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Terminal Alkyne Metathesis: A Further Step Towards Selectivity

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Dedicated to Yves Chauvin, Richard R. Schrock and Robert H. Grubbs, our 2005 Nobel's.

Abstract: Terminal alkyne metathesis has been improved by addition of quinuclidine as an external ligand to the $(t\text{-BuO})_3W{\equiv}CBu\text{-}t$ carbyne complex, giving a yield of 80% during hept-1-yne metathesis. Extension of this system to the co-metathesis of terminal and disubstituted alkynes affords the expected cross-reaction products.

Keywords: alkynes; carbynes; catalysis; metathesis; tungsten

Homogeneous internal alkyne metathesis was first reported to be catalysed by molybdenum/phenols-based catalyst systems, either starting from molybdenum hexacarbonyl as the metal source and thermal or photochemical activation,[1] or from higher oxidation state complexes such as $MoO_2(acac)_2$/aluminium alkyl-based precursors,[2] the latter giving rise to much more active catalysts, allowing the reaction to be applied to functionalized alkynes and to occur at room temperature, Eq. (1).[3]

$$2\ R^1C{\equiv}CR^2 \rightleftharpoons R^1C{\equiv}CR^1 + R^2C{\equiv}CR^2 \quad (1)$$

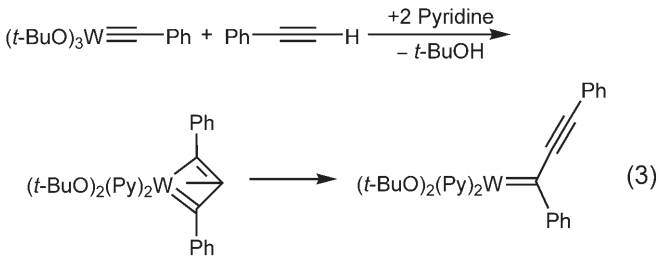
On the other hand well-defined tungsten[4] and molybdenum[5] catalysts were synthesised and also proved to be very efficient catalysts for this reaction.

All those catalysts, as well as others based on molybdenum tris-arylamidocarbynes[6] are presently used in metathesis reactions, ring-closing alkyne metathesis[7] (RCAM) and metathesis polymerisation,[8] using disubstituted alkynes as substrates.

In contrast, there are only few publications dealing with the metathesis reaction of terminal alkynes using metallacarbynes as catalysts, Eq. (2).

$$2\ R^1C{\equiv}CH \longrightarrow R^1C{\equiv}CR^1 + HC{\equiv}CH \quad (2)$$

The first attempts described by Schrock using phenylacetylene as substrate and the well-defined $(t\text{-BuO})_3W{\equiv}CPh$ complex only led to polymer formation, *via* a process where the initial metallacyclobutadiene intermediates are shown to readily deprotonate, giving rise to the production of deprotiometallacycles, which are very efficient terminal alkynes polymerisation species, Eq. (3).[9]



(3)

Another possible reason for the failure of this approach is the observation that in the case of the use of *tert*-butylacetylene as substrate and the *tert*-butylmetallacarbyne $(t\text{-BuO})_3W{\equiv}CBu\text{-}t$, acetylene formed during the first turnover reacts readily with the metallacarbyne to produce the dimeric compound $[W_2(OBu\text{-}t)_6](\mu C_2H_2)$:[10] both processes leading to these two metathesis-inactive complexes may occur , as exemplified in Eq. (4).

$$3(t\text{-BuO})_3W{\equiv}CtBu + 3\ t\text{-BuC}{\equiv}CH \rightleftharpoons \quad (4)$$

$$\mu\text{-}C_2H_2[W(OBu\text{-}t)_3]_2 + t\text{-BuC}{\equiv}CBu\text{-}t + (t\text{-BuO})_2WC_3(Bu\text{-}t)_2 + t\text{-BuOH}$$

On the other hand, we have shown that under specific conditions, and using *alkyl*-substituted terminal alkynes such as hept-1-yne[11] this reaction could be catalytic leading to the expected metathesis products acetylene and dodec-6-yne, Eq. (2). However, after several turnovers, the initial very fast metathesis reac-

tion was irreversibly followed by polymerisation and the metathesis turnover number remained quite low. One interesting feature was the fact that the best results were obtained using diethyl ether as the solvent, suggesting that the coordinating properties of an external ligand may give rise to a stabilisation of the catalytic species vs. their tendency for irreversible deprotonation.

