, 156, 1036, 994, 911, 861, 765, 708, 628, 595, 559 cm^{-1}; MS (EI): *m*/*z* (%): 249 (6) $[M+3]^+$, 248 (64) $[M+2]^+$, 247 (7) $[M+1]^+$, 246 (66) $[M]^+$, 218 (10), 217 (98), 216 (11), 215 (100), 190 (9), 189 (24), 188 (12), 187 (22), 108 (17), 107 (12), 80 (6), 79 (20), 69 (11), 62 (7), 53 (11), 52 (8), 51 (25), 50 (13), 39 (6), 38 (6); HR-MS (EI) ($C_8H_7BrO_4$): calcd 245.9528; found 245.9529.

K_2CO_3 (42.3 g, 306 mmol), *n*Bu_4NI (7.537 g, 20.4 mmol) and 4-methoxybenzyl chloride (47.93 g, 306 mmol) were added to a solution of 4-bromo-3,5-dihydroxy-benzoic methyl ester (25.2 g, 102 mmol) in DMF (400 mL), and the resulting mixture was stirred at 80 °C for 12 h. The reaction was quenched with brine, the aqueous layer was extracted with *tert*-butyl methyl ether, the combined organic layers were washed with brine and dried over Na_2SO_4, and the solvent was evaporated. Crystallization of the residue from pentane/*tert*-butyl methyl ether (1:1) delivered compound **8** as colorless crystals. Evaporation of the mother liquor followed by flash chromatography of the residue (hexanes/ethyl acetate 4:1 → 3:1) afforded a second crop of the title compound as a colorless solid (combined yield: 41.8 g, 84 %). M.p. 100–101 °C; ^{1}H NMR (300.1 MHz, $CDCl_3$): $\delta = 7.40$ (AA′XX′, 4H), 7.30 (s, 2H), 6.90 (AA′XX′, 4H), 5.11 (s, 4H), 3.89 (s, 3H), 3.79 (s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 166.3$, 159.4, 156.2, 129.9, 128.8, 128.2, 113.9, 108.4, 107.3, 70.9, 55.2, 52.4; IR: $\nu = 3082$, 3015, 2997, 2946, 2899, 2836, 1713, 1613, 1584, 1514, 1469, 1436, 1418, 1371, 1331, 1305, 1249, 1227, 1179, 1105, 1030, 992, 923, 876, 857, 823, 806, 779, 765, 743, 651, 631, 566, 528, 507 cm^{-1}; MS (EI): *m*/*z* (%): 486 (<1) $[M]^+$, 455 (<1), 285 (2), 122 (15), 121 (100), 91 (3), 78 (5), 77 (5); HR-MS (CI, isobutane) ($C_{24}H_{23}BrO_6$+H): calcd 487.0756; found 487.0755; elemental analysis calcd (%) for $C_{24}H_{23}BrO_6$ (487.35): C 59.15, H 4.76; found C 59.13, H 4.68.

[4-Bromo-3,5-bis-(4-methoxybenzyloxy)-phenyl]-methanol (9): $LiBH_4$ (8.09 g, 371.4 mmol) was added to a solution of compound **8** (36.2 g, 74.29 mmol) in THF (400 mL). MeOH (15 mL, 371.4 mmol) was then added dropwise to the solution over a period of 30 min at 0 °C and the resulting mixture was refluxed for 3 h. Addition of water at 0 °C, extraction of the aqueous phase with *tert*-butyl methyl ether, drying of the combined organic layers (Na_2SO_4) and evaporation of the solvent delivered alcohol **9** as a colorless solid (33.5 g, 98 %). M.p. 130–131 °C; ^{1}H NMR (300.1 MHz, [D$_6$]acetone): $\delta = 7.44$ (AA′XX′, 4H), 6.94 (AA′XX′, 4H), 6.83 (s, 2H), 5.10 (s, 4H), 4.60 (d, $J = 5.4$ Hz, 2H), 4.33 (t, $J = 5.7$ Hz, 1H), 3.78 (s, 6H); ^{13}C NMR (75.5 MHz, [D$_6$]acetone): $\delta = 160.4$, 157.1, 144.5, 129.8, 114.6, 105.4, 100.5, 71.2, 64.4, 55.5; IR: $\nu = 3500$, 3067, 3039, 2937, 2880, 2842, 1611, 1588, 1516, 1458, 1431, 1378, 1322, 1302, 1249, 1195, 1178, 1097, 1031, 1015, 999, 974, 920, 855, 835, 821, 776, 719, 695, 656, 606, 589, 508 cm^{-1}; MS (EI): *m*/*z* (%): 458 (<1) $[M]^+$, 257 (<1), 122 (11), 121 (100), 91 (3), 78 (4), 77 (4), 51 (1); elemental analysis calcd (%) for $C_{23}H_{23}BrO_5$ (459.34): C 60.14, H 5.05; found C 60.09, H 5.14.

[4-Bromo-3,5-bis-(4-methoxybenzyloxy)-benzyloxy]-*tert*-butyldiphenylsilane (10): Imidazole (1.885 g, 27.69 mmol) and *t*$BuPh_2SiCl$ (7.612 g, 27.69 mmol) were added to a solution of alcohol **9** (10.6 g, 23.08 mmol) in DMF (150 mL) and the resulting mixture was stirred for 12 h. A standard extractive work-up followed by recrystallization of the residue from diethyl ether/pentane (1:1) delivered compound **10** as a colorless solid (13.2 g, 82 %). M.p. 71–73 °C; ^{1}H NMR (300.1 MHz, CD_2Cl_2): $\delta = 7.71–7.68$ (m, 4H), 7.50–7.38 (m, 10H), 6.92 (AA′XX′, 4H), 6.68 (s, 2H), 5.04 (s, 4H), 4.74 (s, 2H), 3.81 (s, 6H), 1.13 (s, 9H); ^{13}C NMR (75.5 MHz, CD_2Cl_2): $\delta =$ 159.9, 156.5, 142.2, 135.9, 133.7, 130.2, 129.3, 129.0, 128.1, 114.2, 104.5, 100.5, 71.0, 65.7, 55.6, 27.0, 19.5; IR: $\nu = 3072$, 3045, 2998, 2955, 2928, 2892, 2855, 1613, 1590, 1514, 1462, 1432, 1388, 1377, 1363, 1328, 1302, 1262, 1247, 1212, 1173, 1114, 1094, 1035, 1008, 976, 940, 925, 825, 808, 744, 703, 689, 654, 637, 618, 573, 505 cm^{-1}; MS (EI): *m*/*z* (%): 698 (<1) $[M+2]^+$, 696 (<1) $[M]^+$, 641 (2), 639 (2), 241 (<1), 199 (<1), 122 (12), 121 (100), 91 (1), 77 (1); elemental analysis calcd (%) for $C_{39}H_{41}BrO_5Si$ (697.74): C 67.13, H 5.92; found C 66.94, H 5.84.

5-Bromo-4-hydroxy-3-methoxybenzaldehyde (12): Bromine (57.75 g, 0.361 mol) was added over a period of 2.5 h to a solution of vanilline **11** (50 g, 0.329 mol) in MeOH (400 mL) at 0 °C and the resulting mixture was stirred at ambient temperature for 1 h. After cooling to 0 °C, water (160 mL) was slowly introduced over a period of 30 min causing the precipitation of a colorless solid. The suspension was stirred for 15 min at ambient temperature and the precipitate was filtered off. Washing with water and pentane followed by drying in vacuo at 60 °C afforded aryl bromide **12** as a colorless solid (72.1 g, 95 %). ^{1}H NMR (300.1 MHz, [D$_6$]acetone): $\delta = 9.81$ (s, 1H), 9.43–9.17 (br s), 7.69 (d, $J = 1.5$ Hz, 1H), 7.43 (d, $J = 1.8$ Hz, 1H), 3.96 (s, 3H); ^{13}C NMR (75.5 MHz, [D$_6$]acetone): $\delta =$ 190.3, 150.6, 149.4, 130.8, 129.6, 110.0, 109.3, 56.8; IR: $\nu = 3298$, 3103, 3072, 3008, 2974, 2942, 2849, 2774, 1675, 1590, 1502, 1464, 1424, 1406, 1354, 1291, 1159, 1046, 971, 855, 830, 794, 680, 585, 537, 519 cm^{-1}; MS (EI): *m*/*z* (%): 233 (9), 232 (98), 231 (76), 230 (100) $[M]^+$, 229 (68), 217 (5), 215 (5), 203 (5), 201 (6), 189 (14), 187 (15), 161 (10), 159 (11), 136 (8), 135 (10), 131 (5), 108 (5), 107 (11), 94 (9), 91 (6), 80 (5), 79 (28), 78 (5), 77 (7), 66 (5), 65 (9), 63 (14), 62 (14), 61 (7), 53 (19), 52 (10), 51 (39), 50 (23), 49 (5), 39 (5), 29 (9); HR-MS (EI) ($C_8H_7BrO_3$): calcd 229.9579; found 229.9577.

5-Bromo-3,4-dimethoxy-benzaldehyde (13): Methyl iodide (52.35 g, 0.369 mol) was added over a period of 1 h to a suspension of aryl bromide **12** (71 g, 0.307 mol) and K_2CO_3 (63.72 g, 0.461 mol) in DMF (700 mL) and stirring was continued for 24 h. Quenching of the mixture with brine, extraction of the aqueous phase with *tert*-butyl methyl ether, washing of the combined organic layers with brine followed by drying (Na_2SO_4) and evaporation of the solvent afforded compound **13** as a colorless solid (73.05 g, 97 %). ^{1}H NMR (300.1 MHz, $CDCl_3$): $\delta = 9.79$ (s, 1H), 7.59 (d, $J =$ 1.8 Hz, 1H), 7.33 (d, $J = 1.8$ Hz, 1H), 3.90 (s, 3H), 3.88 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 189.7$, 154.0, 151.7, 132.9, 128.5, 117.8, 110.1, 60.7, 56.1; IR: $\nu = 3072$, 3051, 3006, 2978, 2945, 2860, 2745, 1693, 1588, 1566, 1487, 1471, 1451, 1420, 1393, 1380, 1313, 1281, 1240, 1212, 1189, 1144, 1133, 1048, 991, 856, 838, 817, 787, 751, 699, 666, 585, 566, 516 cm^{-1}; MS (EI): *m*/*z* (%): 247 (10), 246 (98), 245 (25), 244 (100) $[M]^+$, 243 (15), 231 (25), 229 (26), 175 (12), 173 (12), 158 (5), 157 (5), 135 (8), 122 (7), 107 (6), 94 (40), 93 (6), 79 (12), 77 (11), 76 (6), 75 (8), 74 (5), 66 (6), 65 (10), 63 (10), 62 (9), 53 (7), 51 (18), 50 (15), 29 (5); HR-MS (EI) ($C_9H_9BrO_3$): calcd 243.9735; found 243.9737.

5-Bromo-3,4-dimethoxyphenol (14): A solution of compound **13** (40 g, 0.163 mol) and 3-chloroperbenzoic acid (70 % *w*/*w*, 60.35 g, 0.245 mol) in CH_2Cl_2 (600 mL) was refluxed for 16 h. The reaction mixture was carefully added to vigorously stirred aq. sat. $NaHCO_3$ (1 L) and stirring was continued for an additional 30 min. The aqueous layer was extracted with CH_2Cl_2 and the combined organic phases were successively washed with aq. sat. $NaHCO_3$, aq. sat. $Na_2S_2O_5$ (test for peroxides must be negative after this step) and brine. The organic phase was then dried (Na_2SO_4) and the solvent was evaporated. The residue was dissolved in MeOH (300 mL), conc. HCl/water (1:1, 300 mL) was added and the mixture was stirred for 30 min. The MeOH was then evaporated, the residue was extracted with *tert*-butyl methyl ether, the combined organic layers were washed with brine, dried (Na_2SO_4) and evaporated to afford phenol **14** as a colorless solid which was analytically pure and could be used in the next step without further purification (26.71 g, 70 %). ^{1}H NMR (300.1 MHz, [D$_6$]acetone): $\delta = 8.42$ (br s, 1H), 6.59 (d, $J = 2.7$ Hz, 1H), 6.50 (d, $J = 2.7$ Hz, 1H), 3.80 (s, 3H), 3.68 (s, 3H); ^{13}C NMR (75.5 MHz, [D$_6$]acetone): $\delta = 155.2$, 155.2, 140.5, 117.6, 110.9, 101.3, 60.5, 56.2; IR: $\nu = 3297$, 3083, 2993, 2946, 2836, 1610, 1581, 1500, 1477, 1452, 1430, 1345, 1319, 1261, 1228, 1204, 1183, 1145, 1046, 994, 976, 856, 837, 821, 772, 728, 684, 632, 554 cm^{-1}; MS (EI): *m*/*z* (%): 235 (8), 234 (92), 233 (9), 232 (93) $[M]^+$, 220 (8), 219 (98), 218 (10), 217 (100), 191 (45), 189 (46), 176 (11), 174 (12), 138 (7), 137 (6), 135 (5), 133 (8), 110 (44), 109 (9), 108 (10), 95 (15), 93 (7), 81 (5), 79 (8), 69 (30), 66 (6), 65 (15), 63 (6), 59 (8), 53 (27), 51 (17), 50 (11), 39 (19), 38 (8), 29 (5); HR-MS (EI) ($C_8H_9BrO_3$): calcd 231.9735; found 231.9735.

5-Hydroxy-2,3-dimethoxybenzonitrile (15): CuCN (10.39 g, 116 mmol) was added to a solution of phenol **14** (20.8 g, 89.23 mmol) in DMF (400 mL) and the resulting mixture was refluxed for 12 h. The reaction was quenched by addition of brine, the aqueous layer was extracted with *tert*-butyl methyl ether, the combined organic phases were washed with brine, dried (Na_2SO_4), and evaporated to give nitrile **15** as a pale yellow solid which was analytically pure and could be used in the next step without further purification (14.23 g, 89 %). ^{1}H NMR (300.1 MHz, [D$_6$]acetone): $\delta = 8.85–8.65$ (br s, 1H), 6.79 (d, $J = 2.8$ Hz, 1H), 6.57 (d, $J = 2.9$ Hz, 1H), 3.85 (s, 3H), 3.83 (s, 3H); ^{13}C NMR (75.5 MHz, [D$_6$]acetone): $\delta = 155.0$, 154.7, 145.6, 116.6, 109.3, 107.6, 106.9, 61.7, 56.3; IR: $\nu = 3347$, 3095, 3011, 2982, 2953, 2839, 2241, 1612, 1599, 1502, 1476, 1431, 1360, 1337, 1274, 1243, 1209, 1194, 1163, 1080, 998, 928, 859, 825, 776, 737, 681, 627, 608, 567 cm^{-1}; MS

(EI): *m*/*z* (%): 180 (8), 179 (97) $[M]^+$, 165 (9), 164 (100), 136 (26), 118 (5), 109 (9), 108 (16), 93 (8), 81 (5), 80 (8), 79 (7), 76 (6), 69 (14), 66 (15), 65 (6), 64 (6), 63 (6), 53 (14), 52 (7), 51 (7), 50 (6), 42 (8), 39 (13); HR-MS (EI) ($C_9H_9NO_3$): calcd 179.0582; found 179.0582.

