

# Ring-Closing Olefin Metathesis of 2,2'-Divinylbiphenyls: A Novel and General Approach to Phenanthrenes

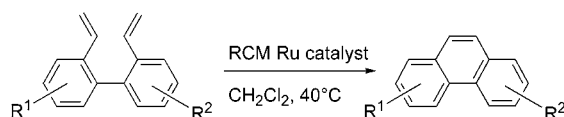
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## ABSTRACT

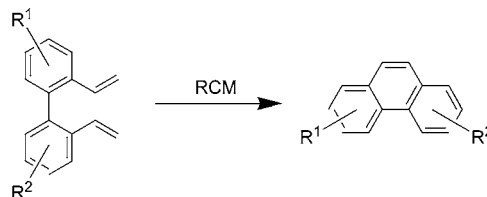


The ring-closing olefin metathesis (RCM) of 2,2'-divinylbiphenyls, using a second-generation RCM ruthenium-based catalyst, leads to differently substituted phenanthrenes in quantitative yield under very mild reaction conditions, independent of both nature and position of the groups present on the biphenyl moiety.

Phenanthrenes represent an important class of organic compounds because they are useful intermediates for natural product synthesis<sup>1</sup> or exhibit various biological activities such as antimalarial,<sup>2</sup> anticancer,<sup>3</sup> and emetic activity.<sup>4</sup> A number of methods are known for the synthesis of phenanthrenes,<sup>1</sup> which use ring annulation,<sup>5</sup> intermolecular,<sup>6</sup> and intramolecular<sup>7</sup> cyclization. The majority of these methods are characterized by limitations such as accessibility of the starting substrates, relatively low overall yield, reaction conditions scarcely compatible with the presence of functional groups, and the lack of well-defined regiocontrol elements. Some of these synthetic methods use as starting materials 2,2'-disubstituted biphenyls, which afford phenanthrenes by

intramolecular condensation,<sup>8</sup> cycloisomerization,<sup>9</sup> metal-catalyzed rearrangement of alkene–alkynes,<sup>10</sup> and photocyclization,<sup>11</sup> depending on the functional group present on the biphenyl moiety. The ready accessibility to differently functionalized biphenyls, by various methods of aryl–aryl coupling,<sup>12</sup> and the success of the ring-closing olefin metathesis (RCM) reaction for the preparation of various compounds,<sup>13</sup> prompted us to check the possibility of obtaining phenanthrenes by RCM of 2,2'-divinylbiphenyls (Scheme 1).<sup>14</sup>

**Scheme 1.** Synthesis of Substituted Phenanthrenes by RCM



We focused our attention on RCM because it is well-known that the mild reaction conditions (ruthenium catalysts,

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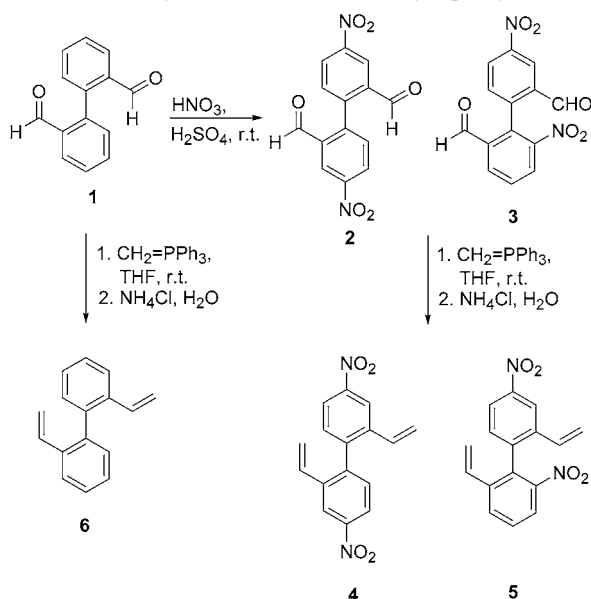
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low temperatures)<sup>15</sup> are well tolerated by many functional groups, which can be introduced on the biphenyl moiety leading to differently substituted phenanthrenes. Here, we present the results we have obtained in the RCM of 2,2'-divinylbiphenyls possessing different substituents on different positions of the biphenyl moiety. We carried out this study to verify the applicability of this method for the synthesis of phenanthrenes.

