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Reactions of aliphatic terminal alkynes with Ti(O*i*Pr)$_4$/BuLi: selectivity, kinetic aspects, and a new tetramerisation process

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Dedicated to our friend and respected colleague Prof. Samir Z. Zard, in recognition of his outstanding contributions to organic chemistry

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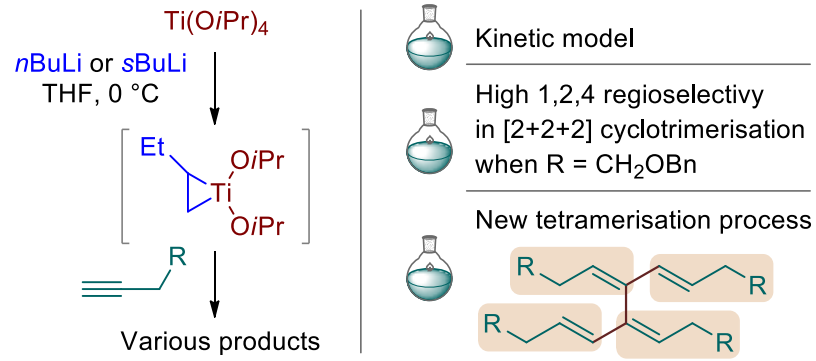
Abstract

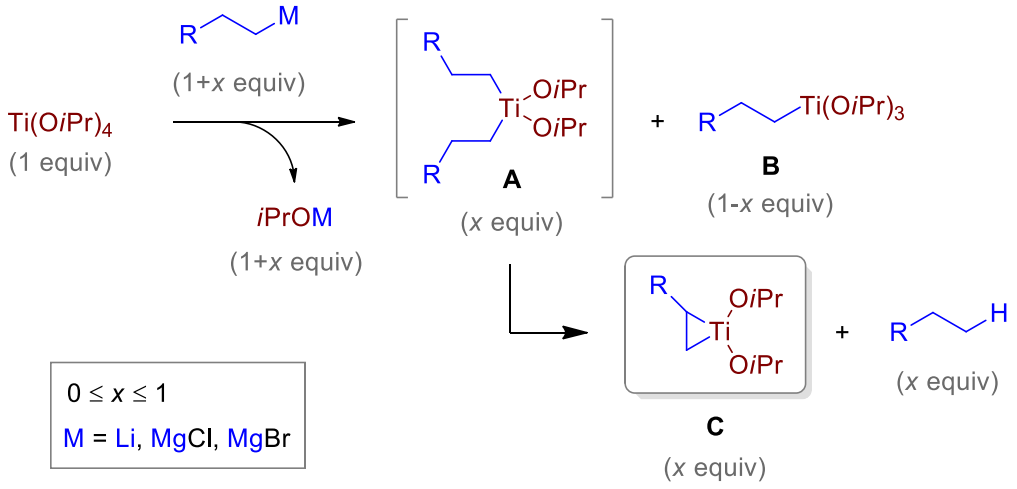
The reactions of terminal aliphatic alkynes with Ti(O*i*Pr)$_4$/*n*BuLi or Ti(O*i*Pr)$_4$/*s*BuLi were investigated. These substrates were transformed more slowly than previously studied 1-aryl acetylene compounds and mixtures of products were generally obtained. This allowed the rate constants of the elementary steps involved to be evaluated. One substrate was shown to undergo cyclotrimerisation with high regioselectivity in favour of the 1,2,4 adduct. Furthermore, an unprecedented tetramerisation process was uncovered.



Keywords: Titanium, alkynes, alkyne-metal complexes, cyclotrimerisation, reaction mechanisms

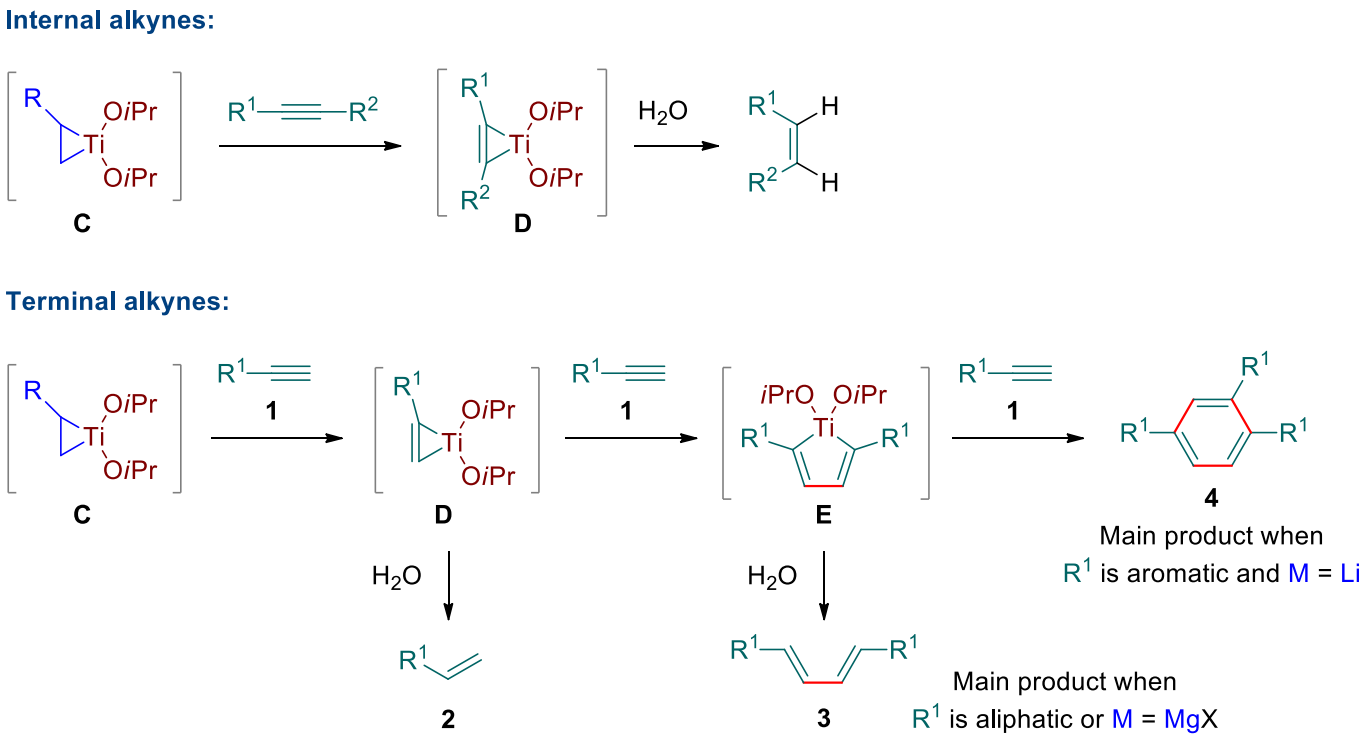
Introduction

Since its early developments at the end of the last century,[1,2] the chemistry associating titanium(IV) isopropoxide and two equivalents of a Grignard reagent[3-5] or, more rarely, an organolithium reagent,[6-11] has evolved into a powerful synthetic tool. Notably, it forms the basis of the classic Kulinkovich, de Meijere and Bertus-Szymoniak cyclopropanation reactions.[3,12-16] All these processes involve the formation of a titanacyclopropane intermediate complex **C**, which can also be viewed as an η^2-alkene complex. It is produced from the unstable dialkyltitanium intermediate **A**, itself generated by two successive transmetallation events, the first one giving the intermediate organotitanium species **B** (Scheme 1).[17]



Scheme 1. The generation of titanacyclopropane species **C** using transmetallation reactions of excess amounts of organolithium or organomagnesium reagents with titanium(IV) isopropoxide.

Complexes of type **C** can react with various organic molecules. Among them, alkynes are particularly interesting substrates.[4] Most studies have been carried out with internal alkynes, from which, titanacyclopropene species **D** are generally produced neatly by ligand exchange, regardless of the polar organometallic reagent used for the generation of **C**: Grignard reagent or organolithium compound (Scheme 2, top). One difference, however, is the thermal stability of the complexes **D** thus produced. In the former case (M = MgX), the temperature should typically be maintained below −30 °C,[18] whereas in the latter situation (M = Li), the titanacyclopropene products **D** display reasonable stability at room temperature and even up to 50 °C.[7] With terminal alkynes **1**, a subsequent process is usually observed in Grignard reagent-based reactions: a titanacyclopentadienyl complex **E** is produced, leading to the formation of diene **3** after hydrolysis (Scheme 2, bottom).[19] In contrast, in organolithium-based transformations, cyclotrimerisation products **4** are obtained from arylacetylene derivatives. These reactions are fast, proceeding to completion in a few minutes at 0 °C.[20] However, alkyl-substituted terminal alkyne substrates react more sluggishly under the same conditions, and lead after hydrolysis to mixtures of alkenes **2**, dienes **3** and cyclotrimerisation products **4**,[20] except when more elevated temperatures are applied, in which case cyclotrimers **4** can be synthesised in good yields.[21]



Scheme 2. Reactions of titanacyclopropane species **C** with disubstituted or monosubstituted alkynes.

Even though this lower reactivity of aliphatic terminal alkynes may be viewed negatively at first glance, it offers an opportunity to get a better understanding of their behaviour under such conditions. In particular, it was anticipated that useful kinetic data and insight on the ligand exchange and dimerisation processes could be extracted by careful studies. The effect of the presence of coordinating groups attached to the alkyne substrate could be investigated as well. To this end, we prepared the series of alkynes displayed in Figure 1, including two hydrocarbon compounds **1a** and **1b**, and derivatives **1c**-**f** having a coordinating benzyl group, located at various distances from the alkyne function.

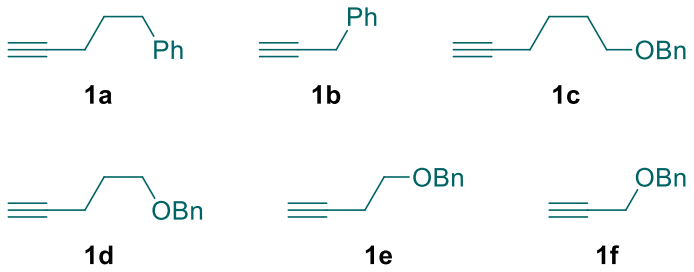


Figure 1. Terminal alkynes **1** used in the present study.