2,3-Dimethoxy-5-(4-methoxybenzyloxy)-benzonitrile (16): K_2CO_3 (12.22 g, 88.39 mmol), nBu$_4$NI (2.177 g, 5.893 mmol) and 4-methoxybenzyl chloride (11.07 g, 70.71 mmol) were added to a solution of nitrile **15** (10.56 g, 58.93 mmol) in DMF (300 mL) and the resulting suspension was stirred at 80 °C for 12 h. Addition of brine was followed by extraction of the aqueous phase with *tert*-butyl methyl ether. The combined organic layers were washed with brine, dried over Na_2SO_4, evaporated, and the residue was triturated with pentane/*tert*-butyl methyl ether (1:1). The precipitate was filtered off and dried in vacuo to give compound **16** as a colorless solid (14.51 g, 82%). M.p. 88–89 °C; ^{1}H NMR (300.1 MHz, $CDCl_3$): $\delta = 7.31$ (AA′XX′, 2H), 6.90 (AA′XX′, 2H), 6.72 (d, $J = 2.8$ Hz, 1H), 6.61 (d, $J = 2.7$ Hz, 1H), 4.09 (s, 2H), 3.91 (s, 3H), 3.82 (s, 3H), 3.80 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 159.7$, 155.2, 153.5, 146.3, 129.3, 127.9, 116.2, 114.1, 106.9, 106.7, 106.4, 70.5, 61.8, 55.9, 55.2; IR: $\nu = 3090$, 3060, 3008, 2978, 2938, 2874, 2839, 2232, 1613, 1597, 1587, 1518, 1493, 1469, 1450, 1424, 1382, 1351, 1304, 1283, 1254, 1235, 1194, 1176, 1156, 1116, 1077, 1025, 993, 934, 873, 864, 827, 816, 785, 771, 743, 635, 617, 543, 526 cm^{-1}; MS (EI): *m*/*z* (%): 299 (2) $[M]^+$, 178 (1), 122 (12), 121 (100), 91 (3), 78 (7), 77 (6), 53 (2), 52 (2), 51 (2); HR-MS (CI, isobutane) ($C_{17}H_{17}NO_4$+H): calcd 300.1236; found 300.1235; elemental analysis calcd (%) for $C_{17}H_{17}NO_4$ (299.33): C 68.22, H 5.72, N 4.68; found C 68.20, H 5.66, N 4.66.

2-[2,3-Dimethoxy-5-(4-methoxybenzyloxy)-phenyl]-4,4-dimethyl-4,5-dihydro-oxazole (18): LiOH (3.21 g, 134.1 mmol) was added to a suspension of compound **16** (8.03 g, 26.83 mmol) in MeOH (200 mL) and water (50 mL) and the resulting mixture was refluxed for 72 h. The MeOH was evaporated and more water (150 mL) was added. Aq. HCl was then introduced at 0 °C to adjust the pH of the aqueous layer to ≈3.5. Extraction of the aqueous layer with ethyl acetate, drying of the combined organic phases (Na_2SO_4) and evaporation of the solvent delivered 2,3-dimethoxy-5-(4-methoxybenzyloxy)-benzoic acid as a colorless solid which had the following analytical and spectroscopic properties (8.37 g, 98%). M.p. 104–105 °C; ^{1}H NMR (300.1 MHz, [D$_6$]acetone): $\delta = 12.30$–10.20 (br s, 1H), 7.40 (AA′XX′, 2H), 6.98 (d, $J = 3.0$ Hz, 1H), 6.94 (AA′XX′, 2H), 6.88 (d, $J = 3.0$ Hz, 1H), 5.03 (s, 2H), 3.88 (s, 3H), 3.87 (s, 3H), 3.79 (s, 3H); ^{13}C NMR (75.5 MHz, [D$_6$]acetone): $\delta = 166.5$, 160.5, 156.1, 154.1, 143.6, 130.3, 129.8, 125.7, 114.6, 106.6, 106.0, 70.1, 61.9, 56.5, 55.5; IR: $\nu = 3436$, 3084, 3056, 3008, 2971, 2935, 2879, 2837, 2618, 1693, 1602, 1585, 1517, 1488, 1460, 1446, 1427, 1412, 1378, 1343, 1305, 1280, 1253, 1207, 1184, 1146, 1112, 1061, 1034, 1020, 960, 931, 907, 858, 847, 823, 799, 782, 767, 725, 679, 630, 606, 532 cm^{-1}; MS (EI): *m*/*z* (%): 319 (1), 318 (5) $[M]^+$, 197 (<1), 137 (2), 122 (13), 121 (100), 91 (3), 78 (5), 77 (5), 53 (2), 52 (1), 51 (2), 39 (2); HR-MS (CI, isobutane) ($C_{17}H_{18}O_6$+H): calcd 319.1182; found 319.1185; elemental analysis calcd (%) for $C_{17}H_{18}O_6$ (318.33): C 64.14, H 5.70; found C 64.20, H 5.62.

A solution of PPh_3 (8.24 g, 31.42 mmol) in pyridine/MeCN (1:1, 50 mL) was added over a period of 30 min to a mixture of 2,3-dimethoxy-5-(4-methoxybenzyloxy)-benzoic acid (2.0 g, 6.283 mmol), 2-amino-2-methyl-propan-1-ol **17** (560 mg, 6.283 mmol), (iPr)$_2$NEt (4.06 g, 31.42 mmol) and CCl_4 (4.833 g, 31.42 mmol) in pyridine/MeCN (1:1, 50 mL) at 0 °C. The resulting mixture was stirred at 80 °C for 16 h, all volatiles were evaporated in vacuo at 60 °C, and the residue was dissolved in ethyl acetate. Water was added, the aqueous layer was extracted with ethyl acetate, the combined organic phases were washed with aq. sat. $CuSO_4$, dried (Na_2SO_4), and the solvent was evaporated. The residue was purified by flash chromatography on silica (hexanes/ethyl acetate 4:1 → 2:1) to deliver oxazoline **18** as a pale yellow solid (1.86 g, 80%). M.p. 89–90 °C; ^{1}H NMR (300.1 MHz, CD_2Cl_2): $\delta = 7.36$ (AA′XX′, 2H), 6.92 (AA′XX′, 2H), 6.87 (d, $J = 2.9$ Hz, 1H), 6.66 (d, $J = 2.9$ Hz, 1H), 4.96 (s, 2H), 4.08 (s, 2H), 3.82 (s, 3H), 3.81 (s, 3H), 3.75 (s, 3H), 1.36 (s, 6H); ^{13}C NMR (75.5 MHz, CD_2Cl_2): $\delta = 161.0$, 160.0, 155.2, 154.5, 143.3, 129.7, 129.3, 123.6, 114.2, 105.8, 104.1, 79.3, 70.6, 67.9, 61.6, 56.3, 55.6, 28.4; IR: $\nu = 3070$, 2965, 2935, 2894, 2836, 1646, 1612, 1588, 1515, 1490, 1465, 1426, 1363, 1337, 1302, 1249, 1192, 1172, 1138, 1112, 1029, 976, 935, 900, 824, 786, 749, 712, 627, 602, 571, 525 cm^{-1}; MS (EI): *m*/*z* (%): 372 (5), 371 (20) $[M]^+$, 356 (2), 340 (5), 122 (13), 121 (100), 91 (2), 78 (3), 77 (3); HR-MS (EI) ($C_{21}H_{25}NO_5$): calcd 371.1733; found 371.1732; elemental analysis calcd (%) for $C_{21}H_{25}NO_5$ (371.43): C 67.91, H 6.78, N 3.77; found C 68.04, H 6.72, N 3.70.

2-[4′-(*tert*-Butyldiphenylsilanyloxymethyl)-6-methoxy-4,2′,6′-tris-(4-methoxybenzyloxy)-biphenyl-2-yl]-4,4-dimethyl-4,5-dihydro-oxazole (19; R^1 = R^2 = PMB, R^3 = TBDPS): A solution of 1,2-dibromoethane (1.265 g, 6.731 mmol) in THF (10 mL) was added over a period of 20 min to a refluxing suspension of Mg powder (654 mg, 26.93 mmol) and aryl bromide **10** (9.393 g, 13.46 mmol) in THF (120 mL) and reflux was continued for another 3 h. Excess magnesium was filtered off, a solution of oxazoline **18** (2.5 g, 6.731 mmol) in THF (40 mL) was added and the resulting mixture was refluxed for 48 h. The reaction was quenched with aq. sat. NH_4Cl, the aqueous layer was extracted with *tert*-butyl methyl ether, the combined organic phases were washed with brine, dried (Na_2SO_4), the solvent was evaporated, and the residue was purified by flash chromatography on silica (hexanes/ethyl acetate 10:1 → 4:1 → 2:1) to afford biaryl **19** as a colorless foam (5.414 g, 84%). ^{1}H NMR (300.1 MHz, CD_2Cl_2): $\delta = 7.74$ (m, 4H), 7.51–7.39 (m, 8H), 7.18 (AA′XX′, 4H), 7.12 (d, $J = 2.4$ Hz, 1H), 6.96 (AA′XX′, 2H), 6.82 (AA′XX′, 4H), 6.72 (d, $J = 2.4$ Hz, 1H), 6.67 (s, 2H), 5.07 (s, 2H), 4.90 (m, 4H), 4.79 (s, 2H), 3.83 (s, 3H), 3.77 (s, 6H), 3.75 (s, 2H), 3.71 (s, 3H), 1.15 (s, 6H), 1.13 (s, 9H); ^{13}C NMR (75.5 MHz, CD_2Cl_2): $\delta = 162.9$, 160.0, 159.5, 159.2, 158.9, 157.8, 142.1, 136.0, 134.0, 131.7, 130.1, 129.9, 129.4, 128.7, 128.1, 117.4, 114.9, 114.3, 114.0, 106.2, 104.0, 101.7, 79.3, 70.5, 70.4, 67.6, 66.2, 56.1, 55.6, 55.5, 28.2, 27.0, 19.6; IR: $\nu = 3070$, 3046, 2959, 2931, 2894, 2857, 2835, 1653, 1612, 1601, 1585, 1515, 1462, 1428, 1359, 1333, 1303, 1249, 1174, 1141, 1106, 1032, 999, 975, 937, 822, 742, 704, 610, 504 cm^{-1}; MS (EI): *m*/*z* (%): 958 (2), 957 (2) $[M]^+$, 838 (3), 837 (8), 836 (11), 821 (3), 820 (4), 297 (2), 256 (2), 122 (9), 121 (100); elemental analysis calcd (%) for $C_{59}H_{63}NO_9Si$ (958.24): C 73.95, H 6.63, N 1.46; found C 73.78, H 6.63, N 1.44.

4′-(*tert*-Butyldiphenylsilanyloxymethyl)-6-methoxy-4,2′,6′-tris-(4-methoxybenzyloxy)-biphenyl-2-carbaldehyde (20; R = PMB): A solution of methyl triflate (351 mg, 2.139 mmol) in CH_2Cl_2 (5 mL) was added dropwise over 15 min to a solution of compound **19** (1.025 g, 1.07 mmol) in CH_2Cl_2 (40 mL) at −10 °C and the resulting solution was stirred for 2 h while the temperature was slowly raised to 0 °C. MeOH/THF (4:1, 15 mL) was introduced at 0 °C followed by the careful addition of $NaBH_4$ (202 mg, 5.349 mmol). After stirring for 3 h at ambient temperature the reaction was quenched with aq. sat. NH_4Cl, the aqueous layer was extracted with CH_2Cl_2, dried (Na_2SO_4), and the solvent was evaporated. Oxalic acid (193 mg, 2.139 mmol) was added to a solution of the residue in THF/H_2O (4:1, 50 mL) and the mixture was stirred for 12 h. Addition of aq. sat. $NaHCO_3$, extraction with *tert*-butyl methyl ether, drying of the combined organic layers (Na_2SO_4), evaporation of the solvent and flash chromatography of the residue on silica (hexanes/ethyl acetate 4:1) afforded aldehyde **20** as a colorless foam (670 mg, 70%). ^{1}H NMR (300.1 MHz, CD_2Cl_2): $\delta =$ 9.67 (s, 1H), 7.74–7.71 (m, 4H), 7.51–7.39 (m, 8H), 7.18 (d, $J = 2.5$ Hz, 1H), 7.08 (AA′XX′, 4H), 6.95 (AA′XX′, 2H), 6.86 (d, $J = 2.4$ Hz, 1H), 6.81 (AA′XX′, 4H), 6.74 (s, 2H), 5.08 (s, 2H), 4.91 (s, 4H), 4.81 (s, 2H), 3.83 (s, 3H), 3.77 (s, 6H), 3.75 (s, 3H), 1.14 (s, 9H); ^{13}C NMR (75.5 MHz, CD_2Cl_2): $\delta = 193.0$, 160.1, 159.8, 159.6, 159.3, 158.0, 143.7, 136.2, 136.0, 133.8, 130.2, 129.9, 129.5, 129.1, 128.8, 128.2, 122.0, 114.3, 114.1, 110.4, 105.4, 103.7, 101.5, 70.4, 66.0, 56.3, 55.6, 55.5, 27.1, 19.6; IR: $\nu = 3070$, 3045, 2998, 2955, 2932, 2856, 2836, 1689, 1612, 1602, 1586, 1515, 1463, 1429, 1374, 1334, 1303, 1282, 1250, 1175, 1151, 1104, 1034, 997, 936, 823, 742, 704, 657, 613, 505 cm^{-1}; MS (EI): *m*/*z* (%): 889 (3), 888 (4) $[M]^+$, 767 (1), 241 (1), 199 (2), 122 (13), 121 (100), 77 (1); elemental analysis calcd (%) for $C_{55}H_{56}O_9Si$ (889.13): C 74.30, H 6.35; found C 74.18, H 6.32.

