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An Investigation of Wall Effects in Microwave-Assisted Ring-Closing Metathesis and Cyclotrimerization Reactions

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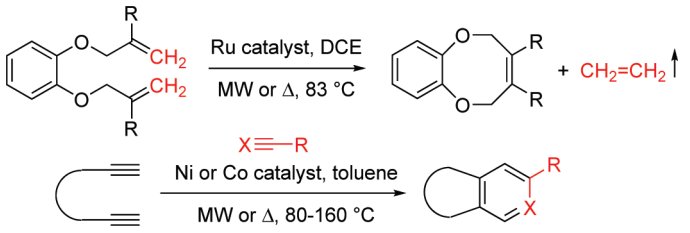

Challenging Ru-catalyzed ring-closing metathesis transformations leading to eight-membered-ring systems and Ni- or Co-catalyzed [2+2+2] cyclotrimerizations were evaluated at elevated temperatures applying microwave dielectric heating or conventional thermal heating in order to investigate the role of wall effects. All reactions were conducted in a dedicated reactor setup that allowed accurate internal reaction temperature measurements using fiber-optic probes for both types of heating modes. For ring-closing metathesis best results were achieved using an open vessel−gas sparging protocol in 1,2-dichloroethane at reflux temperature (83 °C), while cyclotrimerizations were performed under sealed vessel conditions in toluene between 80 and 160 °C. For all studied transformations the results achieved in a single-mode microwave reactor could be reproduced by conventional heating in an oil bath by carefully matching the temperature profiles as close as possible during the entire heating and cooling cycle. In contrast to previous literature reports, no evidence that direct in-core microwave heating can increase catalyst lifetime by minimization or elimination of wall effects was obtained. At the same time, no indication for the involvement of nonthermal microwave effects in these homogeneous transition metal-catalyzed transformations was seen.

Introduction

Traditionally, organic synthesis in an elevated temperature regime is performed by conductive heating applying an external heat source such as an oil-bath or heating mantle. This is a comparatively slow and inefficient method for transferring energy into the system since it depends on convection currents and on the thermal conductivity of the various materials that must be penetrated, and generally results in the temperature of the reaction vessel being higher than that of the reaction mixture. This is particularly true if reactions are performed under reflux conditions, where the temperature of the bath fluid or heating mantle is typically kept 20−50 °C above the boiling point of the reaction mixture in order to ensure an efficient reflux.

In contrast, microwave irradiation produces efficient internal heating (in-core volumetric heating) by direct coupling of microwave energy with the molecules (solvents, reagents, catalysts) that are present in the reaction mixture.[1] Microwave irradiation therefore raises the temperature of the whole volume simultaneously (bulk heating) whereas in the conventionally heated vessel, the reaction mixture in contact with the vessel wall is heated first. Since the reaction vessels employed in modern microwave reactors are typically made

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out of nearly microwave transparent materials such as borosilicate glass, quartz, or Teflon, the radiation passes through the walls of the vessel and the temperature at the inner surface of the reactor wall will (initially) be lower than that of the bulk liquid. The elimination of a hot vessel surface has often been stated as being one of the key advantages of using microwave technology in synthetic organic chemistry,[1] in particular in transition metal-catalyzed transformations where temperature sensitive catalysts can undergo decomposition on hot reactor surfaces (wall effects).[2] It has been argued that the elimination of such a hot surface by in-core volumetric heating can increase the lifetime of the catalyst and therefore may lead to better conversions in a microwave heated as compared to a conductively heated process.[1,2]

In this paper we present a detailed investigation on the putative role and existence of wall effects in conventionally and microwave heated ring-closing metathesis transformations.[3] Ring-closing metathesis chemistry was chosen as a suitable model system for several reasons. First of all, it is well-known that many of the classical transition metal-based catalytic systems used today to perform olefin metathesis chemistry are thermally unstable and will degrade over time, especially when heated to higher temperatures.[3,4] Second, the use of microwave dielectric heating to perform a range of transition metal-catalyzed metathesis protocols,[5] including ring-closing metathesis (RCM),[6−12] cross-metathesis (CM),[13,14] ring-opening metathesis polymerization (ROMP),[15] and several types of alkyne metathesis reactions[16,17] is well documented. In virtually all of these published examples, the use of microwave irradiation has led to significant improvements in terms of reaction rates and/or product yields and purities, compared to conventionally processed reactions, in particular for otherwise difficult to perform metathesis protocols.[5−17] In addition, the use of microwave heating has often allowed a significant reduction in catalyst loading, and therefore an increase in catalyst turnover numbers.[5−17] As a scientific rationale for the observed effects an increased catalyst lifetime by elimination of wall effects due to direct in-core microwave heating was proposed in several publications.[5,7,14,17]

The studies presented herein describe a series of carefully executed experiments involving difficult to perform Ru-catalyzed olefin ring-closing metathesis transformations for the construction of eight-membered-ring systems. In addition, the putative role of wall effects and involvement of nonthermal microwave effects in Ni- and Co-catalyzed [2+2+2] cyclotrimerization reactions was also evaluated.[18]

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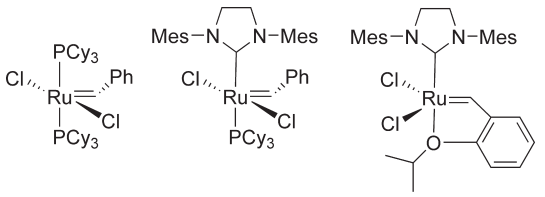


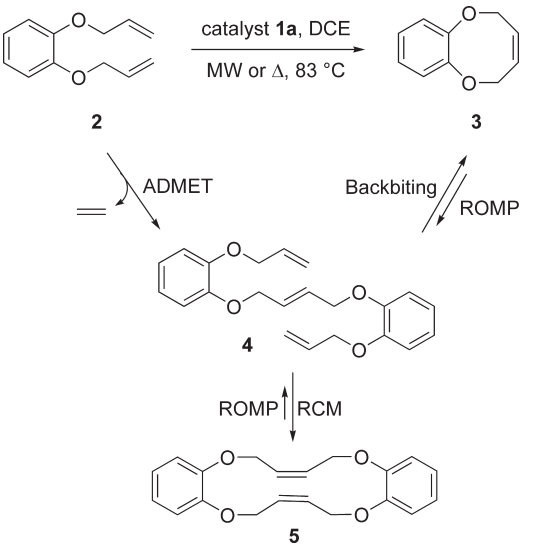
FIGURE 1. Ru-based olefin metathesis catalysts. Cy = cyclohexyl; Mes = 2,4,6-phenyl.

