Inorganica Chimica Acta 378 (2011) 257–263

Contents lists available at SciVerse ScienceDirect

Inorganica Chimica Acta

journal homepage: www.elsevier.com/locate/ica

# Activity of homobimetallic ruthenium alkylidene complexes on intermolecular [2+2+2] cyclotrimerisation reactions of terminal alkynes

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ARTICLE INFO

*Article history:*
Received 15 April 2011
Received in revised form 22 August 2011
Accepted 10 September 2011
Available online 17 September 2011

*Keywords:*
Ruthenium
Cyclotrimerisation
Alkynes
Silicon
Arene ligands

ABSTRACT

The activity of homobimetallic ruthenium alkylidene complexes, [(*p*-cymene)Ru(Cl)(μ-Cl)$_2$Ru(Cl)(=CHPh)(PCy$_3$)] [**Ru-I**] and [(*p*-cymene)Ru(Cl)(μ-Cl)$_2$Ru(Cl)(=CHPh)(IPr)] [**Ru-II**], on intermolecular [2+2+2] cyclotrimerisation reactions of monoynes has been investigated for the first time. It was found that these complexes can catalyse the chemo and regioselective cyclotrimerisation reactions of alkynes at both 25 and 50 °C in polar, aprotic solvents. The catalytic activity of [**Ru-I**] and [**Ru-II**] was compared to other well-known ruthenium catalysts such as Grubbs first generation catalyst [RuCl$_2$(=CHPh)(PCy$_3$)$_2$] [**Ru-III**], [RuCl(μ-Cl)(*p*-cymene)]$_2$ [**Ru-IV**] and [RuCl$_2$(*p*-cymene)PCy$_3$] [**Ru-V**] complexes. To examine the effect of the steric hinderance of substrates on the regioselectivity of the reaction, a series of sterically hindered silicon containing alkynes (**1a, 1b, 1c**) were used. It was shown that the isomeric product distribution of the reaction shifts from 1,2,4-trisubstituted arenes to 1,3,5-trisubstituted arenes as the steric hinderance on the substrates increases. These homobimetallic ruthenium alkylidene complexes also catalysed regio- and chemo-selective cross-cyclotrimerisation reactions between silicon-containing alkynes (**1a, 1b, 1c**) and aliphatic alkynes (**1d–g**).



## 1. Introduction

Compared to conventional strategies, such as electrophilic aromatic substitutions or orthometalation techniques [1], the transition metal catalysed [2+2+2] cyclotrimerisation of alkynes is considerably advantageous in the synthesis of highly substituted benzene derivatives due to its atom-economical and convergent nature [2,3]. Cyclotrimerisation of alkynes is catalysed using a variety of transition metal catalysts including: Co, Fe, Ni, Pd, Re, Rh, Ru and Ta [4–10]. Among them, CpCo complexes (Cp: cyclopentadienyl), such as CpCo(CO)$_2$, have been widely used in the pharmaceutical industry, in the preparation of natural products and in the preparation of functionalised materials [11]. Ni(acac)$_2$/PPh$_3$ [14] and the Wilkinson catalyst, RhCl$_2$(PPh$_3$)$_3$ [15], have also been used to catalyse cyclotrimerisation reactions of alkynes. To control the chemo- and regioselectivity of cyclotrimerisation reactions, a stoichiometric approach was used, which utilised ($\eta^2$-propene)Ti(O-i-Pr)$_2$ [12], and ZrCp$_2$(C$_4$Et$_4$) [13]. A binary metallic system of nickel and zinc phenoxide was reported by Odashima and co-workers [16] as a high chemo and regioselective approach to intermolecular cyclotrimerisation reactions for two different monoynes. Zhou and colleagues reported an efficient binary metallic system of Y[N(TMS)$_2$]$_3$/FeCl$_3$ for the cyclotrimerisation of terminal alkynes. Ruthenium catalysts such as [RuCl(cod)Cp] [17], are widely used in the cyclotrimerisation reactions of alkynes as well as the [2+2+2] cycloaddition of 1,6-diynes with nitriles, isocyanates and isothiocyanates to afford pyridines, bicyclic pyridones and thiopyridones at good yields [18]. The [RuCl(cod)Cp] catalyst has been successfully applied to achieve the chemoselective [2+2+2] cycloaddition of three different alkynes, through the control of the molar ratio of the substrates [19]. Lin et al. reported the activity of an air stable Ru(II) perchloro-cyclobutenonyl complex towards [2+2+2] cyclotrimerisation reactions [20]. Recently, a homobimetallic ruthenium complex, [{Ru($\eta^3$-C$_{10}$H$_{16}$)($\mu$-Cl)Cl}$_2$], was shown to catalyse the cyclotrimerisation reactions of alkynes in aqueous media [21]. Although, there are several reports on the catalytic activity of ruthenium complexes towards inter- and intra-cyclotrimerisation reactions of alkynes, there are few examples using ruthenium alkylidene complexes to mediate [2+2+2] the cycloaddition of alkynes in an intra- or intermolecular fashion. Blechert reported, for the first time that Grubbs first generation catalyst can catalyse the intramolecular [2+2+2] cyclotrimerisation reactions of triynes at good yields [22]. Roy and Das prepared carbohydrate derivatives with Grubbs first generation catalyst utilising the intermolecular cyclotrimerisation reactions [23]. Additionally, this catalyst was used for cross-cyclotrimerisation of diynes with alkynes [15], for solid-supported cyclotrimerisation reactions [24] and for the synthesis of indacenes [25]. More recently, Castells reported that second generation Grubbs and Hoveyda–Grubbs complexes

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doi:10.1016/j.ica.2011.09.023

are efficient catalysts for the cross [2+2+2] cyclotrimerisation of diynes with alkynes and demonstrated that the process was still selective when applied to non-symmetric diynes [26].