1-[4′-(*tert*-Butyldiphenylsilanyloxymethyl)-6-methoxy-4,2′,6′-tris-(4-methoxybenzyloxy)-biphenyl-2-yl]-pent-4-en-1-ol (24a; R = PMB, n = 2, X = CH=CH$_2$): A solution of 3-butenylmagnesium bromide (0.5 M in THF, 2.7 mL, 1.35 mmol) was added dropwise to a solution of aldehyde **20** (400 mg, 0.45 mmol) in THF (20 mL) at 0 °C and the resulting mixture was stirred for 1 h at that temperature. A standard extractive work-up followed by flash chromatography on silica (hexanes/ethyl acetate 4:1) provided alcohol **24a** as a colorless syrup (350 mg, 82%). ^{1}H NMR (300.1 MHz, CD_2Cl_2): $\delta = 7.73$–7.70 (m, 4H), 7.49–7.38 (m, 8H), 7.10 (AA′XX′, 2H), 7.07 (AA′XX′, 2H), 6.94 (AA′XX′, 2H), 6.80 (m, 5H), 6.72 (s), 6.69 (s, 2H), 6.55 (d, $J = 2.3$ Hz, 1H), 5.60 (ddt, $J = 16.9$, 10.2, 6.5 Hz, 1H), 5.04 (s, 2H), 4.91–4.78 (m, 6H), 4.77 (s, 2H), 4.40 (t, $J = 6.5$ Hz, 1H), 3.82 (m, 3H), 3.76 (br s, 6H), 3.70 (br s, 3H), 2.03 (m, 1H), 1.88 (m, 2H), 1.65 (m, 2H), 1.54 (s, 9H); ^{13}C NMR (75.5 MHz, CD_2Cl_2): $\delta = 160.0$, 160.0, 159.7, 159.5, 158.6, 158.2, 157.1, 146.1, 142.7, 139.0, 136.0, 133.8, 130.1, 129.9, 129.8, 129.7, 129.4, 129.1, 128.5, 128.1, 115.2, 114.3, 114.3, 114.2, 114.1, 113.9, 104.6, 104.1, 102.6,

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98.7, 71.1, 70.9, 70.2, 70.0, 66.0, 56.0, 55.6, 55.5, 36.4, 30.4, 27.0, 19.5; IR: $\nu =$ 3452, 3070, 2998, 2955, 2928, 2854, 1639, 1612, 1604, 1585, 1514, 1462, 1428, 1418, 1373, 1323, 1303, 1249, 1175, 1150, 1101, 1032, 999, 911, 822, 777, 742, 702, 607 cm^{-1}; MS (EI): m/z (%): 945 (<1), 944 (<1) $[M]^+$, 824 (2), 823 (3), 808 (2), 807 (3), 806 (4), 752 (2), 751 (3), 688 (2), 687 (4), 629 (2), 122 (14), 121 (100); elemental analysis calcd (%) for $C_{59}H_{64}O_9Si$ (945.24): C 74.97, H 6.82; found C 74.86, H 6.78.

1-[4′-(*tert*-Butyldiphenylsilanyloxymethyl)-6-methoxy-4,2′,6′-tris-(4-methoxybenzyloxy)-biphenyl-2-yl]-hept-6-en-1-ol (24b; R = PMB, n = 4, X = CH=CH$_2$): Prepared as described above from aldehyde **20** (500 mg, 0.562 mmol) and 5-hexenylmagnesium bromide (0.4 M in THF, 4.22 mL, 1.687 mmol). Colorless syrup (430 mg, 79%). ^{1}H NMR (300.1 MHz, CD_2Cl_2): $\delta = 7.71$ (m, 4H), 7.50–7.38 (m, 8H), 7.09 (m, 4H), 6.94 (AA′XX′, 2H), 6.80 (m, 5H), 6.72 (s), 6.69 (s, 2H), 6.56 (d, $J = 2.2$ Hz, 1H), 5.71 (ddt, $J = 17.0$, 10.3, 6.7 Hz, 1H), 5.05 (s, 2H), 4.95–4.83 (m, 6H), 4.77 (s, 2H), 4.37 (t, $J = 6.6$ Hz, 1H), 3.82 (s, 3H), 3.76 (s, 6H), 3.70 (s, 3H), 2.11–1.97 (m, 1H), 1.87 (m, 2H), 1.67–1.48 (m, 2H), 1.23–1.10 (m, 4H), 1.12 (s, 9H); ^{13}C NMR (75.5 MHz, CD_2Cl_2): $\delta = 160.0$, 160.0, 159.7, 159.5, 158.5, 158.2, 157.1, 146.3, 142.6, 139.5, 136.0, 133.8, 130.1, 129.9, 129.8, 129.7, 129.4, 129.1, 128.4, 129.1, 115.3, 114.3, 114.2, 114.1, 114.1, 104.6, 104.2, 102.6, 98.6, 71.5, 70.9, 70.1, 70.0, 66.0, 56.0, 55.6, 55.5, 36.9, 34.0, 29.1, 27.1, 25.7, 19.6; IR: $\nu =$ 3447, 3070, 2998, 2931, 2856, 2835, 1639, 1604, 1585, 1514, 1461, 1428, 1372, 1323, 1303, 1249, 1175, 1150, 1112, 1035, 999, 911, 822, 742, 703, 611, 504 cm^{-1}; MS (EI): m/z (%): 972 (<1) $[M]^+$, 850 (<1), 834 (1), 833 (2), 779 (<1), 715 (1), 657 (<1), 122 (9), 121 (100); elemental analysis calcd (%) for $C_{61}H_{68}O_9Si$ (973.29): C 75.28, H 7.04; found C 75.22, H 7.09.

1-[4′-(*tert*-Butyldiphenylsilanyloxymethyl)-6-methoxy-4,2′,6′-tris-(4-methoxybenzyloxy)-biphenyl-2-yl]-hex-4-yn-1-ol (24c; R = PMB, n = 2, X = C≡CCH$_3$): Prepared as described above from aldehyde **20** (185 mg, 0.208 mmol) and 3-pentynylmagnesium bromide (0.4 M in THF, 1.56 mL, 0.624 mmol). Colorless syrup (174 mg, 87%). ^{1}H NMR (300.1 MHz, CD_2Cl_2): $\delta = 7.73–7.70$ (m, 4H), 7.50–7.39 (m, 8H), 7.14 (AA′XX′, 2H), 7.10 (AA′XX′, 2H), 6.94 (AA′XX′, 2H), 6.84–6.78 (m, 5H), 6.73 (s), 6.72 (s, 2H), 6.56 (d, $J = 2.3$ Hz, 1H), 5.04 (s, 2H), 4.95–4.86 (m, 4H), 4.78 (s, 2H), 4.53 (m, 1H), 3.83 (s, 3H), 3.77 (s), 3.77 (s, 6H), 3.71 (s, 3H), 2.09 (m, 1H), 2.08–1.97 (m, 2H), 1.82–1.65 (m, 2H), 1.60 (t, $J = 2.5$ Hz, 3H), 1.12 (s, 9H); ^{13}C NMR (75.5 MHz, CD_2Cl_2): $\delta = 160.0$, 160.0, 159.7, 159.5, 158.6, 158.4, 157.1, 145.8, 142.6, 136.0, 133.8, 130.2, 129.9, 129.8, 129.6, 129.5, 129.0, 128.7, 128.1, 115.2, 114.3, 114.2, 114.1, 113.8, 104.3, 103.9, 102.6, 98.7, 78.9, 75.8, 70.8, 70.6, 70.2, 70.1, 65.9, 56.0, 55.6, 55.5, 36.7, 27.0, 19.5, 15.7, 3.5; IR: $\nu =$ 3511, 3070, 3047, 2998, 2955, 2932, 2856, 2836, 1604, 1585, 1515, 1462, 1429, 1378, 1323, 1303, 1251, 1175, 1150, 1111, 1035, 1000, 954, 940, 824, 742, 706, 613, 505 cm^{-1}; MS (EI): m/z (%): 956 (<1) $[M]^+$, 818 (1), 763 (<1), 700 (1), 699 (2), 443 (<1), 241 (1), 199 (1), 122 (14), 121 (100), 91 (<1), 77 (1); elemental analysis calcd (%) for $C_{60}H_{64}O_9Si$ (957.25): C 75.28, H 6.74; found C 75.15, H 6.79.

1-[4′-(*tert*-Butyldiphenylsilanyloxymethyl)-6-methoxy-4,2′,6′-tris-(4-methoxybenzyloxy)-biphenyl-2-yl]-oct-6-yn-1-ol (24d; R = PMB, n = 4, X = C≡CCH$_3$): Prepared as described above from aldehyde **20** (1.5 g, 1.687 mmol) and 5-heptynylmagnesium bromide (0.3 M in THF, 11.2 mL, 3.374 mmol). Colorless syrup (1.105 g, 66%): R_f 0.41 (hexanes/ethyl acetate 2:1); ^{1}H NMR (300.1 MHz, CD_2Cl_2): $\delta = 7.76–7.73$ (m, 4H), 7.53–7.41 (m, 8H), 7.13 (m, 4H), 6.97 (AA′XX′, 2H), 6.86–6.82 (m, 5H), 6.76 (s), 6.74 (s, 2H), 6.56 (d, $J = 2.3$ Hz, 1H), 5.08 (s, 2H), 4.96 (s, 2H), 4.92 (s), 4.90 (s, 2H), 4.82 (s, 2H), 4.41 (t, $J = 6.7$ Hz; 1H), 3.84 (s, 3H), 3.79 (s), 3.78 (s, 6H), 3.74 (s, 3H), 2.13 (m, 1H), 1.98–1.92 (m, 2H), 1.72 (t, $J = 2.5$ Hz; 3H), 1.67–1.55 (m, 2H), 1.35–1.25 (m, 4H), 1.15 (s, 9H); ^{13}C NMR (75.5 MHz, CD_2Cl_2): $\delta = 160.0$, 160.0, 159.8, 159.5, 158.6, 158.3, 157.1, 146.2, 142.7, 136.0, 133.8, 130.2, 129.9, 129.8, 129.7, 129.4, 129.1, 128.4, 128.2, 115.3, 114.3, 114.2, 114.1, 114.0, 104.6, 104.2, 102.6, 98.7, 79.5, 75.5, 71.5, 70.9, 70.1, 70.0, 66.0, 56.0, 55.6, 55.5, 36.6, 29.3, 27.1, 25.5, 19.6, 18.8, 3.5; IR: $\nu =$ 3475, 3133, 3070, 3048, 2998, 2932, 2856, 2835, 1604, 1585, 1514, 1461, 1428, 1372, 1323, 1303, 1249, 1174, 1149, 1104, 1033, 999, 822, 742, 703, 612, 504 cm^{-1}; MS (EI): m/z (%): 984 (<1) $[M]^+$, 846 (2), 845 (3), 727 (1), 200 (1), 199 (4), 136 (1), 135 (2), 122 (12), 121 (100), 91 (2), 79 (2), 78 (2), 77 (3), 40 (4); MS (ESI-pos): 1023 $[M+K]^+$, 1007 $[M+Na]^+$; elemental analysis calcd (%) for $C_{62}H_{68}O_9Si$ (985.30): C 75.58, H 6.96; found C 75.65, H 7.08.

Thiocarbonic acid *O*-{1-[4′-(*tert*-butyldiphenylsilanyloxy-methyl)-6-methoxy-4,2′,6′-tris-(4-methoxybenzyloxy)-biphenyl-2-yl]-pent-4-enyl}ester *O*-phenyl ester (25a; R = PMB, n = 2, X = CH=CH$_2$): Phenyl chlorothionoformate (49.3 mg, 0.286 mmol) and pyridine (33.9 mg, 0.428 mmol) were successively added to a solution of alcohol **24a** (135 mg, 0.143 mmol) in CH_2Cl_2 (15 mL) at −20 °C. The resulting solution was stirred for 1 h at −20 °C and for 12 h at ambient temperature. All volatiles were evaporated and the residue was purified by flash chromatography on silica (hexanes/ethyl acetate 6:1 → 4:1) to deliver thiocarbonate **25a** as a colorless foam (145 mg, 94%). ^{1}H NMR (300.1 MHz, CD_2Cl_2): $\delta = 7.72–7.68$ (m, 4H), 7.48–7.21 (m, 11H), 7.12 (AA′XX′, 2H), 7.07 (AA′XX′, 2H), 6.95 (AA′XX′, 2H), 6.83–6.78 (m, 7H), 6.70 (m), 6.65 (m, 2H), 6.64 (d, $J =$ 2.4 Hz, 1H), 6.15 (m, 1H), 5.62 (ddt, $J = 17.0$, 10.4, 6.2 Hz, 1H), 5.05 (s, 2H), 4.96–4.84 (m, 6H), 4.78 (s, 2H), 3.82 (s, 3H), 3.77 (s, 3H), 3.76–3.74 (m, 6H), 1.92 (m, 4H), 1.10 (s, 9H); ^{13}C NMR (75.5 MHz, CD_2Cl_2): $\delta =$ 194.3, 160.0, 159.9, 159.5, 159.3, 158.8, 158.1, 157.3, 153.8, 143.1, 140.5, 138.1, 136.0, 133.9, 130.1, 129.9, 129.8, 129.7, 129.5, 128.7, 128.6, 128.1, 128.0, 126.6, 122.3, 116.0, 114.8, 114.3, 114.1, 114.0, 112.5, 103.6, 103.5, 103.3, 99.4, 84.4, 70.2, 70.0, 69.6, 66.1, 56.2, 55.6, 55.5, 35.0, 29.4, 27.0, 19.5; IR: $\nu =$ 3070, 2998, 2954, 2930, 2856, 2835, 1639, 1605, 1586, 1514, 1490, 1461, 1429, 1365, 1322, 1301, 1249, 1193, 1152, 1105, 1034, 1000, 914, 822, 770, 742, 703, 690, 613, 505 cm^{-1}; MS (EI): m/z (%): 1046 (<1) $[M-H_2S]^+$, 926 (2), 807 (2), 806 (5), 805 (4), 752 (2), 751 (4), 750 (5), 749 (8), 686 (2), 685 (2), 670 (2), 642 (2), 641 (3), 631 (2), 630 (2), 629 (4), 550 (2), 199 (8), 135 (2), 122 (9), 121 (100); elemental analysis calcd (%) for $C_{66}H_{68}O_{10}SSi$ (1081.41): C 73.30, H 6.33; found C 73.41, H 6.30.

Thiocarbonic acid *O*-{1-[4′-(*tert*-butyldiphenylsilanyloxymethyl)-6-methoxy-4,2′,6′-tris-(4-methoxybenzyloxy)-biphenyl-2-yl]-hept-6-enyl}ester *O*-phenyl ester (25b; R = PMB, n = 4, X = CH=CH$_2$): Prepared as described above from alcohol **24b** (380 mg, 0.39 mmol) and phenyl chlorothionoformate (135 mg, 0.781 mmol). Colorless foam (339 mg, 78%). ^{1}H NMR (300.1 MHz, CD_2Cl_2): $\delta = 7.71–7.68$ (m, 4H), 7.47–7.20 (m, 11H), 7.11 (AA′XX′, 2H), 7.07 (AA′XX′, 2H), 6.94 (AA′XX′, 2H), 6.82–6.77 (m, 7H), 6.69 (br s), 6.66 (m, 2H), 6.63 (d, $J = 2.3$ Hz, 1H), 6.13 ("t", $J = 6.4$ Hz, 1H), 5.70 (ddt, $J = 17.0$, 10.2, 6.6 Hz, 1H), 5.04 (br s, 2H), 4.97–4.84 (m, 6H), 4.77 (br s, 2H), 3.82 (m, 3H), 3.77 (s), 3.76 (s), 3.74 (s), 3.73 (s, 9H), 1.85 (m, 4H), 1.22–1.14 (m, 4H), 1.10 (s, 9H); ^{13}C NMR (75.5 MHz, CD_2Cl_2): $\delta =$ 194.3, 160.0, 159.9, 159.5, 159.3, 158.7, 158.1, 157.3, 153.8, 143.1, 140.7, 139.3, 136.0, 133.9, 130.1, 129.9, 129.6, 129.5, 128.7, 128.4, 128.1, 128.1, 126.6, 122.3, 116.0, 114.3, 114.1, 114.0, 112.6, 103.6, 103.5, 103.4, 99.4, 84.8, 70.2, 70.0, 69.6, 66.1, 56.1, 55.6, 55.5, 35.5, 33.9, 29.0, 27.0, 24.6, 19.5; IR: $\nu =$ 3070, 2998, 2931, 2856, 2835, 1639, 1605, 1585, 1514, 1490, 1461, 1429, 1364, 1322, 1302, 1286, 1249, 1193, 1152, 1106, 1034, 998, 938, 912, 823, 769, 742, 704, 690, 611 cm^{-1}; MS (EI): m/z (%): 1074 (<1) $[M-H_2S]^+$, 955 (2), 954 (2), 835 (3), 834 (5), 833 (5), 777 (2), 714 (2), 713 (3), 657 (2), 199 (3), 135 (2), 122 (11), 121 (100); elemental analysis calcd (%) for $C_{68}H_{72}O_{10}SSi$ (1109.47): C 73.62, H 6.54; found C 73.49, H 6.46.