Results and Discussion

Ru-Catalyzed Ring-Closing Metathesis. The mechanism of Ru-catalyzed olefin metathesis has been the subject of intense experimental[19] and theoretical[20] scrutiny. It is generally acknowledged that a metal carbene species is required and that interaction with an olefin substrate leads to four-membered metallacyclobutane intermediates or transition states; cleavage of this intermediate in the opposite sense by which it was formed leads to olefin metathesis, creating a new carbon−carbon double bond and regenerating an active metal carbene.[19,20] The well-known Grubbs-type catalysts (Figure 1) consist of a variety of Ru-based systems of the general formula $[Cl_2(L)(L')Ru{=}C(H)R]$, which in an initiation step generate the reactive 14-electron alkylidene species $[Cl_2(L)Ru{=}C(H)R]$ by reversible dissociation of L′ (PCy_3 for **1a**, **1b**).[21] The reaction temperatures required to overcome this initiation step can lead to decreased catalyst lifetimes, which therefore makes these transformations attractive model reactions for the investigation of wall effects. Successful improvements of the Grubbs first-generation catalyst (G I) **1a** are modifications that either encourage loss of L′,[22] or reduce the tendency of the reactive species $[Cl_2(L)Ru{=}C(H)R]$ to recapture the liberated L′,[23] which competes with the olefin substrate for the unsaturated metal center in $[Cl_2(L)Ru{=}C(H)R]$ (Grubbs second-generation catalyst, G II, **1b**). Alternatively, Hoveyda and co-workers have developed catalyst **1c** (Hoveyda−Grubbs second generation catalyst, HG II), in which L′ is incorporated into a loosely chelating group associated with the carbene ligand that is removed upon the first metathesis event.[24]

The thermal decomposition of Ru olefin metathesis catalysts **1a**−**c** has been studied in detail, and the suggested quite complex decomposition pathways vary significantly between the individual catalyst types, and additionally are influenced by the presence of olefin substrates and other additives.[3,25] Significant catalyst decomposition is generally observed at temperatures above 50 °C within a few hours.[3,25] For most catalysts, the rate of decomposition is related to the rate of the initiation step—a slow rate of L′ dissociation likely to be contributing to a low decomposition rate.[3,25] Clearly, the utility of a given olefin metathesis catalyst will be a function of the rate of olefin metathesis turnover to the rate of catalyst decomposition.[26] With this background the ring-closing olefin metathesis of several difficult substrates utilizing Ru metathesis catalysts **1a**−**c** in an elevated temperature regime was investigated.

SCHEME 1. Ring-Closing Metathesis and Related Metathesis Products of 1,2-Bis(allyloxy)benzene (2)



In 2003, we reported on microwave-assisted ring-closing olefin metathesis chemistry employing Ru catalyst **1b** in dichloromethane (DCM) and a set of standard diene substrates.[9] We have demonstrated that these undemanding RCM reactions leading to five-, six-, and seven-membered heterocycles could be significantly accelerated using microwave heating as compared to reactions performed at room temperature (e.g., 2 min at 60 °C versus 90 min at 25 °C with 0.5 mol % catalyst), but have also found that these rate enhancements were due to a purely thermal effect and not related to any special microwave effect.[9,18] For the current investigations, it was evident that a more difficult RCM process needed to be chosen, requiring longer reaction times, higher temperatures, and possibly also higher catalyst loadings to enforce the influence of wall effects on the overall process. As a first model system we have chosen the RCM of readily available 1,2-bis(allyloxy)benzene (**2**) to provide the eight-membered 2,5-dihydro-1,6-benzodioxocin **3** (Scheme 1). The synthesis of eight-membered rings, common structural elements in numerous natural products, has proven a challenging extension of the metathesis concept.[3,4] Presumably, the kinetics of ring closure, the strain inherent in many eight-membered rings, and the competing metathesis-based oligomerization of reactants and/or products are among the factors contributing to this problem.[27] The RCM process shown in Scheme 1 was first reported by Grubbs and co-workers in 1995, requiring 8 mol % of the first generation Ru catalyst $[Cl_2(PCy_3)_2Ru{=}CHCHC(Ph)_2]$, and 3 h at 55 °C in benzene to produce 75% of benzodioxocin **3**.[27] A subsequent study by König and Horn

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demonstrated that applying 10 mol % catalyst **1a** in DCM at room temperature for 4 h resulted in only 15% of conversion to the desired RCM product **3**, in addition to the formation of the acyclic diene metathesis (ADMET) oligomerization product **4** and the 14-membered macrocycle **5**, resulting from an apparent RCM of linear dimer **4** (10% each).[28] Similar results were observed by Fogg and co-workers: by using 5 mol % of G II catalyst **1b** and a substrate concentration of 0.1 M, an equilibrium of **4**, a cyclic trimer, and **3** was established. On the other hand, at more dilute conditions (0.005 M), no oligomerization products were obtained and direct cyclization to the RCM product was favored, due to the small ring size and backbone rigidity of **3**.[29] Apart from other studies on this RCM at room temperature,[30,31] the only microwave-assisted protocol for the RCM **2** → **3** was reported by Comer and Organ, who achieved a 35% conversion with 1 mol % of G II catalyst **1b** in toluene within 4 min using a continuous flow process (temperature not specified).[10]

Our investigations started with a solvent screen for the RCM process **2** → **3** involving a set of common solvents typically employed in Ru-catalyzed metathesis chemistry such as DCM, 1,2-dichloroethane (DCE), benzene, and toluene. On the basis of the results from these initial screening experiments and upon considering the boiling points of these solvents we have selected DCE as the solvent of choice for all metathesis chemistry described herein. DCE has been frequently used in metathesis transformations in combination with the Ru catalysts shown in Figures 1[3,4] including reactions performed under microwave conditions.[5−17] Because of its comparatively low microwave absorptivity (loss tangent tanδ 0.123),[32] a significant amount of microwave energy is required to heat the reaction mixture. In addition to investigating the potential role of wall effects, this allowed us to concurrently evaluate the influence of selective heating/activation of the polar Ru catalysts by microwave irradiation, and thus the involvement of nonthermal microwave effects.[9,11,12,18] Since we anticipated that many of the planned experiments would have to be performed under open vessel reflux conditions in order to volatilize the formed ethylene from the reaction mixture (see below), the atmospheric boiling point of 83 °C for DCE appeared well suited for these studies.

Comparing the performance of the Ru catalysts **1a**−**c** at room temperature at 1.5 mol % loading for the RCM **2** → **3** (Scheme 1, DCE, 0.02 M, Ar atmosphere) demonstrated that all three catalysts operated with similar efficiency. For example, a 53% conversion of the diene substrate to the RCM product **3** was achieved with G I catalyst **1a** after 3 h. Slightly lower values were obtained for **1b** (48%) and **1c** (43%). Longer exposure to the catalyst (24 h) only slightly increased the conversion (Figure S1 in the Supporting Information). In agreement with previously published results[28,29] we find that apart from the desired RCM product **3**, substantial amounts (20−25%) of oligomerization/cyclodimerization products **4**/**5** are also produced. It should be noted that the formation of these byproducts is reversible and can be minimized by proper choice of experimental conditions (see below).[29,33]