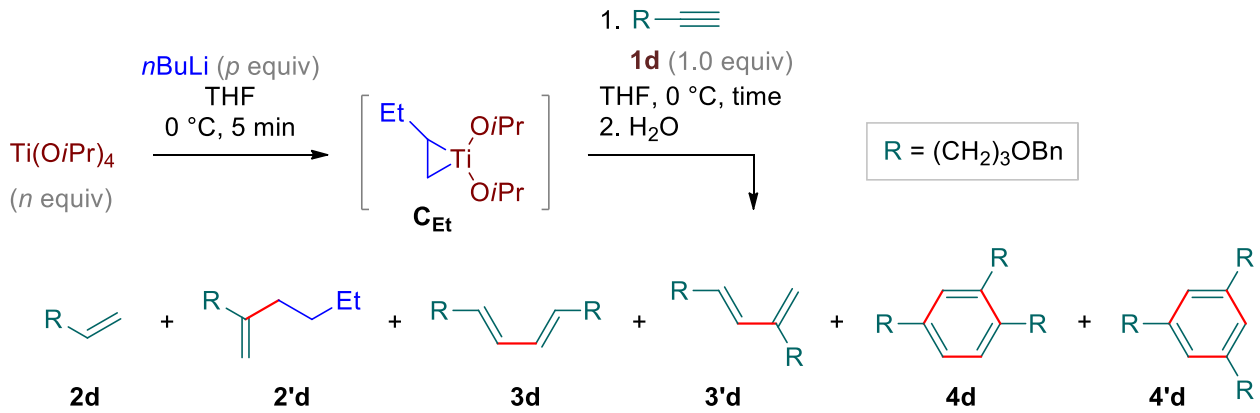
Results and Discussion

Reaction of 5-benzyloxypent-1-yne 1d

Initial experiments were carried out with 5-benzyloxypent-1-yne **1d**, chosen as a benchmark substrate. This alkyne was thus added to THF solutions containing various amounts of titanacyclopropane complex $\mathbf{C}_{Et}$, pre-

formed at 0 °C from Ti(O*i*Pr)$_4$ and *n*BuLi. The results are displayed in Table 1. Unsurprisingly, while total conversion of **1d** was achieved within 20 to 30 minutes when 1 or 2 equiv of **C$_{Et}$** were used (Table 1, entries 1 and 3), more time was required (45 minutes) with 0.5 equiv of **C$_{Et}$** (entries 4–6). Overall, three types of products were observed: alkenes **2d** and **2'd**, resulting from the reaction of one molecule of **1d**; 1,4-disubstituted and 1,3-disubstituted dienes **3d** and **3'd**, having incorporated two units of **1d**; and the cyclotrimerisation adducts **4d** and **4'd**.

Table 1. Reactions of 5-benzyloxypent-1-yne **1d** with Ti(O*i*Pr)$_4$/*n*BuLi, under various conditions[a]

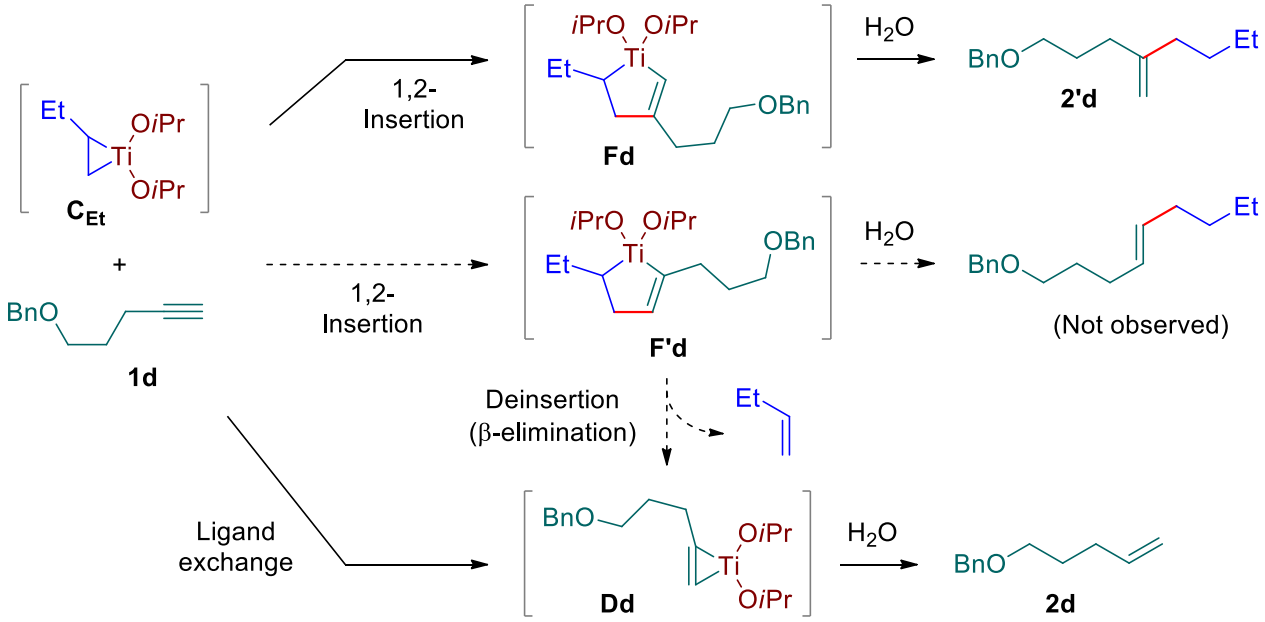


Entry	**C$_{Et}$**[b]	Time (min)	Unreacted **1d**	Alkene **2d**	Alkene **2'd**	Dienes **3d**/**3'd** (ratio)	Trimers **4d**/**4'd** (ratio)
1	≈ 2 equiv	20	2%	24%	12%	33% (49 : 51)	4% (75 : 25)
2	≈ 2 equiv	120	1%	8%	11%	21% (69 : 31)	6% (67 : 33)
3	≈ 1 equiv	30	3%	14%	9%	42% (52 : 48)	12% (67 : 33)
4	≈ 0.5 equiv	20	28%	2%	6%	33% (48 : 52)	13% (69 : 31)
5		30	14%	3%	7%	39% (49 : 51)	18% (67 : 33)
6		45	3%	4%	7%	42% (50 : 50)	20% (70 : 30)

[a] Typical experimental procedure: *n*BuLi solution in hexanes (*p* equiv) was added dropwise, over 1–4 min at 0 °C, to a THF solution of Ti(O*i*Pr)$_4$ (*n* equiv). After 5 min of stirring at 0 °C, the alkyne **1d** (1.0 equiv) was added dropwise. The mixture was stirred for the time indicated and H_2O was then added to hydrolyse the organotitanium species generated. The yields and isomer ratios are estimated by ^{1}H NMR spectroscopy of the crude products. [b] As established in ref. 11, ≈ 1 equiv of **C$_{Et}$** is presumably generated with *n* = 2.2 and *p* = 3.3. For the generation of ≈ 2 or ≈ 0.5 equiv of **C$_{Et}$**, the amounts of reagents were therefore adjusted to *n* = 4.4; *p* = 6.6 or *n* = 1.1; *p* = 1.65, respectively.

Alkene products 2d and 2'd. Alkene **2d** can simply result from protonolysis of the titanacyclopropene intermediate **Dd** formed by net ligand exchange with the alkyne **1d**. The production of the *n*-butyl-substituted derivative **2'd** can be explained by a 1,2-insertion process giving the titanacyclopentene intermediate **Fd** (Scheme 3). This complex appears to be fairly stable (see further below). Its formation is interesting: to the best of our knowledge, examples of intermolecular 1,2-insertion reactions of alkynes into dialkoxytitanacyclopropanes have been scarcely reported;[22-26] the typical mode of reactivity is ligand exchange.[4] Moreover, the high selectivity of the insertion process leading to **Fd** is remarkable. Indeed, three

other constitutional isomers could have been formed, for instance **F'd**. The protonolysis products expected from the latter were not observed.



Scheme 3. The reaction of titanacyclopropane species $\mathbf{C_{Et}}$ with 5-benzyloxypent-1-yne **1d**: ligand exchange *vs* 1,2-insertion.

To try and understand this selectivity, the coordination complexes resulting from initial complexation of $\mathbf{C_{Et}}$ with the alkyne have to be considered (Figure 2). Among these, **Gαα** and **Gαβ** should be kinetically favoured, as steric interactions between the ethyl group of $\mathbf{C_{Et}}$ and the alkyne **1d** are minimised during the approach of the latter. For each possible intermediate, a competition takes place between oxidative coupling, leading to the corresponding 1,2-insertion products, or ligand exchange to produce the titanacyclopropene **Dd**, with departure of 1-butene, a volatile molecule. Two possibilities can be put forward: either **F'd** is not formed at all and the ligand exchange pathway operates exclusively from **Gαα**; or **F'd** is an intermediate in the generation of the titanacyclopropene derivative **Dd**. Recent DFT calculations performed in the context of zirconocene chemistry support a mechanism operating by 1,2-insertion, followed by de-insertion, in ligand exchange reactions of the Negishi reagent with alkenes.[27] Transposition to the present case advocates the competitive formation of **Fd** and **F'd**, and subsequent transformation of the latter into **Dd**, via a transition state looking like **Gαα**. Conversely, our results suggest that **Fd** is stable on the time-scale of our experiments. Indeed, the yield of **2'd** does not drop with increasing reaction times (Table 1, entry 2 *vs* entry 1 and entry 6 *vs* entry 4).

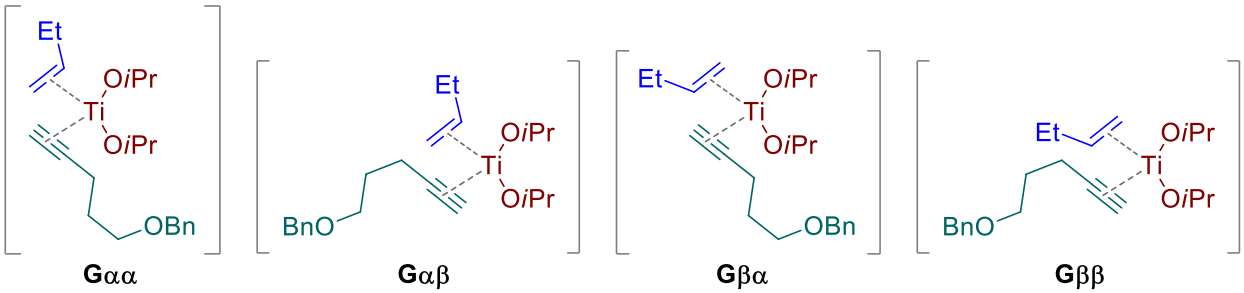
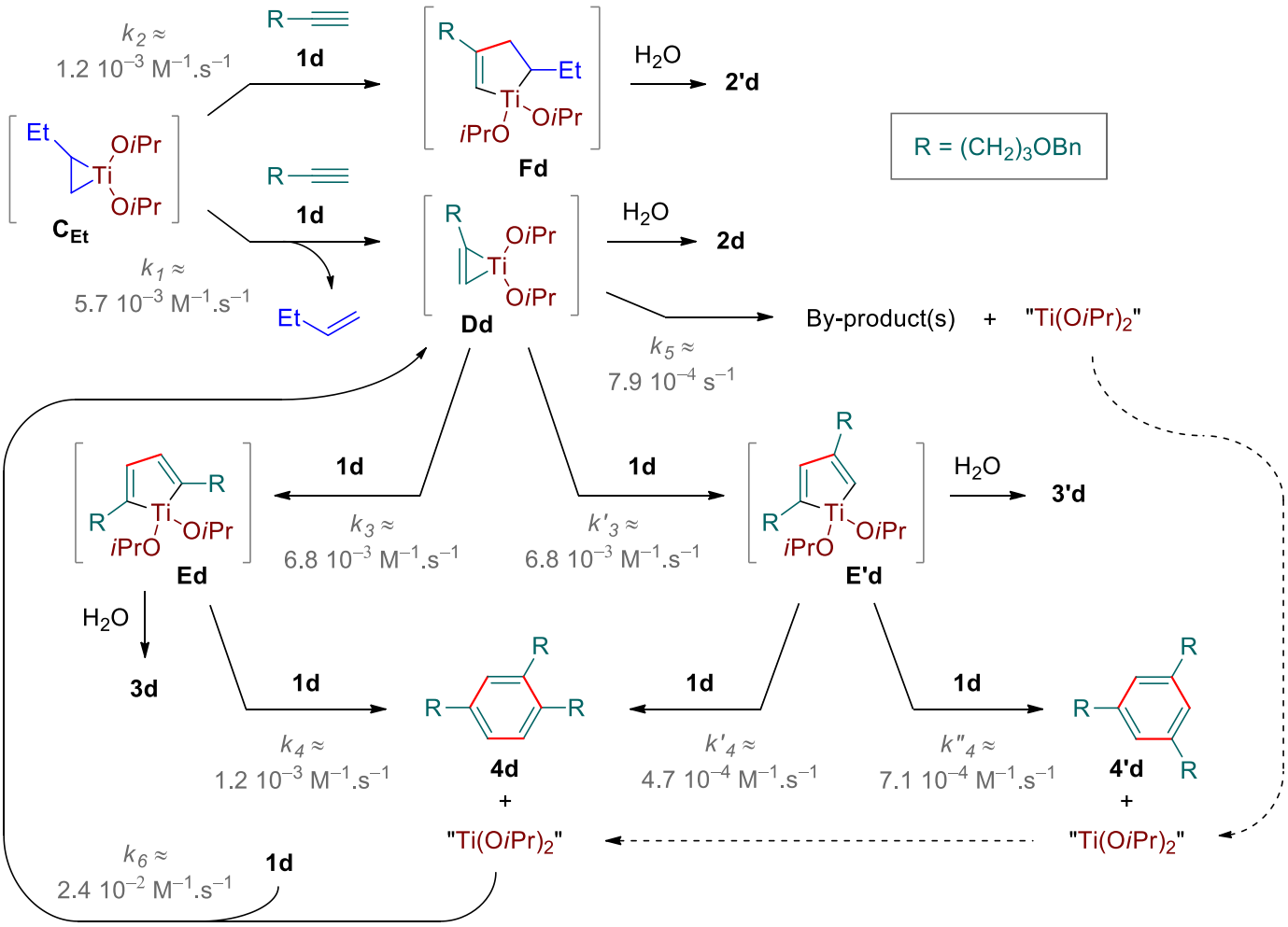


