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Can the $\text{Ti}(\text{O}i\text{Pr})_4/n\text{BuLi}$ Combination of Reagents Function as a Catalyst for [2+2+2] Alkyne Cyclotrimerisation Reactions?^{†‡}

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Catalysis of the cyclotrimerisation of alkynes with the $\text{Ti}(\text{O}i\text{Pr})_4/n\text{BuLi}$ system was studied, leading to the development of a particularly convenient and reliable protocol. This method allows the [2+2+2] cycloaddition reaction to proceed within a few minutes under microwave conditions, with generally good selectivity from a variety of aromatic and aliphatic alkynes.

Introduction

Since the initial discoveries by the group of O. G. Kulinkovich,^{1,2} the combined use of titanium(IV) isopropoxide and excess amounts of Grignard reagents [> 2 equivalents (equiv) vs $\text{Ti}(\text{O}i\text{Pr})_4$] has led the development of a family of powerful synthetic tools.³ Analogous chemistry using organolithium reagents RLi only emerged in the early 2000s, with reports by the group of J. J. Eisch,⁴ although earlier studies on the mono-transmetallation of organolithium reagents with $\text{Ti}(\text{O}i\text{Pr})_4$ had been carried out from the mid-20th century.^{5,6} Using 2 equiv of an organolithium reagent having a β -hydrogen atom with 1 equiv of $\text{Ti}(\text{O}i\text{Pr})_4$, the behaviour of the organometallic species generated is consistent with the titanacyclopentadiene structure **1** (Scheme 1). The conditions described by J. J. Eisch (-78°C then overnight, 25°C) are in fact not applicable because of the low thermal stability of **1** but subsequent work reported by several groups has revealed the synthetic potential of the combination of reagents.^{7–10} Moreover, using non-standard proportions, i.e. 2 equiv of $\text{Ti}(\text{O}i\text{Pr})_4$ and 3 equiv of $n\text{BuLi}$, we showed that **1** can be conveniently and reproducibly generated at 0°C in THF.¹¹

Scheme 1 Generation of the active titanacyclopentadiene complex **1**.

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[†] Dedicated to Prof. Janusz Zakrzewski of the University of Łódź, Poland, on the occasion of his 70th birthday.

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It was also disclosed that terminal alkynes **2** undergo rapid cyclotrimerisation when treated with a solution of **1** prepared in this way (about 1.1 equiv, generated from 2.2 equiv of $\text{Ti}(\text{O}i\text{Pr})_4$ and 3.3 equiv of $n\text{BuLi}$, Scheme 2).¹² Excellent 1,2,4 regioselectivity is observed in the case of aryl-substituted substrates. The mechanism is likely to proceed *via* titanacyclopentadiene and titanacyclopentadiene intermediates **3** and **4**. To account for the eventual formation of the [2+2+2] product **5** (**5'**), several pathways can be put forward, for instance a [4+2] cycloaddition reaction as shown in Scheme 2. Every possibility formally involves extrusion of $\text{Ti}(\text{O}i\text{Pr})_2$ and in principle, the latter could then react with the alkyne starting material **2** to regenerate species **3**, thereby establishing a catalytic cycle.

Results and discussion

Initial investigation

A preliminary study on this prospect was conducted with phenylacetylene **2a**. The first experiment, involving the generation of *ca.* 0.5 equivalent of complex **1**, was not encouraging (Table 1, entry 2 vs entry 1). Conversion of **2a** was not complete and large amounts of diene **6a** were produced, presumably by hydrolysis of unreacted intermediate **4a**

Scheme 2 Alkyne cyclotrimerisation mediated by **1**: previous work and tentative mechanism.

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Table 1 Modification of the initial experimental procedure for the cyclotrimerisation of phenylacetylene **2a**.^a

$\text{Ph-C}\equiv\text{C-Ph} \xrightarrow[\text{(1.0 equiv)}]{\text{[1] (generated at 0 °C) solvent, T °C, time}} \text{Ph-C}_6\text{H}_3\text{-Ph} \text{ (5a)} + \text{Ph-C}_6\text{H}_4\text{-Ph} \text{ (6a)} + \text{2a}$							
Entry	Ti(OiPr) ₄ (equiv)	nBuLi (equiv)	solvent	T (°C)	time	5a/6a/2a ratio ^b	5a yield ^c
1	2.2	3.3	THF	20	20 min	94:06:00	84%
2	1.0	1.5	THF	20	20 min	36:36:28	
3	0.40	0.60	THF	20	20 h	91:09:00	
4	0.20	0.30	THF	20	20 h	60:07:33	
5	0.20	0.30	THF	66 (reflux)	20 h	92:08:00	68%
6	0.10	0.15	THF	66 (reflux)	20 h	27:02:71	
7 ^d	0.20	0.30	THF	66 (reflux)	20 h	81:19:00	55%
8	0.20	0.30	tBuOMe	55 (reflux)	20 h	72:04:24	
9	0.20	0.30	THF	70 (μW) ^e	45 min	91:09:00	
10	0.20	0.30	THF	70 (μW) ^e	30 min	93:07:00	74%
11	0.20	0.30	THF	70 (μW) ^e	10 min	93:07:00	
12	0.10	0.15	THF	70 (μW) ^e	10 min	09:01:90	
13	0.10	0.15	THF	70 (μW) ^e	90 min	15:01:84	