Microwave experiments were conducted in a CEM Discover single mode microwave reactor equipped with a fiber-optic (FO) probe provided by the instrument manufacturer for directly controlling and monitoring the internal reaction temperature in a 10 mL sealed reaction vessel.[34] Recent evidence has demonstrated that in several instances the use of an external infrared (IR) sensor, recording the surface temperature of the vessel, does not accurately reflect the genuine reaction temperature inside the reaction vial and therefore may lead to erroneous results.[34,35] As the G I Ru catalyst **1a** provided the best results at room temperature and we deliberately wanted to use a system that would react to thermal stress such as **1a**,[3,25] this catalyst was used for all subsequent RCM reactions **2** → **3**. Applying sealed vessel microwave heating at an 83 °C set temperature under otherwise identical conditions (0.02 M, Ar atmosphere) resulted in a much faster conversion of the diene. By using 1.5 mol % of catalyst **1a**, a 60% conversion to **3** was obtained after only 5 min of irradiation (1 min ramp time, 4 min hold time at 83 °C). No further improvement in conversion was experienced after 10 min or even 20 min of irradiation (Figure S2 in the Supporting Information). As expected, lower catalyst loadings furnished reduced conversions, but again no improvement was seen by extending the reaction time. These results suggested that either the catalyst essentially had decomposed after 5 min, or that the metathesis system had reached an equilibrium state. It should be emphasized that olefin metathesis is essentially a fully reversible set of [2+2] cycloaddition−cycloreversion equilibria, although in practice for RCM complete reversibility is rare due to the release of ethylene.[29,33] In a sealed microwave vial, however, ethylene cannot be removed from the equilibrium potentially leading to unproductive metathetical exchange.[33] Indeed, control experiments have shown that benzodioxocin **3** when exposed to ethylene and Ru catalysts **1a** or **1b** in a sealed reactor will revert to diene **2** and oligomerization/cyclodimerization products **4** and **5** (in particular under more concentrated conditions).[36]

On the basis of these thoughts we next moved to an open vessel microwave setup and an experimental protocol that would ensure the complete volatilization of the formed ethylene gas. Reiser and co-workers have already demonstrated in 2005 that the combination of microwave irradiation with inert gas sparging (to remove ethylene from the equilibrium) is a technique that can be successfully utilized to perform challenging RCM transformations.[8] For this purpose a 10 mL round-bottomed flask was attached to a reflux condenser and placed in the cavity of a CEM Discover

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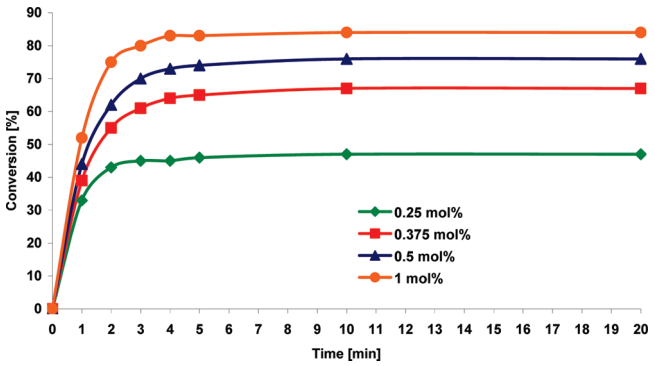

FIGURE 2. Conversion over time for the ring-closing metathesis of 1,2-bis(allyloxy)benzene (**2**) to metathesis product **3** at different Ru catalyst **1a** concentrations (Scheme 1). Conditions: DCE (0.02 M), open vessel microwave heating (150 W constant power), 83 °C reflux, Ar sparging. HPLC peak area percent (215 nm).

microwave system. Inert gas sparging was provided by a gentle Ar stream through a glass capillary fitted through the reflux condenser. In addition, the flask contained a magnetic stir bar and a fiber-optic (FO) temperature probe immersed into the reaction mixture (5 mL) (see the Experimental Section and Figure S3 in the Supporting Information for further details). Microwave experiments were performed in constant power mode under reflux conditions and magnetic stirring, monitoring the temperature of the reaction mixture by the FO sensor. A constant magnetron power of 150 W resulted in a heating ramp of ~55 s to achieve reflux temperature (83 °C) and also ensured a steady reflux of the reaction mixture for the duration of the experiment.

The RCM reaction **2** → **3** shown in Scheme 1 (DCE, 0.02 M) was investigated under reflux conditions at 83 °C with Ru catalyst **1a**, using four different catalyst loadings: 0.25, 0.375, 0.5, and 1.0 mol %. As can be seen in Figure 2, conversions compared to the sealed vessel experiments (Figure S2 in the Supporting Information) were markedly increased, with 85% conversion attained after 5 min with 1 mol % catalyst loading. Similar to the sealed vessel experiments, however, after 3 min very little further improvements in conversions were seen, suggesting complete catalyst decomposition after this period. While in the initial phases of the metathesis event the reaction mixture contained considerable quantities of oligomerization and cyclodimerization products **4** and **5**, after 5 min the amount of the ADMET product **4** was reduced to 3%, clearly demonstrating the reversible nature of these Ru-catalyzed metathesis events (Table S1 in the Supporting Information). The amount of cyclodimerization product **5** could be minimized to ~9% by executing the RCM under more dilute conditions at 0.01 M diene concentration. Using these carefully optimized conditions (MW, 83 °C, 5 min, Ar sparging, 1 mol % **1a**, 0.01 M) provided the desired 2,5-dihydro-1,6-benzodioxocin **3** in 85% isolated yield after chromatography, a marked improvement over the previously published methods.[10,27−31]

At this stage the stability of G I Ru catalyst **1a** in DCE at the reaction temperature of 83 °C was evaluated. For this purpose, samples of the catalyst were heated without substrate in DCE under reaction conditions with microwave irradiation for 5, 10, or 15 min, before adding the diene substrate **2** and continued heating for an additional 5 min period. As seen in Table 1, for low catalyst loadings (0.25 and 0.5 mol %) this pretreatment results in a significant reduction in metathesis activity, presumably as a result of progressive catalyst decomposition. For higher catalyst loadings (1.0 and 1.5 mol %) the effect is almost unnoticeable as even after 15 min of catalyst preheating there appears to be still enough active Ru catalyst present in the reaction mixture to afford high levels of conversion in the metathesis event.

With these data on catalyst stability and an optimized metathesis protocol in hand we ultimately performed comparison experiments between microwave and conventionally heated RCM reactions **2** → **3** (Scheme 1). For this purpose the complete open vessel reaction setup consisting of round-bottomed flask, reflux condenser, gas sparging line, and FO temperature sensor was moved from the microwave cavity into a preheated oil bath placed on a conventional hot plate/stirrer (Figure S3 in the Supporting Information). Using the internal FO probe it was demonstrated that an oil bath temperature of ~180 °C leads to the same ramp time as under microwave conditions, raising the temperature of the 5 mL reaction mixture from ambient conditions to 83 °C within ~50 s (Figure S4 in the Supporting Information). For the actual RCM comparison experiments we have intentionally used a suboptimal catalyst loading of only 0.5 mol % in order to be able to detect any effect of increased catalyst decomposition as a result of wall effects in the conventionally heated experiment (cf. Table 1). To our surprise, the conversion rates achieved by conventional heating at 83 °C—with all other reaction parameters being the same—were virtually identical for the corresponding microwave runs (Figure S5 in the Supporting Information). When lower oil bath temperatures were used (140 and 160 °C), the rate of the metathesis reaction was slower during the first 1−2 min as a result of the slower heating ramp to 83 °C, but finally reached nearly the same conversion levels as the 180 °C bath temperature experiments (see Figures S5 and S6 in the Supporting Information). Therefore, despite an oil bath temperature in the conventionally heated experiment of 180 °C, potentially leading to a wall surface temperature nearly 100 °C above the temperature of the reaction mixture of 83 °C, no wall effects were evident. In fact, no apparent advantage of performing this RCM transformation under microwave dielectric heating compared to conductive heating was observed and the HPLC-UV traces obtained from the crude reaction mixtures of both types of heating experiments were virtually identical (see Figure S7 in the Supporting Information).