Another point which was at the origin of our renewed interest in this reaction comes from other data reported in the mid 1980s related to the fact that upon addition of pyridine to the dimeric complex $[W_2(OBu\text{-}t)_6](\mu\text{-}C_2H_2)$, $[W_2(OBu\text{-}t)_6](\mu\text{-}C_2H_2)(py)$ was formed and shown to be in equilibrium with the monomeric tunsgstacarbyne methylidyne species (t-BuO)$_3$W≡CH;[10] furthermore, the use of quinuclidine as ligand has proved to be very useful to stabilise trisalkoxycarbyne complexes *via* formation of stable, isolable (t-BuO)$_3$W≡CR(Quin) 1:1 adducts, including the methylidyne (t-BuO)$_3$W≡CH(Quin), Eq. (5).[12]

$$\mu\text{–}C_2H_2[W(OBu\text{-}t)_3]_2 + 2\ \text{Quin} \rightleftharpoons 2\ (t\text{-BuO})_3W{\equiv}CH(\text{Quin}) \quad (5)$$

We anticipated, therefore, that the use of coordinating ligands, and particularly these two amines, would provide a useful way for controlling the reaction course, due to some stabilisation of the methylidyne intermediates.

In Table 1 are reported selected results related to the metathesis reaction of hept-1-yne using 4 mol% carbyne catalyst (t-BuO)$_3$W≡CBu-t and equimolar amounts of potentially coordinating ligands as modifiers at different temperatures.

As reported in previous papers in this field,[11] one main feature during this reaction is the fact that the metathesis reaction rapidly stops and that the transformation rapidly moves towards polymerisation. This observation was confirmed in almost all runs conducted with the phosphorus- and nitrogen-based ligands (runs 1–5, Table 1), leading to poor yields and selectivities of metathesis at room temperature.

In contrast, the use of quinuclidine (runs 6 and 7), although reducing the reaction rate, gave increased amounts of metathesis products: 73% metathesis selectivity was even maintained after 1 hour. The same observation was confirmed using diethyl ether as solvent (run 8), but the metathesis only occurs during 15 min to reach a 41% maximum conversion, and no further transformation of the alkyne was observed (run 8).

Knowing that a temperature increase benefits metathesis *vs.* polymerisation,[11] further experiments were conducted at 80 °C (runs 10–12). Although pyridine itself gave rise to a slight increase, the use of quinuclidine as modifier gave the best yield ever reported for this reaction, as expected: an 80% yield at 91% conversion (87% selectivity) was attained under these conditions.

Due to the relative stability of the (t-BuO)$_3$W≡CBu-t/quinuclidine catalyst, we next undertook to follow the reaction using ^{1}H NMR spectroscopy. The *in situ* ^{1}H NMR spectrum of the catalytic reaction re-

Table 1. Metathesis of 1-heptyne by the Schrock carbyne with different ligands.[a]

Entry	Ligand	Reaction time [min]	T [°C]	Solvent	Conversion[b] [%]	Metathesis[c] Yield [%]	Metathesis selectivity [%]
1	-	60	RT	Toluene	93	23	25
2	Triphenylphosphine	60	RT	Toluene	99	12	12
3	Tris-*o*-tolylphosphine	60	RT	Toluene	97	16	16.5
4	Pyridine	60	RT	Toluene	77	24	31
5	Triethylamine	60	RT	Toluene	56	22	39
6	Quinuclidine	60	RT	Toluene	51	37	73
7	Quinuclidine	1	RT	Toluene	28	22	78
8	Quinuclidine	15	RT	Diethyl ether	41	30	73
9	–	1 (60)	RT	Diethyl ether	91 (>99)	25,7 (23)	28 (23)
10	–	1 (60)	80	Toluene	78 (>99)	33 (26)	42 (26)
11	Pyridine	1 (60)	80	Toluene	53 (>99)	44 (37)	83 (37)
12	Quinuclidine	1 (60)	80	Toluene	91 (>99)	80 (70)	88 (70)