To date, no examples of intermolecular cyclotrimerisation reactions of monoynes catalysed using homobimetallic ruthenium alkylidene complexes have been reported. In this study, we report the activity of homobimetallic ruthenium alkylidene complexes (Scheme 1) on the intermolecular [2+2+2] cyclotrimerisation reactions of monoynes and the chemo- and regio-selective cross-intermolecular cyclotrimerisation reactions of two different alkynes.

## 2. Experimental

### 2.1. Materials

All manipulations were carried out under an inert atmosphere of nitrogen using Schlenk techniques. 3-Trimethylsiloxy-1-propyne (**1a**), 3-(trimethylsilyloxy)-1-butyne (**1b**), [(1,1-dimethyl-2-propynyl)-oxy]trimethylsilane (**1c**), 1-heptyne (**1d**), 1-octyne (**1e**), 1-dodecyne (**1f**) and 1-tetradecyne (**1g**) were purchased from Sigma–Aldrich and used as received. Grubbs first generation catalyst $[RuCl_2(=CHPh)(PCy_3)_2]$ [**Ru-III**] and $[RuCl_2(p\text{-cymene})]_2$ [**Ru-IV**] were purchased from Sigma–Aldrich and used as received, [(*p*-cymene)Ru(Cl)($\mu$-Cl)$_2$Ru(Cl)(=CHPh)($PCy_3$)] [**Ru-I**] [(*p*-cymene)Ru(Cl)($\mu$-Cl)$_2$Ru(Cl)(=CHPh)(IPr)] [**Ru-II**] (IPr: 1,3-bis(2,6-diisopropylphenyl)-imidazoline) and $[RuCl_2(p\text{-cymene})PCy_3]$ [**Ru-V**] were synthesised according to the literature [27,28]. Toluene, THF, dichloromethane and acetone were purchased from Sigma–Aldrich and distilled under Na/benzophenone, $P_2O_5$ and $CaCl_2$, respectively and stored under an inert atmosphere of nitrogen.

### 2.2. Instrumentation

$^1$H and $^{13}$C NMR spectra were recorded at 25 °C with a Bruker GmbH 400 MHz high performance digital FT NMR spectrometer using $CDCl_3$ as a solvent. Tetramethylsilane was used for the $^1$H and $^{13}$C NMR reference. GC–MS analyses were performed with a Shimadzu GC–MS QP5050A using an Optima column, 5–1.0 μm (50 m × 0.32 mm) and a temperature range of 50–300 °C (10 °C/min). The carrier gas was helium with a flow rate of 1 mL/min.

### 2.3. Procedure for intermolecular [2+2+2] cyclotrimerisation reactions of silicon containing terminal alkynes

#### 2.3.1. Representative procedure for the preparation of 1,3,5-tris((trimethylsilyloxy)methyl)benzene (**2a**) and 1,2,4-tris((trimethylsilyloxy)methyl)benzene (**3a**)

A reactor was charged with [**Ru-II**] (0.030 mmol) and **1a** (0.75 mmol) in 1 ml of dry THF under a nitrogen atmosphere. The reaction mixture was stirred at 50 °C for 15 h. Aliquots taken periodically from the reaction mixture were analysed by GC–MS. The solvent was evaporated and crude product mixture was passed through a plug of silica gel to remove catalytic impurities. The final product was a mixture of 1,3,5-trisubstitued (**2a**) and 1,2,4-trisubstitued (**3a**) arene isomers (Scheme 2). The mixtures were analysed by $^1$H and $^{13}$C NMR.

#### 2.3.2. 1,3,5-tris((Trimethylsilyloxy)methyl)benzene (**2a**)

$^1$H NMR ($CDCl_3$; ppm): 7.32 (s, 3H), 4.73 (s, 6H), 0.12 (s, 27H). $^{13}$C NMR ($CDCl_3$; ppm): 141.67, 123.30, 68.10, 0.41, MS [EI 70 eV] *m*/*z* 384 [$M^+$].

#### 2.3.3. 1,2,4-tris((Trimethylsilyloxy)methyl)benzene (**3a**)

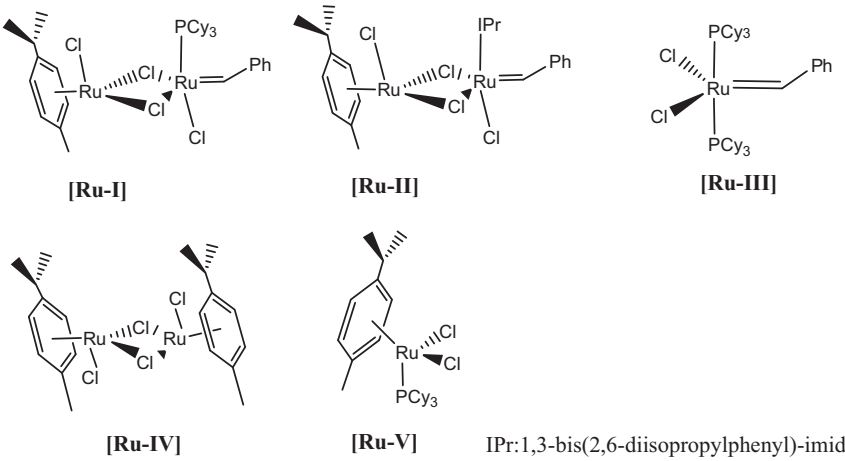
$^1$H NMR ($CDCl_3$; ppm): 7.28 (s, 1H), 7.20 (d, *J* = 7.40 Hz, 1H), 7.10 (d, *J* = 7.40 Hz, 1H), 4.75 (s, 2H), 4.70 (s, 2H), 4.51 (d, *J* = 6.5 Hz, 2H), 0.14 (s, 9H), 0.12 (s, 18H). $^{13}$C NMR ($CDCl_3$; ppm): 140.0, 138.10, 136.72, 127.34, 125.90, 125.40, 65.10, 63.20, 62.0, 1.93, MS [EI 70 eV] *m*/*z* 384 [$M^+$].