We hypothesized that the catalyst amount utilized in the RCM transformation **2** → **3** (Scheme 1) was possibly too low in order to detect any effect of catalyst decomposition on the hot reactor surface. Therefore, an even more demanding RCM reaction involving the formation of a tetrasubstituted double bond within an eight-membered-ring system was considered. The formation of tetrasubstituted double bonds is one of the most challenging transformations for Ru-based olefin metathesis catalysts.[3,4] This transformation typically requires the application of second-generation-type catalysts and high loadings.[37] For ease of preparation and based

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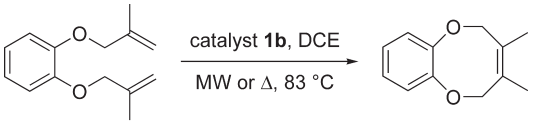
TABLE 1. Effect of Catalyst Preheating on Conversion in the Ring-Closing Metathesis of 1,2-Bis(allyloxy)benzene (2) (Scheme 1)[a]

catalyst loading **1a** (mol %)	preheating time (min)	reaction time (min)	conv (%)[b]
0.25	0	5	46
0.25	5	5	20
0.25	10	5	11
0.25	15	5	7
0.5	0	5	74
0.5	5	5	62
0.5	10	5	58
0.5	15	5	47
1.0	0	5	83
1.0	5	5	83
1.0	10	5	82
1.0	15	5	80
1.5	10	5	85
1.5	15	5	85

[a]Conditions: DCE (0.02 M), open vessel microwave heating (150 W constant power), 83 °C reflux, Ar sparging. [b]HPLC-UV peak area percent (215 nm). Overall conversion to metathesis product **3**.

SCHEME 2. Ring-Closing Metathesis of 1,2-Bis(2-methylallyloxy)-benzene (6)



6 **7**

on the apparent similarity with our first model system (Scheme 1), we have decided to investigate the RCM reaction of 1,2-bis(2-methylallyloxy)benzene (**6**) with the three Ru-based catalysts **1a**−**c** applying our optimized open vessel−gas sparging conditions at elevated temperature (Scheme 2). To the best of our knowledge, this RCM process has never been reported in the literature.

Applying open vessel−gas sparging conditions with microwave irradiation at 83 °C in DCE, the performance of catalysts **1a**−**c** was evaluated. In agreement with previous studies,[3,4,37] we found that the G I Ru system **1a** exhibits almost no activity in this exceedingly difficult RCM reaction (Figure S8 in the Supporting Information). Both the G II catalyst **1b** and the HG II system **1c** show significant activity and by using 10 mol % of **1b** diene conversions up to 64% could be achieved after 2 h. Regardless of the catalyst loading (1.5, 5, or 10 mol %), by using **1b** as a metathesis catalyst a plateau is reached in the conversion after ~1 h with very little progress being made after that period. It is interesting to note that the HG II system **1c** is evidently more stable than G II catalyst **1b** since even after 1 h of irradiation, metathesis conversion still increases with Ru catalyst **1c**, although the overall level of conversion is lower compared to G II catalyst **1b** (Figure S8 in the Supporting Information). This behavior is related to the fact that in HG II catalyst **1c** initiation requires breakage of the comparatively strong Ru−O chelation as a first step. Therefore, this catalyst is initialized much more slowly than **1b** and does need a high temperature to reach a reasonable amount of activity.[4] For our evaluation of wall effects we have therefore selected the "less stable" Ru catalyst **1b**. Not surprisingly, conversions are significantly lower when this reaction is performed under sealed vessel conditions (~25% with 10 mol % **1b**), and little progress in the metathesis event is made after the first 20 min probably due to unproductive metathetical exchange (Figure S8 in the Supporting Information).[33]

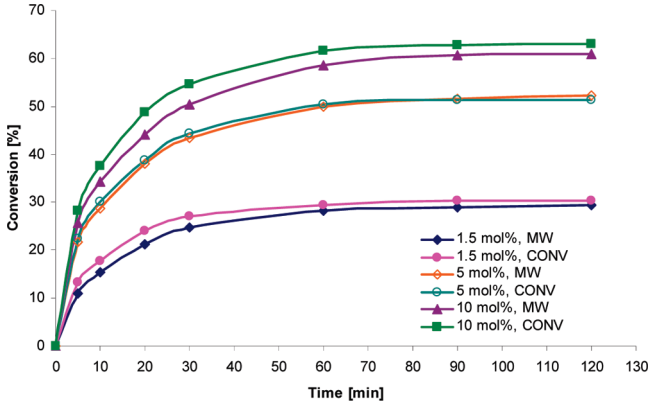


FIGURE 3. Conversion over time for the ring-closing metathesis of 1,2-bis(2-methylallyloxy)benzene (**6**) to RCM product **7** at different catalyst (**1b**) concentrations (Scheme 2). Conditions: DCE (0.02 M), 83 °C reflux, open vessel microwave heating (MW, 150 W constant power) or oil bath heating (CONV, 180 °C bath temperature), Ar sparging. HPLC peak area percent (215 nm).

To achieve complete conversion of diene **6** in the RCM, the portionwise addition of catalyst **1b** was evaluated.[8] Adding an additional amount of 10 mol % of **1b** after 1 h open vessel−gas sparging conditions at 83 °C (20 mol % in total, 0.02 M diene concentration), complete conversion was achieved after an additional 1 h heating period (Figure S9 in the Supporting Information). From this experiment, the desired RCM product benzodioxocin **7** was isolated after chromatography in 71% yield. Applying a 5 + 5 mol % catalyst addition cycle provided 87% overall conversion after 2 h. The fact that the conversion following this stepwise regime is significantly higher compared to the experiment where 10 mol % of catalyst was added in the beginning (64%) clearly points to catalyst decomposition as being the limiting factor in this difficult RCM reaction (Figure S9 in the Supporting Information).