Figure 2. Regioisomer complexes resulting from complexation of **1d** with the titanacyclopropane $\mathbf{C_{Et}}$.

Alkene/diene/trimer selectivity. It is expected that the lower the relative amounts of titanium reagent $\mathbf{C_{Et}}$, the more products incorporating more than one molecule of **1d** should be formed, i.e. dienes **3d**/**3'd** and trimers **4d**/**4'd**. This is verified by the experimental results (Table 1, compare entries 1, 3 and 6). It is noteworthy that the production of dienes **3d** and **3'd** is, in fact, especially favoured, even using 2 equivalents of complex $\mathbf{C_{Et}}$. Indeed, they are still formed in 33% yield, while the alkenes **2d** and **2'd** are produced in 24% and 12% yields, respectively (entry 1). The rapid reaction of **Dd** with another molecule of alkyne **1d** is thus difficult to avoid. Indeed, at −40 °C, more dienes than alkene products are detected after 30 minutes of reaction with 1 equiv of $\mathbf{C_{Et}}$, in spite of the incomplete conversion of **1d** (see the supporting information for detail). In contrast, incorporation of the third molecule of **1d**, leading to the trimers **4d** and **4'd**, proves to be comparatively slow, as evidenced by the relatively low yields observed, even using a small amount of $\mathbf{C_{Et}}$ (entry 6). This is consistent with the necessity to apply heat to achieve good yields in the cyclotrimerisation of terminal aliphatic alkynes.[21]

Finally, the stability of the organometallic species formed was evaluated by extending the reaction time to two hours, with 2 equiv of $\mathbf{C_{Et}}$ (entry 2 *vs* entry 1). Most starting material **1d** had already been converted after 20 minutes and after the prolonged reaction time, a significant drop was observed in the yields of dienes **3d** and **3'd** (21% vs 33%). Since the yields of trimers **4d** and **4'd** did not increase to the same extent, this can be interpreted as partial decomposition of the titanacyclopentadienes **Ed** and **E'd**, especially of the 1,3-substituted complex **E'd**, as judged by the higher **3d**/**3'd** ratio after two hours. The results also reveal the particular instability of the titanacyclopentene complex **Dd**: the yield of the corresponding alkene **2d** dropped from 24% to 8%. In contrast, no significant change in the yield of **2'd** was observed, indicating that the titanacylopentene complex **Fd** can be considered to be stable at 0 °C for at least two hours.

Kinetic aspects. With most elementary steps of the transformation of alkyne **1d** being understood, and with results having been obtained under various relative concentrations of the reactants and with different reaction times, extraction of useful kinetic data seemed feasible. To this end, an empirical approach was implemented. It consisted of adjusting the values of the relevant kinetic constants by an iterative trial/error process, so that transformations simulated with an online tool[28,29] would match the experimental results as closely as possible. It must be noted that in the absence of detail on the decomposition pathways of some of the organometallic species involved, as well as on the exact mechanism leading to the cyclotrimerised products, significant simplification could not be avoided. Namely, only decomposition of complex **Dd** was taken into account, to produce "by-products" and regenerate titanium(II) species "Ti(O*i*Pr)$_2$". The latter was also considered to be produced during the elementary step leading to the cyclotrimerized products, which is consistent with the possibility to run these reactions with catalytic amounts of organometallic reagents.[21] The resulting mechanistic model is presented in Scheme 4.



Scheme 4. Simplified mechanistic model for the reaction of **1d**. Kinetic constant values were evaluated by an empirical approach (see main text).

The validity of this simplified model is supported by the rather good agreement observed between the experimental yields and the simulated end concentrations of the organometallic species involved, with a variety of starting concentrations of reactants and reaction times. This is illustrated graphically in Figure 3.

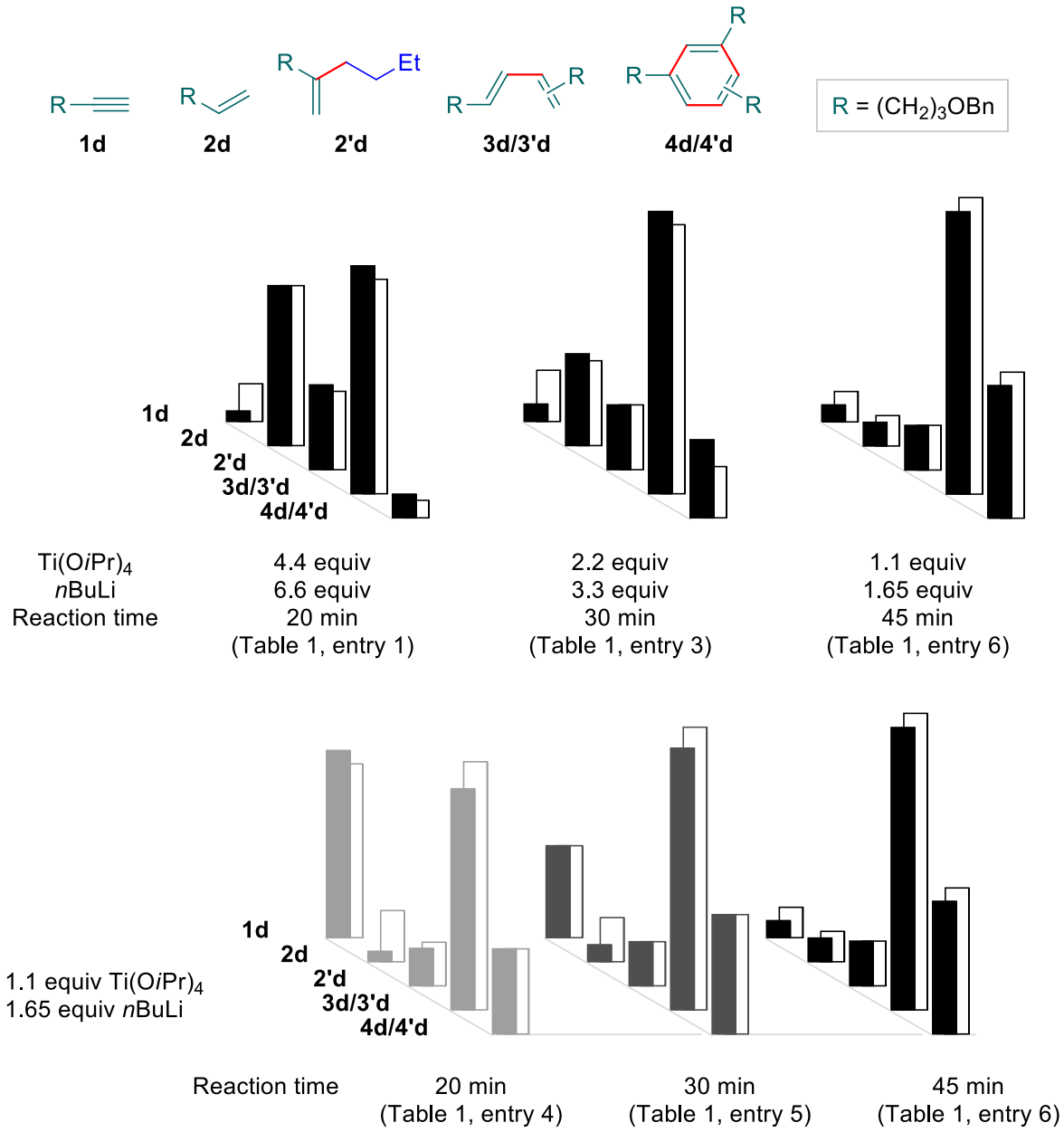
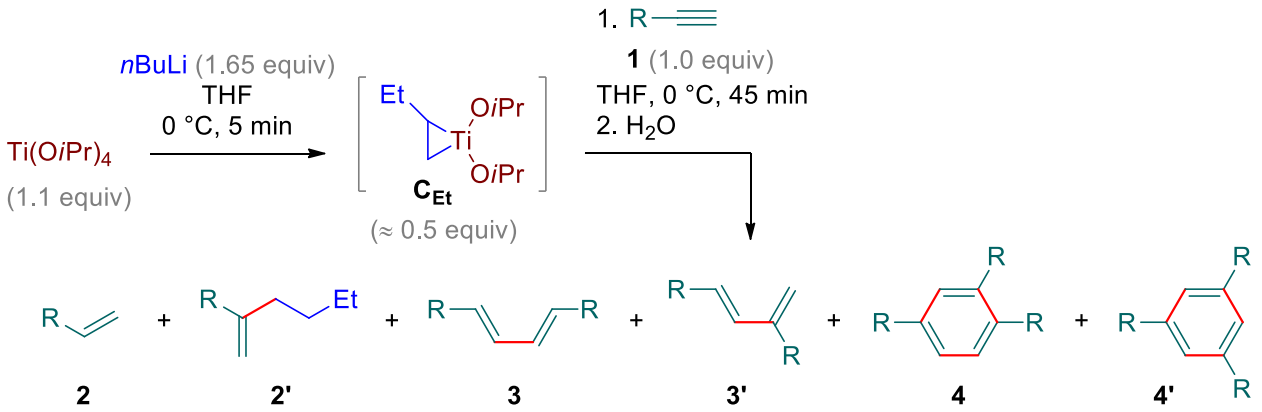


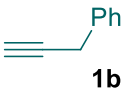
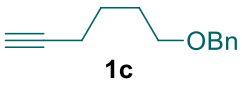
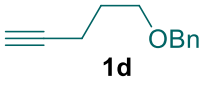
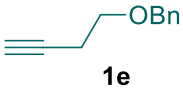
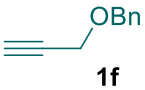
Figure 3. Graphical representation of the product distribution under various conditions. Experimental yields are represented by plain bars and are to be compared with the simulated yields, represented by hollow bars. These were calculated according to the simplified mechanistic model shown in Scheme 4.