#### 2.3.4. 1,3,5-tris(1-(Trimethylsilyloxy)ethyl)benzene (**2b**)

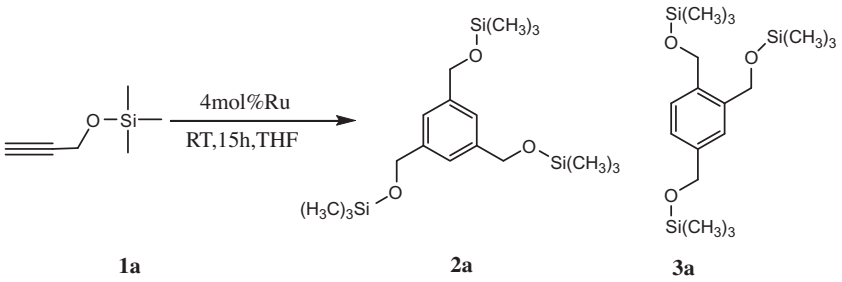
$^1$H NMR ($CDCl_3$; ppm): 7.29 (s, 3H), 4.50 (q, 3H), 1.50 (d, *J* = 6.8 Hz, 9H), 0.12 (s, 27 H). $^{13}$C NMR ($CDCl_3$; ppm): 145.0, 121.0, 72.10, 25.20, 1.93. MS [EI 70 eV] *m*/*z* 426 [$M^+$].

#### 2.3.5. 1,2,4-tris(1-(Trimethylsilyloxy)ethyl)benzene (**3b**)

$^1$H NMR ($CDCl_3$; ppm): 7.25 (s, 1H), 7.21 (d, *J* = 7.44 Hz, 1H), 7.05 (d, *J* = 7.44 Hz, 1H), 4.51(q, 1H), 4.40 (q, 2H), 4.30 (m, 2H), 0.14 (s, 9H), 0.12 (s, 18H). $^{13}$C NMR ($CDCl_3$; ppm): 143.0, 140.20, 137.55, 126.0, 122.85, 122.30, 69.84, 68.30, 68.14, 23.40, 23.06, 1.93. MS [EI 70 eV] *m*/*z* 426 [$M^+$].




**Scheme 1.** Various ruthenium complexes, which were used in intermolecular [2+2+2] cyclotrimerisation reactions of monoynes.




**Scheme 2.** Representative cyclotrimerisation reaction of **1a**.

*2.3.6. 1,3,5-tris(2-(Trimethylsilyloxy)propan-2-yl)benzene (**2c**)*

$^1$H NMR ($CDCl_3$; ppm): 7.20 (s, 1H), 1.45 (s, 18H), 0.12 (s, 27H). $^{13}$C NMR ($CDCl_3$; ppm): 148.40, 123.0, 76.64, 30.10, 1.94. MS [EI 70 eV] *m*/*z* 468 [$M^+$].

*2.3.7. 1,2,4-tris(2-(Trimethylsilyloxy)propan-2-yl)benzene (**3c**)*

This compound could only be detected by GC–MS. Amount of the isomer was too low to detect by $^{13}$C and $^1$H NMR. MS [EI 70 eV] *m*/*z* 468 [$M^+$].

*2.4. Procedure for intermolecular [2+2+2] cross-cyclotrimerisation reactions of alkyne **1a** with 1-heptyne (**1d**), 1-octyne (**1e**), 1-dodecyne (**1f**) and 1-tetradecyne (**1g**)*

*2.4.1. Representative procedure for the preparation of 1,2-bis(trimeth ylosiloxyl methyl)-4-heptyl-benzene (**2e**) and 1,3-bis(trimethylosil oxylmethyl)-4-heptyl-benzene (**3e**)*

To a mixture of [**Ru-IV**] (0.039 mmol) and **1a** (1.625 mmol) in 1.5 ml dry THF, 450 μL of a THF solution of 1-octyne (0.325 mmol) was added in nine aliquots of 50 μL over a period of 30 min. The reaction mixture was stirred for 48 h at 50 °C. Aliquots were taken periodically from the reaction mixture and analysed by GC–MS. The solvent was evaporated and the crude product mixture was passed through a plug of silica gel to remove catalytic impurities. The mixture was then analysed by $^1$H and $^{13}$C NMR. The final product was determined to be a mixture of **2e**, **3e** and **2a**.

*2.4.2. 1,2-bis(Trimethylosiloxyl methyl)-4-pentyl-benzene (**2d**)*

$^1$H NMR ($CDCl_3$; ppm): 7.26 (s, 1H), 7.16 (d, *J* = 7.55 Hz, 1H), 7.12 (d, *J* = 7.55 Hz, 1H), 4.62 (s, 2H), 4.48 (d, *J* = 6.40 Hz, 2H), 2.67 (m, 2H), 1.58 (m, 2H), 1.34–1.25 (m, 4H), 0.89 (t, 3H), 0.14 (s, 9H), 0.12 (s, 9H). $^{13}$C NMR ($CDCl_3$; ppm): 141.0, 137.0, 133.2, 129.84, 125.87, 125.49, 64.21, 62.55, 33.63, 31.31, 29.35, 22.57, 14.10, 1.94. MS [EI 70 eV] *m*/*z* 352 [$M^+$].

*2.4.3. 1,3-bis(Trimethylosiloxyl methyl)-4-pentyl-benzene (**3d**)*

$^1$H NMR ($CDCl_3$; ppm): 7.22 (d, *J* = 7.81 Hz, 1H), 7.19 (s, 1H), 6.94 (d, *J* = 7.84 Hz, 1H), 4.59 (d, 2H), 4.40 (d, *J* = 6.50 Hz, 2H), 2.69 (m, 2H), 1.58 (m, 2H), 1.33–1.25 (m, 4H), 0.89 (t, 3H), 0.14 (s, 9H), 0.12 (s, 9H). $^{13}$C NMR ($CDCl_3$; ppm): 141.54, 139.70, 137.10, 129.10, 127.30, 127.21, 64.24, 62.45, 33.67, 31.32, 29.40, 22.59, 14.11, 1.93. MS [EI 70 eV] *m*/*z* 352 [$M^+$].