Comparison experiments between microwave heating and conventional heating were conducted as described above for our first model reaction (Scheme 1) using open vessel−gas sparging conditions and a 180 °C oil bath temperature to mimic the heating profile obtained under microwave conditions. As demonstrated in Figure 3, using carefully controlled reaction conditions no difference between metathesis experiments performed under microwave conditions and in an oil bath could be detected, regardless if a 1.5, 5, or 10 mol % quantity of Ru catalyst **1b** was employed. It therefore appears that the putative hot reactor wall in the oil bath experiment does not play any significant role in the thermal decomposition of the metathesis catalyst (or of intermediates in the catalytic cycle),[38] and that direct in-core microwave heating, conversely, cannot extend catalyst lifetime. Thus, no evidence for the existence of previously suggested wall effects was seen in these elevated temperature metathesis reactions.[5,7,14,17] The results described herein are

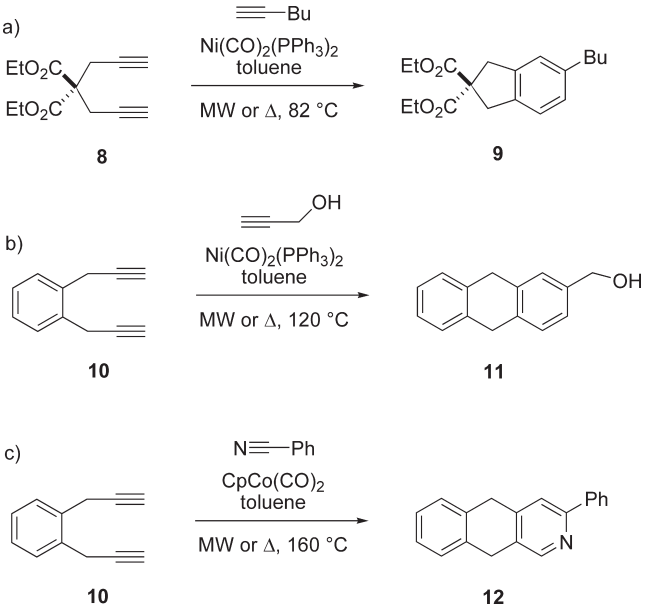
(38) We noted, however, that the deposition of Ru metal on the vessel walls at the end of the metathesis reactions was significantly more prominent in conventionally heated experiments as compared to the microwave runs (confirmed by ICP-MS measurements). This phenomenon, while not having any influence on the rate of the RCM transformations, is under further investigation in our laboratories.

in agreement with recent studies reported from our laboratory utilizing reaction vessels made out of strongly microwave-absorbing silicon carbide (SiC) in microwave-assisted transformations.[39] Using this technique the occurrence of wall effects has to be expected since the SiC ceramic will heat rapidly and will transfer the heat by standard conductive mechanisms to the reaction mixture. However, for virtually all studied cases, including transition metal-catalyzed transformations, no significant difference in conversion, yield, or product purity was seen comparing microwave chemistry performed in SiC vials with experiments conducted in standard Pyrex vessels at the same reaction temperature.[39] This is also in line with other microwave/oil bath comparison studies involving metal-catalyzed transformations recently performed in our laboratories.[40]

Since the metathesis reactions were performed with 150 W of constant power and the chosen solvent DCE is only moderately microwave absorbing, it is also evident that the electromagnetic field does not exert any nonthermal microwave[9,12] or "activation/reenergizing"[11] effects on the Ru catalyst in solution, or influences the catalytic cycle or the metathesis events in any other way than involving changes in the bulk reaction temperature.

Ni- and Co-Catalyzed [2+2+2] Cyclotrimerizations. During the past few decades the transition metal-catalyzed [2+2+2] cyclotrimerization reaction of alkynes and other reaction partners has emerged as an efficient method for the synthesis of carbo- and heterocyclic structures, including applications in total synthesis.[41] The classical [2+2+2] cyclotrimerization reaction involves the reaction of three alkynes or two alkynes and a nitrile to form benzenes or pyridines. Such reactions are typically conducted under homogeneous Co, Ni, Ru, and Rh catalysis, although other transition metals have been used as well.[41] It is assumed that in the first steps of the cyclotrimerization reaction two alkyne molecules sequentially displace two ligand molecules (often CO) from the metal center. The resulting π complex rearranges to produce a reactive metallocyclopentene intermediate that subsequently adds the remaining alkyne (or nitrile) to ultimately produce a six-membered aromatic ring.[41] Since

SCHEME 3. Ni- and Co-Catalyzed [2+2+2] Cyclotrimerization Reactions



2006, an increasing number of reports have advocated the use of microwave heating for these transition metal-catalyzed processes, generally providing improved yields in shorter reaction times.[42−46] In some instances, control experiments performed by conductive heating at the same monitored temperature were reported to result in much lower conversions/product yields,[43−46] and in other cases provided no product at all.[45,46]

Evaluating the published examples,[42−46] we initially hypothesized that the reported enhancements seen in microwave-assisted [2+2+2] cyclotrimerization chemistry, rather than being the result of nonthermal microwave effects,[46] could be due to the minimization of wall effects using direct in-core microwave heating, leading to enhanced catalyst lifetimes. To elucidate the role of microwave irradiation in these [2+2+2] cyclotrimerizations in more detail we decided to reinvestigate three recently published examples, where the reported differences between sealed vessel microwave and conventional heating at the same temperature were most prominent (Scheme 3). To accurately compare the results obtained by direct sealed vessel microwave heating with the outcome of a conventionally heated reaction at the same temperature we have used a sealed 10 mL Pyrex vial in combination with a CEM Discover microwave system that allows us to perform both types of transformations in the identical reaction vessel and to monitor the internal reaction temperature in both experiments directly with a FO probe device.[34] This system has the advantage that the same reaction vessel and the same method of temperature measurement is used. In this way all parameters apart from the mode of heating are identical and therefore a fair comparison

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between microwave heating and thermal heating can be made.[34]

The first model system (Scheme 3a) involved the [2+2+2] cyclotrimerization of diethyl dipropargyl malonate (**8**) with 1-hexyne in toluene leading to the fused benzene **9**. Using 10 mol % $Ni(CO)_2(PPh_3)_2$ as a catalyst and 10 equiv of 1-hexyne, Teske and Deiters were able to achieve complete conversion of **8** and a 78% isolated yield of product **9** within only 2 min of microwave irradiation.[45] These experiments were conducted in power control mode with 300 W of constant magnetron output power, leading to a continuous temperature rise from 25 to 82 °C (IR sensor) within the 2 min duration of the experiment. Remarkably, repeating the exact same experiment in an oil bath (82 °C final temperature, 92 °C bath temperature) for 2 min did not lead to any cyclotrimerization product **9**.[45] Repeating the general experimental conditions reported by Teske and Deiters as close as possible, but performing temperature-controlled microwave experiments in combination with an internal FO sensor, we were able to obtain comparable results. Using 300 W of maximum magnetron power and a ~3 min heating ramp to 82 °C, followed by a 2 min hold time at 82 °C also provided consistently complete conversion of diyne **8** (GC-MS) and led to a 70% yield of cyclotrimerization product **9**. The reasons for performing a temperature-controlled run rather than a power-controlled experiment are related to the better control of reaction temperature, which is an important factor if accurate comparisons with conventionally heated experiments are required.[34,35] In this context, it should be emphasized that comparison studies between microwave and conventional heating experiments should not only take the final reaction temperature into account, but must also provide for similar heating and cooling profiles. In particular for short overall reaction times, the ramp time will become important. In the present case, an appropriate adjustment of the utilized maximum microwave power (300 W) led to a ramp time of ~3 min in the microwave run, which was comparable to the heating profile that could be achieved in an oil bath experiment (Figure S10 in the Supporting Information). In our hands, performing the cyclotrimerization reaction **8**→**9** with conductive heating using the same 10 mL sealed Pyrex vessel fitted with an internal FO probe, but immersing the complete setup into a preheated oil bath led in essence to the same result as using microwave heating: conversions of >99% with an isolated yield of 61% of cyclotrimerization product **3** were achieved. Importantly, as shown in Figure S10 (Supporting Information) the reaction temperature profiles for both the conventionally and the microwave heated cyclotrimerizations were very similar.