Reactions of other substrates

The reactions of the other terminal alkynes **1a**-**c** and **1e**-**f** were investigated as well, again with various proportions of organometallic reagents. For the sake of clarity, only the results obtained with ≈ 0.5 equiv of $\mathbf{C_{Et}}$ are presented (Table 2).

Table 2. Reactions of alkynes **1a**-**f** with Ti(O*i*Pr)$_4$/*n*BuLi (1.1 and 1.65 equiv respectively), at 0 °C[a]



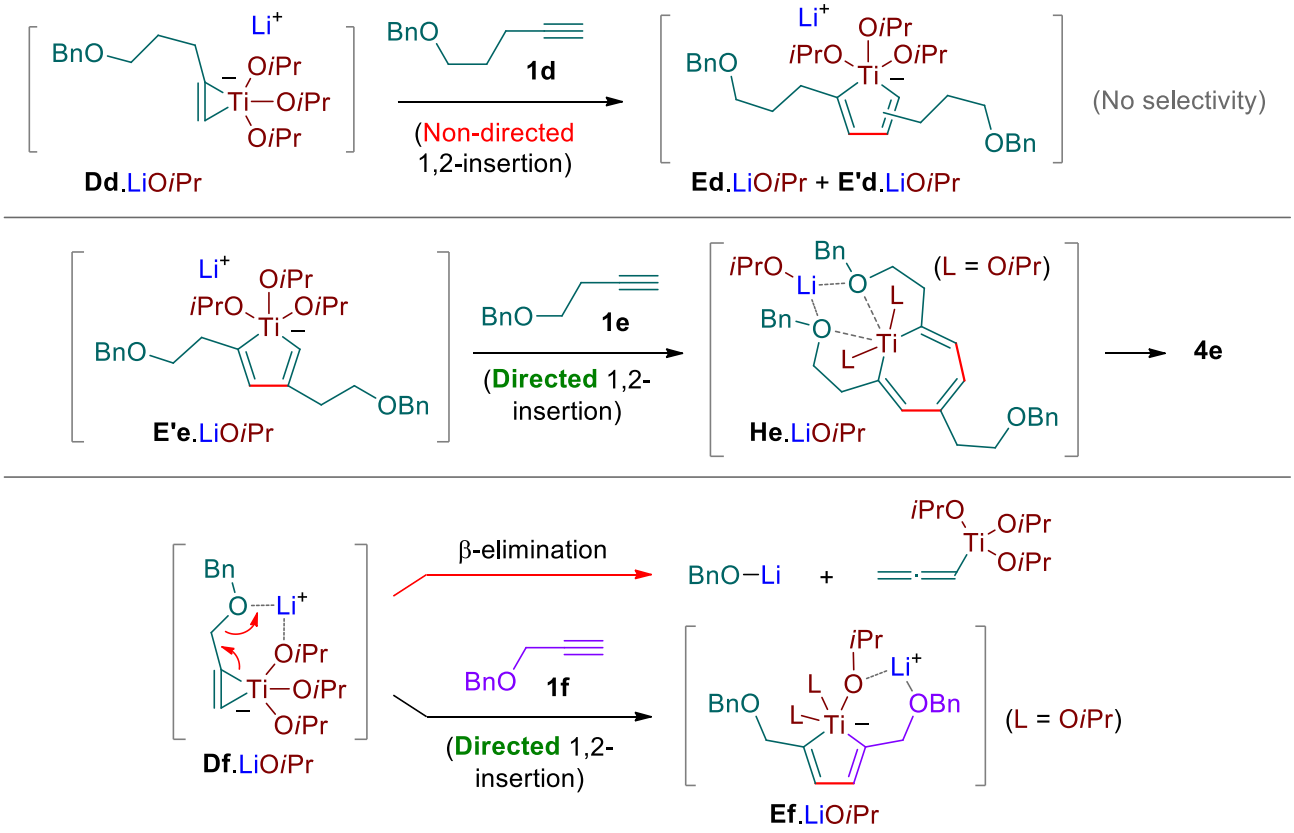
Entry	Substrate	Unreacted **1**	Alkene **2**	Alkene **2'**	Dienes **3**/**3'** (ratio)	Trimers **4**/**4'** (ratio)
1	 **1a**	3%	5%	8%	44% (50 : 50)	20% (60 : 40)
2	 **1b**	3%	5%	5%	31% (55 : 45)	31% (71 : 29)
3	 **1c**	7%	5%	7%	37% (47 : 53)	14% (66 : 34)
4	 **1d**	3%	4%	7%	42% (50 : 50)	20% (70 : 30)
5	 **1e**	2%	2%	5%	25% (57 : 43)	36% (95 : 5)
6[b]	 **1f**	7%	3%	4%	26% (92 : 8)	18% (>95 : 5)

[a] Typical experimental procedure: *n*BuLi solution in hexanes (1.65 equiv) was added dropwise, over 1-5 min at 0 °C, to a THF solution of Ti(O*i*Pr)$_4$ (1.1 equiv). After 5 min of stirring at 0 °C, the alkyne **1** (1.0 equiv) was added dropwise. The mixture was stirred for 45 min and H_2O was then added to hydrolyse the organotitanium species generated. The yields and isomer ratios are estimated by ^{1}H NMR spectroscopy of the crude products. [b] Benzyl alcohol was formed in an estimated 27% yield.

These experiments show that alkynes **1a**-**c** behave very similarly to **1d** (Table 2, entries 1–4). In particular and interestingly, the presence of the coordinating benzyloxy groups of **1c** or **1d**, located three or four atoms away from the C≡C triple bond, does not appear to have any significant effect on the yields or selectivities of the formation of the dienes **3** or the cyclotrimers **4** (entries 3-4 *vs* entries 1-2). This is consistent with the earlier formulated hypothesis that titanacyclopropene and titanacyclopentadiene intermediates **D**, **E** and **E'** exist as "ate" complexes formed by coordination of lithium isopropoxide produced during the generation of **C$_{Et}$**.[11,17,20,30,31] Accordingly, 1,2-insertion of **1c** or **1d** into the titanacyclopropene complexes **Dc** or **Dd** could not be directed efficiently by the ether function (Scheme 5, top).

In contrast, high regioselectivity was observed in the formation of the titanacyclopentadiene **Ef** from **1f**, with a **3f**/**3'f** diene product ratio of 92:8 (entry 6), and, consequently, in the production of the [2+2+2] cyclotrimerisation adduct **4f**. To explain this, one can invoke the participation of a Li$^+$ cation, the coordination

of which with both an isopropoxyl ligand of **Df** and the incoming alkyne benzyl ether **1f** could effectively direct the 1,2-insertion elementary step (Scheme 5, bottom). Similar directing interactions would be conceivable as well in the cases of **1c**-**e** but they would become increasingly weak with longer chains separating the ether and the alkyne functions, because of the entropic cost associated with reaching the corresponding transition states. Such an effect may nonetheless marginally operate in the case of **1e** [**3e**/**3'e** ratio 57:43 (entry 5)] but not starting from **1c** or **1d** [ratio ca. 50:50 (entries 3−4)]. The comparatively low cumulative yields of diene **3f** and trimer **4f** can be explained by the competitive β-elimination of a benzyloxide anion from the titanacylopropene **Df** (Scheme 5, bottom) or the titanacyclopentadiene **Ef**,[32,33] as evidenced by the presence of benzyl alcohol in the crude product.

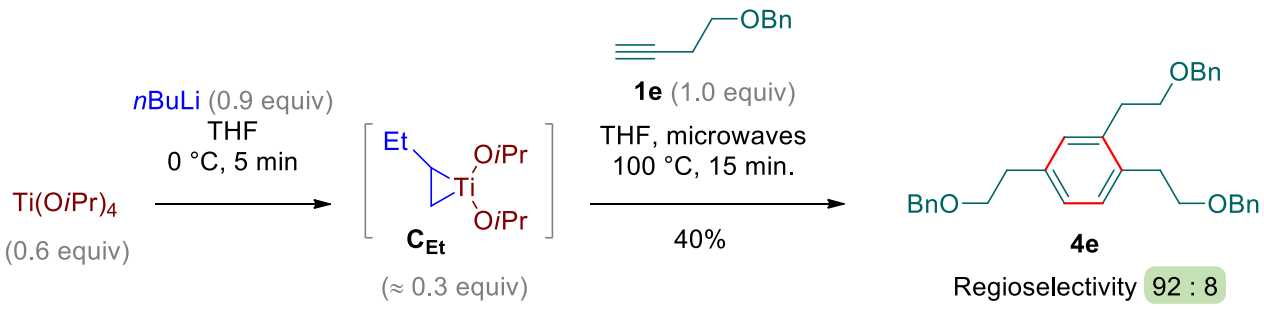


Scheme 5. Tentative explanations for the levels of selectivity observed in 1,2-insertion reactions involving benzyl ethers **1d**-**f**. Titanium ate complexes / aggregates with two molecules of LiO*i*Pr could be envisaged as well.

Comparison of the results observed with **1e** and **1d** is also interesting (entry 5 *vs* entry 4). Starting from **1e**, more cyclotrimerised compounds are produced (36% *vs* 20%), with markedly higher selectivity in favour of the 1,2,4-isomer (95:5 vs 70:30). This is all the more remarkable since the titanacyclopropene precursors **Ee** and **E'e** of the cyclotrimerised products are present in approximately equal quantities, as indicated by the ratio of the diene hydrolysis products **3e**/**3'e** (57:43). The 1,4-disubstituted isomer **Ee** is expected to give the 1,2,4-isomer **4e**. However, it it does not appear to be consumed faster than **E'e**, which suggests that the reaction of **E'e** with a third molecule of alkyne **1e** is unusually selective, in favour of the formation of **4e** as well. To account for this, we are again tentatively proposing a directing effect involving a lithium cation and leading to the preferential formation of the bimetallic aggregate **He** (Scheme 5, middle). This directing interaction makes

the reactions of titanacyclopentadienes **Ee**/**E'e** not only more selective but also faster, as evidenced by the comparatively higher yields of cyclotrimerised products **4e**/**4'e** and lower yields of dienes **3e**/**3'e** (Table 2, entry 5 *vs* all other entries).