*2.4.4. 1,2 -bis (trimethylosiloxyl methyl) -4-heptyl-benzene (**2e**)*

$^1$H NMR ($CDCl_3$; ppm): 7.25 (s, 1H), 7.16 (d, *J* = 7.51 Hz, 1H), 7.10 (d, *J* = 7.51 Hz, 1H), 4.62 (s, 2H), 4.48 (d, *J* = 6.40 Hz, 2H), 2.69 (m, 2H), 1.58 (m, 2H), 1.33–1.25 (m, 6H), 0.89 (t, 3H), 0.14 (s, 9H), 0.12 (s, 9H). $^{13}$C NMR ($CDCl_3$; ppm): 141.3, 137.2, 133.1, 129.85, 125.90, 125.49, 64.21, 62.55, 33.66, 31.30, 30.92, 29.42, 22.62, 14.09, 1.93. MS [EI 70 eV] *m*/*z* 366 [$M^+$].

*2.4.5. 1,3-bis(trimethylosiloxyl methyl)-4-heptyl-benzene (**3e**)*

$^1$H NMR ($CDCl_3$; ppm): 7.23 (d, *J* = 7.70 Hz, 1H), 7.19 (s, 1H), 6.94 (d, *J* = 7.71 Hz, 1H), 4.59(d, 2H), 4.40 (d, *J* = 6.42 Hz, 2H), 2.69 (m,2H), 1.58 (m, 2H), 1.33–1.25 (m, 6H), 0.89 (t, 3H), 0.14 (s, 9H), 0.12 (s, 9H). $^{13}$C NMR ($CDCl_3$; ppm): 141.66, 139.95, 137.14, 128.96, 127.30, 127.11, 64.21, 62.55, 33.66, 31.30, 30.92, 29.42, 22.62, 14.09, 1.93. MS [EI 70 eV] *m*/*z* 366 [$M^+$].

*2.4.6. 1,2-bis(Trimethylosiloxyl methyl)-4-decyl-benzene (**2f**)*

This compound could only be detected by GC–MS. Amount of the isomer was too low to detect by $^{13}$C and $^1$H NMR. MS [EI 70 eV] *m*/*z* 422 [$M^+$].

*2.4.7. 1,3-bis(Trimethylosiloxyl methyl)-4-decyl-benzene (**3f**)*

$^1$H NMR ($CDCl_3$; ppm): 7.24 (d, *J* = 7.68 Hz, 1H), 7.18 (s, 1H), 6.93 (d, *J* = 7.67 Hz, 1H), 4.60(d, 2H), 4.40 (d, *J* = 6.40 Hz, 2H), 2.70 (m, 2H), 1.58 (m, 2H), 1.42–1.22 (m, 15H), 0.89 (t, 3H), 0.14 (s, 9H), 0.12 (s, 9H). $^{13}$C NMR ($CDCl_3$; ppm): 142.0, 140.61, 137.63, 129.05, 127.72, 127.88, 64.25, 62.59, 33.70, 31.30, 30.92, 29.42, 29.10, 29.0, 28.75, 23.40, 22.62, 14.09, 1.93. MS [EI 70 eV] *m*/*z* 422 [$M^+$].

*2.4.8. 1,2-bis(Trimethylosiloxyl methyl)-4-dodecyl-benzene (**2g**)*

This compound could only be detected by GC–MS. Amount of the isomer was too low to detect by $^{13}$C and $^1$H NMR. MS [EI 70 eV] *m*/*z* 450 [$M^+$].

*2.4.9. 1,3-bis(Trimethylosiloxyl methyl)-4-dodecyl-benzene (**3g**)*

$^1$H NMR ($CDCl_3$; ppm): 7.24 (d, *J* = 7.66 Hz, 1H), 7.18 (s, 1H), 6.94 (d, *J* = 7.66 Hz, 1H), 4.61 (d, 2H), 4.39 (d, *J* = 6.45 Hz, 2H), 2.70 (m, 2H), 1.58 (m, 2H), 1.42–1.20 (m, 19H), 0.89 (t, 3H), 0.14 (s, 9H), 0.12 (s, 9H). $^{13}$C NMR ($CDCl_3$; ppm): 142.1, 140.65, 137.69, 129.15, 127.80, 127.80, 64.24, 62.57, 33.70, 31.30, 30.92, 29.80 29.42, 29.30, 29.10, 29.0, 28.75, 23.40, 22.62, 14.09, 1.93. MS [EI 70 eV] *m*/*z* 450 [$M^+$].

## 3. Results and discussion

In this study, several ruthenium complexes (Scheme 1), Grubbs first generation catalysts [**Ru-III**], [(*p*-cymene)Ru(Cl)(μ-Cl)$_2$ Ru(Cl)(=CHPh)($PCy_3$)] [**Ru-I**], ([(*p*-cymene)(Cl)Ru(μ-Cl)$_2$Ru(Cl) (IPr)-(CHPh) [**Ru-III**], [(*p*-cymene)$RuCl_2$]$_2$ [**Ru-IV**] and [(*p*-cymene)$RuCl_2PCy_3$] [**Ru-V**] were tested on intermolecular cyclotrimerisation reactions of terminal alkynes. The activity of homobimetallic ruthenium complexes [**Ru-II**] and [**Ru-III**] towards cyclotrimerisation reactions of monoynes were compared to other well-known ruthenium complexes, such as [**Ru-I**] and [**Ru-IV**].