Thiocarbonic acid *O*-{1-[4′-(*tert*-butyldiphenylsilanyloxymethyl)-6-methoxy-4,2′,6′-tris-(4-methoxybenzyloxy)-biphenyl-2-yl]-hex-4-ynyl}ester *O*-phenyl ester (25c; R = PMB, n = 2, X = C≡CCH$_3$): Prepared as described above from alcohol **24c** (670 mg, 0.7 mmol) and phenyl chlorothionoformate (242 mg, 194 μL, 1.4 mmol). Colorless foam (717 mg, 94%). ^{1}H NMR (300.1 MHz, CD_2Cl_2): $\delta = 7.73–7.69$ (m, 4H), 7.49–7.22 (m, 11H), 7.18 (AA′XX′, 2H), 7.07 (AA′XX′, 2H), 6.96 (AA′XX′, 2H), 6.86–6.80 (m, 6H), 6.78 (d, $J = 2.3$ Hz, 1H), 6.72 (s, 1H), 6.65 (s, 1H), 6.64 (d, $J = 2.3$ Hz, 1H), 6.20 (t, $J = 5.6$ Hz, 1H), 5.05 (s, 2H), 4.95 (s, 2H), 4.92–4.83 (m, 2H), 4.79 (s, 2H), 3.83 (s), 3.82 (s, 3H), 3.78 (s), 3.77 (s, 3H), 3.75 (s, 3H), 3.73 (s), 3.72 (br s, 3H), 2.09–2.02 (m, 4H), 1.67 (m, 3H), 1.11 (s, 9H); ^{13}C NMR (75.5 MHz, CD_2Cl_2): $\delta =$ 194.1, 160.0, 159.9, 159.6, 159.3, 158.9, 158.2, 157.4, 153.8, 143.0, 140.1, 136.0, 133.8, 133.8, 130.1, 129.9, 129.8, 129.6, 129.5, 128.9, 128.8, 128.1, 128.0, 126.6, 122.3, 116.1, 114.3, 114.1, 114.0, 112.3, 103.6, 103.4, 103.1, 99.6, 83.7, 78.2, 76.2, 70.3, 70.1, 69.6, 66.0, 56.2, 55.6, 55.5, 35.4, 27.0, 19.5, 15.2, 3.6; IR: $\nu =$ 3069, 3044, 2998, 2955, 2931, 2856, 2835, 1605, 1585, 1514, 1490, 1461, 1429, 1365, 1322, 1302, 1275, 1249, 1192, 1151, 1104, 1032, 999, 821, 770, 742, 703, 690, 612, 503 cm^{-1}; MS (ESI-pos): 1131 $[M+K]^+$, 1115 $[M+Na]^+$, 1099 $[M+Li]^+$, 961 $[M - C_6H_5OH - COS+Na]^+$, 939 $[M - C_6H_5OH - COS+H]^+$; elemental analysis calcd (%) for $C_{67}H_{68}O_{10}SSi$ (1093.42): C 73.60, H 6.27; found C 73.49, H 6.18.

Thiocarbonic acid *O*-{1-[4′-(*tert*-butyldiphenylsilanyloxymethyl)-6-methoxy-4,2′,6′-tris-(4-methoxybenzyloxy)-biphenyl-2-yl]-oct-6-ynyl}ester *O*-phenyl ester (25d; R = PMB, n = 4, X = C≡CCH$_3$): Prepared as described above from alcohol **24d** (1.0 g, 1.015 mmol) and phenyl chlorothionoformate (350 mg, 281 μL, 2.03 mmol). Colorless foam (1.03 g, 90%). ^{1}H NMR (300.1 MHz, CD_2Cl_2): $\delta = 7.74–7.70$ (m, 4H), 7.49–7.22 (m, 11H), 7.15 (AA′XX′, 2H), 7.10 (AA′XX′, 2H), 6.97 (AA′XX′, 2H), 6.87–6.80 (m,

7H), 6.72–6.66 (m, 3H), 6.15 (t, $J = 6.5$ Hz, 1H), 5.07 (s, 2H), 4.97 (s, 2H), 4.93–4.91 (m, 2H), 4.80 (s, 2H), 3.84 (m, 3H), 3.79 (s), 3.78 (s, 3H), 3.76 (s, 6H), 1.97–1.83 (m, 4H), 1.72 (t, $J = 2.5$ Hz, 3H), 1.33–1.18 (m, 4H), 1.14 (s), 1.12 (s, 9H); ^{13}C NMR (75.5 MHz, CD_2Cl_2): $\delta = 194.3$, 160.0, 159.9, 159.5, 159.3, 158.8, 158.1, 157.3, 153.8, 143.1, 140.6, 136.0, 133.9, 133.9, 130.1, 129.9, 129.7, 129.5, 128.7, 128.5, 128.2, 128.1, 126.6, 122.4, 116.1, 114.3, 114.1, 114.0, 112.6, 103.7, 103.5, 103.3, 99.4, 84.7, 79.3, 75.6, 70.2, 69.9, 69.7, 66.1, 56.1, 55.6, 55.6, 35.2, 29.1, 27.1, 24.4, 19.6, 18.8, 3.5; IR: $\nu = 3039$, 3070, 2998, 2932, 2856, 2835, 1605, 1585, 1514, 1490, 1461, 1429, 1419, 1364, 1322, 1303, 1288, 1249, 1193, 1152, 1105, 1034, 999, 939, 822, 770, 742, 704, 691, 613, 504 cm^{-1}; MS (ESI-pos): 1143 $[M+Na]^+$, 989 $[M - C_6H_5OH - COS+Na]^+$, 967 $[M - C_6H_5OH+COS+H]^+$; elemental analysis calcd (%) for $C_{69}H_{72}O_{10}SSi$ (1121.48): C 73.90, H 6.47; found C 74.06, H 6.40.

***tert*-Butyl-[2′-methoxy-2,6,4′-tris-(4-methoxybenzyloxy)-6′-pent-4-enyl-biphenyl-4-ylmethoxy]-diphenylsilane (26a; R = PMB, *n* = 2, X = CH=CH$_2$)**: nBu$_3$SnH (172 mg, 0.592 mmol) and AIBN (9.7 mg, 0.059 mmol) were added to a solution of thiocarbonate **25a** (320 mg, 0.296 mmol) in toluene (30 mL) and the resulting mixture was stirred at 75 °C for 12 h. Evaporation of the solvent followed by flash chromatography of the residue on silica (hexanes (ca. 1 L), then hexanes/ethyl acetate 10:1 → 6:1) afforded compound **26a** as a colorless oil (268 mg, 97%). ^{1}H NMR (300.1 MHz, CD_2Cl_2): $\delta = 7.72$ (m, 4H), 7.49–7.39 (m, 8H), 7.12 (AA′XX′, 4H), 6.94 (AA′XX′, 2H), 6.81 (AA′XX′, 4H), 6.69 (s, 2H), 6.56 (m, 1H), 6.50 (m, 1H), 5.65 (ddt, $J = 16.9$, 10.2, 6.6 Hz, 1H), 5.02 (s, 2H), 4.95–4.84 (m, 6H), 4.78 (s, 2H), 3.82 (m, 3H), 3.77 (m, 6H), 3.71 (m, 3H), 2.36 (t, $J = 7.8$ Hz, 2H), 1.90 (m, 2H), 1.52 (m, 2H), 1.12 (s, 9H); ^{13}C NMR (75.5 MHz, CD_2Cl_2): $\delta = 159.9$, 159.5, 159.4, 158.8, 157.8, 144.2, 142.2, 139.3, 136.0, 133.9, 130.1, 130.0, 129.8, 128.7, 128.7, 128.1, 116.2, 114.6, 114.3, 114.3, 114.1, 106.5, 104.0, 97.0, 70.2, 70.1, 66.1, 55.9, 55.6, 55.5, 33.8, 33.7, 29.8, 27.1, 19.6; IR: $\nu = 3070$, 3047, 2998, 2954, 2932, 2857, 2835, 1638, 1612, 1602, 1584, 1514, 1462, 1429, 1418, 1373, 1324, 1303, 1249, 1174, 1150, 1111, 1035, 1000, 954, 912, 823, 741, 704, 612, 505 cm^{-1}; MS (EI): m/z (%): 929 (1), 928 (1) $[M]^+$, 810 (1), 809 (4), 808 (9), 807 (12), 241 (2), 199 (1), 135 (2), 123 (1), 122 (22), 121 (100), 91 (1), 77 (1); elemental analysis calcd (%) for $C_{59}H_{64}O_8Si$ (929.24): C 76.26, H 7.03; found C 76.30, H 7.03.

***tert*-Butyl-[6′-hept-6-enyl-2′-methoxy-2,6,4′-tris-(4-methoxybenzyloxy)-biphenyl-4-ylmethoxy]-diphenylsilane (26b; R = PMB, *n* = 4, X = CH=CH$_2$)**: Prepared as described above from thiocarbonate **25b** (325 mg, 0.293 mmol). Colorless oil (230 mg, 82%). ^{1}H NMR (300.1 MHz, CD_2Cl_2): $\delta = 7.72$ (m, 4H), 7.50–7.39 (m, 8H), 7.13 (AA′XX′, 4H), 6.96 (AA′XX′, 2H), 6.81 (AA′XX′, 4H), 6.69 (s, 2H), 6.57 (d, $J = 2.3$ Hz, 1H), 6.50 (d, $J = 2.3$ Hz, 1H), 5.75 (ddt, $J = 17.0$, 10.2, 6.6 Hz, 1H), 5.03 (s, 2H), 4.96–4.86 (m, 2H), 4.92 (s, 4H), 4.78 (s, 2H), 3.83 (s, 3H), 3.77 (s, 6H), 3.71 (s, 3H), 2.34 (t, $J = 7.8$ Hz, 2H), 1.91 (m, 2H), 1.42 (m, 2H), 1.30–1.11 (m, 4H), 1.12 (s, 9H); ^{13}C NMR (75.5 MHz, CD_2Cl_2): $\delta = 159.9$, 159.5, 159.4, 158.7, 157.8, 144.5, 142.2, 139.6, 136.0, 133.9, 130.1, 129.8, 128.6, 128.1, 116.2, 114.7, 114.2, 114.1, 106.4, 104.0, 96.9, 70.2, 70.1, 66.1, 55.9, 55.6, 55.5, 34.1, 34.0, 30.4, 29.3, 29.1, 27.1, 19.6; IR: $\nu = 3070$, 2998, 2931, 2856, 1639, 1612, 1602, 1580, 1514, 1462, 1429, 1418, 1373, 1323, 1303, 1249, 1174, 1150, 1111, 1035, 999, 939, 910, 822, 742, 704, 613, 505 cm^{-1}; MS (EI): m/z (%): 957 (2), 956 (3) $[M]^+$, 837 (5), 836 (12), 835 (15), 241 (2), 122 (15), 121 (100); elemental analysis calcd (%) for $C_{61}H_{68}O_8Si$ (957.29): C 76.54, H 7.16; found C 76.64, H 7.10.

***tert*-Butyl-[6′-hex-4-ynyl-2′-methoxy-2,6,4′-tris-(4-methoxybenzyloxy)-biphenyl-4-ylmethoxy]-diphenylsilane (26c; R = PMB, *n* = 2, X = C≡CCH$_3$)**: Prepared as described above from thiocarbonate **25c** (621 mg, 0.568 mmol). Colorless oil (444 mg, 83%). ^{1}H NMR (300.1 MHz, CD_2Cl_2): $\delta = 7.71$ (m, 4H), 7.49–7.38 (m, 8H), 7.12 (AA′XX′, 4H), 6.94 (AA′XX′, 2H), 6.81 (AA′XX′, 4H), 6.68 (s, 2H), 6.56 (d, $J = 2.3$ Hz, 1H), 6.50 (d, $J = 2.3$ Hz, 1H), 5.01 (s, 2H), 4.91 (s, 4H), 4.77 (s, 2H), 3.83 (s, 3H), 3.76 (s, 6H), 3.69 (s, 3H), 2.42 ("t", $J = 7.7$ Hz, 2H), 1.94 (m, 2H), 1.67 (t, $J = 2.4$ Hz, 3H), 1.56 (m, 2H), 1.11 (s, 9H); ^{13}C NMR (75.5 MHz, CD_2Cl_2): $\delta = 159.9$, 159.5, 159.4, 158.8, 157.8, 143.6, 142.2, 136.0, 133.8, 130.1, 130.0, 129.8, 129.8, 128.7, 128.1, 116.3, 114.5, 114.2, 114.1, 106.5, 103.9, 97.1, 79.3, 75.7, 70.2, 70.1, 66.1, 55.9, 55.6, 55.5, 33.3, 30.0, 27.0, 19.5, 18.7, 3.5; IR: $\nu = 3070$, 3045, 2997, 2954, 2932, 2857, 1602, 1580, 1514, 1461, 1428, 1372, 1323, 1303, 1249, 1174, 1150, 1105, 1035, 1000, 940, 824, 742, 704, 611, 506 cm^{-1}; MS (EI): m/z (%): 941 (1), 940 (2) $[M]^+$, 820 (2), 819 (2), 818 (3), 699 (<1), 241 (<1), 199 (<1), 122 (9), 121 (100), 77 (<1); elemental analysis calcd (%) for $C_{60}H_{64}O_8Si$ (941.25): C 76.56, H 6.85; found C 76.63, H 6.96.