[a] Reactions were carried out using hept-1-yne (190 μL, 1,45 micromoles), *n*-decane (100 μL), solvent (5 mL), 4 mol% catalyst and equimolar amounts of extra ligand.
[b] Conversions were determined by GC using *n*-decane as internal standard.
[c] Determined by GC, using the amount of dodec-6-yne as reference – no other internal alkyne was detected in the liquid phase.

corded after 5 min at room temperature, using a 10/1 hept-1-yne/catalyst ratio (Figure 1), revealed several species in solution.

The most characteristic signal is a singlet at $\delta = 5.15$ where WH satellites are observed ($J_{HW} = 90$ Hz) corresponding to the (t-BuO)$_3$W≡CH(Quin) methylidyne complex, already described by Schrock.[12]

Several signals are detected in the $\delta = 3.8$–4.2 range, among which three may be assigned to a triplet corresponding to the methylene group of the alkylidyne propagating species (t-BuO)$_3$W≡CCH_2CH$_2$Pr-(Quin) ($J_{HH} = 8$ Hz): the ^{1}H NMR analysis of a metathesis reaction conducted with non-4-yne under these conditions using the same catalyst gave the multiplet pattern (**b)** corresponding to the α methylene protons in the mixture of the [W]≡CCH_2CH$_2$CH$_3$ and [W]≡CCH_2Pr propagating species.

Finally, the singlet at $\delta = 10.71$ with an unusual J_{WH} coupling of 30 Hz (the J_{WH} values of the β hydrogen in metallacyclobutadienes are usually in the range 11.6–15.3 Hz,[9]) can be ascribed to the two α protons in a monosubstituted metallacyclobutadiene, which could only give rise to degenerate metathesis and may well be considered as dormant species which, upon hept-1-yne removal, could restore the methylidyne active species in the catalytic cycle. This assumption is in agreement with the fact that this species is the most stable over time: this downfield signal only decreases when the two signals corresponding to the propagating metallacarbynes have disappeared. Accordingly, new carbene signals arising from the deprotonation process [Eq. (3)] appear progressively in the $\delta = 8.4$–13 range, together with those corresponding to the production of polymer, only after the disappearance of these former three species.

The identification of stable methylidyne species during catalysis could explain the increasing amounts of metathesis products, but the presence of the singlet at $\delta = 10.71$ may also lead to the conclusion that quinuclidine also stabilises metallacyclobutadiene intermediates *via* complexation. This avoids or inhibits at least in part the deprotonation process, and probably also contributes to some extent to the metathesis productivity enhancement.

Although this catalytic system gives unprecedented results concerning linear terminal alkyne metathesis (hept-1-yne being a model for these linear alkynes), attempts to extend this procedure to other typical substrates such as phenylacetylene and *tert*-butylacetylene failed, with a complete polymerisation in the case of phenylacetylene and no reaction in the case of *tert*-butylacetylene. This last result is in agreement with previous studies using this sterically hindered substrate on Schrock's catalyst.[11]

These two last results clearly limit the use of the (t-BuO)$_3$W≡CBu-t(quinuclidine) catalyst to the metathesis of linear alkynes. Nevertheless, due to its propensity to metathesise both terminal and disubstituted alkynes, we next attempted a cross-metathesis reaction using equimolar amounts of hept-1-yne and dec-5-yne, with the quinuclidine modified catalyst (3.5

