# Ruthenium-catalysed conversion of triynes to benzene derivatives—a novel metathesis cascade

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**In a novel application of [$PhCH_2$=$Ru(PCy_3)_2Cl_2$] 1, triynes are isomerised to benzene derivatives; a cascade of four metathesis reactions is proposed as a mechanistic explanation.**

Cyclotrimerisation of acetylenes is catalysed by a variety of transition metal catalysts[1] and provides easy access to highly substituted benzene derivatives.[2] Cobalt[3] and rhodium[4] catalysts have been used to make this reaction the key step in a number of elegant natural product syntheses. Metallacyclooligoolefins are believed to be pivotal intermediates in the acetylene trimerisation catalytic cycle.[5] An exception is the palladium-catalysed reaction *via* vinylpalladium intermediates.[6]

Another approach to transform acetylenes into benzene derivatives is the metathesis of mono-[7] or bis-acetylenic[8] compounds with stoichiometric amounts of transition metal carbonyl carbene complexes with subsequent CO insertion. These methodologies have also found ample application in efficient constructions of structurally complex synthetic targets.[9]

Mechanistically interesting is the conversion of an alkylidyne complex to a benzylidene complex with 3 equiv. of an acetylene by a metathesis cascade.[10]

However, a catalytic metathesis process for the isomerisation of triynes to benzene derivatives has not yet been described.

In several instances, it has been shown that ruthenium carbene complexes derived from Grubbs' metathesis catalyst **1**[11] insert intramolecular C≡C triple bonds regioselectively, with metallacyclobutenes as likely intermediates.[12] Recent work shows that intermolecular additions of such carbene complexes to C≡C triple bonds also proceed regioselectively.[13]

Ring-closing olefin metathesis employing **1** is a well established reaction.[14] In general, ruthenium-catalysed ring-closing olefin metatheses are initiated by the *in situ* transformation of the stable benzylidene complex **1** into a reactive methylidene complex as the active catalytic species.[15] However, far less reactive[15] ruthenium benzylidene complexes similar to **1** were also involved as catalytic species in ring-closing olefin metatheses.[16]

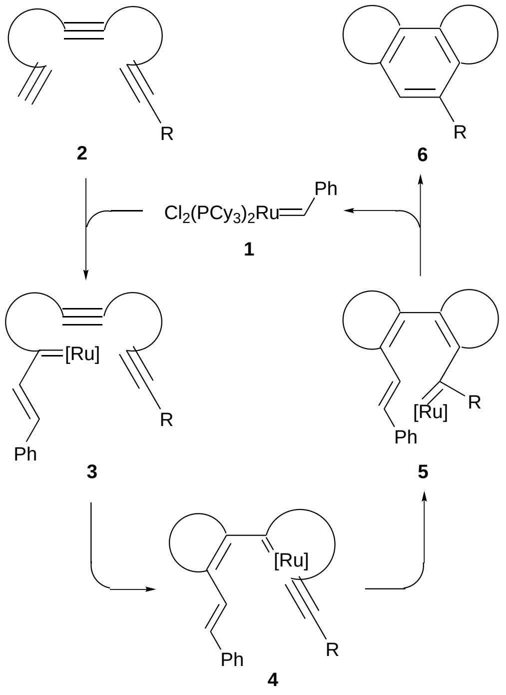
Metathesis catalytic cycles usually commence with a regioselective addition of the catalytic species to the substrate's least hindered site as is suggested by the outcome of conversions of substrates with differently substituted C≡C and C=C bonds.[17]

Based on these findings, we projected a metathesis cascade process for the isomerisation of acyclic triynes to benzene derivatives by **1** (Scheme 1).

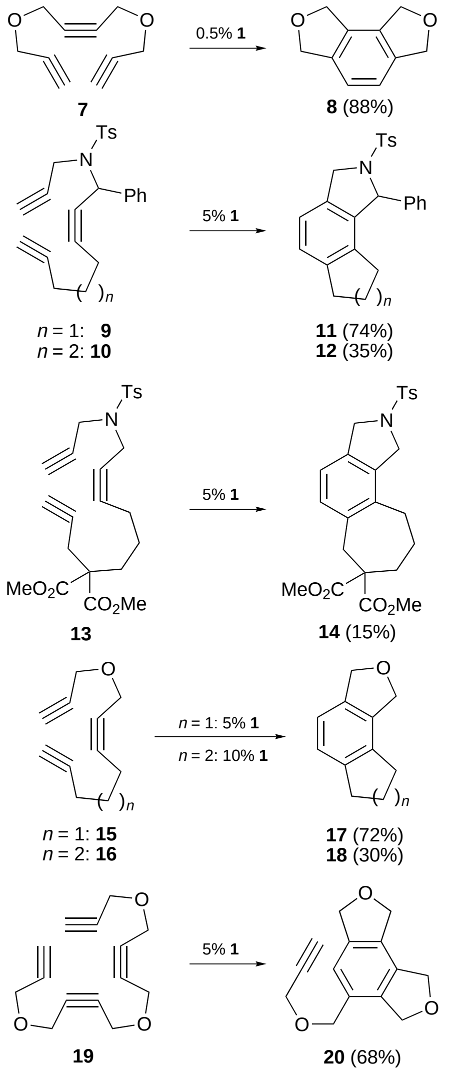
In an initial intermolecular reaction, ruthenium benzylidene complex **1** adds to the least hindered triple bond of triyne **2**. The resulting vinyl carbene complex **3** undergoes an intramolecular metathesis reaction *via* **4** to produce a conjugated carbene complex **5**, with two of the newly formed double bonds embedded in ring structures and thus forced to be *Z*. This is a prerequisite for the final ring-closing olefin metathesis step which releases benzylidene complex **1**, thus making the entire process catalytic. The formation of an aromatic system **6** should provide a strong driving force for the overall reaction cascade.