The choice of method for synthesizing the 2,2'-divinylbiphenyl systems depends on the nature of the substituents as well as their position on the biphenyl moiety.

The unsubstituted 2,2'-divinylbiphenyl as well as the nitro-substituted substrates were prepared starting from 2,2'-diformylbiphenyl **1** (Scheme 2), obtained by Ullmann cou-

**Scheme 2.** Synthesis of the 2,2'-Divinylbiphenyls **4–6**

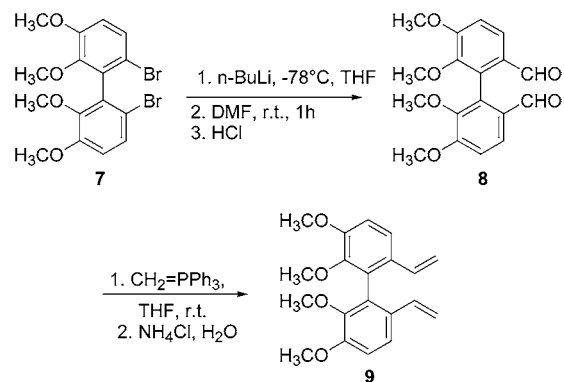


pling of 2-iodobenzaldehyde.<sup>16</sup> Nitration of **1**, under the experimental conditions used for obtaining 3-nitrobenzaldehyde,<sup>17</sup> afforded a mixture of the two isomers **2** and **3**, which were not separable by recrystallization or by flash chromatography. The Wittig reaction performed on the isomeric mixture afforded the corresponding olefins in nearly quan-

titative yield, which were separated by flash chromatography giving the two isomeric divinyl derivatives **4** and **5**. The structure of **5** was determined by <sup>1</sup>H NMR analysis (coupling constant and NOE measurements). In turn, 2,2'-divinylbiphenyl **6** was obtained in nearly quantitative yield by Wittig reaction on **1**.

The vinyl groups of compound **9** were introduced in two steps starting from compound **7**, prepared as already described<sup>18</sup> (Scheme 3).

**Scheme 3.** Synthesis of 5,5',6,6'-Tetramethoxy-2,2'-divinylbiphenyl **9**



According to Scheme 3, standard metal–halide exchange (BuLi/−78 °C/THF) on compound **7** followed by quenching with *N,N*-dimethylformamide and acidic workup afforded, in quantitative yield, the corresponding diformyl derivative **8**, which was subjected to standard Wittig reaction, giving quantitatively the 2,2'-divinylbiphenyl derivative **9**. The use of the two-step procedure was necessary because attempts at introducing directly the vinyl groups by cross-coupling of **7** with vinyl organometallic reagents<sup>19</sup> were unsuccessful.

The synthesis of the unsymmetrical 2,2'-divinylbiphenyl derivative **14** (Scheme 4) required a different approach both for building up the biphenyl system and for the introduction of the two vinyl groups.

Classical Suzuki–Miyaura<sup>20</sup> coupling of 3-methoxyphenylboronic acid and 2-iodobenzaldehyde gave in excellent yield the unsymmetrical biphenyl **10**.

Bromination of **10** using BTMA·Br<sub>3</sub> at room temperature<sup>21</sup> afforded **11** as sole product in quantitative yield, whose chemical structure was confirmed by <sup>1</sup>H NMR analysis (coupling constant and NOE measurements). The first vinyl group was introduced at this step by reacting **11** with methyltriphenylphosphonium ylide under standard conditions; the vinyl derivative **12** was obtained in 94% yield after flash chromatography. The second vinyl group was introduced by formylation (DMF) of the lithium derivative, obtained by standard metal–halide exchange, followed by Wittig reaction on the aldehyde **13**, as previously described for the preparation of **9**. Compound **14** was obtained in 60% yield from **12**, after chromatographic purification.