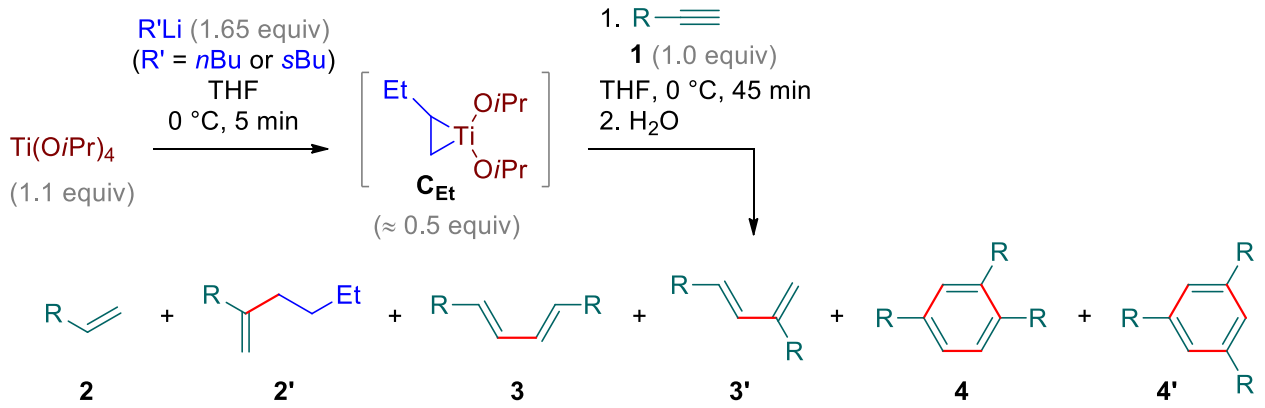
Thermal activation using microwave irradiation. Considering the good regioselectivity observed in the formation of the cyclotrimerised product **4e** (Table 2, entry 4), it seemed interesting to investigate the reaction of **1e** under our earlier developed conditions for the cyclotrimerisation of alkynes, that involved the same combination of reagents, used in lower amounts and with microwave heating.[21] Indeed, among the various methods reported for the cyclotrimerisation of alkynes, only few lead to satisfactory selectivities starting from alkyl-substituted acetylene derivatives.[34,35] Gratifyingly, when **1e** was heated at 100 °C under microwave conditions in the presence of pre-formed complex $\mathbf{C_{Et}}$, the high regioselectivity of the formation of **4e** was preserved, notwithstanding the moderate isolated yield (Scheme 6). Starting from compounds **1a**, **1b** or **1c**, regioselectivities were around 70 : 30 (see the supporting information for detail), *i.e.* comparable to the 65 : 35 selectivity we had previously observed starting from 1-heptyne under the same conditions.[21]



Scheme 6. Reaction of alkyne **1e** using lower amounts of reagents and under microwave conditions. Similar results were obtained at higher temperature (140 °C).

The use of *s*BuLi in place of *n*BuLi. The influence of the nature of the organolithium reagent was next explored. Substrates **1b**-**1e** were submitted to the same reaction conditions as before, except for the use of *s*-butyllithium instead of *n*-butyllithium. The very same titanacyclopropane intermediate $\mathbf{C_{Et}}$ was expected to be generated again, together with *s*BuTi(O*i*Pr)$_3$ **B*s***. However, these two organometallic compounds could interact differently with each other and/or form different aggregates.[11] The results, compared with those obtained using *n*-butyllithium, are presented in Table 3. Significant deviations are observed, the most striking being a much-reduced formation of cyclotrimerisation products **4**/**4'** when *s*BuLi is employed (entry 2 *vs* entry 1; entry 4 *vs* entry 3; entry 6 *vs* entry 5 and entry 8 *vs* entry 7). Nevertheless, this is not counterbalanced with a corresponding increase in the production of dienes **3**/**3'**. On the contrary, the latter is marginally reduced, with a slightly modified proportion of the two isomers, in the favour of **3'**. A change is observed in the **4**/**4'** ratio as well, with a consistent moderate increase of the relative amount of **4'**. Finally, and perhaps most importantly, a new tetrameric product was detected. This is the subject of the next subsection.

Table 3. Comparison of the reactions of substrates **1b**-**e** with Ti(O*i*Pr)$_4$/*n*BuLi or Ti(O*i*Pr)$_4$/*s*BuLi, at 0 °C[a]



Entry	Substrate	R'Li	Unreacted **1**	Alkene **2**	Alkene **2'**	Dienes **3**/**3'** (ratio)	Trimers **4**/**4'** (ratio)
1	 **1b**	*n*BuLi	3%	5%	5%	31% (55 : 45)	31% (71 : 29)
2[b]		***s*BuLi**	12%	5%	3%	29% (41 : 59)	5% (64 : 36)
3	 **1c**	*n*BuLi	7%	5%	7%	37% (47 : 53)	14% (66 : 34)
4		***s*BuLi**	11%	7%	8%	33% (44 : 56)	4% (56 : 44)
5	 **1d**	*n*BuLi	3%	4%	7%	42% (50 : 50)	20% (70 : 30)
6[b]		***s*BuLi**	15%	6%	4%	30% (45 : 55)	4% (60 : 40)
7	 **1e**	*n*BuLi	2%	2%	5%	25% (57 : 43)	36% (95 : 5)
8		***s*BuLi**	3%	6%	4%	22% (44 : 56)	16% (91 : 9)

[a] Typical experimental procedure: *n*BuLi or *s*BuLi solution in hexanes or cyclohexane (1.65 equiv) was added dropwise, over 0.5-8 min at 0 °C, to a THF solution of Ti(O*i*Pr)$_4$ (1.1 equiv). After 5 min of stirring at 0 °C, the alkyne **1** (1.0 equiv) was added dropwise. The mixture was stirred for 45 minutes and H_2O was then added to hydrolyse the organotitanium species generated. The yields and isomer ratios are estimated by ^{1}H NMR spectroscopy of the crude products. [b] Mean values are given for the yields, calculated from the similar results of two runs carried out under essentially the same conditions.

An unexpected tetramerisation reaction

Incidentally, an unprecedented transformation was discovered in the course of the experiments involving the use of *s*-butyllithium. Indeed, the crude products of reactions involving 1.1 equiv of Ti(O*i*Pr)$_4$ and 1.65 equiv of *s*BuLi were found to contain the unexpected tetraene products **5b**-**e**, in variable amounts depending on the substrates **1b**-**e** and on the precise reaction conditions (Figure 4). The formation of these molecules, which we are giving the informal name "Marie-Anne tetramers", was never observed using Ti(O*i*Pr)$_4$ and *n*BuLi in any of the proportions investigated, and only traces, at most, were detected using 2.2 equiv of Ti(O*i*Pr)$_4$ and 3.3 equiv of *s*BuLi.

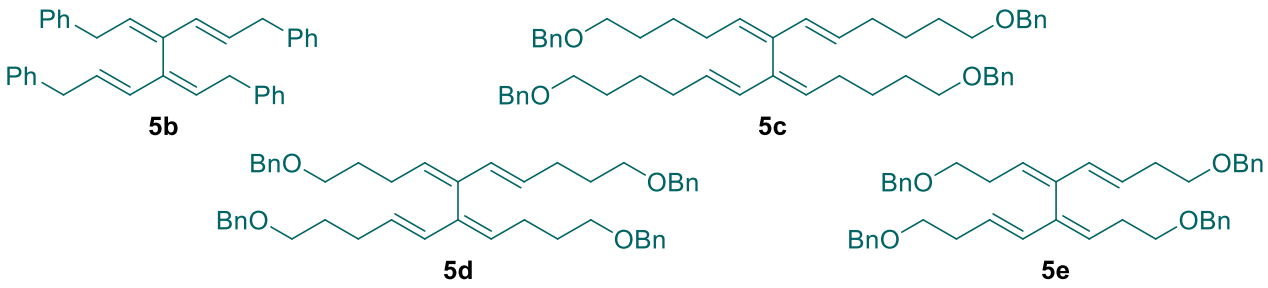


Figure 4. Structures of the unexpected tetraene co-products **5b**-**e**.

Compound **5b** was formed in the highest yield, which reached 32% in one experiment. It could then be isolated by trituration with MeOH and recrystallisation from EtOAc. It was fully characterised and its structure was confirmed by X-ray crystallography of a single crystal. Two views are presented in Figure 5. The conformation of this compound is interesting. It can be seen as the association of two *s-trans* 1,3-diene subunits. They are linked by a C–C σ bond, with a dihedral angle of about 79°. Therefore, one can consider that there is practically no conjugation between the two dienyl systems. Moreover, it is likely that there is a significant rotation energy barrier around the "central" σ bond. It is thus tempting to predict that atropoisomers would be observed if a chiral analogue could be made, either by a hypothetical synthetic method from small building blocks, or by a selective post-functionalisation reaction performed on molecules of type **5**.

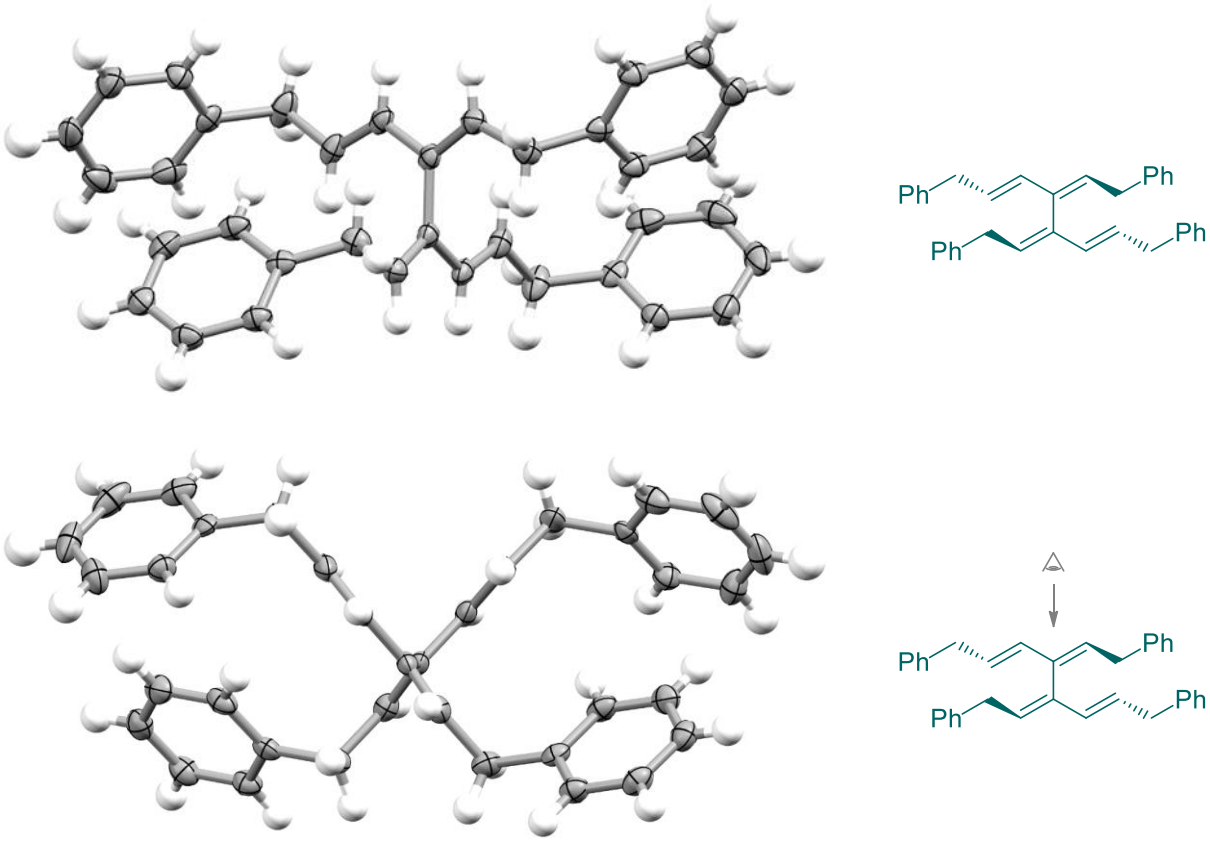
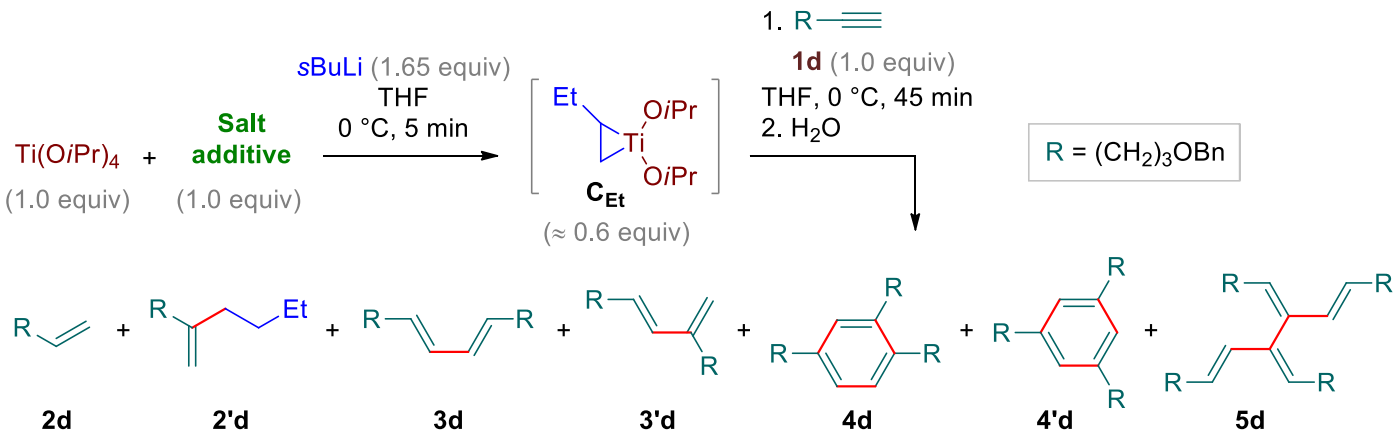