^a Experimental procedure, unless otherwise stated: a solution of **1** in the dry solvent indicated, generated at 0 °C from Ti(OiPr)₄ and nBuLi, was added dropwise to a cold (0 °C) solution of **2a** in the same solvent. The mixture was then stirred at T °C for the time indicated. ^b Qualitative estimation obtained by ¹³C NMR spectroscopy. ^c Isolated yield. ^d A simplified experimental procedure was applied, whereupon **1** was generated in the presence of the alkyne. ^e "μW" stands for heating by microwave irradiation.

(structure **4** in Scheme 2 with R = Ph). Better results could be obtained by extending the reaction time to 20 h, even with decreased amounts of Ti(OiPr)₄ and nBuLi (entry 3). Further decrease to 0.1 equiv of **1** led to lower conversion of **2a** (entry 4) but gratifyingly, heating the reaction mixture at reflux restored reactivity (entry 5). An attempt made at simplifying the procedure by generating the active complex **1** directly in the presence of the alkyne reactant led to a somewhat inferior result (entry 7). Switching the solvent to tBuOMe was unsatisfactory, with lower conversion of **2a** (entry 8), as well as the production of polymeric material.⁵ We next investigated the effect of microwave irradiation (entries 9–13). Much faster production of the cyclotrimerisation product **5a** was observed (entry 11). Finally, attempts at further decreasing the amount of catalyst **1** down to less than 0.1 equiv led to poor results (entries 6, 12 and 13).

Development of a better procedure, under microwave conditions

This first set of experiments had established that complex **1** could catalyse the cyclotrimerisation of **2a** but the experimental protocol remained somewhat tedious. Indeed, it involved pre-formation of species **1** in a separate vessel (procedure A). We sought to simplify this procedure in two ways, either by generating **1** in the presence of **2a** [Table 2, entry 2, (procedure B)], as had been attempted already under standard reflux conditions (Table 1, entry 7), or by adding **2a** directly into the solution of pre-formed **1** [Table 2, entry 3, (procedure C)]. When procedure B was applied, comparatively large amounts of undesired polymer compounds were

produced again. This problem was minimised with the convenient procedure C and little difference was observed with the results obtained with procedure A (Table 2, entry 3 vs entry 1).⁶ However, the amounts of Ti(OiPr)₄ and nBuLi could not be reduced further, even using freshly distilled THF from sodium/benzophenone. Moreover, at times, we experienced difficulties reproducing our results. This is not surprising since in practice, the septum on the reaction vial must be quickly replaced with a cap for the microwave apparatus, which causes introduction of a small quantity of oxygen and traces of water. Eventually, our best result was obtained with 0.14 equiv of Ti(OiPr)₄ and 0.21 equiv of nBuLi, corresponding to 0.07 equiv of complex **1** (Table 2, entry 4).

One experiment performed with Cp₂TiCl₂ instead of Ti(OiPr)₄ left **2a** essentially unscathed, with the production of minor amounts of unidentified new compounds. More interestingly, when Grignard reagents were used, the cyclotrimerisation of **2a** proceeded with strikingly modified regioselectivity (Scheme 3). Indeed, the 1,3,5-triphenyl isomer **5'a**, which had not been observed so far, was now produced in comparatively large amounts, suggesting the extensive formation of the titanacyclopentadiene intermediate complex **4'a**. Explanation for this phenomenon is not straightforward, especially if one remembers that when treated with Ti(OiPr)₄ and a Grignard reagent in Et₂O at low temperature, phenylacetylene **2a** is transformed selectively into (E,E)-1,4-diphenylbutadiene **6a**.¹³ However, similar selectivity in [2+2+2] cycloaddition reactions has been reported by the group of S. Okamoto using a reagent system composed of Ti(OiPr)₄ (1 equiv), Mg powder (3 equiv) and Me₃SiCl (2 equiv).¹⁴

Table 2 Cyclotrimerisation studies performed with phenylacetylene **2a**, under microwave conditions.