***tert*-Butyl-[6′-methoxy-2,6,4′-tris-(4-methoxybenzyloxy)-2′-oct-6-ynyl-biphenyl-4-ylmethoxy]-diphenylsilane (26d; R = PMB, *n* = 4, X = C≡CCH$_3$)**: Prepared as described above from thiocarbonate **25d** (995 mg, 0.887 mmol). Colorless oil (650 mg, 76%). ^{1}H NMR (300.1 MHz, CD_2Cl_2): $\delta = 7.74–7.70$ (m, 4H), 7.50–7.39 (m, 8H), 7.13 (AA′XX′, 4H), 6.95 (AA′XX′, 2H), 6.82 (AA′XX′, 4H), 6.69 (s, 2H), 6.56 (d, $J = 2.3$ Hz, 1H), 6.50 (d, $J = 2.3$ Hz, 1H), 5.03 (s, 2H), 4.92 (s, 4H), 4.78 (s, 2H), 3.83 (s, 3H), 3.77 (s, 6H), 3.71 (s, 3H), 2.34 ("t", $J = 7.7$ Hz, 2H), 1.96 (m, 2H), 1.71 (t, $J = 2.6$ Hz, 3H), 1.45–1.18 (m, 6H), 1.12 (s, 9H); ^{13}C NMR (75.5 MHz, CD_2Cl_2): $\delta = 159.9$, 159.5, 159.4, 158.7, 157.8, 144.4, 142.2, 136.0, 133.9, 130.1, 130.0, 129.8, 128.6, 128.1, 116.2, 114.7, 114.2, 114.1, 106.4, 104.0, 96.9, 79.6, 75.4, 70.2, 70.1, 66.1, 55.9, 55.6, 55.5, 34.0, 30.1, 29.3, 29.0, 27.1, 19.6, 18.8, 3.5; IR: $\nu = 3070$, 3046, 2998, 2931, 2835, 1612, 1602, 1580, 1514, 1462, 1428, 1418, 1371, 1323, 1302, 1249, 1174, 1150, 1102, 1035, 999, 938, 822, 742, 703, 612, 505 cm^{-1}; MS (EI): m/z (%): 969 (<1), 968 (1) $[M]^+$, 849 (3), 848 (7), 847 (10), 122 (9), 121 (100); elemental analysis calcd (%) for $C_{62}H_{68}O_8Si$ (969.30): C 76.83, H 7.07; found C 76.72, H 7.11.

[2′-Methoxy-2,6,4′-tris-(4-methoxybenzyloxy)-6′-pent-4-enyl-biphenyl-4-yl]-methanol (27a; R = PMB, *n* = 2, X = CH=CH$_2$): TBAF·3H$_2$O (22.9 mg, 0.073 mmol) was added to a solution of compound **26a** (45 mg, 0.048 mmol) in THF (5 mL) and the mixture was stirred for 2 h. The solvent was evaporated and the residue was purified by flash chromatography on silica (hexanes/ethyl acetate 1:1) affording alcohol **27a** as a colorless oil (33 mg, 99%). ^{1}H NMR (300.1 MHz, CD_2Cl_2): $\delta = 7.41$ (AA′XX′, 2H), 7.13 (AA′XX′, 4H), 6.94 (AA′XX′, 2H), 6.82 (AA′XX′, 4H), 6.71 (s, 2H), 6.55 (d, $J = 2.3$ Hz, 1H), 6.48 (d, $J = 2.3$ Hz, 1H), 5.64 (ddt, $J = 17.0$, 10.4, 6.6 Hz, 1H), 5.02 (s, 2H), 4.94 (s, 4H), 4.90–4.82 (m, 2H), 4.66 (brs, 2H), 3.82 (s, 3H), 3.77 (s, 6H), 3.67 (s, 3H), 2.34 (t, $J = 7.8$ Hz, 2H), 1.92–1.84 (m, 3H), 1.48 (m, 2H); ^{13}C NMR (75.5 MHz, CD_2Cl_2): $\delta = 159.9$, 159.5, 159.5, 158.7, 158.0, 144.1, 142.4, 139.3, 129.9, 129.8, 128.8, 128.8, 116.0, 115.3, 114.3, 114.2, 114.0, 106.5, 104.7, 97.0, 70.3, 70.1, 65.7, 55.9, 55.6, 55.6, 33.8, 33.7, 29.8; IR: $\nu = 3427$, 3072, 3037, 2997, 2933, 2865, 2835, 1638, 1612, 1602, 1580, 1515, 1461, 1430, 1418, 1376, 1322, 1303, 1249, 1175, 1150, 1103, 1033, 1000, 913, 822, 774, 705, 626, 514 cm^{-1}; MS (EI): m/z (%): 691 (2), 690 (4) $[M]^+$, 571 (2), 570 (6), 569 (9), 450 (1), 449 (2), 241 (1), 156 (1), 122 (15), 121 (100), 91 (1), 78 (1), 77 (2); HR-MS (ESI-pos) ($C_{43}H_{46}O_8$+Na): calcd 713.3090; found 713.3084; elemental analysis calcd (%) for $C_{43}H_{46}O_8$ (690.83): C 74.76, H 6.71; found C 74.80, H 6.65.

[6′-Hept-6-enyl-2′-methoxy-2,6,4′-tris-(4-methoxybenzyloxy)-biphenyl-4-yl]-methanol (27b; R = PMB, *n* = 4, X = CH=CH$_2$): Prepared as described above from compound **26b** (210 mg, 0.219 mmol). Colorless oil (150 mg, 95%). ^{1}H NMR (300.1 MHz, CD_2Cl_2): $\delta = 7.41$ (AA′XX′, 2H), 7.14 (AA′XX′, 4H), 6.94 (AA′XX′, 2H), 6.83 (AA′XX′, 4H), 6.70 (s, 2H), 6.55 (d, $J = 2.3$ Hz, 1H), 6.48 (d, $J = 2.3$ Hz, 1H), 5.73 (ddt, $J = 17.0$, 10.2, 6.7 Hz, 1H), 5.02 (s, 2H), 4.95 (s, 4H), 4.95–4.85 (m, 2H), 4.66 (brs, 2H), 3.82 ("s", 3H), 3.77 ("s", 6H), 3.67 ("s", 3H), 2.32 (t, $J = 7.8$ Hz, 2H), 1.87 (m, 3H), 1.40 (m, 2H), 1.25–1.12 (m, 4H); ^{13}C NMR (75.5 MHz, CD_2Cl_2): $\delta = 159.9$, 159.5, 159.5, 158.7, 158.0, 144.5, 142.4, 139.7, 130.0, 129.8, 128.7, 116.0, 115.4, 114.2, 114.1, 114.0, 106.4, 104.8, 96.9, 70.3, 70.1, 65.7, 55.9, 55.6, 55.6, 34.1, 33.9, 30.3, 29.2, 29.0; IR: $\nu = 3427$, 3071, 2997, 2931, 2855, 2836, 1639, 1612, 1602, 1580, 1514, 1461, 1430, 1418, 1377, 1322, 1303, 1248, 1174, 1150, 1102, 1034, 1000, 966, 909, 823, 705, 626, 512 cm^{-1}; MS (EI): m/z (%): 719 (2), 718 (3) $[M]^+$, 689 (1), 688 (2), 599 (2), 598 (4), 597 (6), 568 (1), 567 (2), 241 (2), 123 (1), 122 (18), 121 (100), 91 (1), 77 (2); elemental analysis calcd (%) for $C_{45}H_{50}O_8$ (718.89): C 75.18, H 7.01; found C 75.25, H 7.11.

[6′-Hex-4-ynyl-2′-methoxy-2,6,4′-tris-(4-methoxybenzyloxy)-biphenyl-4-yl]-methanol (27c; R = PMB, *n* = 2, X = C≡CCH$_3$): Prepared as described above from compound **26c** (78 mg, 0.083 mmol). Colorless oil (54 mg, 99%). ^{1}H NMR (300.1 MHz, CD_2Cl_2): $\delta = 7.40$ (AA′XX′, 2H), 7.14 (AA′XX′, 4H), 6.93 (AA′XX′, 2H), 6.82 (AA′XX′, 4H), 6.71 (s, 2H), 6.55 (d, $J = 2.3$ Hz, 1H), 6.47 (d, $J = 2.3$ Hz, 1H), 5.00 (s, 2H), 4.94 (s, 4H), 4.66 (d, $J = 5.7$ Hz, 2H), 3.82 (s, 3H), 3.77 (s, 6H), 3.66 (s, 3H), 2.40 ("t", $J = 7.7$ Hz, 2H), 1.92 (m, 2H), 1.81 (t, $J = 5.9$ Hz, 1H), 1.68 (t, $J = 2.5$ Hz, 3H), 1.54 (m, 2H); ^{13}C NMR (75.5 MHz, CD_2Cl_2): $\delta = 159.9$, 159.6, 159.5, 158.7, 158.0, 143.5, 142.4, 129.9, 129.8, 129.7, 128.8, 116.1, 115.2, 114.2, 114.0, 106.5, 104.7, 97.1, 79.3, 75.7, 70.3, 70.1, 65.7, 55.9, 55.6, 55.6, 33.3, 30.0, 18.7, 3.5; IR: $\nu = 3439$, 3063, 3035, 2997, 2933, 2864, 2835, 1612, 1603, 1584, 1514, 1461, 1431, 1417, 1383, 1323, 1303, 1248, 1174, 1149, 1102, 1032, 999, 821, 773 cm^{-1}; MS (EI): m/z (%): 703 (<1), 702 (2) $[M]^+$, 582 (1), 581 (2), 461 (<1), 122 (9), 121 (100), 91 (1), 77 (<1); HR-MS (ESI-pos) ($C_{44}H_{46}O_8$+Na): calcd 725.3090; found 725.3092; elemental analysis calcd (%) for $C_{44}H_{46}O_8$ (702.84): C 75.19, H 6.60; found C 75.26, H 6.55.

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[2′-Methoxy-2,6,4′-tris-(4-methoxybenzyloxy)-6′-oct-6-ynyl-biphenyl-4-yl]-methanol (27d; R = PMB, n = 4, X = C≡CCH$_3$): Prepared as described above from compound **26d** (620 mg, 0.64 mmol). Colorless oil (450 mg, 96%). ^{1}H NMR (300.1 MHz, CD_2Cl_2): δ = 7.44 (AA′XX′, 2H), 7.18 (AA′XX′, 4H), 6.98 (AA′XX′, 2H), 6.86 (AA′XX′, 4H), 6.75 (s, 2H), 6.60 (d, 1H, J = 2.4 Hz), 6.52 (d, J = 2.4 Hz, 1H), 5.05 (s, 2H), 4.98 (s, 4H), 4.68 (br s, 2H), 3.84 (s, 3H), 3.80 (s, 6H), 3.70 (s, 3H), 2.37 ("t", J = 7.8 Hz, 2H), 2.15 (m, 1H), 1.95 (m, 2H), 1.77 (t, J = 2.5 Hz, 3H), 1.48–1.20 (m, 6H); ^{13}C NMR (75.5 MHz, CD_2Cl_2): δ = 159.9, 159.5, 159.5, 158.7, 157.9, 144.3, 142.6, 130.0, 129.8, 128.7, 116.0, 115.3, 114.2, 114.0, 106.5, 104.8, 96.9, 79.7, 75.5, 70.3, 70.0, 65.7, 55.9, 55.6, 55.5, 34.0, 30.0, 29.1, 28.9, 18.7, 3.5; IR: ν = 3435, 3071, 2998, 2932, 2857, 2835, 1612, 1602, 1580, 1515, 1461, 1430, 1418, 1376, 1322, 1302, 1248, 1175, 1150, 1101, 1065, 1033, 1000, 972, 822, 769, 624, 511 cm^{-1}; MS (EI): m/z (%): 731 (1), 730 (2) $[M]^+$, 610 (2), 609 (5), 314 (<1), 294 (2), 122 (11), 121 (100); HR-MS (CI, isobutane) ($C_{46}H_{50}O_8$+H): calcd 731.3584; found 731.3582; elemental analysis calcd (%) for $C_{46}H_{50}O_8$ (730.90): C 75.59, H 6.90; found C 75.66, H 7.06.

4′-Bromomethyl-2-methoxy-4,2′,6′-tris-(4-methoxybenzyloxy)-6-pent-4-enyl-biphenyl (28a; R = PMB, n = 2, X = CH=CH$_2$): A solution of alcohol **27a** (20 mg, 0.029 mmol) and triethylamine (4.4 mg, 0.043 mmol) in CH_2Cl_2 (10 mL) at 0 °C was treated with methanesulfonic anhydride (7.6 mg, 0.043 mmol). The resulting mixture was stirred at that temperature for 30 min prior to quenching with aqueous saturated $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2, the combined organic phases were dried (Na_2SO_4) and the solvent was evaporated. LiBr (25.1 mg, 0.29 mmol) was added to a solution of the residue in THF (10 mL) and the resulting mixture was stirred at 60 °C for 2 h. The precipitate was filtered off, the filtrate was diluted with water, the aqueous phase was extracted with diethyl ether, the combined organic layers were dried (Na_2SO_4), the solvent was evaporated and the residue was purified by flash chromatography on silica (hexanes/ethyl acetate 3:1) to deliver bromide **28a** as a colorless oil (16 mg, 73% over both steps). ^{1}H NMR (300.1 MHz, CD_2Cl_2): δ = 7.40 (AA′XX′, 2H), 7.13 (AA′XX′, 4H), 6.93 (AA′XX′, 2H), 6.82 (AA′XX′, 4H), 6.74 (s, 2H), 6.53 (d, J = 2.4 Hz, 1H), 6.47 (d, J = 2.3 Hz, 1H), 5.59 (m, 1H), 5.00 (s, 2H), 4.93 (s, 4H), 4.89–4.80 (m, 2H), 4.52 (s, 2H), 3.82 (s, 3H), 3.77 (s, 6H), 3.67 (s, 3H), 2.31 (t, J = 7.8 Hz, 2H), 1.87 (m, 2H), 1.46 (tt, 2H, J = 9.5, 7.5 Hz); ^{13}C NMR (75.5 MHz, CD_2Cl_2): δ = 159.9, 159.6, 158.7, 157.9, 144.1, 139.2, 138.6, 129.8, 129.7, 129.6, 128.8, 116.7, 115.5, 114.4, 114.2, 114.1, 107.2, 106.5, 97.0, 70.4, 70.1, 55.9, 55.6, 55.6, 34.9, 33.7, 33.6, 29.8; IR: ν = 3071, 3034, 2997, 2931, 2864, 2834, 1638, 1613, 1601, 1577, 1514, 1461, 1430, 1418, 1377, 1324, 1303, 1248, 1174, 1151, 1100, 1033, 999, 911, 822, 654, 635, 513 cm^{-1}; MS (ESI-pos): 775 $[M+Na]^+$, 753 $[M+H]^+$; elemental analysis calcd (%) for $C_{43}H_{45}BrO_7$ (753.73): C 68.52, H 6.02; found C 68.58, H 6.12.