Figure 5. Two views of the X-ray structure of compound **5b**. Ellipsoids are drawn at the 50% probability level.

The formation of products **5** was first observed using an already in-use bottle of *s*-butyllithium that had been opened at an unknown date. When another, freshly opened bottle of *s*BuLi was later employed, smaller amounts of the same compounds were detected. Experiments were then conducted with the deliberate introduction of various alkali metal salts, to see if the earlier results could be reproduced more faithfully. We also wanted to investigate whether these additives could exercise some influence on the product distribution, for instance by inducing the formation of different organometallic aggregates.

The effect of various inorganic salt additives. Reactions of starting alkyne **1d**, conducted in the presence of NaCl, LiCl, LiBr, LiOMe, LiOH or Li_2SO_4, led to the results presented in Table 4. Under the conditions applied, involving 1.0 equiv of Ti(O*i*Pr)$_4$ and 1.65 equiv of *s*BuLi, high conversion was generally observed. The yield of the tetramer **5d**, however, was found to be uniformly somewhat lower with the additives (entries 2-8 *vs* entry 1). Apart from this observation, it was found that the use of 1 equiv LiCl or 2 equiv LiBr leads to a significant increase of the amounts of trimers **4d**/**4'd**, at the expense of the alkene and diene products (entries 3 and 5).

Table 4. Effect of inorganic salt additives on the reaction of alkyne **1d** with Ti(O*i*Pr)$_4$/*s*BuLi[a]

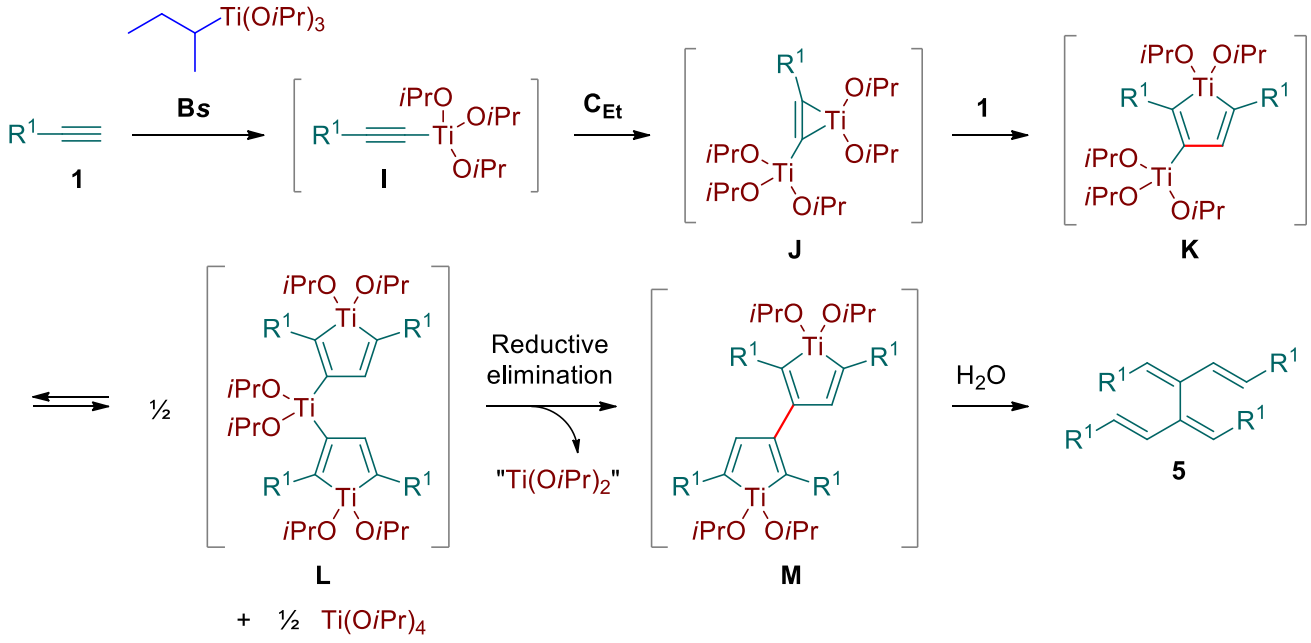


Entry	Salt additive	Unreacted **1d**	Alkene **2d**	Alkene **2'd**	Dienes **3d**/**3'd** (ratio)	Trimers **4d**/**4'd** (ratio)	Tetramer **5d**
1	None	2%	9%	7%	30% (50 : 50)	7% (62 : 38)	11%
2	**NaCl**	3%	11%	8%	32% (57 : 43)	12% (54 : 46)	7%
3	**LiCl**	3%	3%	4%	25% (58 : 42)	26% (58 : 42)	3%
4	**LiBr**	10%	3%	4%	24% (52 : 48)	19% (59 : 41)	3%
5	**LiBr**[b]	2%	3%	6%	18% (65 : 35)	26% (54 : 46)	1%
6	**LiOMe**	4%	10%	7%	30% (56 : 44)	12% (58 : 42)	4%
7	**LiOH**	4%	8%	7%	34% (33 : 47)	10% (62 : 38)	8%
8	**Li_2SO_4**	2%	9%	7%	31% (57 : 43)	10% (58 : 42)	5%

[a] Typical experimental procedure: *s*BuLi solution in cyclohexane (1.65 equiv) was added dropwise, over 1.5 min at 0 °C, to a THF solution of Ti(O*i*Pr)$_4$ (1.0 equiv) and the salt additive (1.0 equiv). After 5 min of stirring at 0 °C, the alkyne **1d** (1.0 equiv) was added dropwise. The mixture was stirred for 45 min and H_2O was then added to hydrolyse the organotitanium species generated. The yields and isomer ratios are estimated by ^{1}H NMR spectroscopy of the crude products. [b] Two equivalents of LiBr were used.

Similar experiments were conducted with the Ti(O*i*Pr)$_4$/*n*BuLi system. Under otherwise identical conditions, the results did not reveal any significant influence of the salt additives.

Mechanism of the formation of compounds 5. Elucidation of the mechanism of the production of tetramers **5** requires additional studies that remain to be carried out. In the meantime, a tentative proposal is presented in Scheme 7. A distinct possibility is that dimetallated species **J** are involved. The formation of such complexes, by the metallation of alkynyltitanium complexes **I** under related conditions, has been described by I. Marek's research group.[36,37] In the present case, **I** could be formed by the deprotonation of **1** with a sufficiently basic organometallic species, for instance **B*s***, of which one equivalent is produced during the generation of $\mathbf{C_{Et}}$, and which is more basic than the primary organotitanium compound **B** resulting from the use of *n*BuLi. Insertion of another molecule of the alkyne **1** into **J** would deliver the titanacycle **K**. Disproportionation of the latter could result in the formation of **L** and, from there, the bis(titanacyclopentadiene) **M**. Finally, hydrolysis of this complex would produce **5**. We intend to probe this mechanism in the near future.



Scheme 7. Tentative mechanism accounting for the formation of the tetramers **5**.

Conclusions and Perspectives

In summary, in THF at 0 °C, terminal aliphatic alkynes generally lead to mixtures of products when they are reacted with the titanacyclopropane $\mathbf{C_{Et}}$ generated from Ti(O*i*Pr)$_4$/*n*BuLi or Ti(O*i*Pr)$_4$/*s*BuLi. After hydrolysis, the major products obtained are typically diene regioisomers that incorporate two molecules of the starting alkynes, even when a two-fold excess of $\mathbf{C_{Et}}$ is engaged.

These results indicate that the insertion of the second molecule of alkyne, to form titanacyclopentadiene species **E** or **E'**, is faster than the initial ligand exchange process that leads to the monosubstituted titanacyclopropene intermediate **D**. In other words, the terminal aliphatic alkyne substrates react faster with **D** than with $\mathbf{C_{Et}}$. The reaction of a third molecule of alkyne is then slower. A more detailed kinetic model, with

rate constant values, could be proposed for the specific transformation of alkyne **1d**, based on the results of a series of experiments involving various reaction times and proportions of reactants.

The outcomes of the reactions of terminal aliphatic alkynes is in sharp contrast with those of terminal 1-arylalkynes under the same conditions, which react rapidly and effciently to form the cyclotrimerised products **4**, with high regioselectivity in favour of the 1,2,4 isomers.[20,21] With terminal aliphatic alkynes, the insertion step that generates the titanacyclopentadiene species **E** or **E'** typically proceeds with little or no selectivity. The same is true for the formation of the minor cyclotrimer products **4**/**4'**. A notable exception is the behaviour of 4-benzyloxybut-1-yne **1e**, which gives comparatively higher yields of these cycloadducts and high 1,2,4 regioselectivity.

The use of *s*BuLi in place of *n*BuLi results in a minimisation of the production of cyclotrimers **4**/**4'**, albeit without any positive impact on the yields of the diene products. Nevertheless, when suitable proportions of reagents are employed, the interesting competitive formation of new compounds **5** incorporating four molecules of alkyne, assembled in a fully regio- and stereo-selective manner, takes place more or less marginally, in yields of up to 32%. In the near future, we are going to probe the mechanism put forward in Scheme 7 and devote efforts to improve the yields and extend the formation of homotetramers **5** to the controlled production of heterotetramers.