$\text{Ph-C}\equiv\text{C-Ph} \xrightarrow[\text{(1.0 equiv)}]{\text{[1] (generated at 0 °C) microwaves THF, 100 °C}} \text{Ph-C}_6\text{H}_3\text{-Ph} \text{ (5a)} + \text{Ph-C}_6\text{H}_4\text{-Ph} \text{ (6a)} + \text{2a}$							
Entry	Ti(OiPr) ₄ (equiv)	nBuLi (equiv)	solvent	procedure ^a	time (min)	5a/6a/2a ratio ^b	5a yield ^c
1 ^d	0.20	0.30	THF	A ^e	30	93:07:00	74%
2	0.20	0.30	THF	B	30	100:0:0 ^f	
3	0.20	0.30	THF	C	30	91:06:03	72%
4	0.14	0.21	THF	C	30	95:05:00	71%
5	0.10	0.15	THF	C	30	54:03:43	
6	0.10	0.15	THF	C	60	34:03:63	
7	0.070	0.105	THF	C	30	13:00:87	

^a Procedure A: a solution of **1** in dry THF, generated at 0 °C from Ti(OiPr)₄ and nBuLi, was added dropwise to a cold (0 °C) solution of **2a** in THF. The mixture was then heated with a microwave apparatus for 30 minutes. Procedure B: as Procedure A except nBuLi was added dropwise, at 0 °C, to a solution of **2a** and Ti(OiPr)₄ in dry THF. Procedure C: **2a** was added to a solution of **1** in dry THF, generated at 0 °C from Ti(OiPr)₄ and nBuLi. The mixture was then heated with a microwave apparatus for the time indicated. ^b Qualitative estimation obtained by ¹³C NMR spectroscopy. ^c Isolated yield. ^d Entry 1 is taken from Table 1 (entry 10) for comparison purposes. ^e Reaction performed at 70 °C. ^f Polymeric by-products were observed.

Scheme 3 Comparison of the uses of $n\text{BuLi}$ and Grignard reagents in the titanium-catalysed cyclotrimerisation of phenylacetylene **2a**.

Optimised conditions and scope

To circumvent the reproducibility issues encountered at the lowest loadings of $\text{Ti}(\text{O}i\text{Pr})_4$ and $n\text{BuLi}$ and even, occasionally, with 0.2 equiv of $\text{Ti}(\text{O}i\text{Pr})_4$ and 0.3 equiv of $n\text{BuLi}$, one could consider excluding water and oxygen more rigorously from the system. This, of course, would be inconvenient, costly and hazardous, with the routine use of a glove box and distillation of THF over sodium. Given the low cost and wide availability of both $\text{Ti}(\text{O}i\text{Pr})_4$ and $n\text{BuLi}$, we chose a more practical solution consisting in increasing their amounts to 0.6 and 0.9 equivalents respectively. The reaction could not be considered truly catalytic any longer but became more efficient (**5a** was isolated in 84% yield from **2a**) and, more importantly, perfectly reliable. The results of the reactions of several terminal alkynes, under these conditions, are presented in Table 3. Moderate to excellent yields and high regioselectivities in favour of the 1,2,4 products **5a–d** were achieved with arylacetylene derivatives **2a–d**. The reactivity of **2e** was non-typical (see next paragraph). Enyne substrates 1-ethynylcyclohexene **2f** and 2-methyl-1-buten-3-yne **2g** reacted with excellent regioselectivity as well but **5f** and **5g** were produced in low yields, together with a number of unidentified by-products. More interestingly, hept-1-yne **2h** was converted into the [2+2+2] adduct **5h** in 86% yield. This is remarkable, since the same transformation had performed poorly under the previously developed conditions (2.2 equiv of $\text{Ti}(\text{O}i\text{Pr})_4$ and 3.3 equiv of $n\text{BuLi}$ at room temperature), with large amounts of diene by-products.¹² These experimental results suggest that the reaction of the third molecule of **2h** with the titanacyclopentadiene intermediates **4/4'** is more difficult than in the case of **2a** but can be sufficiently accelerated upon heating. Another difference with the reaction of **2a** is the lower regioselectivity (**5h/5'h** $\approx 65:35$), indicating that the 1,3-disubstituted intermediate complex **4'h** is produced in significant amounts. The reactions of the bulkier substrates 3,3-dimethyl-but-1-yne **2i** and cyclopropylacetylene **2j** proceeded with better selectivities (86:14 and 89:11 respectively) but in somewhat lower yields, perhaps because of their volatility.

Table 3 Titanium-mediated cyclotrimerisation reactions of terminal alkynes, performed under simplified and reliable conditions.^a

^a Unless indicated otherwise, all the yields are for isolated products. **5/5'** regioisomeric ratios are indicated in parentheses. ^b The starting alkyne was added as a solution in THF. ^c **5e** was formed together with a hydro-defluoro-substitution product (total yield 63%). The 39% yield indicated is for **5e** only. ^d Yield estimated by ¹H NMR spectroscopy.⁵

Unexpected hydro-dehalo-substitution

Intriguing hydro-dehalo-substitution processes were observed when halophenylacetylene substrates were engaged (Scheme 4). The single hydro-dehalo-substitution products **7e**, **7k** and **7l** are formed predominantly,⁵ with remarkable selectivity in the case of the fluoro substrates **2e** and **2k**. The hydro-dehalo-substitution appears to be more facile with chloro derivatives, as evidenced by the low yield (6%) of the trichloro product **5l** and the significant formation of mono-chloro by-products **8l** and **9l**.⁵ Work-up of the reaction mixture with D_2O did not result in any deuterium atom incorporation into the products. Interestingly, the phenomenon is significantly minimised when only 0.3 equiv of $\text{Ti}(\text{O}i\text{Pr})_4$ and 0.6 equiv of $n\text{BuLi}$ are employed, instead of 0.6 and 0.9 equiv respectively.⁵ This suggests that $n\text{BuTi}(\text{O}i\text{Pr})_3$ might play a key role in the reduction process. Moreover, when purified **5e** is submitted to the reaction conditions again, the defluorinated molecule **7e** is formed in significant amounts. This is consistent with a hydro-dehalo-substitution reaction taking place after the alkyne cyclotrimerisation process. A tentative mechanistic proposal is presented in Scheme 5.