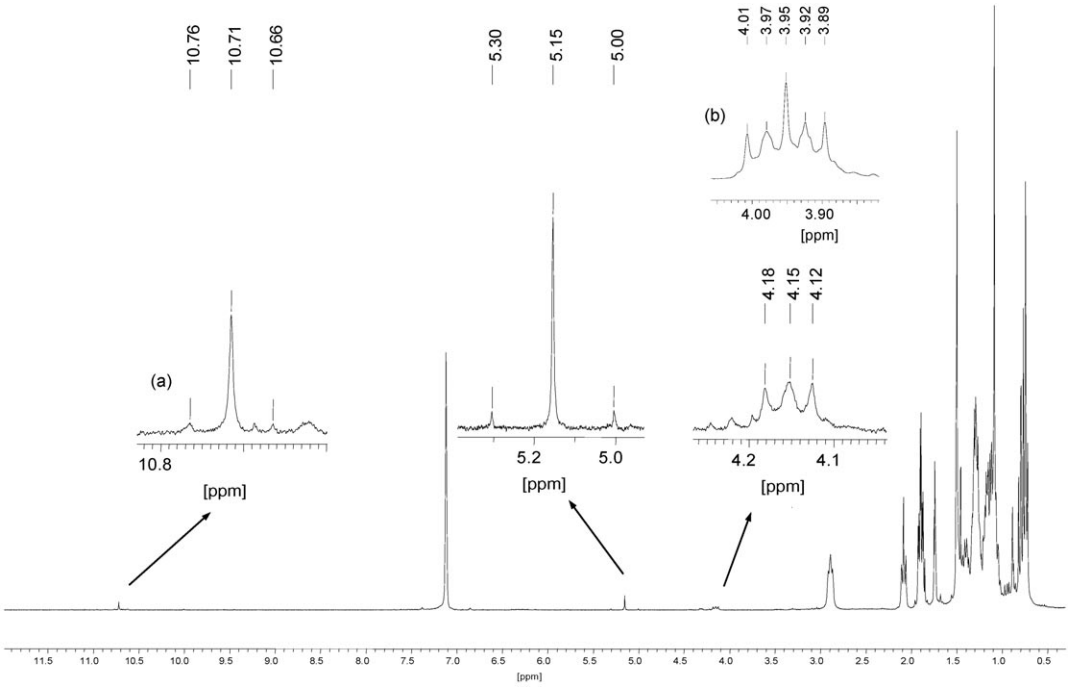
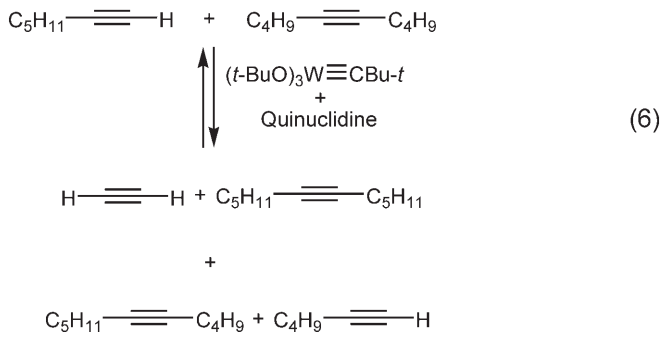


Figure 1. NMR spectrum (**a**) of hept-1-yne metathesis over the (t-BuO)$_3$W≡CBu-t/quinuclidine system, and part of the spectrum (**b**) obtained using non-4-yne on the same catalyst.

mol%) in toluene for 1 hour at room temperature ([Eq. (6)].



(6)

GC analyses using *n*-decane as internal standard showed that all the expected products coming from homo- and *cross*-metathesis were obtained (mol%): *hex-1-yne* (10.6), hept-1-yne (6.8), dec-5-yne (22.9), *undec-5-yne* (25.5), dodec-6-yne (7.3).

This successful cross-metathesis reaction led us to attempt ring-closing metathesis of $HC{\equiv}C(CH_2)_3O(CH_2)_2C{\equiv}CC_3H_7$, where both internal and terminal alkynes are present in the substrate. The ether function in the substrate, as might be expected from results obtained using diethyl ether as solvent, does not inhibit the reaction: a 25% yield into the ring-closure product was obtained.[13] This preliminary result also illustrates the possibility of applications in ring-closing metathesis of terminal alkynes.