### 3.1. Intermolecular [2+2+2] cyclotrimerisation reactions of silicon containing alkynes

To optimise the reaction conditions, alkyne **1a** was reacted with [**Ru-II**] and [**Ru-IV**] under a variety of reaction conditions (Scheme 2). The first tests were carried out in THF with 4% mol of [**Ru-II**] at room temperature. The reaction was monitored by GC–MS by taking aliquots from the reaction mixture. After no improvement in yield was observed, the solvent was evaporated and the organic products were purified by passing the reaction mixture through a silica column using ethyl acetate as the eluent. The resulting product mixture was found to be an isomeric mixture of 1,2,4- and 1,3,5-substituted benzene derivatives confirmed by both GC–MS and NMR analyses.

Using the **[Ru-II]** catalyst, the reaction proceeded smoothly and within 15 h, a yield of 94% (**2a:3a**; 20:80) cyclotrimerisation products, **2a** and **3a**, was achieved. Using the [**Ru-IV**] catalyst only 43% yield was obtained, (**2a**:**3a**; 19:81) and the [**Ru-V**] catalyst yielded 30% (**2a:3a**; 35:65). To increase the yields using the [**Ru-IV**] and [**Ru-V**] catalysts, the respective reaction mixtures were heated. At 50 °C, a sharp increase in the activity of the reaction mixture containing [**Ru-IV**] was observed. Compound **1a** was completely transformed into **2a** and **3a** with a 4% catalytic loading of [**Ru-IV**] in THF. [**Ru-IV**] demonstrated the best catalytic performance at 50 °C, with a yield of 100% of the cyclotrimerisation product within 4 h. No improvement in the yield was obtained when the reaction was carried out at higher temperatures, such as 60, 70 and 80 °C.

Toluene, dichloromethane, acetone and THF were tested to determine the best reaction solvent and the results are listed on Table 1. Among these solvents, toluene gave relatively poor results, considering both the time and regioselectivity of the reaction. Homobimetallic complexes are also sparingly soluble in toluene. The use of polar solvents demonstrated slightly better performances. The results on Table 1 indicate that acetone and THF are comparable solvents when considering regioselectivity and yield values. However, in addition to higher regioselectivity, THF demonstrated slightly better catalytic activity compared to the other solvents. It was observed that the reaction times for the cyclotrimerisation of **1a** could be reduced from 72 to 15 h with a slight increase in yield and regioselectivity when using THF as the solvent.

After the best reaction conditions were determined, the catalytic activity of [**Ru-I**], [**Ru-II**], [**Ru-III**], [**Ru-IV**] and [**Ru-V**] were tested on the intermolecular [2+2+2] cyclotrimerisation reactions of the silicon containing substrate **1a**. The results are summarised on Table 2. First, the tests were carried out at room temperature with a catalytic loading of 4% mol catalyst in THF using **1a** as the substrate. Grubbs first generation catalyst [**Ru-III**], which is a well-known alkylidene complex, was used to catalyse this reaction. The reaction was completed within 15 h with a yield of 90% (**2a**:**3a**; 16:84). Homobimetallic ruthenium alkylidene complexes [**Ru-I**] and [**Ru-II**] gave a yield of 94% (**2a:3a**; 20:80) and 92% (**2a:3a**; 18:82), respectively. [**Ru-IV**] and [**Ru-V**] demonstrated poor catalytic activity at room temperature where yields of only 43% (**2a**:**3a**; 19:81) and 23% (**2a:3a**; 40:60), respectively, were achieved. No improvement in yield was observed after 20 h. The [**Ru-V**] catalyst was not used in any further studies because of its low catalytic activity and regioselectivity towards intermolecular cyclotrimerisation reactions of **1a**. The catalytic activity difference between [**Ru**]-**I**, **II**, **III** and [**Ru**]-**IV**, **V** can possibly be explained by the presence of the alkylidene group on [**Ru-I**], [**Ru-II**] and [**Ru-III**]. It has been reported in literature that ruthenium arene fragments are capable of forming mono or bis-alkylidene complexes in polar solvents at relatively high temperatures [29]. Considering this fact, it is possible that at room temperature the metathetic cascade route, compared to the metallacycle pathway, would be the predominant reaction pathway for the ruthenium alkylidene complexes.

**Table 1**
Solvent effect on cyclotrimerisation reactions of terminal alkynes.

| Solvent | Yield[a] (%) | Time (h) | Isomer ratio (**2a**:**3a**) |
|---|---|---|---|
| Toluene | 80 | 72 | 28:72 |
| Dichloromethane | 90 | 24 | 23:77 |
| Acetone | 93 | 18 | 20:80 |
| THF | 94 | 15 | 20:80 |

[a] 0.030 mmol [**Ru-I**] was added to a 1 ml THF solution of alkyne **1a** (0.724 mmol) at room temperature. The reaction mixture was periodically analysed by GC–MS.

The second tests were carried out at 50 °C. The activity of [**Ru-III**] stayed nearly the same, but regioselectivity of the reaction decreased from (**2a:3a**) 16:84 to 25:75. When catalysed by [**Ru-I**] and [**Ru-II**], the cyclotrimerisation reaction of **1a** proceeded with 95% (**2a:3a**; 21:79) and 98% (**2a**:**3a**; 21:79) yields of the trisubstituted arene isomers **2a:3a**, respectively. The reaction carried out with [**Ru-IV**] at 50 °C yielded 100% (**2a:3a**; 20:80) within 4 h. The homobimetallic alkylidene complexes [**Ru-I**] and [**Ru-II**] and monometallic alkylidene complexes [**Ru-III**] can catalyse the intermolecular cyclotrimerisation reactions at room temperature with high regioselectivity. However at 50 °C, a slight decrease in regioselectivity, but an increment in yield was observed.