Scheme 4 Reactions of haloarylacetylene substrates **2e**, **2k** and **2l**.

Scheme 5 Tentative mechanism for the formation of hydro-dehalo-substitution products.

According to this hypothesis, an aryltitanium intermediate complex, e.g. **10e** starting from **5e**, would be generated by oxidative addition of a C-halogen bond onto “Ti(OiPr)₂”. Subsequent reaction with *n*BuTi(OiPr)₃, by σ -bond metathesis, would lead to the new complex **11e**. Eventually, intramolecular hydrogen atom transfer, analogous to the initial formation of **1** from *n*Bu₂Ti(OiPr)₂, would produce **7e** and regenerate **1**. The latter would thus function as a catalyst in this transformation and the source of hydrogen atom would be *n*BuTi(OiPr)₃. It is interesting to note that in the ¹³C NMR spectra of **5e**, **5k** and

5l, the most downfield C-halogen signals belong to the very aryl groups where the hydro-dehalo-substitution take place preferentially. This is reasonable, since it corresponds to oxidative addition of the most polarised carbon-halogen bonds. Nonetheless, further work is still needed, and will be carried out, in order to support this mechanistic picture more decisively or rule it out.

Disubstituted alkyne substrates

Finally, the possibility to extend the titanium-mediated cyclotrimerisation process to internal alkynes **12** was briefly examined (Table 4). The reactions of but-2-yne **12a** and 1-phenylprop-1-yne **12d** afforded the corresponding hexasubstituted benzene derivatives **13a** and **13d** in satisfactory yields, **13d** being obtained with good selectivity (88:12). In contrast, oct-4-yne **12b**, diphenylacetylene **12c** and 1-phenylpent-1-yne **12e** gave poor results, suggesting that the transformation does not tolerate internal alkyne substrates having both substituents larger than a methyl group. Interestingly, in the case of the reaction of **12b**, which gave hexapropylbenzene **13b** in low yield (14%), no trace of diene resulting from hydrolysis of the titanacyclopentadiene intermediate of type **4** was observed. The only by-product is (Z)-oct-4-ene, the presence of which presumably results from hydrolysis of unreacted titanacyclopentadiene complex. The limiting factor thus appears to be the reaction of the second molecule of **12b**. A similar situation is met starting from **12c** and **12e**, with substantial amounts of cis-stilbene and (Z)-1-phenylpent-1-ene being produced, while neither diene resulting from dimerisation nor cyclotrimerised product **13** are observed.

Table 4 Titanium-mediated cyclotrimerisation reactions of disubstituted alkynes **12**.^a

^a Typical experimental procedure as in Table 3.⁵ Unless indicated otherwise, all the yields are for isolated products. The **13d**/**13'd** ratio is indicated in parentheses. ^b Yield estimated by ¹H NMR spectroscopy. Only partial conversion took place and the production of (Z)-oct-4-ene, in about 28% yield, was also observed.

Conclusions

To conclude, our new results demonstrate that the $\text{Ti}(\text{OiPr})_4/n\text{BuLi}$ system can function as a catalyst for the cyclotrimerisation of alkynes. However, the use of 0.6 equiv of $\text{Ti}(\text{OiPr})_4$ and 0.9 equiv of $n\text{BuLi}$ with respect to the alkyne substrate gives the most reliable results. Although these new conditions cannot be applied to the heterocyclotrimerisation reactions we developed earlier, which require the stoichiometric preparation of titanacyclopropene complexes from internal alkynes,¹² they represent a dramatic improvement over our previously described alkyne homocyclotrimerisation method, as summarised in Scheme 6. In addition, comparison with the few other Ti-catalysed processes reported in the literature¹⁵ reveals significant advantages, notably the low cost and direct availability of the reagent system, as well as the practicability of the experimental procedure.

Experimental section

For general information, see the ESI.[†] Compounds **5a**,^{12,16} **5'a**,¹⁷ **5b**,^{12,15b,18} **5c**,¹⁹ **5d**,^{12,18a,20} **5e**,^{18a,21} **5f**, **5'f**,²² **5g**,²³ **5'g**,^{23a} **5h**,^{12,24} **5'h**,²⁴ **5i**,²⁵ **5'i**,²⁶ **5j**, **5'j**,²⁷ **5l**,^{18,19,20} **9l**,^{18b} **13a**,²⁶ **13b**,²⁸ **13d**²⁹ and **13'd**^{29a} have already been described and their analytical data are in good agreement with those reported in the literature.⁵

General procedure (GP) for the cyclotrimerisation reactions under optimised conditions.