Overall, the data collected during this work can serve as a foundation for future research on the controlled oligomerisation of terminal alkynes. The improved understanding of the factors leading to good selectivities will facilitate the design of new substrates, better suited for achieving enhanced efficiency and control in low-valent titanium-mediated processes.

Experimental Section

General. Titanium(IV) isopropoxide was purchased from Sigma Aldrich, distilled under reduced pressure (≈ 70 °C at 2 mbar) and stored under argon for several months. *n*-Butyllithium (2.5 M solution in hexanes) and sec-butyllithium (1.4 M solution in cyclohexane) were purchased from Sigma-Aldrich and titrated once a month. Tetrahydrofuran was purified using a MB SPS-800 solvent purification system (MBRAUN). Petroleum ether (40−60 °C fraction) was distilled at 450 mbar before use. Other solvents and commercial reagents were used as received, without purification.

All reactions were carried out under argon. The glassware, septa, syringes and needles were dried in a desiccator under vacuum (ca. 20 mbar), in the presence of $CaCl_2$. The reaction vessels and the magnetic stirring bars were dried in an oven (120-130 °C) overnight or, alternatively, heated with a heat gun under a stream of argon. In either case, the flasks were allowed to cool down to room temperature under a gentle stream of argon before the introduction of the solvent and the reactants.

Flash column chromatography was performed on VWR Chemicals or Merck silica gel 60 (40–63 µm). Concentration under reduced pressure was carried out using rotary evaporators at 40 °C.

Melting points were determined using a Stuart SMP40 apparatus. Infrared spectra were recorded with a Perkin-Elmer 2000 or a Perkin-Elmer Spectrum Two FT-IR spectrometer. NMR spectra were recorded with an AVANCE 400 Bruker spectrometer (^{1}H at 400.2 MHz, ^{13}C at 100.6 MHz). Chemical shifts δ are given in parts per million (ppm), referenced to the peak of tetramethylsilane, defined at δ = 0.00 for ^{1}H and ^{13}C NMR, or to the solvent peak [in $CDCl_3$: δ = 7.26 (residual $CHCl_3$) for ^{1}H NMR and δ = 77.0 for ^{13}C NMR]. Multiplicities are abbreviated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad). Coupling

constants *J* are given in Hz and are rounded to the closest multiple of 0.5. HRMS spectra were recorded using a tims-TOF mass spectrometer (Bruker). The electrospray source was used in positive mode.

In the description of compounds, all the NMR chemical shifts indicated were measured from our spectra. When available, literature data were used for comparison/confirmation purposes. A number of products could not be isolated in pure form but were obtained in mixture with one or two other compounds; occasionally more. In such cases, assignment of the signals was done by combining several methods: careful analysis of 1D and 2D (COSY, HSQC and/or HMBC) NMR spectra, use of known data for some of the constituents of the mixture (if applicable), analogy with other products of similar structure, either obtained in this work or described in the literature, and use of the NMR spectra simulation tools available on the nmrshiftdb2 platform (http://www.nmrshiftdb.org; accessed in January 2024). Sometimes, all the signals of a given new product could be identified in this way, notwithstanding the fact that it had not been perfectly isolated. Quite often however, only a few of the signals could be assigned with a sufficient degree of certainty. In such cases, only these selected characteristic signals are provided.

Typical procedure for the reactions of terminal alkynes 1 with organometallic species generated from Ti(O*i*Pr)$_4$/*n*BuLi or Ti(O*i*Pr)$_4$/*s*BuLi

Transformation of alkyne 1d with Ti(O*i*Pr)$_4$/*n*BuLi, under the conditions of Table 1, entries 4-6. *n*-Butyllithium solution (2.27 M in hexanes, 1.65 equiv, 3.30 mmol, 1.45 mL) was added dropwise, over 1.25 min, at 0 °C, to a solution of titanium(IV) isopropoxide (1.10 equiv, 2.20 mmol, 651 µL) in THF (5.0 mL). The solution turned yellow, then orange and then brown. After 5 minutes of stirring at 0 °C, it had turned black and 5-benzyloxypent-1-yne **1d** (1.00 equiv, 2.00 mmol, 348 mg) was added dropwise, over 1.33 min. After 20 minutes of stirring at 0 °C, part of the solution (1.0 mL) was taken out using a syringe and introduced into another flask under Ar, at 0 °C. H_2O (0.1 mL) was added to this flask. After 15 minutes of stirring, the septum was removed to expose it to air and stirring was continued for 10 more minutes. The white mixture was then filtered through a pad of sand, $MgSO_4$, celite and sand [from bottom to top; rinsing with Et_2O (6.0 mL)] and concentrated under reduced pressure (down to 50-60 mbar) to afford the crude product corresponding to *t* = 20 minutes (yellow oil; 33.4 mg). The same operation was repeated after 30 minutes of reaction at 0 °C, to afford the crude product corresponding to *t* = 30 minutes (yellow oil; 62.1 mg). Finally, after 45 minutes of reaction at 0 °C, the remaining solution was treated with H_2O (0.3 mL) and the same procedure was applied as for the two intermediate crude products (the filtration pad was rinsed with 12 mL of Et_2O). The crude product corresponding to *t* = 45 minutes was obtained as a yellow oil (293 mg). Each of the three samples was analysed by ^{1}H NMR spectroscopy to give the qualitative estimation of the product yields shown in Table 6; entries 4, 5 and 6.

5-Benzyloxypent-1-ene (2d).[38] ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 1.72 (2 H, tt, *J* 7.5, 6.5), 2.15 (2 H, tddd, *J* 7.5, 6.5, 1.5, 1.0), 3.49 (2 H, t, *J* 6.5), 4.50 (2 H, s), 4.96 (1 H, ddt, *J* 10.0, 2.0, 1.0), 5.02 (1 H, ddt, *J* 17.0, 2.0, 1.5), 5.82 (1 H, ddt, *J* 17.0, 10.0, 6.5), 7.29 (1 H, m), 7.32−7.37 (4 H, m). ^{13}C NMR ($CDCl_3$, 100.6 MHz): *δ* 28.9, 30.3, 69.7, 72.9, 114.7, 127.5, 127.6, 128.3, 138.3.

4-Methyleneoctoxymethylbenzene (2'd). ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 0.90 (3 H, t, *J* 7.5), 1.30 (2 H, qt, *J* 7.5, 7.0), 1.40 (2 H, tt, *J* 7.5, 7.0), 1.76 (2 H, tt, *J* 7.5, 6.5), 2.01 (2 H, br t, *J* 7.5), 2.09 (2 H, br t, *J* 7.5), 3.48 (2 H, t, *J* 6.5), 4.50 (2 H, s), 4.71 (2 H, br s), 7.28 (1 H, m), 7.31−7.37 (4 H, m). ^{13}C NMR ($CDCl_3$, 100.6 MHz): *δ* 14.0, 22.5, 27.9, 30.0, 32.4, 35.8, 70.1, 72.9, 108.7, 127.5, 127.6, 128.3, 138.6, 149.5.

[(*E*,*E*)-10-Benzyloxydeca-4,6-dienoxy]methylbenzene (3d). Viscous colourless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 1.71 (4 H, tt, *J* 7.5, 6.5), 2.16 (4 H, br td, *J* 7.5, 7.0), 3.48 (4 H, t, *J* 6.5), 4.50 (4 H, s), 5.55 (2 H, m), 6.00 (2 H, m), 7.25−7.31 (2 H, m), 7.31−7.37 (8 H, m). ^{13}C NMR ($CDCl_3$, 100.6 Hz): *δ* 29.2, 29.4, 69.7, 72.9, 127.5, 127.6,

128.3, 130.7, 131.7, 138.6. HRMS (EI) (performed on a a 43 : 57 mixture of **3d** and **3'd**): *m/z* 259.1701 ([M−Bn]$^+$ $C_{17}H_{23}O_2^+$ requires 259.1693).

[(*E*)-9-benzyloxy-4-methylene-non-5-enoxy]methylbenzene (3'd). Viscous colourless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 1.72 (2 H, tt, *J* 7.5, 6.5), 1.79 (2 H, tt, *J* 7.5, 6.5), 2.19 (2 H, tdd, *J* 7.5, 7.0, 1.5), 2.27 (2 H, td, *J* 7.5, 1.0), 3.48 (2 H, t, *J* 6.5), 3.49 (2 H, t, *J* 6.5), 4.50 (2 H, s), 4.51 (2 H, s), 4.86 (1 H, br s), 4.89 (1 H, br s), 5.70 (1 H, dt, *J* 16.0, 7.0), 6.06 (1 H, dt, *J* 16.0, 1.5), 7.25-7.31 (2 H, m), 7.31−7.37 (8 H, m). ^{13}C NMR ($CDCl_3$, 100.6 Hz): *δ* 28.3, 28.6, 29.4, 29.4, 69.7, 70.0, 72.9, 72.9, 113.5, 127.5, 127.5, 127.6, 127.6, 128.3, 128.3, 129.5, 132.3, 138.6, 138.6, 145.6.

1,2,4-Tris(3-benzyloxyproyl)benzene (4d). Colourless liquid. IR (neat) (performed on a 49 : 51 mixture of **4d** and **4'd**): *v* 2927 (m), 2854 (m), 1495 (w), 1452 (m), 1352 (m), 1204 (w), 1099 (s), 1075 (m), 1027 (m), 734 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 1.84−1.95 (6 H, m), 2.64 (2 H, br t, *J* 7.5), 2.68 (4 H, br t, *J* 8.0), 3.46−3.52 (6 H, m), 4.50 (6 H, br s), 6.94 (1 H, dd, *J* 7.5, 2.0), 6.96 (1 H, d, *J* 2.0), 7.04 (1 H, d, *J* 7.5), 7.24−7.37 (15 H, m). ^{13}C NMR ($CDCl_3$, 100.6 MHz): *δ* 28.6, 29.0, 31.07, 31.14, 31.4, 31.9, 69.6, 69.80, 69.81, 72.8, 72.9, 72.9, 126.0, 127.5, 127.5, 127.5, 127.6, 127.6, 127.6, 128.3, 128.3, 128.3, 129.2, 129.4, 137.1, 138.6, 138.6, 138.6, 139.5, 139.7. HRMS (ESI) (performed on a 49 : 51 mixture of **4d** and **4'd**): m/z 523.3223 ([MH]$^+$ $C_{36}H_{43}O_3^+$ requires 523.3207), 545.3043 ([MNa]$^+$ $C_{36}H_{42}NaO_3^+$ requires 545.3026), 561.2784 ([MK]$^+$ $C_{36}H_{42}KO_3^+$ requires 561.2766).

1,3,5-Tris(3-benzyloxyproyl)benzene (4'd). Colourless liquid. ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 1.84−1.95 (6 H, m), 2.64 (6 H, br t, *J* 7.5), 3.48 (6 H, t, *J* 6.5), 4.50 (6 H, s), 6.82 (3 H, s), 7.24−7.37 (15 H, m). ^{13}C NMR ($CDCl_3$, 100.6 MHz): *δ* 31.4, 32.3, 69.6, 72.9, 126.1, 127.5, 127.6, 128.3, 138.6, 142.0.