4′-Bromomethyl-6-hept-6-enyl-2-methoxy-4,2′,6′-tris-(4-methoxybenzyloxy)-biphenyl (28b; R = PMB, n = 4, X = CH=CH$_2$): Prepared as described above from alcohol **27b** (140 mg, 0.195 mmol). Colorless oil (117 mg, 77%). ^{1}H NMR (300.1 MHz, CD_2Cl_2): δ = 7.43 (AA′XX′, 2H), 7.16 (AA′XX′, 4H), 6.96 (AA′XX′, 2H), 6.85 (AA′XX′, 4H), 6.77 (s, 2H), 6.57 (d, J = 2.3 Hz, 1H), 6.50 (d, J = 2.2 Hz, 1H), 5.76 (ddt, J = 17.0, 10.2, 6.7 Hz, 1H), 5.03 (s, 2H), 4.96 (s, 4H), 4.93–4.87 (m, 2H), 4.54 (s, 2H), 3.83 (s, 3H), 3.79 (s, 6H), 3.70 (s, 3H), 2.33 (t, J = 7.8 Hz, 2H), 1.91 (m, 2H), 1.41 (m, 2H), 1.27–1.14 (m, 4H); ^{13}C NMR (75.5 MHz, CD_2Cl_2): δ = 159.9, 159.6, 158.6, 157.9, 144.4, 139.6, 138.5, 129.8, 129.8, 129.7, 128.8, 116.8, 115.5, 114.2, 114.1, 114.1, 107.2, 106.5, 96.9, 70.4, 70.0, 55.9, 55.6, 55.6, 34.9, 34.1, 33.9, 30.4, 29.2, 29.0; IR: ν = 3071, 3035, 2998, 2931, 2856, 2836, 1639, 1613, 1576, 1514, 1457, 1419, 1377, 1325, 1303, 1254, 1175, 1151, 1098, 1033, 1000, 955, 912, 825, 773, 757, 706, 675, 655, 635, 594, 517 cm^{-1}; MS (ESI-pos): 819 $[M+K]^+$, 803 $[M+Na]^+$, 781 $[M+H]^+$; elemental analysis calcd (%) for $C_{45}H_{49}BrO_7$ (781.78): C 69.14, H 6.32; found C 69.06, H 6.25.

4′-Bromomethyl-6-hex-4-ynyl-2-methoxy-4,2′,6′-tris-(4-methoxybenzyloxy)-biphenyl (28c; R = PMB, n = 2, X = C≡CCH$_3$): Prepared as described above from alcohol **27c** (330 mg, 0.47 mmol). Colorless oil (274 mg, 76%). ^{1}H NMR (300.1 MHz, CD_2Cl_2): δ = 7.42 (AA′XX′, 2H), 7.17 (AA′XX′, 4H), 6.96 (AA′XX′, 2H), 6.85 (AA′XX′, 4H), 6.77 (s, 2H), 6.57 (d, J = 2.3 Hz, 1H), 6.50 (d, J = 2.3 Hz, 1H), 5.03 (s, 2H), 4.96 (s, 4H), 4.54 (s, 2H), 3.83 (s, 3H), 3.79 (s, 6H), 3.69 (s, 3H), 2.43 ("t", J = 7.7 Hz, 2H), 1.96 (m, 2H), 1.72 (t, J = 2.5 Hz, 3H), 1.57 (m, 2H); ^{13}C NMR (75.5 MHz, CD_2Cl_2): δ = 159.9, 159.6, 159.6, 158.7, 158.0, 143.4, 138.5, 129.8, 129.7, 129.6, 128.9, 116.6, 115.6, 114.2, 114.1, 107.1, 106.5, 97.1, 79.3, 75.7, 70.5, 70.1, 55.9, 55.6, 55.6, 34.8, 33.2, 30.0, 18.6, 3.6; IR: ν = 3067, 3034, 2999, 2958, 2929, 2864, 2835, 1613, 1577, 1515, 1458, 1419, 1379, 1326, 1304, 1250, 1173, 1153, 1101, 1034, 999, 818, 772, 704, 655, 634, 505 cm^{-1}; MS (ESI-pos): 787 $[M+Na]^+$; elemental analysis calcd (%) for $C_{44}H_{45}BrO_7$ (765.74): C 69.02, H 5.92; found C 69.11, H 5.84.

4′-Bromomethyl-2-methoxy-4,2′,6′-tris-(4-methoxybenzyloxy)-6-oct-6-ynyl-biphenyl (28d; R = PMB, n = 4, X = C≡CCH$_3$): Prepared as described above from alcohol **27d** (438 mg, 0.599 mmol). Colorless oil (385 mg, 81%). ^{1}H NMR (300.1 MHz, CD_2Cl_2): δ = 7.41 (AA′XX′, 2H), 7.15 (AA′XX′, 4H), 6.95 (AA′XX′, 2H), 6.84 (AA′XX′, 4H), 6.75 (s, 2H), 6.55 (d, J = 2.3 Hz, 1H), 6.48 (d, J = 2.3 Hz, 1H), 5.02 (s, 2H), 4.95 (s, 4H), 4.53 (s, 2H), 3.83 (s, 3H), 3.78 (s, 6H), 3.69 (s, 3H), 2.31 ("t", J = 7.8 Hz, 2H), 1.94 (m, 2H), 1.74 (t, J = 2.5 Hz, 3H), 1.44–1.14 (m, 6H); ^{13}C NMR (75.5 MHz, CD_2Cl_2): δ = 159.9, 159.6, 158.6, 157.9, 144.3, 138.5, 129.8, 129.7, 129.7, 128.8, 116.8, 115.5, 114.2, 114.1, 107.2, 106.4, 96.9, 79.6, 75.4, 70.4, 70.1, 55.9, 55.6, 55.6, 34.9, 34.0, 30.0, 29.2, 28.9, 18.8, 3.5; IR: ν = 3064, 3035, 2999, 2934, 2858, 2836, 1612, 1600, 1578, 1514, 1461, 1431, 1419, 1376, 1324, 1303, 1248, 1175, 1152, 1100, 1034, 1000, 954, 824, 736, 705, 655, 635, 517 cm^{-1}; MS (ESI-pos): 815 $[M+Na]^+$; elemental analysis calcd (%) for $C_{46}H_{49}BrO_7$ (793.80): C 69.60, H 6.22; found C 69.54, H 6.18.

2-Methoxy-4,2′,6′-tris-(4-methoxybenzyloxy)-6-pent-4-enyl-4′-undec-10-enyl-biphenyl (29; R = PMB): A solution of 9-decenylmagnesium bromide (0.3 M in THF, 1.93 mL, 0.578 mmol) was added dropwise to a solution of bromide **28a** (218 mg, 0.289 mmol) and Li_2CuCl_4 (0.1 M in THF, 289 μL, 0.029 mmol) in THF (12 mL) at −20 °C. The color of the mixture gradually changed from red to black. After stirring for 1 h at −20 °C, the reaction was quenched with aq. sat. NH_4Cl, the aqueous layer was extracted with diethyl ether, the combined organic phases were dried (Na_2SO_4) and evaporated, and the residue was purified by flash chromatography on neutral alumina (hexanes/ethyl acetate 8:1 → 6:1) to give diene **29** as a colorless oil (152 mg, 65%). ^{1}H NMR (300.1 MHz, CD_2Cl_2): δ = 7.40 (AA′XX′, 2H), 7.12 (AA′XX′, 4H), 6.93 (AA′XX′, 2H), 6.81 (AA′XX′, 4H), 6.52 (m, 3H), 6.46 (d, J = 2.2 Hz, 1H), 5.83 (ddt, J = 17.0, 10.2, 6.7 Hz, 1H), 5.59 (ddt, J = 17.0, 10.4, 6.5 Hz, 1H), 5.30–4.80 (m, 4H), 5.00 (s, 2H), 4.90 (s, 4H), 3.82 (s, 3H), 3.77 (s, 6H), 3.67 (s, 3H), 2.60 (t, J = 7.7 Hz, 2H), 2.31 (t, J = 7.8 Hz, 2H), 2.05 (m, 2H), 1.86 (m, 2H), 1.64 (m, 2H), 1.50–1.25 (m, 14H); ^{13}C NMR (75.5 MHz, CD_2Cl_2): δ = 159.9, 159.5, 159.4, 158.8, 157.7, 144.3, 144.1, 139.7, 139.3, 130.2, 129.8, 128.8, 116.3, 114.2, 114.2, 114.0, 113.6, 106.7, 106.5, 97.0, 70.3, 70.0, 55.9, 55.6, 55.6, 36.9, 34.2, 33.8, 33.7, 31.7, 29.9, 29.9, 29.9, 29.8, 29.5, 29.4; IR: ν = 3075, 2997, 2925, 2854, 1639, 1612, 1601, 1585, 1576, 1515, 1462, 1439, 1418, 1374, 1321, 1302, 1248, 1192, 1174, 1152, 1104, 1036, 1000, 909, 823, 627, 517 cm^{-1}; MS (EI): m/z (%): 813 (2), 812 (3) $[M]^+$, 693 (4), 692 (8), 691 (9), 572 (2), 571 (3), 122 (14), 121 (100); elemental analysis calcd (%) for $C_{53}H_{64}O_7$ (813.09): C 78.29, H 7.93; found C 78.15, H 8.06.

6-Hept-6-enyl-2-methoxy-4,2′,6′-tris-(4-methoxybenzyloxy)-4′-non-8-enyl-biphenyl (30; R = PMB): Prepared as described above from bromide **28b** (98 mg, 0.125 mmol) and 7-octenylmagnesium bromide (0.3 M in THF, 627 μL, 0.251 mmol). Colorless oil (67 mg, 66%). ^{1}H NMR (300.1 MHz, CD_2Cl_2): δ = 7.42 (AA′XX′, 2H), 7.14 (AA′XX′, 4H), 6.95 (AA′XX′, 2H), 6.83 (AA′XX′, 4H), 6.55 (d, J = 2.5 Hz, 1H), 6.54 (s, 2H), 6.48 (d, J = 2.3 Hz, 1H), 5.86 (ddt, J = 17.0, 10.2, 6.6 Hz, 1H), 5.75 (ddt, J = 17.0, 10.2, 6.7 Hz, 1H), 5.07–4.86 (m, 4H), 5.03 (s, 2H), 4.93 (s, 4H), 3.83 (s, 3H), 3.78 (s, 6H), 3.69 (s, 3H), 2.62 (t, J = 7.7 Hz, 2H), 2.32 (t, J = 7.8 Hz, 2H), 2.09 (m, 2H), 1.90 (m, 2H), 1.65 (m, 2H), 1.47–1.10 (m, 14H); ^{13}C NMR (75.5 MHz, CD_2Cl_2): δ = 159.9, 159.5, 159.4, 158.8, 157.7, 144.6, 144.0, 139.7, 139.7, 130.2, 129.9, 129.8, 128.8, 116.3, 114.2, 114.1, 114.0, 113.7, 106.7, 106.4, 96.9, 70.3, 70.0, 55.9, 55.6, 55.6, 36.9, 34.2, 34.2, 33.9, 31.6, 30.4, 29.8, 29.5, 29.4, 29.3, 29.0; IR: ν = 3073, 3035, 2997, 2927, 2854, 1639, 1612, 1601, 1585, 1576, 1514, 1462, 1418, 1374, 1321, 1302, 1248, 1174, 1151, 1103, 1036, 1000, 910, 823, 756, 627, 512 cm^{-1}; MS (EI): m/z (%): 813 (2), 812 (4) $[M]^+$, 693 (2), 692 (6), 691 (12), 122 (9), 121 (100); HR-MS (CI, isobutane) ($C_{53}H_{64}O_7$+H): calcd 813.4730; found 813.4730; elemental analysis calcd (%) for $C_{53}H_{64}O_7$ (813.09): C 78.29, H 7.93; found C 78.22, H 7.86.

4′-Dodec-10-ynyl-6-hex-4-ynyl-2-methoxy-4,2′,6′-tris-(4-methoxybenzyloxy)-biphenyl (31; R = PMB): Prepared as described above from bromide **28c** (265 mg, 0.346 mmol) and 9-undecynylmagnesium bromide (0.3 M in THF, 3.46 mL, 1.038 mmol). Colorless oil (232 mg, 80%). ^{1}H NMR (300.1 MHz, CD_2Cl_2): δ = 7.41 (AA′XX′, 2H), 7.15 (AA′XX′, 4H), 6.95 (AA′XX′, 2H), 6.84 (AA′XX′, 4H), 6.56 (d, 1H), 6.55 (s, 2H), 6.48 (d, J = 2.3 Hz, 1H), 5.02 (s, 2H), 4.93 (s, 4H), 3.83 (s, 3H), 3.78 (s, 6H), 3.68 (s, 3H), 2.62 (t, J = 7.8 Hz, 2H,), 2.41 (t, J = 7.7 Hz, 2H), 2.13 (m, 2H), 1.93 (m, 2H), 1.77 (t, J = 2.6 Hz, 3H), 1.70 (t, J = 2.5 Hz, 3H), 1.70–1.29 (m, 16H);

^{13}C NMR (75.5 MHz, CD_2Cl_2): δ = 159.9, 159.5, 159.4, 158.8, 157.7, 144.1, 143.6, 130.2, 129.8, 128.8, 116.4, 114.2, 114.0, 113.5, 106.7, 106.5, 97.1, 79.6, 79.4, 75.7, 75.5, 70.3, 70.1, 55.9, 55.6, 55.6, 36.9, 33.3, 31.6, 30.0, 29.9, 29.9, 29.6, 29.6, 29.3, 19.0, 18.7, 3.5, 3.5; IR: ν = 3062, 3035, 2994, 2925, 2854, 2835, 1606, 1577, 1515, 1462, 1436, 1420, 1384, 1363, 1344, 1322, 1302, 1248, 1177, 1166, 1148, 1104, 1086, 1061, 1037, 993, 960, 922, 857, 830, 814, 767, 746, 719, 649, 627, 608, 565, 519, 504 cm^{-1}; MS (EI): *m*/*z* (%): 836 (3) $[M]^+$, 835 (4), 717 (2), 716 (6), 715 (11), 566 (1), 122 (9), 121 (100); HR-MS (CI, isobutane) ($C_{55}H_{64}O_7$+H): calcd 837.4730; found 837.4724; elemental analysis calcd (%) for $C_{55}H_{64}O_7$ (837.11): C 78.91, H 7.71; found C 79.08, H 7.80.

4′-Dec-8-ynyl-2-methoxy-4,2′,6′-tris-(4-methoxybenzyloxy)-6-oct-6-ynyl-biphenyl (32; R = PMB): Prepared as described above from bromide **28d** (260 mg, 0.328 mmol) and 7-nonynylmagnesium bromide (0.3 M in THF, 3.28 mL, 0.983 mmol). Colorless oil (200 mg, 73%). ^{1}H NMR (300.1 MHz, CD_2Cl_2): δ = 7.41 (AA′XX′, 2H), 7.14 (AA′XX′, 4H), 6.94 (AA′XX′, 2H), 6.83 (AA′XX′, 4H), 6.54 ("d", 1H), 6.54 (s, 2H), 6.47 (d, *J* = 2.3 Hz, 1H), 5.02 (s, 2H), 4.92 (s, 4H), 3.82 (s, 3H), 3.78 (s, 6H), 3.68 (s, 3H), 2.64 ("t", *J* = 7.7 Hz, 2H), 2.31 ("t", *J* = 7.7 Hz, 2H), 2.13 (m, 2H), 1.93 (m, 2H), 1.77 (t, *J* = 2.6 Hz, 3H), 1.73 (t, *J* = 2.5 Hz, 3H), 1.72–1.15 (m, 16H); ^{13}C NMR (75.5 MHz, CD_2Cl_2): δ = 159.9, 159.5, 159.4, 158.8, 157.7, 144.5, 144.0, 130.2, 129.8, 129.8, 128.8, 116.3, 114.2, 114.0, 113.6, 106.7, 106.4, 96.9, 79.6, 79.6, 75.5, 75.3, 70.3, 70.0, 55.9, 55.6, 55.5, 36.9, 34.0, 31.6, 30.0, 29.7, 29.6, 29.4, 29.2, 29.2, 29.0, 19.0, 18.8, 3.5; IR: ν = 3063, 3034, 2998, 2931, 2856, 2837, 1612, 1601, 1585, 1576, 1514, 1462, 1429, 1418, 1372, 1322, 1302, 1249, 1174, 1152, 1103, 1036, 1000, 824, 756, 736, 628, 515 cm^{-1}; MS (EI): *m*/*z* (%): 837 (3), 836 (4) $[M]^+$, 835 (4), 717 (3), 716 (11), 715 (22), 241 (1), 122 (18), 121 (100); HR-MS (CI, isobutane) ($C_{55}H_{64}O_7$+H): calcd 837.4730; found 837.4727; elemental analysis calcd (%) for $C_{55}H_{64}O_7$ (837.11): C 78.91, H 7.71; found C 79.07, H 7.82.