$n\text{BuLi}$ (≈ 2.0 M solution in hexanes, 0.900 equiv, 2.70 mmol) was added dropwise, over 1 min, into a solution of $\text{Ti}(\text{OiPr})_4$ (0.600 equiv, 1.80 mmol) in dry THF (4.0 mL), in a flame-dried 10 mL microwave vial, under argon at 0 °C. After 5 min of stirring at 0 °C, the alkyne substrate (1.00 equiv, 3.00 mmol) was then added dropwise. The septum on the vial was quickly replaced with the suitable sealed cap and the vial was

immediately heated with the microwave synthesis reactor (100 °C, 15 min). After cooling, 2 M HCl aqueous solution (10 mL) was added. The mixture was stirred at r.t. for 15 min, then extracted with Et_2O (3×10 mL). The combined organic phases were dried over MgSO_4 , filtered and concentrated under reduced pressure to afford the crude product.

Cyclotrimerisation of phenylacetylene **2a**.

Catalytic reaction performed at reflux (Table 1, entry 5). $n\text{BuLi}$ (2.14 M solution in hexanes, 0.300 equiv, 1.80 mmol, 841 μL) was added dropwise, over 2.5 min, into a solution of $\text{Ti}(\text{OiPr})_4$ (0.200 equiv, 1.20 mmol, 355 μL) in dry THF (8.0 mL), under argon at 0 °C. After 5 min of stirring at 0 °C, the resulting solution was added dropwise, over 2.5 min, into a solution of phenylacetylene **2a** (1.00 equiv, 6.00 mmol, 660 μL) in THF (1.0 mL) at 15 °C. The mixture was then heated at reflux for 20 h. After cooling, 2 M HCl aqueous solution (15 mL) was added. The mixture was stirred at r.t. for 15 min, then extracted with Et_2O (3×15 mL). The combined organic phases were dried over MgSO_4 , filtered and concentrated under reduced pressure to afford the crude product. Purification by flash column chromatography on silica gel (EtOAc /petroleum ether, gradient from 0 to 10%) afforded pure 1,2,4-triphenylbenzene **5a** (418 mg, 1.36 mmol, 68%).

Catalytic reaction performed under microwave conditions, with a simplified procedure (Table 2, entry 3 and Scheme 3, top). $n\text{BuLi}$ (2.34 M solution in hexanes, 0.300 equiv, 900 μmol , 385 μL) was added dropwise, over 1 min, into a solution of $\text{Ti}(\text{OiPr})_4$ (0.200 equiv, 600 μmol , 178 μL) in dry THF (4.5 mL), in a flame-dried 10 mL microwave vial, under argon at 0 °C. After 5 min of stirring at 0 °C, **2a** (1.00 equiv, 3.00 mmol, 330 μL) was added dropwise. The septum on the vial was quickly replaced with the suitable sealed cap and the vial was immediately heated with the microwave synthesis reactor (100 °C, 30 min). After cooling, 2 M HCl aqueous solution (10 mL) was added. The mixture was stirred at r.t. for 15 min, then extracted with Et_2O (3×10 mL). The combined organic phases were dried over MgSO_4 , filtered and concentrated under reduced pressure to afford the crude product. Purification by flash column chromatography on silica gel (EtOAc /petroleum ether, gradient from 0 to 2%) afforded pure **5a** (222 mg, 725 μmol , 72%).

Catalytic reaction performed under microwave conditions with $i\text{PrMgCl}$ (Scheme 3, bottom). $i\text{PrMgCl}$ (1.73 M solution in THF, 0.300 equiv, 900 μmol , 520 μL) was added dropwise, over 1 min, into a solution of $\text{Ti}(\text{OiPr})_4$ (0.200 equiv, 600 μmol , 178 μL) in dry THF (4.5 mL), in a flame-dried 10 mL microwave vial, under argon at 0 °C. After 5 min of stirring at 0 °C, **2a** (1.00 equiv, 3.00 mmol, 330 μL) was added dropwise. The septum on the vial was quickly replaced with the suitable sealed cap and the vial was immediately heated with the microwave synthesis reactor (100 °C, 30 min). After cooling, 2 M HCl aqueous solution (10 mL) was added. The mixture was stirred at r.t. for 15 min, then extracted with Et_2O (3×10 mL).

Scheme 6 Comparison of the two terminal alkyne cyclotrimerisation methods developed by our group.

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The combined organic phases were dried over MgSO_4 , filtered and concentrated under reduced pressure to afford the crude product (380 mg, brown sticky oil). ^{13}C NMR analysis showed full conversion of the starting material and the production of 1,2,4- and 1,3,5-triphenylbenzene **5a** and **5'a** in 60 : 40 ratio. Purification by flash column chromatography on silica gel (EtOAc /petroleum ether, gradient from 0 to 2%) afforded a 58 : 42 mixture of **5a** and **5'a** (197 mg, 642 μmol , 64%).