The activity/selectivity observed in these reactions using this simple Schrock carbyne/quinuclidine-modified catalyst are of interest from a synthetic point of view: the metathesis yield could be enhanced to 80% using a simply modified catalyst in 4 mol% catalytic amounts. Accordingly, this catalyst may be used for either cross-metathesis reactions or ring-closing metathesis involving either mixed terminal/disubstituted α,ω-diynes or terminal α,ω diynes. It has to be emphasised, however, that presently the reaction is limited to the use of linear alkynes, although some functional groups such as an ether function can be tolerated. Further studies are underway using this concept, *via* the synthesis of other modified tunsgtenacarbyne complexes which may be applicable to other alkynes, as these results could then pave the way for a new synthetic tool in organic chemistry.

Experimental Section

All experiments were carried out under argon in a glovebox or using Schlenk techniques. Solvents were purchased from SDS or Scharlau Company. Toluene and decane (Aldrich) were dried over sodium and distilled under nitrogen. Triethylamine and pyridine were dried over KOH and distilled under argon . Alkynes (Aldrich or GFS Chemicals) were dried over CaH_2 and distilled under argon. Quinuclidine (Aldrich) was purified by sublimation prior to use. Benzene-d_6 (Eurisotop) was dried over sodium and distilled under argon. All solvents were degassed by three freeze-pump-thaws prior to use. $(t\text{-BuO})_3W{\equiv}CBu\text{-}t$ was synthesised as described in the literature.[4a]

GC analyses were performed on a CHROMPACK CP-9002 equipped with a CPSil-8CB column. ^1H NMR spectra were measured on a Bruker Avance 300.13 MHz spectrometer; the residual ^1H signal of benzene-d_6 was used as reference. The amount of dodec-6-yne was calculated on the basis of a calibration curve made with pure dodec-6-yne and *n*-decane. Metathesis yields were calculated on the basis of dodec-6-yne formed:

$$\%\ \text{metathesis} = (2n_{\text{dodec-6-yne}}/ni_{\text{hept-1-yne}}) \times 100,$$

where $n_{\text{dodec-6-yne}}$ refers to the amount of dodec-6-yne produced (in mol) and $ni_{\text{hept-1-yne}}$ refers to the initial amount of hept-1-yne used for the reaction (in mol).

General Procedure for Alkyne Metathesis

A round-bottom flask was charged with hept-1-yne (0.19 mL, 1.48 mmol), toluene (5 mL), *n*-decane (0.1 mL) and a magnetic stirring bar. The solution was stirred at 80 °C. A Schlenk flask was charged with $(t\text{-BuO})_3W{\equiv}CBu\text{-}t$ (0.024 g, 0.05 mmol), quinuclidine (0.005 g, 0.05 mmol), toluene (1 mL) and a magnetic stir bar. The solution was stirred at room temperature for 15 min and then added to the previous solution with a syringe. Aliquots were withdrawn during the reaction, quenched with methanol to precipitate the undesired polymer, and then analysed by GC.

The same procedure was used for alkyne cross-metathesis, except that an equimolar amount of dec-5-yne (0.27 mL, 1.48 mmol) was added together with hept-1-yne.

General Procedure for Ring-Closing Alkyne Metathesis

In a Schlenk tube were added under argon 1-(pent-4-ynyloxy)-oct-3-yne (0.05 g, 0.26 mmol), toluene (12 mL), and decane (0,1 mL) as internal standard. The solution was stirred at 80 °C and 1 mL of the catalytic solution consisting of $(t\text{-BuO})_3W{\equiv}CBu\text{-}t$ (0.012 g, 0.025 mmol) and quinuclidine (0.003 g, 0,025 mmol) in toluene was added to the reaction mixture. Stirring was continued for 1 hour at the same temperature. The reaction was then quenched with methanol and the products analysed by GC. A conversion of 80% of the starting material was observed with the formation of 25% of the cyclic metathesis product was confirmed by GC-MS.

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