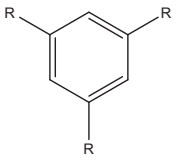
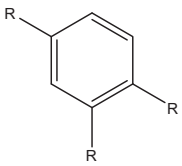
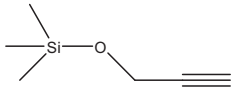
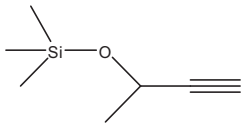
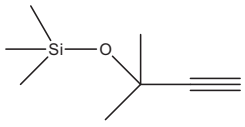
Next, a study was performed to determine the effect of the substrate on the cyclotrimerisation reactions. For this purpose a set of three silicon containing alkynes, **1a**, **1b** and **1c** were selected and their effect on the reaction yield and regioselectivity was investigated (Table 2). Alkyne **1b**, a more sterically hindered alkyne than **1a**, was reacted with 4% mol catalysts in THF at room temperature. The best conversion value of 53% (**2b:3b**; 76:24) was obtained using [**Ru-II**]. The [**Ru-IV**] catalysed reaction showed the best regioselectivity with a relatively lower yield of both **2b** and **3b**, (32% **2b**:**3b**; 80:20) at room temperature. At 50 °C, the [**Ru-II**] catalysed cyclotrimerisation reaction was completed within 22 h with a small increase in yield (65%; **2b:3b**; 76:24). Under these conditions, [**Ru-IV**] demonstrated the best results for both regioselectivity (**2b**:**3b**; 84:16) and yield (70%). Next, alkyne **1c** was reacted with various ruthenium catalysts under pre-determined reaction conditions. None of our Ru-complexes catalysed this reaction at room temperature. However at 50 °C, [**Ru-I**], [**Ru-II**] and [**Ru-IV**] yielded corresponding arenes **2c** and **3c** with 20% (**2c:3c**; 80:20), 30% (**2c:3c**; 90:10) and 24% (**2c**:**3c**; 83:17) yields, respectively.

Considering these results, the regioselectivity of the reaction shifts from a 1,2,4-(**3a–c**) to a 1,3,5-(**2a–c**) trisubstituted arene isomer formation based on the increasing steric hinderance of the substrate. The reaction of **1b** and **1c** demonstrated that the metathetic cascade route produces the less hindered corresponding arenes **2b** and **2c** as the major products. Additionally, traces of dimerisation and acyclic trimerisation products were observed by GC–MS during the cyclotrimerisation reactions of **1b** and **1c** with our catalytic system. Comparing these observed manifolds, we can conclude that the steric effect of the substrate has a direct effect on product distribution and yield.

### 3.2. Intermolecular [2+2+2] cross cyclotrimerisation reactions of two alkynes

To obtain chemo- and regioselective cross-cyclotrimerisation products, **1a** was reacted with various alkynes. To date, a few successful strategies have been employed to overcome the poor chemo- and regio-selectivity of intermolecular cyclotrimerisation reactions between two or three alkynes. Odashima and co-workers employed a binary metal system to obtain a chemoselective process for the intermolecular cross-cyclotrimerisation reactions between two or three alkynes with the slow addition of one of

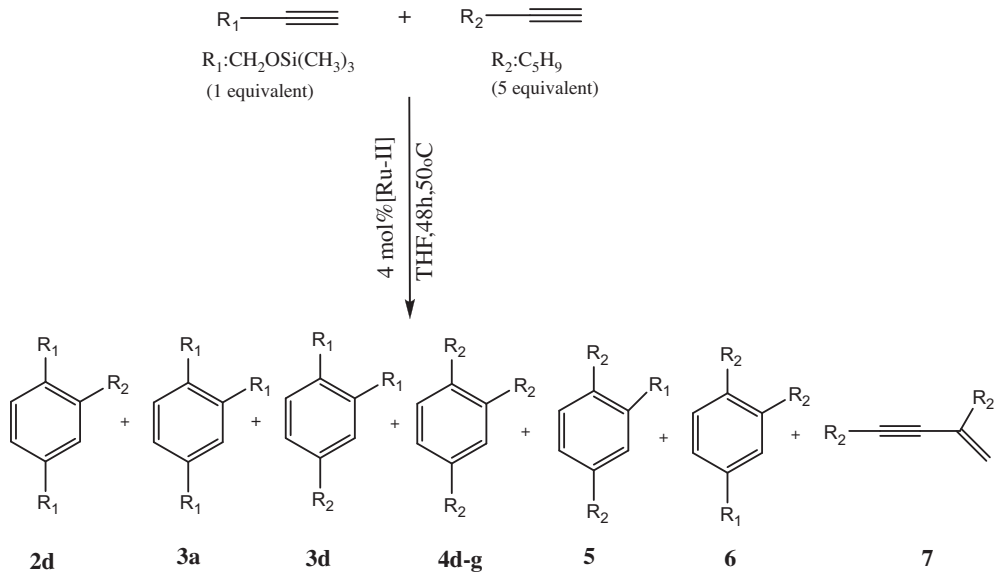
**Table 2**
Cyclotrimerisation reactions of alkynes **1a**, **1b** and **1c** with various ruthenium catalysts.

| Alkyne | Temperature (°C) | Catalyst | Time (h) | Yield[a](%) | Products | |
|---|---|---|---|---|---|---|
| | | | | |  **2a-c** |  **3a-c** |
|  **(1a)** | 25 | [**Ru-I**] | 15 | 94 | 20 | 80 |
| | | [**Ru-II**] | 15 | 92 | 18 | 82 |
| | | [**Ru-III**] | 15 | 90 | 16 | 84 |
| | | [**Ru-IV**] | 15 | 43 | 19 | 81 |
| | | [**Ru-V**] | 20 | 30 | 35 | 65 |
| | 50 | [**Ru-I**] | 12 | 90 | 25 | 75 |
| | | [**Ru-II**] | 10 | 95 | 21 | 79 |
| | | [**Ru-III**] | 8 | 98 | 21 | 79 |
| | | [**Ru-IV**] | 4 | 100 | 20 | 80 |
|  **(1b)** | 25 | [**Ru-I**] | 15 | 45 | 77 | 23 |
| | | [**Ru-II**] | 15 | 53 | 76 | 24 |
| | | [**Ru-III**] | 15 | 42 | 74 | 26 |
| | | [**Ru-IV**] | 15 | 32 | 80 | 20 |
| | 50 | [**Ru-I**] | 28 | 50 | 76 | 24 |
| | | [**Ru-II**] | 20 | 55 | 78 | 22 |
| | | [**Ru-III**] | 22 | 65 | 76 | 24 |
| | | [**Ru-IV**] | 24 | 70 | 84 | 16 |
|  **(1c)** | 25 | [**Ru-I**] | 48 | 0 | 0 | 0 |
| | | [**Ru-II**] | 48 | 0 | 0 | 0 |
| | | [**Ru-III**] | 48 | 0 | 0 | 0 |
| | | [**Ru-IV**] | 48 | 0 | 0 | 0 |
| | 50 | [**Ru-I**] | 72 | 6 | 59 | 41 |
| | | [**Ru-II**] | 72 | 20 | 80 | 20 |
| | | [**Ru-III**] | 72 | 30 | 90 | 10 |
| | | [**Ru-IV**] | 72 | 24 | 83 | 17 |