Reaction performed under optimised conditions (Table 3). General procedure **GP** was applied with **2a**. Purification of the crude product (420 mg, brown sticky oil) by flash column chromatography on silica gel (EtOAc /petroleum ether, gradient from 0 to 2%) afforded pure **5a** (257 mg, 839 μmol , 84%).

Cyclotrimerisation reactions of terminal alkynes **2b-j** (Table 3).

1,2,4-Tris(*p*-tolyl)benzene 5b. General procedure **GP** was applied with **2b**. Purification of the crude product by flash column chromatography on silica gel (EtOAc /petroleum ether, gradient from 0 to 2%) afforded pure **5b** (273 mg, 783 μmol , 78%).

1,2,4-Tris(4-*tert*-butylphenyl)benzene 5c. General procedure **GP** was applied with **2c**. Purification of the crude product (685 mg, brown sticky oil) by flash column chromatography on silica gel (EtOAc /petroleum ether, gradient from 0 to 2%) afforded pure **5c** (436 mg, 918 μmol , 92%).

1,2,4-Tris(4-methoxyphenyl)benzene 5d. General procedure **GP** was applied with **2d**. Purification of the crude product (685 mg, brown sticky oil) by flash column chromatography on silica gel (EtOAc /petroleum ether, gradient from 1 to 10%) afforded pure **5d** (225 mg, 567 μmol , 57%).

1,2,4-Tris(4-fluorophenyl)benzene 5e and 1,2-bis(4-fluorophenyl)-4-phenyl-benzene 7e. General procedure **GP** was applied with **2e** [added into the reaction mixture as a solution in THF (0.5 mL)]. Analysis of the crude product (370 mg, brown sticky oil) by ^{13}C NMR spectroscopy showed full conversion of the starting material and the production of **5e** and **7e** in an estimated 65 : 35 ratio. Purification by flash column chromatography on silica gel (EtOAc /petroleum ether, gradient from 0 to 5%) afforded pure **5e** (36.8 mg, 103 μmol , 10%) and a 55 : 45 mixture of **5e** and **7e** (187 mg, 292 and 239 μmol respectively). The yields obtained for both compounds are thus 39% (**5e**) and 24% (**7e**).

7e. White solid. ^1H NMR (CDCl_3 , 400 MHz): δ 6.94 (2 H, br dd, J 9.0, 8.5), 6.95 (2 H, br dd, J 9.0, 8.5), 7.09–7.16 (4 H, m), 7.38 (1 H, br t, J 7.5), 7.47 (2 H, br t, J 7.5), 7.47 (1 H, d, J 8.0), 7.62 (1 H, br d, J 2.0), 7.63 (1 H, br dd, J 8.0, 2.0), 7.66 (2 H, br d, J 7.5). ^{13}C NMR (CDCl_3 , 100.6 MHz): δ 115.0 (4 C, br d, J 21.5), 126.3, 127.1, 127.6, 128.9, 129.3, 131.0, 131.33 (d, J 8.0), 131.38 (d, J 8.0), 136.8 (d, J 3.0), 137.2 (d, J 3.0), 138.4, 139.9, 140.3, 140.6, 161.80 (d, J 246.5), 161.83 (d, J 246.5). HRMS (EI): m/z 342.1209 (M^{+} , $\text{C}_{24}\text{H}_{16}\text{F}_2^{+}$ requires 342.1215). Note: this compound was not obtained in pure form but as a mixture with **5e**.

1,2,4-Tri(cyclohexen-1-yl)benzene 5f and 1,3,5-tri(cyclohexen-1-yl)benzene 5'f. General procedure **GP** was applied with **2f** but the work-up was performed as follows: H_2O (0.5 mL) was added and the mixture was stirred at r.t. for 30 min, before being filtered through a short pad of sand, MgSO_4 , celite and sand (from bottom to top) (rinsing: Et_2O). The combined organic phases were dried over MgSO_4 and filtered. *trans*-Cinnamic acid (200 μmol , 29.6 mg) was added as an internal standard and the solution was concentrated under reduced pressure to afford the crude product. ^1H NMR analysis, with comparison of the integrals of relevant signals, showed that **5f** and **5'f** had been produced in 19% yield (ratio 97 : 3).

1,2,4-Triisopropenylbenzene 5g and 1,3,5-triisopropenylbenzene 5'g. General procedure **GP** was applied with **2g**. Purification of the crude product (278 mg) by flash column chromatography on silica gel (pentane) afforded pure **5g** (11.2 mg) and a 90 : 10 mixture of **5g** and the 1,3,5 isomer **5'g** (3.0 mg). The total amount of triisopropenylbenzene isomers isolated is thus 13.2 mg (66.6 μmol , 7%).