Since a reaction time of 2 min is not well suited for an accurate kinetic study comparing microwave and conventional heating, the Ni-catalyzed [2+2+2] cyclotrimerization of 1,2-dipropargylbenzene (**10**) with propargyl alcohol was selected as a more appropriate example (Scheme 3b). Deiters and coworkes have reported that using 10 mol % of $Ni(CO)_2(PPh_3)_2$ catalyst and 10 equiv of propargyl alcohol a 66% yield of 9,10-dihydroanthracene **11** was obtained after 10 min of microwave heating in toluene at 120 °C.[44] Applying conventional heating under otherwise identical conditions furnished only 35% of the target compound **11**.[44] Again, for comparison purposes, a temperature-controlled microwave experiment was performed applying 300 W of initial microwave power, which allowed ramping the temperature from 25 °C to the desired set temperature of 120 °C within 4 min. This was followed by a 5 min hold time at 120 °C (total irradiation time of 9 min), and a subsequent cooling step to 50 °C within ~5 min (overall processing time 14 min). For this experiment standard cooling by compressed air in the microwave instrument was switched off in order to match the cooling obtained in the conventionally heated experiment (Figure S11 in the Supporting Information). This protocol consistently provided complete conversion of starting diyne **10** and led to a 64% isolated yield of 9,10-dihydroanthracene **11**. In our hands, control experiments with conductive heating in an oil bath following a similar temperature profile (Figure S11 in the Supporting Information) also led to complete GC-MS conversion and furnished a 67% yield of **11**.

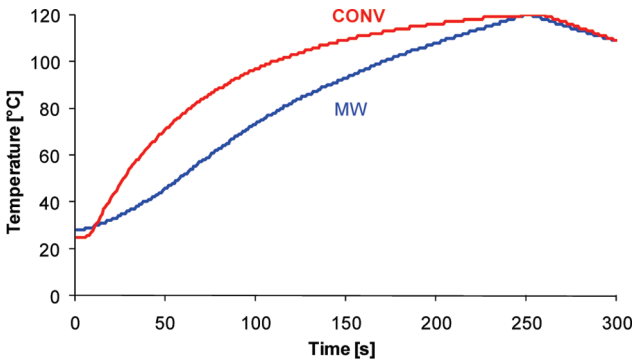

FIGURE 4. Temperature profiles obtained with internal FO sensors for conventionally (CONV) and microwave (MW) heated [2+2+2] cyclotrimerizations of 1,2-dipropargylbenzene (**10**) with propargyl alcohol in toluene (Scheme 3b). Conditions: 300 W maximum microwave power, 120 °C set temperature; 135 °C oil bath temperature.

To obtain further insights into the kinetics of this cyclotrimerization we have performed additional experiments evaluating the progress of the reaction after only 5 min overall reaction time. To our surprise, under these conditions the conventionally heated cyclotrimerization went to complete conversion, whereas the microwave heated run furnished only 18% conversion. A further reduction of the reaction time to 4 min provided a similar situation: 56% conversion for the conventionally heated experiment and 11% conversion for the microwave heated run. Based on a careful evaluation of the temperature−time histories for these experiments we believe that these results are a consequence of the fact that the heating of 4 mL of toluene in an oil bath to 120 °C is actually faster than applying microwave heating (Figure 4). Since toluene is a low-absorbing solvent (tanδ 0.040),[32] microwave dielectric heating to 120 °C in a 300 W single-mode reactor is not particularly efficient.[47] Integration of the reaction temperature profiles obtained with internal FO probes shown in Figure 4 revealed that the average temperature during the ramp time period (0−4 min) is significantly higher in the oil bath experiment (94 °C) as compared to the microwave run (79 °C). Therefore, the higher conversions with conventional heating are not surprising.

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Since it appeared that the Ni-catalyzed [2+2+2] cyclotrimerization **10** → **11** is rather sensitive to temperature we additionally evaluated this transformation at a lower reaction temperature. At 100 °C the cyclotrimerization was exceedingly slow, with only 5−15% conversion being observed after 5 min for both the conventionally and microwave heated experiments. Prolongation of the reaction time to 10 or 20 min at 100 °C did not lead to any improvement in conversion for both modes of heating. To determine if catalyst decomposition has a role in these events we performed a microwave experiment where the reaction mixture was first heated to 100 °C for 10 min, followed immediately by heating to 120 °C for an additional 10 min. Since the second heating step at the optimum reaction temperature did not lead to any improvement in conversion it can be assumed that the 10 min treatment at 100 °C provided sufficient thermal energy to trigger a deactivation of the Ni catalyst

As a final example in this series we studied the Co-catalyzed [2+2+2] cyclotrimerization of diyne **10** with benzonitrile leading to 9,10-dihydro-2-azaanthracene **12** (Scheme 3c). Using 120 °C reaction temperature for 20 min in toluene, 10 equiv of benzonitrile, and 20 mol % $CpCo(CO)_2$ as catalyst, Deiters and co-workers have reported an 87% isolated yield of 2-azaanthracene **12** under microwave conditions, compared to only 8% applying conventional heating.[44] In our hands, this Co-catalyzed [2+2+2] cyclotrimerization required 160 °C to lead to complete conversion within 20 min under microwave conditions and furnished a 78% isolated product yield of **12**. Performing an oil bath experiment with a similar temperature profile as in the microwave run (Figure S12 in the Supporting Information) also gave full conversion and a similar isolated product yield (75%). At a temperature of 150 °C, for example, the level of conversion for both types of experiments was significantly lower, but in the same range (62% microwave versus 59% oil bath).