All of the 2,2'-divinylbiphenyl derivatives were subjected to the RCM reaction, using commercial first-generation<sup>13</sup> or

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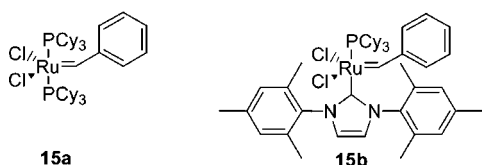
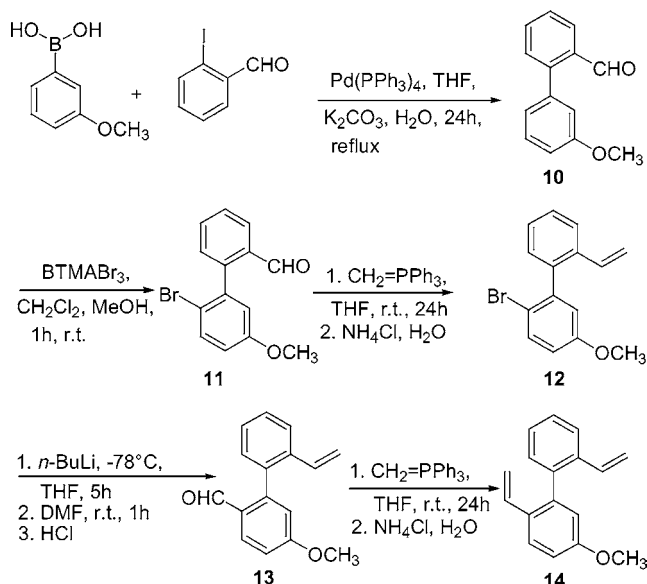
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**Scheme 4.** Synthesis of 5-Methoxy-2,2'-divinylbiphenyl **14**



**Figure 1.** Structure of first-generation (**15a**) and second-generation (**15b**) ruthenium-carbene catalysts.

second-generation<sup>22</sup> ruthenium-carbene catalysts (Figure 1), to evaluate the effects of both nature and position of the biphenyl substituents on the outcome of the reaction.

The obtained results are listed in Table 1. All the reactions were carried out under the experimental condition usually employed for RCM.

In a typical run the catalyst (5% mol) was added to a  $10^{-2}$  M solution of the substrate in dry solvent. The mixture was stirred at the reported temperature (Table 1), and the reaction was interrupted when TLC or GC analysis showed that the substrate conversion did not proceed further.

The reaction of 2,2'-divinylbiphenyl **6** in  $\text{CH}_2\text{Cl}_2$  at room temperature afforded a complete conversion of the substrate in 2 h, giving chemically pure phenanthrene in quantitative yield (entry 1). By contrast, under the same reaction conditions the RCM of 5,5',6,6'-tetramethoxy-2,2'-divinylbiphenyl **9** did not take place; not even doubling the catalyst amount or prolonging the reaction time had any beneficial

**Table 1.** RCM of 2,2'-Divinylbiphenyls to Phenanthrenes

Entry	Substrate	Product	Solvent	T <sup>o</sup> C	Cat	t(h)	Yield
1			$\text{CH}_2\text{Cl}_2$	25	<b>15a</b>	2	100
2			$\text{CH}_2\text{Cl}_2$	25	<b>15a</b>	2	0 <sup>(a)</sup>
3	<b>9</b>	<b>16b</b>	$\text{CH}_2\text{Cl}_2$	40	<b>15a</b>	24	30
4	<b>9</b>	<b>16b</b>	Toluene	110	<b>15a</b>	24	30
5	<b>9</b>	<b>16b</b>	$\text{CH}_2\text{Cl}_2$	40	<b>15b</b>	2	100
6			$\text{CH}_2\text{Cl}_2$	40	<b>15a</b>	24	50
7	<b>4</b>	<b>16c</b>	$\text{CH}_2\text{Cl}_2$	40	<b>15b</b>	2	100
8			$\text{CH}_2\text{Cl}_2$	40	<b>15b</b>	2	100
9			$\text{CH}_2\text{Cl}_2$	40	<b>15a</b>	24	87
10	<b>14</b>	<b>16e</b>	$\text{CH}_2\text{Cl}_2$	40	<b>15b</b>	2	100