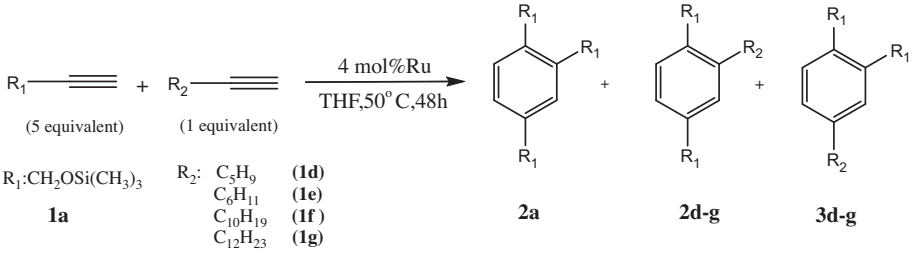
[a] 0.030 mmol [**Ru**] was added to a 1 ml THF solution of alkyne **1a–c** (0.724 mmol). The reaction mixture was periodically analysed by GC–MS.

the alkynes to the reaction medium. An intramolecular version of this process has been successfully employed using a diyne and excess of an alkyne.

To determine the best reaction conditions for the cross-cyclotrimerisation of monoynes, **1a** and **1d** (1-heptyne) were reacted with Ru catalysis under various reaction conditions to achieve a high chemo- and regioselective process. The effect of the **1a**/**1d–g** ratio on chemoselectivity of the reaction was initially investigated. One molar equivalent of alkyne **1a** was reacted with 1 M equivalent of **1d** in THF at room temperature using a 4% mol of [**Ru-II**]. After 72 h, GC–MS analysis revealed that only trace amounts of the cyclotrimerisation products were formed under these conditions.




**Scheme 3.** Representative cross-cyclotrimerisation reactions of excess **1d** (5 mol equivalent) and **1a** (1 mol equivalent).




**Scheme 4.** Representative cross-cyclotrimerisation reactions of excess **1a** (5 mol equivalent) and **1d**–**g** (1 mol equivalent).

The reaction was also carried out at 50 °C and resulted in no cross-cyclotrimerisation products; however, **2a**, 3a and **4d** were formed. When a mixture of a mol equivalent of **1a** and a 5 mol equivalent of **1d** were reacted under the same conditions, chemoselectivity of the reaction was completely lost, resulting in a mixture of trisubstituted arenes (Scheme 3). The products of the reaction between **1a** and **1d** in a 1:5 ratio demonstrated that the homodimerisation of **1d** and the homo cyclotrimerisation of **1a** and **1d** are the major competitive reactions. The preceding experiments revealed that an excess amount of alkyne **1d–g** present in the reaction media has a negative impact on the regio- and chemoselectivity of the cross-cyclotrimerisation reaction.

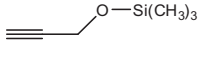
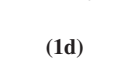
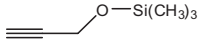
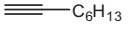
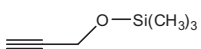
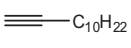
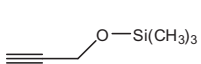
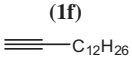
The slow addition of **1d** to the reaction media may offer a possible solution to the chemoselectivity problem. To demonstrate this, **1d** was added slowly to a solution containing a 5 mol equivalent of **1a** (**1a:1d**; 5:1) and [**Ru-II**] (4% mol). The mixture was then stirred at 50 °C for 48 h (Scheme 4). GC–MS analysis revealed a mixture of the regioisomeric cycloadducts **2d** and **3d**, which were formed by the chemoselective coupling of two molecules of **1a** and one molecule of **1d** (77% yield; **2d**:**3d**; 87:13).

After the best reaction conditions were determined, the catalytic activity of [**Ru-I**], [**Ru-II**], [**Ru-III**] and [**Ru-IV**] were tested on cross-intermolecular cyclotrimerisation reactions of **1a** and **1d–g** (Table 3). [**Ru-III**], a monometallic ruthenium alkylidene complex, demonstrated poor catalytic activity on the cross-cyclotrimerisation reactions that take places between **1a** and the aliphatic alkynes **1d–g**, which follow a metathetic cascade route. [**Ru-I**], which is a homobimetallic analog of [**Ru-III**] that combines a ruthenium-arene fragment bridged by chlorine atoms, revealed relatively high activity for regio- and chemoselective cross-cyclotrimerisation reactions of two different alkynes. The reaction of **1a** and **1d** was catalysed by [**Ru-III**] under the optimum reaction conditions resulting in a 28% yield of **2d** and **3d** (**2d:3d**; 88:12). A sharp increase to a 75% yield of in **2d** and **3d** (**2d:3d**; 86:14) was observed when [**Ru-I**], the homobimetallic analog of [**Ru-III**], was employed as a catalyst. Another slight increase in yield (77%, **2d**:**3d**; 87:13) was observed when [**Ru-II**] was employed as a catalyst. However, among these catalysts, [**Ru-IV**] demonstrated the best catalytic activity towards cross cyclotrimerisation reactions. The [**Ru-IV**] catalysed reactions provided a high yield of **2d** and **3d** (81%, **2d**:**3d**; 81:19).