Therefore, for all three examples of [2+2+2] cyclotrimerizations studied herein (Scheme 3), it is evident that microwave heated experiments—within experimental error—will give the same results as conventionally heated experiments provided that similar temperature−time histories are realized for both types of heating modes. For the comparatively short overall reaction times of these [2+2+2] cyclotrimerizations it is essential to not only take the final reaction temperature into account when comparing different heating modes, but also to match heating and cooling profiles as close as possible. As demonstrated for the Ni-catalyzed [2+2+2] cyclotrimerization of 1,2-dipropargylbenzene (**10**) with propargyl alcohol (Scheme 3b), a mismatch in the heating ramp can lead to significant differences in product distribution, in particular if the reaction is sensitive to minor changes in reaction temperature. We believe that previous claims to the observations of apparent microwave enhancements in these transformations are due to inaccurate temperature measurements, in particular to the use of external IR sensors.[43−46]

Conclusion

The elimination of a hot reactor surface common to conductive heat transfer principles using external heating sources has often been stated as being one of the key advantages of using microwave technology in synthetic organic chemistry. It can be argued that the elimination of such wall effects by direct in-core microwave heating can increase the lifetime of catalysts or other temperature-sensitive species in the reaction mixture and therefore may lead to better conversions in a microwave heated as compared to a conductively heated process. In this paper we have presented a detailed investigation of the putative role and existence of wall effects in conventionally and microwave heated Ru-catalyzed ring-closing metathesis and Ni- and Co-catalyzed [2+2+2] cyclotrimerizations. These synthetically valuable processes were chosen as model transformations since several previous reports have found significant rate and yield enhancements when these reactions were performed with microwave heating compared to the results obtained in an oil bath at the same measured reaction temperature. In our hands, carefully conducted control experiments for challenging ring-closing metathesis reactions and [2+2+2] cyclotrimerizations revealed that in all cases the results obtained with microwave irradiation could be reproduced also with conventional heating. The lifetime and activity of the transition metal catalysts was not influenced in any way by the heating mode, clearly demonstrating the absence of any specific or nonthermal microwave effects, and also revealing no apparent involvement of wall effects. Of critical importance for our control experiments was the use of internal fiber-optic probes as accurate temperature measurement devices in *both* the microwave and the conventionally heated reactors, and a careful matching of not only the final reaction temperatures and times but also of heating and cooling ramps. For reactions lasting only a few minutes, the temperature−time history during the heating and cooling stages will be important and must be carefully matched in order to obtain valid results. We suspect that in the previously published studies referred to herein, the claimed differences between microwave and conventional heating were the result of inaccurate temperature measurements often using external IR temperature probes, in addition to the fact that other important process parameters such as stirring rate or vessel geometry were most likely not properly considered. On the basis of the results presented herein it appears that the often suggested ability of a hot reactor wall to trigger unwanted thermal side reactions for well-agitated small scale organic reaction mixtures of low viscosity needs to be reconsidered. Correspondingly, the notion that microwave heating will have a significant advantage over conventional heating in minimizing or eliminating these wall effects needs to be reevaluated.

Experimental Section

Microwave Irradiation Experiments. All microwave irradiation experiments described herein were performed with a single-mode Discover Labmate System from CEM Corporation, using either a standard cylindrical Pyrex vessel for sealed vessel processing (capacity 10 mL) or a 10 mL Pyrex round-bottomed flask for open vessel reflux chemistry. Experiments were performed with temperature control mode (sealed vessel processing) or in constant power mode (open vessel reflux processing). In all experiments the internal reaction temperature was monitored by a FO probe sensor as previously reported.[34] Conventional heating was performed with a standard hot plate/magnetic stirrer, using a diethylene glycol bath.[34,35] All relevant comparison experiments were repeated at least three times in order to guarantee statistical

relevance. The given values of conversion in the text refer to the mean value of typically three experiments.

Ring-Closing Metathesis Reactions under Open Vessel Conditions: General Procedure. In an oven-dried 10 mL round-bottomed flask equipped with a magnetic stir bar, 0.1 mmol of diene starting material **2**[48] or **6**,[49] respectively, was purged for 5 min with Ar. Subsequently, the given amounts of Ru catalysts (stock solution in DCE) in Figures 2 and 3 and Figures S1, S5, S8, and S9 in the Supporting Information, respectively, and DCE (so that a total volume of 5 mL is reached) were added. A reflux condenser was attached, the fiber-optic probe and glass capillary for Ar purging were immersed through the reflux condenser into the solution (Figure S3, Supporting Information), and the setup was placed in either the microwave instrument (irradiation at 150 W constant power) or in a preheated oil bath for the times specified in Figures 1 and 2 and Figures S1, S5, S8 and S9 in the Supporting Information, respectively. For reaction monitoring 50 μL samples were taken with a glass capillary after the indicated times (see Figures 2 and 3 and Figures S1, S5, S8, and S9 in the Supporting Information) and diluted with 0.8 mL MeCN for HPLC analysis.

2,5-Dihydrobenzo-1,6-dioxocin (3, Scheme 1). In an oven-dried 25 mL round-bottomed flask equipped with a magnetic stir bar, 28.5 mg (0.15 mmol) of diene **2**[48] was purged for 5 min with Ar. A 1 mol % sample of G I (600 μL of a 2 mM stock solution in DCE) and 14.4 mL of DCE (total volume of 15 mL) were added. A reflux condenser was attached, the fiber-optic probe and glass capillary for Ar purging were immersed through the reflux condenser into the solution, and the setup was placed in the microwave instrument and irradiated at 150 W constant power (FO temperature 83 °C) with Ar-sparging for 5 min. The solvent was evaporated and the mixture was purified by silica gel column chromatography (petroleum ether/ethyl acetate: 10/1) to give 28 mg (85%) of RCM product **3** as a light yellow oil and 96% purity (HPLC at 215 nm). ^{1}H NMR (300 MHz, DMSO-d_6) δ 6.95 (s, 4H), 5.88−5.91 (m, 2H), 4.86 (d, J = 4.3 Hz, 4H). ^{13}C NMR (90 MHz, $CDCl_3$) δ 148.0, 129.4 123.7, 122.5, 70.1. MS-EI m/z 162 (M^+). The spectroscopic data of this material were in agreement with published values.[27]

3,4-Dimethyl-2,5-dihydrobenzo-1,6-dioxocin (7, Scheme 2). In an oven-dried 10 mL round-bottomed flask equipped with a magnetic stir bar, 21.8 mg (0.1 mmol) of diene **6**[49] was purged for 5 min with Ar. A 10 mol % sample of G II (1 mL of a 0.01 M stock solution in DCE) and 4 mL of DCE (that a total volume of 5 mL is reached) were added. A reflux condenser was attached, the fiber-optic probe and glass capillary for Ar purging were immersed through the reflux condenser into the solution, and the setup was placed in the microwave instrument and irradiated at 150 W constant power (FO temperature 83 °C) with Ar-sparging for 1 h. After cooling to 50 °C another 10 mol % of G II was added and again heated at 150 W constant power with Ar-sparging for 1 h. For isolation two experiments were combined (total 0.2 mmol). The solvent was evaporated and the mixture was purified by silica gel column chromatography (petroleum ether/ethyl acetate: 15/1) to provide 27 mg (71%) of RCM product **7** as a light yellow oil in 93% purity (HPLC at 215 nm). ^{1}H NMR (300 MHz, DMSO-d_6) δ 6.92 (s, 4H) 4.78 (s, 4H), 1.57 (s, 6H). MS-EI m/z 218 (M^+). The spectroscopic data of this material were in agreement with published values.[50]