Ring closing olefin metathesis—Preparation of compound (*E*,*Z*)-35 (R = PMB)

Method A: A solution of diene **29** (65 mg, 0.08 mmol) and ruthenium carbene **33** (3.3 mg, 0.004 mmol, 5 mol%) in CH_2Cl_2 (35 mL) was refluxed for 4 h. The solvent was evaporated and the residue was purified by flash chromatography on silica (hexanes/ethyl acetate 6:1) to afford olefin **35** as a colorless oil (49 mg, 78%). The product consisted of a mixture of isomers (*E*:*Z* = 1.2:1).

Method B: A solution of diene **29** (150 mg, 0.184 mmol) and ruthenium indenylidene complex **34** (8.5 mg, 0.009 mmol, 5 mol%) in CH_2Cl_2 (60 mL) was refluxed for 1 h. Workup as described above delivered olefin **35** (110 mg, 76%) as a mixture of isomers (*E*:*Z* = 1:1.1). Colorless syrup. ^{1}H NMR (600.2 MHz, CD_2Cl_2): δ [*E*-isomer] = 7.40 (AA′XX′, 2H), 7.14 (AA′XX′, 4H), 6.94 (AA′XX′, 2H), 6.83 (AA′XX′, 4H), 6.54 (d, *J* = 2.4 Hz, 1H), 6.54 (s, 2H), 6.46 (d, 1H, *J* = 2.4 Hz), 5.24 (m, 1H), 5.04 (m, 1H), 5.01 (s, 2H), 4.93 (m, 4H), 3.82 (s, 3H), 3.78 (s, 6H), 3.67 (s, 3H), 2.63 (t, *J* = 6.8 Hz, 2H), 2.34 (m, 2H), 1.87 (m, 4H), 1.66 (m, 2H), 1.55–1.05 (m, 14H); δ [*Z*-isomer] = 7.40 (AA′XX′, 2H), 7.14 (AA′XX′, 4H), 6.94 (AA′XX′, 2H), 6.82 (AA′XX′, 4H), 6.55 (d, *J* = 2.4 Hz, 1H), 6.53 (s, 2H), 6.46 (d, *J* = 2.4 Hz, 1H), 5.35 (m, 1H), 5.27 (m, 1H), 5.01 (s, 2H), 4.90 (m, 4H), 3.82 (s, 3H), 3.78 (s, 6H), 3.67 (s, 3H), 2.65 (t, *J* = 6.2 Hz, 2H), 2.29 (m, 2H), 1.87 (m, 4H), 1.65 (m, 2H), 1.55–1.05 (m, 14H); ^{13}C NMR (150.9 MHz, CD_2Cl_2): δ [*E*-isomer] = 159.9, 159.5, 159.4, 158.8, 157.7, 144.6, 144.0, 130.6, 130.4, 130.2, 129.9, 129.8, 128.8, 116.4, 114.2, 114.0, 113.6, 106.9, 106.6, 96.9, 70.3, 70.1, 55.9, 55.6, 55.6, 36.3, 33.7, 32.5, 31.6, 30.7, 30.2, 27.9, 27.7, 27.4, 27.2, 27.1, 26.4; δ [*Z*-isomer] = 159.9, 159.5, 159.5, 158.8, 157.7, 144.7, 143.4, 130.2, 130.2, 130.1, 129.9, 129.8, 128.9, 116.4, 114.2, 114.0, 113.7, 107.2, 106.0, 96.9, 70.4, 70.1, 55.9, 55.6, 55.6, 36.3, 34.2, 31.5, 30.5, 29.1, 28.7, 28.4, 28.2, 28.0, 27.0, 26.9, 26.3; IR [*E*:*Z* = 1.2:1]: ν = 3068, 3035, 3001, 2926, 2853, 1613, 1603, 1585, 1514, 1460, 1442, 1417, 1383, 1320, 1303, 1248, 1173, 1151, 1100, 1033, 1000, 966, 821 cm^{-1}; [*Z*-isomer]: ν = 3064, 2999, 2927, 2854, 1612, 1602, 1585, 1576, 1514, 1460, 1442, 1418, 1371, 1338, 1320, 1302, 1248, 1174, 1151, 1103, 1034, 1000, 822, 755, 719, 629, 514 cm^{-1}; MS (EI): *m*/*z* (%): [*E*:*Z* = 1.2:1] 785 (2), 784 (3) $[M]^+$, 665 (1), 664 (4), 663 (7), 543 (2), 390 (1), 241 (<1), 122 (10), 121 (100), 91 (<1), 77 (<1); *m*/*z* (%) [*Z*-isomer]: 785 (1), 784 (2) $[M]^+$, 665 (1), 664 (3), 663 (4), 543 (<1), 421 (<1), 241 (<1), 122 (9), 121 (100), 91 (<1), 78 (1), 77 (1); MS (ESI-pos): 785 $[M+H]^+$; HR-MS (CI, isobutane) ($C_{51}H_{60}O_7$+H): calcd 785.4417; found 785.4415; elemental analysis calcd (%) for $C_{51}H_{60}O_7$ (785.03): C 78.03, H 7.70; found C 78.09, H 7.75.

Ring closing olefin metathesis—Preparation of compound (*E*,*Z*)-36 (R = PMB)

Method A: A solution of diene **30** (65 mg, 0.08 mmol) and ruthenium carbene **33** (3.3 mg, 0.004 mmol, 5 mol%) in CH_2Cl_2 (20 mL) was refluxed for 2 h. The solvent was evaporated and the residue was purified by flash chromatography on silica (hexanes/ethyl acetate 10:1 → 6:1) to afford olefin **36** as a pale yellow oil (46 mg, 0.059 mmol, 73%). The product consisted of a mixture of isomers (E:Z = 5.8:1).

Method B: A solution of diene **30** (80 mg, 0.098 mmol) and ruthenium indenylidene complex **34** (4.5 mg, 0.0049 mmol, 5 mol%) in CH_2Cl_2 (40 mL) was refluxed for 3 h. Workup as described above afforded olefin **36** (65 mg, 0.083 mmol, 84%) as mixture of isomers (*E*:*Z* = 6.9:1). ^{1}H NMR (600.2 MHz, CD_2Cl_2): δ [*E*-isomer] = 7.42 (AA′XX′, 2H), 7.15 (AA′XX′, 4H), 6.95 (AA′XX′, 2H), 6.83 (AA′XX′, 4H), 6.57 (d, *J* = 2.3 Hz, 1H), 6.50 (s, 2H), 6.47 (d, *J* = 2.3 Hz, 1H), 5.24 (m, 2H), 5.02 (s, 2H), 4.93 (s, 4H), 3.83 (s, 3H), 3.78 (s, 6H), 3.69 (s, 3H), 2.61 (t, *J* = 6.5 Hz, 2H), 2.22 (m, 2H), 1.96 (m, 2H), 1.91 (m, 2H), 1.59 (m, 2H), 1.39 (m, 2H), 1.35–1.05 (m, 12H); ^{1}H NMR (300.1 MHz, CD_2Cl_2): δ [*Z*-isomer] = 7.41 (AA′XX′, 2H), 7.14 (AA′XX′, 4H), 6.94 (AA′XX′, 2H), 6.82 (AA′XX′, 4H), 6.54 (d, *J* = 2.3 Hz, 1H), 6.49 (s, 2H), 6.47 (d, *J* = 2.4 Hz, 1H), 5.37–5.24 (m, 2H), 5.01 (s, 2H), 4.92 (s, 4H), 3.82 (s, 3H), 3.77 (s, 6H), 3.69 (s, 3H), 2.61 (t, *J* = 6.2 Hz, 2H), 2.24 (m, 2H), 2.05–1.87 (m, 4H), 1.63–1.02 (m, 16H); ^{13}C NMR (150.9 MHz, CD_2Cl_2): δ [*E*-isomer] = 159.9, 159.5, 159.5, 158.8, 157.5, 144.9, 143.7, 131.5, 130.6, 130.2, 129.9, 129.8, 128.8, 116.3, 114.2, 114.0, 113.8, 107.2, 106.2, 96.9, 70.3, 70.1, 55.9, 55.6, 55.5, 36.6, 34.5, 33.4, 31.8, 31.8, 31.3, 29.8, 29.6, 29.0, 28.5, 28.5, 27.8; ^{13}C NMR (75.5 MHz, CD_2Cl_2): δ [*Z*-isomer] = 159.9, 159.5, 159.5, 158.8, 157.5, 144.9, 143.7, 130.5, 130.2, 129.9, 129.9, 129.8, 128.8, 116.3, 114.2, 114.0, 113.7, 107.3, 106.5, 96.9, 70.3, 70.0, 55.9, 55.6, 55.5, 36.8, 35.0, 31.6, 30.9, 30.5, 29.8, 29.7, 29.1, 28.7, 28.6, 27.8, 26.8; IR [*E*:*Z* = 5.8:1]: ν = 3062, 2997, 2927, 2852, 1612, 1602, 1576, 1514, 1461, 1440, 1418, 1370, 1321, 1302, 1249, 1174, 1151, 1100, 1034, 1000, 967, 822, 753, 626, 511 cm^{-1}; [*Z*-isomer]: ν = 3064, 3001, 2926, 2851, 1618, 1600, 1585, 1573, 1515, 1462, 1419, 1375, 1338, 1301, 1249, 1191, 1157, 1113, 1031, 1000, 856, 824, 758, 708, 644, 632, 596, 517 cm^{-1}; MS (EI): *m*/*z* (%): [*E*:*Z* = 5.8:1] 785 (3), 784 (5) $[M]^+$, 664 (7), 663 (13), 543 (1), 241 (1), 122 (13), 121 (100); *m*/*z* (%) [*Z*-isomer]: 785 (3), 784 (5) $[M]^+$, 665 (2), 664 (5), 663 (9), 543 (1), 241 (1), 122 (9), 121 (100); MS (ESI-pos): 785 $[M+H]^+$; HR-MS (CI, isobutane) ($C_{51}H_{60}O_7$+H): calcd 785.4417; found 785.4414; [*Z*-isomer] ($C_{51}H_{60}O_7$+H): calcd 785.4417; found 785.4411; elemental analysis calcd (%) for $C_{51}H_{60}O_7$ (785.03): C 78.03, H 7.70; found C 78.11, H 7.79.

Ring closing alkyne metathesis—Preparation of compound 37 (R = PMB)

Method A: A solution of diyne **31** (63 mg, 0.075 mmol) and [(tBuO)$_3$W≡CCMe$_3$] (3.6 mg, 0.0075 mmol, 10 mol%) in toluene (40 mL) was stirred at 80 °C for 16 h. The solvent was evaporated and the residue was purified by flash chromatography on silica (hexanes/ethyl acetate 6:1 → 4:1) to afford alkyne **37** as a colorless solid (38 mg, 64%).

Method B: A solution of diyne **31** (200 mg, 0.239 mmol), $Mo(CO)_6$ (6.3 mg, 0.0239 mmol, 10 mol%) and 4-trifluoromethylphenol (38.7 mg, 0.239 mmol) in chlorobenzene (60 mL) was refluxed for 4 h while a gentle stream of Ar was bubbled through the solution. The solvent was evaporated and the residue was purified by flash chromatography on neutral alumina (hexanes/ethyl acetate 10:1 → 6:1) to deliver alkyne **37** (155 mg, 83%) as a colorless solid. M.p. 136–139 °C; ^{1}H NMR (300.1 MHz, CD_2Cl_2): δ = 7.39 (AA′XX′, 2H), 7.15 (AA′XX′, 4H), 6.93 (AA′XX′, 2H), 6.82 (AA′XX′, 4H), 6.55 (m, 2H), 6.49 (d, *J* = 2.4 Hz, 1H), 6.47 (d, *J* = 2.3 Hz, 1H), 4.99 (s, 2H), 4.92 (s, 4H), 3.82 (s, 3H), 3.77 (s, 6H), 3.67 (s, 3H), 2.64 (t, *J* = 6.4 Hz, 2H), 2.42 (m, 2H), 2.08–1.93 (m, 4H), 1.72–1.20 (m, 16H); ^{13}C NMR (75.5 MHz, CD_2Cl_2): δ = 159.9, 159.5, 159.4, 158.9, 157.7, 143.9, 143.7, 130.2, 129.8, 128.9, 116.5, 114.2, 114.0, 113.5, 107.0, 106.5, 97.0, 80.4, 80.3, 70.4, 70.1, 56.0, 55.6, 55.6, 36.2, 33.8, 30.4, 29.4, 28.2, 28.2, 28.0, 28.0, 27.4, 27.1, 19.1, 18.3; IR: ν = 3072, 3035, 2997, 2928, 2853, 1612, 1602, 1576, 1514, 1461, 1440, 1418, 1375, 1321, 1302, 1248, 1174, 1152, 1103, 1034, 1000, 941, 823, 768, 625, 516 cm^{-1}; MS (EI): *m*/*z* (%): 783 (3), 782 (4) $[M]^+$, 663 (2), 662 (6), 661 (9), 541 (2), 122 (9), 121 (100); HR-MS (CI, isobutane) ($C_{51}H_{58}O_7$+H): calcd 783.4261; found 783.4266; elemental analysis calcd (%) for $C_{51}H_{58}O_7$ (783.02): C 78.23, H 7.47; found C 78.18, H 7.46.

Method C: A SmithProcess vial (10 mL) containing a magnetic stir bar was charged with diyne **31** (20 mg, 0.024 mmol), 4-trifluoromethylphenol (3.9 mg, 0.024 mmol), $Mo(CO)_6$ (0.6 mg, 0.002 mol%) and chlorobenzene (2.5 mL). The vial was sealed and evacuated through a cannula, and the

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resulting mixture was heated to 150 °C in a microwave oven (SmithCreator reactor) for 5 min. Work-up as described above provided cycloalkyne **37** as a colorless solid (13 mg, 69 %). The analytical and spectroscopic data are identical with those compiled above.