1,2,4-Tripentylbenzene 5h and 1,3,5-tripentylbenzene 5'h. General procedure **GP** was applied with **2h**. Analysis of the crude product by ^1H NMR spectroscopy showed full conversion of the starting material and the production of **5h** and **5'h** in an estimated 65 : 35 ratio. Minor diene by-products **4h** and **4'h** made purification difficult and they were therefore destroyed by the following treatment: concentrated H_2SO_4 (0.5 mL) was added dropwise to the crude product at 0 $^\circ\text{C}$. After 15 min of stirring at r.t., H_2O (20 mL) was added dropwise at 0 $^\circ\text{C}$ and the mixture was extracted with Et_2O (3×20 mL). The combined organic phases were dried over MgSO_4 , filtered and concentrated under reduced pressure. Purification of the residue (351 mg, brown oil) by flash column chromatography on silica gel (petroleum ether) afforded a 62 : 38 mixture of **5h** and **5'h** (247 mg, 530 and 330 μmol respectively). The yields obtained for both compounds are thus 53% (**5h**) and 33% (**5'h**). **1,2,4-Tri(*tert*-butyl)benzene 5i and 1,3,5-tri(*tert*-butyl)benzene 5'i.** General procedure **GP** was applied with **2i**. Purification of the crude product (360 mg, orange oil) by flash column chromatography on silica gel (petroleum ether) afforded a 90 : 10 mixture of **5i** and **5'i** (121 mg, 491 μmol , 49%).

1,2,4-Tricyclopropylbenzene 5j and 1,3,5-tricyclopropylbenzene 5'j. General procedure **GP** was applied with **2j**. Purification by flash column chromatography on silica gel (pentane) afforded pure **5j** (28.1 mg, 142 μmol , 14%) and a 86 : 14 mixture of **5j** and **5'j** (52.7 mg, 229 and 37 μmol respectively). The yields obtained for both compounds are thus 37% (**5j**) and 4% (**5'j**).

Cyclotrimerisation reactions of halo substrates **2k-l** (Scheme 4).

1,2,4-Tris(2-fluorophenyl)benzene 5k and 1,2-bis(2-fluorophenyl)-4-phenyl-benzene 7k. General procedure **GP** was applied with **2k**. Analysis of the crude product by ^{13}C NMR spectroscopy showed full conversion of the starting material and the production of **5k** and **7k** in an estimated 55 : 45 ratio. Purification by flash column chromatography on silica gel

(EtOAc/petroleum ether, gradient from 0 to 2%) afforded pure **5k** (4.2 mg, 11.7 μ mol, 1%) and a 52 : 48 mixture of **5k** and **7k** (198 mg, 286 and 264 μ mol respectively). The yields obtained for both compounds are thus 30% (**5k**) and 26% (**7k**).

5k. Colourless oil. ^1H NMR (CDCl_3 , 400 MHz): δ 6.94 (1 H, ddd, J 10.0, 8.0, 1.0), 6.95 (1 H, ddd, J 10.0, 8.0, 1.0), 7.02 (2 H, br d, J 7.5), 7.13–7.24 (5 H, m), 7.23 (1 H, br t, J 7.5), 7.34 (1 H, tdd, J 8.0, 5.0, 2.0), 7.52 (1 H, d, J 8.0), 7.54 (1 H, dd, J 8.0, 2.0), 7.64 (1 H, br s), 7.67 (1 H, ddd, J 8.0, 2.0, 1.5). ^{13}C NMR (CDCl_3 , 100.6 MHz): δ 115.3 (2 C, d, J 22.5), 116.2 (d, J 22.5), 123.6 (d, J 3.0), 123.6 (d, J 3.0), 124.4 (d, J 3.5), 128.5, 129.02 (d, J 8.0), 129.03 (d, J 8.0), 129.2 (d, J 8.0), 130.8, 130.8, 131.3 (d, J 2.5), 131.8 (2 C, br s), 135.0, 135.4, 135.8, 159.4 (d, J 247.0), 159.5 (d, J 246.5), 159.8 (d, J 248.0). The signals of carbons C3, C11 and C19 could not be identified with certainty. ^{19}F NMR (CDCl_3 , 282.4 MHz): δ -117.76 (1 F, br m), -115.32 (2 F, br m). HRMS (EI): m/z 360.1130 ($\text{M}^{++} \text{C}_{24}\text{H}_{15}\text{F}_3^{++}$ requires 360.1120).

7k. Colourless oil. ^1H NMR (CDCl_3 , 400 MHz): δ 6.91–6.97 (2 H, m), 6.98–7.04 (2 H, m), 7.36 (1 H, br t, J 7.5), 7.45 (2 H, br t, J 7.5), 7.52 (1 H, d, J 8.0), 7.12–7.24 (4 H, m), 7.63–7.70 (2 H, m), 7.66 (2 H, br d, J 8.0). ^{13}C NMR (CDCl_3 , 100.6 MHz): δ 115.3 (2 C, d, J 22.5), 123.5 (d, J 3.0), 123.6 (d, J 3.0), 126.5, 127.2, 127.5, 128.8, 129.4, 128.9 (d, J 7.5), 129.0 (d, J 7.5), 131.1, 131.7 (2 C, br s), 134.5, 136.0, 140.3, 140.8, 159.4 (d, J 247.0), 159.4 (d, J 247.0). The signals of carbons C9 and C17 could not be identified with certainty. ^{19}F NMR (CDCl_3 , 282.4 MHz): δ -115.38 (2 F, br m). HRMS (EI): m/z 342.1221 ($\text{M}^{++} \text{C}_{24}\text{H}_{16}\text{F}_2^{++}$ requires 342.1215). Note: this compound was not obtained in pure form but as a mixture with other reduction compounds in minor amounts and with **5k**.