<sup>a</sup> Reacting **9** for 24 h or using 10% mol of **15a** gave the same result.

effect (entry 2). The lack of reactivity of this substrate can be attributed to the presence of the 6,6' substituents which impart conformational rigidity to the biphenyl system, preventing the coplanar disposition of the two phenyl rings and hence the cyclization.<sup>23</sup> On increasing the reaction temperature to 40 °C, the RCM did take place, however, but afforded only 30% yield of the phenanthrene derivative (entry 3). A further increase in reaction temperature (refluxing toluene) afforded the same result (entry 4).

These poor results prompted us to check the second-generation ruthenium carbene catalyst **15b**, which is known

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to often afford a higher yield of metathesis product<sup>24</sup> with respect to the use of **15a**. Much to our delight, with **15b** as the RCM catalyst a complete conversion of the substrate to **16b** occurred after 2 h reaction at reflux in dichloromethane; the phenanthrene derivative was obtained in quantitative yield (entry 5). The RCM of the 4,4'-dinitro-2,2'-divinylbiphenyl **4**, performed in the presence of **15a** as catalyst, afforded the corresponding phenanthrene derivative in only 50% yield after 24 h reaction at 40 °C. Since the presence of substituents at 4,4' positions of the biphenyl system does not affect the conformational flexibility of 2,2'-disubstituted biphenyl systems the lower yield with respect to the RCM of **6** can be attributed to the electronic character of the nitro groups. The effect of the electronic properties of the substituents on the efficiency of the ring closure is unusual, since it is known, for example, that chromenes having substituents such as NO<sub>2</sub> or OMe could be prepared with the same efficiency.<sup>25</sup>

By contrast, when **15b** was used as catalyst for the RCM of **4**, a quantitative yield of the corresponding phenanthrene was obtained, after only 2 h of reaction in dichloromethane at reflux (entry 7). Also, compound **5**, where one of the nitro groups is at the position 6 of the biphenyl moiety, underwent the RCM in 2 h, affording the corresponding substituted phenanthrene in quantitative yield. These results point to the much greater effectiveness of the second generation Grubbs catalyst in the RCM reactions of 2,2'-divinylbiphenyls. The trend observed with substrates **4** and **9** was also confirmed in the case of **14**. When the RCM of this substrate was performed in the presence of **15a**, 24 h were required to

obtain a high yield of the corresponding phenanthrene (entry 9), whereas in the presence of catalyst **15b**, a quantitative yield of the cyclization product was achieved only after 2 h of reaction (entry 10).

In conclusion, the RCM of 2,2'-divinylbiphenyls has proven to be a general method for obtaining high yields of substituted phenanthrenes. Using the ruthenium-carbene complex **15a** as catalyst the reaction gives results that depend on the conformational rigidity of the biphenyl moiety as well as the electronic properties of the substituents. The use of the ruthenium-carbene complex **15b** as catalyst affords quantitative yields of the phenanthrene derivative independent of the structure of the starting biphenyl. In addition, the ready accessibility to differently substituted 2,2'-divinylbiphenyls makes this approach very attractive. The sole limitation of this method is the impossibility to obtain phenanthrenes having substituents at positions 9 and 10. Nevertheless, these derivatives can be easily obtained by electrophilic aromatic substitution on phenanthrene.

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**Supporting Information Available:** Full experimental details including procedure for the preparation of the biphenyl derivatives as well as the analytical and spectroscopic data of all new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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