1,4-Bis(2-(allyloxy)phenoxy)but-2-ene (4) and 6,9,16,19-Tetrahydrodibenzo[*b*,*j*][1,4,9,12]tetraoxacyclohexadecin (5, Scheme 1). The known[28,29] byproducts **4** and **5** were obtained in pure form (>98% HPLC at 215 nm) from more concentrated metathesis experiments (0.30 M for **4**; 0.09 M for **5**) with use of G I catalyst **1a**.[36] Data for linear dimer **4**: colorless solid, mp 84 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.91 (s, 8H), 6.05−6.12 (m, 4H), 5.43 (d, J = 14.4 Hz, 2H), 5.29 (d, J = 10.8, 2H), 4.61−4.65 (m, 8H). ^{13}C NMR (90 MHz, $CDCl_3$) δ 148.5, 133.5, 128.6, 121.3, 117.5, 114.4, 76.6, 69.9. MS-EI m/z 352 (M^+). Cyclodimer **5**: colorless solid, mp 145−158 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.94−6.96 (m, 8H), 6.17 (m, 4H), 4.62 (m, 8H). ^{13}C NMR (90 MHz, $CDCl_3$) δ 149.7, 128.4, 122.2, 116.9, 70.3. MS-EI m/z 324 (M^+). The spectroscopic data of these materials were in agreement with published values.[28,29]

[2+2+2] Cyclotrimerization Reaction of Diethyl Dipropargyl Malonate (8) with 1-Hexyne (Scheme 3a). To a flame-dried 10 mL CEM microwave process vial equipped with a stir bar were added diethyl dipropargyl malonate (**8**)[51] (12 mg, 0.05 mmol) and anhydrous toluene (2 mL). The vial was purged with Ar for 10 min before 1-hexyne (58 μL, 0.50 mmol) and $Ni(CO)_2(PPh_3)_2$ catalyst (3.20 mg, 0.005 mmol) were added. The reaction mixture was purged again with Ar for 20 min before being sealed tight by using the CEM Discover pressure/fiber-optic attenuator[34] and was subsequently placed into the CEM Discover microwave unit or a preheated oil bath (86 °C) to be heated for 5 min (Figure S10, Supporting Information, see main text for details). After allowing the reaction mixture to cool to room temperature, a 50 μL sample was transferred into a syringe, filtered via a syringe filter, diluted with EtOAc (1 mL), and subjected to GC-MS analysis. For isolation, the crude reaction mixtures from three experiments were pooled, concentrated under vacuo, and purified by flash chromatography with hexanes/EtOAc as eluent to provide 33.4 mg (70%, microwave) and 29 mg (61%, oil bath), respectively, of pure diethyl 5-butyl-1*H*-indene-2,2-dicarboxylate (**9**) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.93 (t, J = 7.2 Hz, 3 H), 1.25 (t, J = 7.1 Hz, 6 H), 1.34 (m, 2 H), 1.58 (m, 2 H), 2.56 (t, J = 7.8 Hz, 2 H), 3.57 (s, 4 H), 4.20 (q, J = 7.1 Hz, 4 H), 6.97 (d, J = 7.6 Hz, 1H), 7.01 (s, 1H), 7.08 (d, J = 7.6 Hz, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 14.0, 22.4, 33.8, 35.5, 40.1, 40.4, 60.6, 61.6, 123.8, 124.1, 127.1, 137.1, 140.0, 141.7, 171.8. The spectral data are in agreement with the previously published values.[52]

[2+2+2] Cyclotrimerization Reaction of 1,2-Dipropargylbenzene (10) with Propargyl Alcohol (Scheme 3b). To a flame-dried 10 mL CEM microwave process vial equipped with a stir bar were added 1,2-dipropargylbenzene (**10**)[53] (20 mg, 0.13 mmol) and anhydrous toluene (4 mL). The vial was purged with Ar for 10 min before adding propargyl alcohol (77 μL, 1.3 mmol) and $Ni(CO)_2(PPh_3)_2$ catalyst (8.30 mg, 0.013 mmol). The reaction mixture was purged again with Ar for 20 min before being sealed tight by using the CEM Discover pressure/fiber-optic attenuator[34] and was subsequently placed into the CEM Discover microwave unit or a preheated oil bath (135 °C) to be heated for 10 min (Figure S11, Supporting Information; see main text for details). After the reaction mixture was allowed to cool to room temperature, a 50 μL sample was transferred into a syringe, filtered via a syringe filter, diluted with EtOAc (1 mL), and subjected to GC-MS analysis. For isolation, the crude reaction mixtures from three experiments were pooled, concentrated under vacuo, and purified by flash chromatography with hexanes/EtOAc as eluent to provide 52 mg (64%, microwave) and 55 mg (67%, oil bath), respectively, of pure 9,10-dihydro-2-(hydroxymethyl)anthracene (**11**) as a yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.59 (s, 1 H), 3.92 (s, 3 H), 4.65 (s, 2H), 7.16

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(m, 3 H), 7.28 (m, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 36.1, 36.4, 65.6, 125.1, 126.4, 126.9, 127.2, 127.6, 127.8, 136.5, 136.8, 137.3, 139.0, 142.8. The spectral data are in agreement with previously published values.[44] The product is unstable and will oxidize easily to the aromatic anthracene product.[44]

[2+2+2] Cyclotrimerization Reaction of 1,2-Dipropargylbenzene (10) with Benzonitrile (Scheme 3c). To a flame-dried 10 mL CEM microwave process vial equipped with a stir bar were added 1,2-dipropargylbenzene (**10**)[53] (20 mg, 0.13 mmol), benzonitrile (134 μL, 1.3 mmol), and anhydrous toluene (4 mL). The capped vial was purged with Ar for 30 min before adding $CpCo(CO)_2$ catalyst (1.60 μL, 0.013 mmol). The reaction vial was sealed tight by using the CEM Discover pressure/fiber-optic attenuator[34] and was subsequently placed into the CEM Discover microwave unit or a preheated oil bath (180 °C) to be heated for 20 min (Figure S12, Supporting Information; see the main text for details). After the reaction mixture was allowed to cool to room temperature, a 50 μL sample was transferred into a syringe, filtered via a syringe filter, diluted with EtOAc (1 mL), and subjected to GC-MS analysis. For isolation, the crude reaction mixtures from three experiments were pooled, concentrated under vacuo, and purified by flash chromatography with hexanes/EtOAc as eluent to provide 78 mg (78%, microwave) and 75 mg (75%, oil bath) of pure 3-phenyl-5,10-dihydrobenzoisoquinoline (**12**) as yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.97 (m, 4H), 7.23 (m, 2H), 7.30 (m, 2H), 7.39 (d, J = 6.4 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 7.63 (s, 1H), 7.97 (d, J = 8.0 Hz, 2H), 8.59 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 32.7, 35.8, 119.4, 126.7, 126.8, 127.0, 127.9, 128.0, 128.8, 128.9, 131.1, 135.0, 135.6, 139.7, 146.5, 148.4, 155.6. The spectral data are in agreement with previously published values.[44] The product is unstable and will oxidize easily to the aromatic aza-anthracene product.[44]

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Supporting Information Available: Description of general experimental procedures, images, and heating profiles for all reactions. This material is available free of charge via the Internet at http://pubs.acs.org.