To test our concept, we treated the easily accessible triyne **7**[18] as a 2 M solution in $CH_2Cl_2$ with 5 mol% of **1** (Scheme 2). The desired tetrasubstituted benzene derivative **8** was obtained in excellent yield after only seconds of vigorous reaction. Optimisation revealed that as little as 0.5 mol% of **1** is sufficient to convert all starting material of **7** as a 1 M solution in $CH_2Cl_2$ in an exothermic reaction within 2 h.† The small amount of catalyst necessary for this supposedly four-fold metathesis cascade is remarkable since most applications of catalyst **1** require several mol%;[14] *e.g.* 20 mol% of **1** has been used in macrocycle syntheses.[19]

To explore the scope of this novel acetylene oligomerisation to see which ring sizes might be accessible, acyclic triynes **9**, **10** and **13** were treated with **1** (Scheme 2). Compared to the formation of **8** from **7**, larger amounts of **1** and longer reaction times were required in all cases for complete conversion. Whereas indane derivative **11** was obtained in good yield from its acyclic precursor **9** after 12 h, the structurally similar **10** gave an only moderate yield of the tetralin **12**. Compound **13** was isomerised in poor yield to benzene derivative **14** with an annulated seven-membered ring. In the latter cases, the desired conversions proceeded slowly (2 d) and the competing formation of obviously polymeric byproducts explains the diminished yields. A similar trend was observed in the formation of indane derivative **17** and tetralin derivative **18** from their respective precursors **15** and **16**. Again, the indane



**Scheme 1** Cy = cyclohexyl



**Scheme 2** Ts = *p*-$MeC_6H_4SO_2$

derivative was obtained in good yield after 12 h, whereas the tetralin derivative was formed in a moderate yield along with polymeric byproducts in a sluggish reaction (2 d). We assume that benzene derivatives with two annulated five-membered rings are generally formed in good yields from acetylenic precursors by reaction with **1**. This was confirmed by further investigations with triynes similar to **7** (yields of 67% or higher).

The tetraacetylenic **19** could potentially be converted to either a cyclooctatetraene or a pentasubstituted benzene **20**. However, when **19** was treated with **1**, **20** was found to be the exclusive product. The long reaction time of 2 d for this conversion can be rationalised by the known susceptibility of the reactivity of ruthenium carbene complexes to steric hindrance;[15] in contrast to all other examples shown in Scheme 2, the final ring-closing olefin metathesis step of the catalytic cycle (Scheme 1) starts from a disubstituted carbene complex **5** (R ≠ H). Only a few examples of ring-closing olefin metatheses involving such ruthenium intermediates are known.[17] A sterically demanding and thus less reactive carbene complex **5** should make this final step slow and rate determining. Despite the slow reaction, **20** was isolated in good yield.

In conclusion, this novel application of **1** expands the scope of the versatile synthetic tool of acetylene cyclooligomerisation by employment of a catalyst which is commercially available and tolerates a wide range of functionalities.

## Footnotes and References

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† Synthesis of **8**: **7**[18] (80 mg; 0.49 mmol) was dissolved in $CH_2Cl_2$ (0.25 ml). After addition of **1** (0.25 ml of a solution of 8 mg of **1** in 1 ml of $CH_2Cl_2$; 2.5 μmol; 0.5 mol%), the colour of the mixture turned from red to brown within seconds. The reaction was complete after 2 h at ambient temperature (GC and TLC). Evaporation of the solvent and column chromatography of the residue (hexane–*tert*-butyl methyl ether, 9 : 1) gave **8** (70 mg; 88%). Spectroscopic data were consistent with the literature.[18]

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*Received in Liverpool, UK, 4th August 1997; 7/05718K*