Ring closing alkyne metathesis—Preparation of compound 38 (R = PMB)

Method A: A solution of diyne **32** (80 mg, 0.096 mmol) and [(*t*BuO)$_3$W≡CCMe$_3$] (4.5 mg, 0.0096 mmol, 10 mol %) in toluene (20 mL) was stirred at 80 °C for 16 h. The solvent was evaporated and the residue was purified by flash chromatography on silica (hexanes/ethyl acetate 10:1 → 6:1 → 4:1) to give cycloalkyne **38** as a colorless solid (46 mg, 61 %).

Method B: A solution of diyne **32** (45 mg, 0.054 mmol), Mo(CO)$_6$ (1.4 mg, 0.0054 mmol, 10 mol %) and 4-trifluoromethylphenol (8.7 mg, 0.054 mmol) in chlorobenzene (30 mL) was refluxed for 6 h while a gentle stream of Ar was bubbled through the solution. After evaporation of the solvent, the residue was purified by flash chromatography on neutral alumina (hexanes/ethyl acetate 10:1 → 6:1) to give alkyne **38** (32 mg, 76 %) as a colorless solid. M.p. 131 – 134 °C; ^{1}H NMR (300.1 MHz, CD$_2$Cl$_2$): δ = 7.41 (AA′XX′, 2H), 7.15 (AA′XX′, 4H), 6.94 (AA′XX′, 2H), 6.83 (AA′XX′, 4H), 6.56 (d, J = 2.3 Hz, 1H), 6.51 (m, 2H), 6.47 (d, J = 2.3 Hz, 1H), 5.01 (s, 2H), 4.94 (s, 4H), 3.82 (s, 3H), 3.78 (s, 6H), 3.69 (s, 3H), 2.63 (t, J = 6.4 Hz, 2H), 2.25 (m, 2H), 2.16 – 2.03 (m, 4H), 1.68 – 1.05 (m, 16H); ^{13}C NMR (75.5 MHz, CD$_2$Cl$_2$): δ = 159.9, 159.5, 158.8, 157.6, 144.8, 143.5, 130.2, 129.8, 129.8, 128.7, 116.3, 114.2, 114.0, 113.7, 107.1, 106.1, 96.9, 80.7, 80.3, 70.2, 70.0, 55.9, 55.6, 55.5, 36.2, 34.3, 31.6, 30.8, 29.8, 29.2, 28.8, 28.6, 28.4, 28.0, 19.3, 18.7; IR: ν = 3063, 3036, 3013, 2927, 2852, 1612, 1600, 1585, 1573, 1514, 1461, 1443, 1418, 1375, 1356, 1338, 1301, 1247, 1194, 1173, 1157, 1115, 1074, 1053, 1030, 1000, 954, 927, 855, 838, 824, 774, 759, 730, 710, 665, 646, 632, 604, 517 cm^{-1}; MS (EI): *m*/*z* (%): 783 (2), 782 (3) $[M]^+$, 663 (1), 662 (4), 661 (9), 241 (1), 122 (10), 121 (100), 77 (1); HR-MS (CI, isobutane) ($C_{51}H_{58}O_7$+H): calcd 783.4261; found 783.4259; elemental analysis calcd (%) for $C_{51}H_{58}O_7$ (783.02): C 78.23, H 7.47; found C 78.20, H 7.55.

Method C: A SmithProcess vial (10 mL) containing a magnetic stir bar was charged with diyne **32** (27 mg, 0.032 mmol), 4-trifluoromethylphenol (5.2 mg, 0.032 mmol), Mo(CO)$_6$ (0.9 mg, 0.003 mol %) and chlorobenzene (3 mL). The vial was sealed and evacuated through a cannula, and the resulting mixture was heated to 150 °C in a microwave oven (SmithCreator reactor) for 5 min. Work-up as described above provides cycloalkyne **38** as a colorless solid (18 mg, 71 %). The analytical and spectroscopic data are identical with those compiled above.

Preparation of (*Z*)-35 by Lindlar reduction of cycloalkyne 37: Commercially available Lindlar catalyst (20 mg) was added to a solution of alkyne **37** (105 mg, 0.134 mmol) and quinoline (20 μL) in ethyl acetate (15 mL). The flask was flushed with H_2 (two freeze/thaw cycles) and the reaction mixture was stirred under H_2 (1 atm) for 6 h. The mixture was filtered through a pad of Celite, the Celite was carefully washed with ethyl acetate, and the combined organic phases were washed with 2 N HCl and dried over Na_2SO_4. Evaporation of the solvent followed by flash chromatography of the residue on silica (hexanes/ethyl acetate 10:1 → 6:1) afforded olefin (*Z*)-**35** as a colorless oil (101 mg, 0.129 mmol, 96 %). The analytical and spectroscopic data were identical in all respects to those compiled above.

Preparation of (*Z*)-36 by Lindlar reduction of cycloalkyne 38: Commercially available Lindlar catalyst (40 mg) was added to a solution of alkyne **38** (145 mg, 0.185 mmol) in ethyl acetate/MeOH (10:1, 20 mL) and quinoline (10 μL). The flask was flushed with H_2 (two freeze/thaw cycles) and the mixture was stirred under H_2 (1 atm) for 2 h. Workup as described above followed by flash chromatography of the crude product on silica (hexanes/ethyl acetate 10:1 → 6:1) afforded olefin (*Z*)-**36** as a colorless oil (141 mg, 0.18 mmol, 97 %). The analytical and spectroscopic data were identical in all respects to those compiled above.

Turriane 3: Pd/C (10 % w/w, 40 mg) was added to a solution of olefin **36** (*E*:*Z* = 5.8:1; 40 mg, 0.051 mmol) in ethyl acetate/EtOH (1:1, 15 mL, containing two drops of water). The flask was flushed with H_2 (two freeze/thaw cycles) and the mixture was stirred under H_2 (1 atm) for 24 h. The catalyst was filtered off through a pad of Celite, the filtrate was evaporated and the residue was purified by flash chromatography on silica (hexanes/ethyl acetate 10:1 → 4:1 → 2:1) to give turriane **3** as a pale yellow oil (19 mg, 87 %). ^{1}H NMR (300.1 MHz, CD$_2$Cl$_2$): δ = 6.49 (d, J = 2.3 Hz, 1H), 6.42 (d, J = 2.3 Hz, 1H), 6.37 (s, 2H), 4.64 (br s, < 3H, OH), 3.71 (s, 3H), 2.57 (t, J = 6.7 Hz, 2H), 2.27 (m, 2H), 1.67 – 1.05 (m, 24H); ^{13}C NMR (75.5 MHz, CD$_2$Cl$_2$): δ = 160.3, 158.4, 154.2, 148.3, 145.1, 109.3, 109.0, 107.9, 107.7, 97.8, 56.2, 35.8, 33.9, 31.7, 30.8, 29.5, 28.7, 28.3, 28.0, 27.8, 27.8, 27.7, 27.4, 27.4, 27.2; IR: ν = 3409, 2926, 2854, 1635, 1605, 1584, 1523, 1459, 1435, 1334, 1259, 1157, 1105, 1082, 1033, 1000, 943, 838, 723, 636, 583, 520 cm^{-1}; MS (EI): *m*/*z* (%): 428 (5), 427 (29), 426 (100) $[M]^+$, 425 (4), 384 (4), 260 (10), 245 (4), 243 (6), 137 (2); HR-MS (EI) ($C_{27}H_{38}O_4$): calcd 426.2770; found 426.2771; elemental analysis calcd (%) for $C_{27}H_{38}O_4$ (426.60): C 76.02, H 8.98; found C 76.15, H 9.06.

Turriane 4

Method A: Olefin (*Z*)-**35** (80 mg, 0.102 mmol) was dissolved in 1,3,5-trimethoxybenzene (~ 2 g) at 70 °C. $SnCl_2$ (19.3 mg, 0.102 mmol) and TMSCl (129 μL, 1.019 mmol) were added and the resulting mixture was stirred at 70 °C for 30 min. Addition of water followed by extraction with ethyl acetate, drying of the combined organic layers (Na_2SO_4) and evaporation of the solvent provided a residue which was first subjected to flash chromatography on silica (hexanes/ethyl acetate 10:1 (750 mL) → 6:1 → 4:1 → 2:1) followed by further purification of the product containing fractions by preparative HPLC, thus providing turriane **4** as a colorless waxy solid (17 mg, 39 %).

Method B: $BF_3 \cdot OEt_2$ (118 μL, 0.943 mmol) was added via syringe over 2 min to a solution of olefin (*Z*)-**35** (37 mg, 0.047 mmol) in EtSH (2 mL) at − 20 °C and the resulting mixture was stirred at ambient temperature for 16 h. The reaction was quenched with aq. sat. $NaHCO_3$, the organic phase was extracted with ethyl acetate, the combined organic layers were dried (Na_2SO_4) and evaporated, and the residue was purified by flash chromatography on silica (hexanes/ethyl acetate 10:1 → 6:1 → 4:1 → 2:1) followed by further purification of the product containing fractions by preparative HPLC to afford turriane **4** as a colorless waxy solid (10 mg, 50 %). ^{1}H NMR (400.1 MHz, CD$_2$Cl$_2$): δ = 6.50 (d, J = 2.3 Hz, 1H), 6.43 (d, J = 2.3 Hz, 1H), 6.38 (s, 2H), 5.40 – 5.24 (m, 2H, OH), 4.63 (br s, 2H, OH), 3.71 (s, 3H), 2.60 (t, J = 6.2 Hz, 2H), 2.27 (m, 2H), 1.87 (m, 4H), 1.68 – 1.58 (m, 2H), 1.50 – 1.42 (m, 2H), 1.35 – 1.15 (m, 12H); ^{13}C NMR (100.6 MHz, CD$_2$Cl$_2$): δ = 160.3, 158.5, 154.2, 148.0, 144.8, 130.7, 129.5, 109.2, 109.1, 107.9, 97.9, 56.2, 35.7, 33.6, 31.8, 30.4, 29.1, 28.8, 28.5, 28.2, 28.0, 27.1, 27.1, 26.3; IR: ν = 3411, 3004, 2927, 2855, 1633, 1604, 1585, 1522, 1457, 1433, 1336, 1259, 1188, 1158, 1105, 1085, 1036, 1001, 841, 818, 721, 700, 637, 521 cm^{-1}; MS (EI): *m*/*z* (%): 426 (5), 425 (30), 424 (100) $[M]^+$, 423 (5), 273 (3), 272 (4), 271 (3), 261 (3), 260 (18), 259 (3), 257 (6), 245 (5), 244 (3), 243 (9), 241 (5), 229 (3), 227 (4), 213 (3), 163 (3), 137 (3), 81 (3), 69 (3), 67 (3), 55 (6), 41 (4); HR-MS (EI) ($C_{27}H_{36}O_4$): calcd 424.2614; found 424.2615; elemental analysis calcd (%) for $C_{27}H_{36}O_4$ (424.58): C 76.38, H 8.55; found C 76.31, H 8.46.

Turriane 5: $BF_3 \cdot OEt_2$ (176 μL, 1.401 mmol) was added through a syringe over 2 min to a solution of olefin (*Z*)-**36** (55 mg, 0.07 mmol) in EtSH (2 mL) at − 20 °C and the resulting mixture was stirred at ambient temperature for 16 h. The reaction was quenched with aq. sat. $NaHCO_3$, the aqueous layer was extracted with ethyl acetate, the combined organic phases were dried (Na_2SO_4) and evaporated, and the residue was purified by flash chromatography on silica (hexanes/ethyl acetate 10:1 → 6:1 → 4:1 → 2:1) followed by further purification of the product containing fractions by preparative HPLC, thus delivering turriane **5** (16 mg, 54 %) as a colorless waxy solid. ^{1}H NMR (400.1 MHz, CD$_2$Cl$_2$): δ = 6.48 (d, J = 2.3 Hz, 1H), 6.44 (d, J = 2.3 Hz, 1H), 6.35 (s, 2H), 5.30 (m, 2H), 5.15 (br s, 1H, OH), 4.62 (br s, 2H, OH), 3.73 (s, 3H), 2.57 (t, J = 6.3 Hz, 2H), 2.24 (m, 2H), 1.94 (m, 4H), 1.63 – 1.10 (m, 16H); ^{13}C NMR (100.6 MHz, CD$_2$Cl$_2$): δ = 160.4, 158.4, 154.1, 148.3, 145.1, 130.3, 130.1, 109.5, 109.0, 108.1, 108.0, 97.8, 56.2, 36.3, 34.5, 31.4, 31.2, 30.3, 29.8, 29.5, 29.2, 28.8, 28.7, 27.7, 26.9; IR: ν = 3495, 3323, 3001, 2926, 2853, 1628, 1615, 1587, 1538, 1485, 1462, 1425, 1364, 1337, 1317, 1270, 1213, 1185, 1152, 1092, 1067, 1025, 1003, 834, 818, 713, 667, 637 cm^{-1}; MS (EI): *m*/*z* (%): 426 (5), 425 (29), 424 (100) $[M]^+$, 423 (4), 272 (3), 260 (11), 257 (4), 245 (5), 243 (8), 241 (4), 227 (3), 137 (3), 67 (3), 55 (5), 41 (4); HR-MS (EI) ($C_{27}H_{36}O_4$): calcd 424.2614; found 424.2612; elemental analysis calcd (%) for $C_{27}H_{36}O_4$ (424.58): C 76.38, H 8.55; found C 76.46, H 8.40.

DNA cleavage assay

Representative procedure: A solution of purified scDNA (2 μL of a stock solution containg ca. 400 μg mL^{-1}) [ΦX174 RF1 DNA, purchased from MBI Fermentas GmbH, St. Leon-Rot, Germany; the EDTA contained in the commercial sample was removed according to the Qiaex II protocol for desalting and concentrating DNA by using a Qiaex II Gel Extraction Kit] was incubated at 37 °C for the time given in the Figure with the respective turriane derivative (2 μL of a 2 mM stock solution), Cu(OAc)$_2$ (2 μL of a

1 mM stock solution), *n*-butylamine (2 μL of a 20 mM stock solution), aq. NaCl (3 μL of a 0.5 mM stock solution) in water (complemented to give a total volume of 20 μL). The mixture was quenched with loading buffer (BioRad laboratories) and the DNA resolved by electrophoresis (Powerpac 300, BioRad) (85 V, 1 h) on a 0.8% agarose gel (containing ethidium bromide) in Tris/boronic acid buffer (BioRad). The bands detected by UV were analyzed and processed using the Bio Doc II software (Biometra).

Acknowledgement

Generous financial support by the Deutsche Forschungsgemeinschaft (Leibniz award to A.F.), the Fonds der Chemischen Industrie (Kekulé stipend to F.S.), and the European Union (Marie-Curie stipend to A.R.) is gratefully acknowledged. We thank Mrs. C. Wirtz and Dr. R. Mynott for their help with the interpretation of some of the NMR spectra and for the unequivalent assignment of the stereochemistry of the RCM products. Moreover, we are indebted to Mr. A. Deege and co-workers for preparative HPLC separations.

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Received: November 5, 2001 [F3655]