Cyclotrimerisation of alkyne 1e under microwave conditions. *n*-Butyllithium solution (2.20 M in hexanes, 0.900 equiv, 2.70 mmol, 1.23 mL) was added dropwise, over 1 minute, at 0 °C, to a solution of titanium(IV) isopropoxide (0.600 equiv, 1.80 mmol, 534 µL) in THF (4.0 mL), in a flame-dried 10 mL microwave vial. After 5 minutes of stirring at 0 °C, 4-benzyloxybut-1-yne **1e** (1.00 equiv, 3.00 mmol, 481 mg) was added dropwise to the dark solution. The septum on the vial was quickly replaced with the suitable sealed cap and the vial was immediately heated with an Anton Paar Monowave 300 Microwave Synthesis Reactor (100 ° C, 15 min). After cooling, H_2O (0.5 mL) was added. After 30 minutes of stirring, the mixture was then filtered through a pad of sand, $MgSO_4$, celite and sand (from bottom to top; rinsing with Et_2O) and concentrated under reduced pressure (down to 50 mbar only) to afford a yellow oil (390 mg). Analysis by ^{1}H NMR spectroscopy revealed the presence of the [2+2+2] cyclotrimerisation adducts **4e** and **4'e**, in a 92:8 ratio and an estimated 50% combined yield. Purification by flash column chromatography (EtOAc/petroleum ether, gradient from 2% to 20%) afforded relatively pure diene **3'e** (23.9 mg, 74.1 µmol, 5%) and a 92 : 8 mixture of pure **4e** and **4'e** (192 mg, 399 µmol, 40%).

[(*E*)-7-Benzyloxy-3-methylene-hept-4-enoxy]methylbenzene (3'e). ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 2.42 (2 H, td, *J* 7.0, 1.0), 2.54 (2 H, td, *J* 7.0, 1.0), 3.50 (2 H, t, *J* 7.0), 3.61 (2 H, t, *J* 7.0), 4.51 (2 H, s), 4.52 (2 H, s), 4.94 (1 H, br s), 4.97 (1 H, br s), 5.72 (1 H, dt, *J* 16.0, 7.0), 6.13 (1 H, br d, *J* 16.0), 7.24−7.36 (10 H, m).

1,2,4-Tris(2-benzyloxyethyl)benzene (4e). Colourless oil. IR (neat): *v* 2929 (w), 2855 (m), 1495 (w), 1453 (m), 1360 (m), 1204 (w), 1092 (s), 1074 (s), 1027 (m), 733 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 2.87 (2 H, t, *J* 7.0), 2.94 (4 H, t, *J* 7.5), 3.62 (2 H, t, *J* 7.5), 3.62 (2 H, t, *J* 7.5), 4.49 (2 H, s), 4.50 (2 H, s), 4.51 (2 H, s), 3.66 (2 H, t, *J* 7.0), 7.01 (1 H, dd, *J* 7.5, 1.5), 7.04 (1 H, d, *J* 1.5), 7.10 (1 H, d, *J* 7.5), 7.24−7.35 (15 H). ^{13}C NMR ($CDCl_3$, 100.6 MHz): *δ* 32.7, 33.1, 35.9, 71.0, 71.0, 71.3, 72.91, 72.95, 72.95, 127.0, 127.5, 127.5, 127.5, 127.6, 127.6, 127.6, 128.3, 128.3, 128.3, 129.8, 130.4, 134.7, 136.8, 136.9, 138.35, 138.35, 138.38. MS (ESI): *m/z* 355.1, 373.2 ([M−OBn]$^+$), 445.3, 463.1, 503.3 ([MNa]$^+$), 539.2.

1,3,5-Tris(2-benzyloxyethyl)benzene (4'e). ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 2.88 (6 H, t, *J* 7.0), 3.66 (6 H, t, *J* 7.0), 4.51 (6 H, s), 6.93 (3 H, s), 7.24−7.35 (15 H). ^{13}C NMR ($CDCl_3$, 100.6 MHz), characteristic signals: *δ* 36.2, 72.9, 127.5.

Synthesis and isolation of "Marie-Anne tetramer" (5b). *s*-Butyllithium solution (1.14 M in cyclohexane, 1.65 equiv, 3.30 mmol, 2.89 mL) was added dropwise, over 2 minutes, at 0 °C, to a solution of titanium(IV) isopropoxide (1.10 equiv, 2.20 mmol, 651 µL) in THF (5.0 mL). The solution turned yellow, then orange and then dark brown. After 5 minutes of stirring at 0 °C, it had turned black and 3-phenylprop-1-yne **1b** (1.00 equiv, 2.00 mmol, 249 µL) was added dropwise, over 4 minutes. The mixture was stirred at 0 °C for an additional 45 minutes. H_2O (0.5 mL) was then added. After 15 minutes of stirring, the septum was removed to expose the mixture to air and stirring was continued for 10 more minutes. The mixture was then filtered through a pad of sand, $MgSO_4$, celite and sand [from bottom to top; rinsing with Et_2O (20 mL)] and concentrated under reduced pressure (down to 100 mbar only) to afford a yellow oil (390 mg). Analysis by ^{1}H NMR spectroscopy revealed the presence of **1b**, **2b**, **2'b**, **3b**, **3'b**, **4b**, **4'b** and **5b** in estimated yields of 12%, 5%, 3%, 12%, 17%, 4%, 2% and 28%, respectively. After thorough concentration under reduced pressure, the residue (yellow oil, 212 mg) was triturated with MeOH (1.0 mL). In the freezer, a solid separated from the MeOH solution. The liquid was removed when still cold. The solid residue was allowed to warm to 20 °C and dried under reduced pressure. A yellow gum was obtained (116 mg). The process was repeated with 0.5 mL of MeOH, to afford yellow crystals (94.9 mg). Recrystallisation from EtOAc (0.5 mL) gave pure tetramer **5b** (35.1 mg). A second batch (35.2 mg) was obtained by another recrystallisation from the mother liquor. Total for **5b**: 70.3 mg, 151 µmol, 30%.

Allylbenzene (2b).[39] ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 3.39 (2 H, ddd, *J* 6.5, 1.5, 1.0), 5.07 (1 H, ddt, *J* 10.0, 1.5, 1.0), 5.08 (1 H, dq, *J* 17.0, 1.5), 5.97 (1 H, ddt, *J* 17.0, 10.0, 6.5), 7.19 (2 H, br d, *J* 8.0), 7.20 (1 H, br t, *J* 7.5), 7.29 (2 H, br dd *J* 8.0, 7.5). ^{13}C NMR ($CDCl_3$, 100.6 MHz): *δ* 40.2, 115.8, 126.0, 128.4, 128.6, 137.4, 140.0.

2-Methylenehexylbenzene (2'b). ^{1}H NMR ($CDCl_3$, 400 MHz), characteristic signals: *δ* 0.88 (3 H, t, *J* 7.0), 1.97 (2 H, br t, *J* 8.0), 4.72 (1 H, br s), 4.81 (1 H, br s). ^{13}C NMR ($CDCl_3$, 100.6 MHz), characteristic signals: *δ* 13.8, 22.2, 29.6, 34.9, 42.8, 110.7, 149.0.

[(2*E*,4*E*)-6-Phenylhexa-2,4-dienyl]benzene (3b).[40] White solid. M.p. 74.0−75.1 °C (from EtOAc); litt. 75 °C (from MeOH).[41] ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 3.40 (4 H, d, *J* 6.5), 5.75 (2 H, m, distorted dt, *J* 14.5, 6.5), 6.08 (2 H, m, *J* 14.5), 7.18 (4 H, br d, *J* 7.5), 7.19 (2 H, br t, *J* 7.5), 7.28 (4 H, br t, *J* 7.5). ^{13}C NMR ($CDCl_3$, 100.6 MHz): *δ* 39.0, 126.0, 128.4, 128.6, 131.2, 131.5, 140.3.

[(2*E*)-4-Benzylpenta-2,4-dienyl]benzene (3'b). ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 3.40 (2 H, d, *J* 7.0), 3.55 (2 H, s), 4.82 (1 H, br s), 5.09 (1 H, br s), 5.86 (1 H, dt, *J* 15.5, 7.0), 6.19 (1 H, br d, *J* 15.5), 7.09 (2 H, br d, *J* 7.5), 7.13−7.31 (8 H, m). ^{13}C NMR ($CDCl_3$, 100.6 Hz): *δ* 38.9, 39.0, 116.5, 125.9, 126.0, 128.2, 128.4, 128.5, 128.9, 129.5, 133.0, 139.6, 140.3, 144.9.

1,2,4-Tribenzylbenzene (4b).[42] Orange oil. ^{1}H NMR ($CDCl_3$, 400 MHz), characteristic signals: *δ* 3.88 (2 H, s), 3.91 (2 H, s), 3.93 (2 H, s), 7.05 (4 H, br d, *J* 7.5), 7.12-7.30 (11 H, m). ^{13}C NMR ($CDCl_3$, 100.6 Hz): *δ* 38.6, 39.0, 41.5, 125.9, 125.9, 125.9, 127.1, 128.3, 128.3, 128.3, 128.6, 128.7, 128.8, 130.7, 131.3, 136.8, 138.9, 139.3, 140.5, 140.6, 141.2.

1,3,5-Tribenzylbenzene (4'b).[42,43] Orange oil. ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 3.89 (6 H, s), 6.86 (3 H, s), 7.12-7.30 (15 H, m). ^{13}C NMR ($CDCl_3$, 100.6 Hz): *δ* 41.8, 125.9, 127.5, 128.3, 128.9, 141.1, 141.3.

[(2*E*,4*Z*,5*Z*,6*E*)-8-Phenyl-4,5-bis(2-phenylethylidene)octa-2,6-dienyl]benzene (5b). Colourless crystals, mp 74.9−77.0 °C (from EtOAc). IR (neat): *ν* 3061 (w), 3025 (w), 3010 (w), 2890 (w), 2836 (w), 1599 (w), 1492 (m), 1453 (m), 1432 (w), 1077 (w), 960 (s), 920 (w), 747 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 3.30 (4 H, AB part of an ABX system, δ_A 3.27, δ_B 3.32, J_{AB} 16.0, J_{AX} 6.5, J_{BX} 8.0), 3.40 (4 H, dd, *J* 7.0, 1.5), 5.72 (2 H, dt, *J* 15.5, 7.0),

5.79 (2 H, dd, *J* 8.0, 6.5), 6.16 (2 H, dt, *J* 15.5, 1.5), 7.06 (4 H, br d, *J* 7.5), 7.13 (4 H, br d, *J* 7.5), 7.14−7.22 (8 H, m, H6 or H13, H7), 7.25 (4 H, br dd, *J* 7.5, 7.0). ^{13}C NMR ($CDCl_3$, 100.6 Hz): *δ* 35.7, 39.0, 125.8, 125.9, 128.4, 128.4, 128.53, 128.54, 129.6, 130.9, 132.5, 136.9, 140.5, 140.7. HRMS (ES$^+$): *m/z* 467.2729 (MH^+ $C_{36}H_{35}^+$ requires 467.2733). CCDC-2311234 contains the supplementary crystallographic data for this compound. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

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Supplementary Material

Experimental detail on the preparations of the alkyne substrates **1c**-**f** and on their transformations; detail on the analyses of the crude product mixtures; characterisation data, copies of ^{1}H and ^{13}C NMR spectra; detail on the kinetic simulations and determination of rate constants, as well as crystallographic detail for compound **5b** are available as Supporting Information.

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