### 3.3. Activity of ruthenium complexes

[**Ru-I**], which consists of two ruthenium fragments, can be synthesised by reacting [**Ru-III**] and [**Ru-IV**] in dichloromethane at room temperature for 2 h. In our study, we demonstrated that both [**Ru-III**] and [**Ru-IV**] can be used to catalyse the intermolecular cyclotrimerisation reactions of **1a** in quantitative yields. Although no mechanistic studies have been performed, it is possible that the mechanism for this intermolecular cyclotrimerisation reactions may be originating from both metathesis cascade route and metallacycle route considering the nature of the homobimetallic catalysts. Additionally, it has been reported in literature that the reactions catalysed with [**Ru-III**] follows a metathetic cascade route which is favourable at both 25 °C and higher temperatures [23,15]. Similar studies have reported that ruthenium arene complexes such as [**Ru-IV**] catalyse the cyclotrimerisation reactions of alkynes following a metallacycle route [18,21,22]. It has been reported in literature that ruthenium arene fragments can also form bis-alkylidene complexes which are active as expected [29]. Therefore, Ru-arene fragment of [**Ru-I**], [**Ru-II**] and [**Ru-IV**] may react

**Table 3**
Cross-cyclotrimerisation reactions of **1a** and **1d**–**g** with various ruthenium catalysts.

| $R^1$ | $R^2$ | $R^1/R^2$ | Yield[a,b] (%) | Catalyst | Product (%) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | **2d–g** | **3d–g** | **4** | **5** | **6** | **7**[c] | **8** |
|  |  | 10 | 75 | [**Ru-I**] | 86 | 14 | 0 | 0 | 0 | 30 | 0 |
| | | | 77 | [**Ru-II**] | 87 | 13 | 0 | 0 | 0 | 30 | 0 |
| | | | 28 | [**Ru-III**] | 88 | 12 | 0 | 0 | 0 | 32 | 0 |
| **(1d)** | | | 81 | [**Ru-IV**] | 81 | 19 | 0 | 0 | 0 | 33 | 0 |
|  |  | 10 | 61 | [**Ru-I**] | 90 | 10 | 0 | 0 | 0 | 32 | 0 |
| | | | 63 | [**Ru-II**] | 90 | 10 | 0 | 0 | 0 | 25 | 0 |
| | | | 22 | [**Ru-III**] | 92 | 8 | 0 | 0 | 0 | 33 | 0 |
| **(1e)** | | | 65 | [**Ru-IV**] | 88 | 12 | 0 | 0 | 0 | 25 | 0 |
|  |  | 10 | 25 | [**Ru-I**] | 89 | 11 | 0 | 0 | 0 | 34 | 0 |
| | | | 27 | [**Ru-II**] | 89 | 11 | 0 | 0 | 0 | 30 | 0 |
| | | | 11 | [**Ru-III**] | 90 | 10 | 0 | 0 | 0 | 32 | 0 |
| **(1f)** | | | 30 | [**Ru-IV**] | 88 | 12 | 0 | 0 | 0 | 30 | 0 |
|  |  | 10 | 25 | [**Ru-I**] | 88 | 12 | 0 | 0 | 0 | 39 | 0 |
| | | | 27 | [**Ru-II**] | 88 | 12 | 0 | 0 | 0 | 40 | 0 |
| | | | 8 | [**Ru-III**] | 90 | 10 | 0 | 0 | 0 | 36 | 0 |
| **(1g)** | | | 28 | [**Ru-IV**] | 89 | 11 | 0 | 0 | 0 | 40 | 0 |

[a] Yield was based on aliphatic alkynes (**1d**–**g**).
[b] 0.030 mmol [**Ru**] was added to a 1 ml THF solution of alkyne **1a**–**c** (0.724 mmol) and stirred for 48 h at 50 °C. The reaction mixture was periodically analysed by GC–MS.
[c] Yield was based on **1a**.

with a terminal alkyne in highly polar solvents at relatively high temperatures to form an active bis-alkylidene complex. Thus making two mechanisms, metathesis cascade and metallacycle route are difficult to distinguish from each other at 50 °C.

The comparable high activity of [**Ru-III**] with our homobimetallic ruthenium systems [**Ru-I**], [**Ru-II**] and [**Ru-IV**] towards the cyclotrimerisation reaction of **1a** indicated that this reaction proceeded through both a metathetic cascade, considering the relatively similar activity of [**Ru-III**], [**Ru-I**] and [**Ru-II**] and a metallacycle route [**Ru-IV**]. Combining these manifolds observations, we can conclude that it is possible for two ruthenium centres (ruthenium alkylidene and the ruthenium arene [**Ru-I**] and [**Ru-II**]) to be active towards cyclotrimerisation reactions.

## 4. Conclusion

In conclusion, we have shown that homobimetallic ruthenium alkylidene complexes [**Ru-I**] and [**Ru-II**] are efficient catalysts for the transformation of alkynes to substituted arenes by chemo- and regio-selective intermolecular-[2+2+2] cyclotrimerisation reactions. These ruthenium complexes promote the catalytic cyclotrimerisation of less sterically hindered alkynes in a selective manner with 1,2,4-trisubstituted arenes. Conversely, the processes favours the formation of 1,3,5-trisubstituted arenes with sterically hindered alkynes. The catalytic systems were also capable of forming substituted arenes through the cross-intermolecular cyclotrimerisation of two monoynes. Considering the nature of the homobimetallic alkylidene complexes, it is possible that these transformations can follow both cascade metathetic and metallacycle routes depending upon the reaction conditions.

## Acknowledgments

We thank the Scientific and Technological Research Council of Turkey (TUBITAK, 107T084) and Hacettepe University (080160 1008) for research support.

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