1,2,4-Tris(4-chlorophenyl)benzene 5l, 1,2-bis(4-chlorophenyl)-4-phenyl-benzene 7l, 1-(4-chlorophenyl)-2,4-diphenyl-benzene 8l and 1-(4-chlorophenyl)-2,5-diphenyl-benzene 9l. General procedure **GP** was applied with **2l** [added into the reaction mixture as a solution in THF (0.5 mL)]. Analysis of the crude product (422 mg, orange oil) by ^{13}C NMR spectroscopy showed full conversion of the starting material and the presence of **7l** as the major product of the reaction. Purification by flash column chromatography on silica gel (EtOAc/petroleum ether, gradient from 0 to 2%) afforded a 27 : 73 mixture of **5l** and **7l** (78.7 mg, 55.3 and 149 μ mol respectively), pure **7l** (6 mg, 16.0 μ mol, 2%) and a mixture of **7l** with other reduced compounds (ratio dichloro/monochloro compounds 28 : 72 as determined by MS; 75.5 mg, 60.3 and 155 μ mol respectively). Assuming **7l** is the sole dichloro product, the yields obtained are thus 6% (**5l**), 23% (**7l**) and 16% (**9l** and isomers).

7l. Colourless oil. ^1H NMR (CDCl_3 , 400 MHz): δ 7.09 (2 H, br d, J 8.5), 7.11 (2 H, br d, J 8.5), 7.23 (2 H, br d, J 8.5), 7.24 (2 H, br d, J 8.5), 7.38 (1 H, br t, J 7.5), 7.47 (1 H, d, J 8.0), 7.47 (2 H, br dd, J 8.0, 7.5), 7.61 (1 H, br d, J 2.0), 7.66 (2 H, br d, J 8.0), 7.66 (1 H, br dd, J 8.0, 2.0). ^{13}C NMR (CDCl_3 , 100.6 MHz): δ 126.6, 127.1, 127.6, 128.32, 128.34, 128.9, 129.3, 131.03, 131.06, 131.10, 132.84, 132.92, 138.1, 139.2, 139.56, 139.64, 140.2, 140.9. HRMS (EI; performed on a 73 : 27 mixture of **7l** and **5l**): m/z 374.0639 ($\text{M}^{++} \text{C}_{24}\text{H}_{16}^{35}\text{Cl}_2^{++}$ requires 374.0624).

8l. ^{13}C NMR (CDCl_3 , 100.6 MHz), characteristic signals (tentative proposal): δ 126.2, 126.8, 129.5, 138.1, 140.9, 141.1. Note: this compound was not obtained in pure form. It is proposed that as one of the contaminants observed in a mixture containing **7l** and **9l**.⁵

Cyclotrimerisation reactions internal alkynes **12a-e** (Table 4).

Hexamethylbenzene 13a. General procedure **GP** was applied with **12a**. Purification of the crude product (177 mg, yellow solid) by flash column chromatography on silica gel (petroleum ether) afforded pure **13a** (97.8 mg, 603 μ mol, 60%).

Hexapropylbenzene 13b. General procedure **GP** was applied with **12b**. ^1H and ^{13}C NMR analyses of the crude product (orange oil) showed the presence of starting **12b** as the main component (58%), (*Z*)-oct-4-ene (28%) and **13b** (14%).

Hexaphenylbenzene 13c. General procedure **GP** was applied with **12c**. Analysis of the crude product by ^1H and ^{13}C NMR spectroscopy showed that it contained essentially only starting material **12c** and *cis*-stilbene in 83:17 ratio. **13c** was not detected.

1,2,4-Trimethyl-3,5,6-triphenyl-benzene 13d and 1,3,5-trimethyl-2,4,6-triphenyl-benzene 13'd. General procedure **GP** was applied with **12d**. Purification of the crude product (412 mg, brown oil) by flash column chromatography on silica gel (EtOAc/petroleum ether, gradient from 0 to 5%) afforded a 82 : 18 mixture of **13d** and **13'd** (208 mg, 597 μ mol, 60%).

1,2,4-Triphenyl-3,5,6-tripropyl-benzene 13e and 1,3,5-triphenyl-2,4,6-tripropyl-benzene 13'e. General procedure **GP** was applied with **12e**. Analysis of the crude product by ^1H and ^{13}C NMR spectroscopy showed that it contained essentially only starting material **12e** and (*Z*)-1-phenyl-pent-1-ene in 61:39 ratio. Neither **13e** nor **13'e** were detected.

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Conflicts of interest

There are no conflicts to declare.

Notes and references

§ See the supporting information for detail.*

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