

Alkyne metathesis: toward simplicity and efficiency

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Abstract—No catalyst pre-activation, no suicide alkyne, and no additive is required in an extremely simple procedure for the metathesis of alkyl-, alkenyl-, and aryl-propynes: just mix $\text{Mo}(\text{CO})_6$, *p*-chlorophenol, and the alkyne in 1,2-dichloroethane, heat at 85 °C for 9–24 h, and the symmetrical alkyne is produced in ca. 95% yield.

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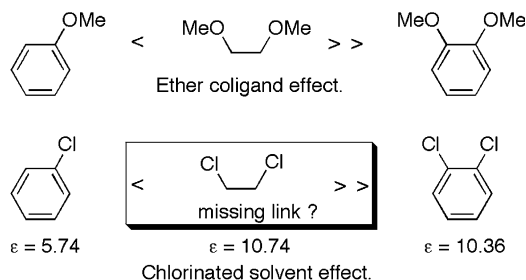
1. Introduction

Alkyne metathesis is an equilibrium process devoid of stereochemical ambiguity. It is attractive for the design of acetylenic molecules of either kinds: symmetrical, or disymmetrical (by recourse to the ring-closing trick via transient coupling of the reactants). Today, highly efficient well-defined catalytic precursors can manage functional substrates at low temperature.¹ They however require fine chemical design under strictly anhydrous and anaerobic conditions, and thus the know-how of trained specialists. By contrast, the original *in situ* Mortreux' system can be quickly generated at low cost and without difficulty,² but can efficiently manage only robust hydrocarbon substrates at high temperature.³

Facing this limitation, but aware of the advantage of the system, we proposed a threefold modification of the original procedure allowing for metathesis of phenylpropyne at *low* temperature (50 °C):⁴ (i) precatalyst generation at high temperature; (ii) addition of 4 Å molecular sieves (MS); (iii) addition of an ether co-ligand. The beneficial co-ligand effect of dimethoxyethane (DME) or diphenoxyethane (DPE) had indeed been previously noticed with other catalytic precursors,⁵ and was recently confirmed for a related system using *o*-fluorophenol instead of *p*-chlorophenol ligands.^{6,7} Nonetheless,

the modified system remains of academic interest: the turnover frequency is indeed low, and the simplicity of the original Mortreux' system has been lost. During preliminary trials for further optimization, the accelerating efficiency of several ether co-ligands was compared: 1,2-dimethoxybenzene (veratrole) had no effect, while anisole was less effective than ethylene diethers (DME, DPE).^{4,8} We also observed that replacing chlorobenzene for *o*-dichlorobenzene (a commonly used solvent at high temperature)^{3,9} killed the catalytic activity at 50 °C.⁸ Noticing the structural analogy between the 'solvent effect' and 'ether effect' (Scheme 1), we may try to extrapolate this trend: the solvent missing link is hereafter addressed for an exploratory, but representative set of simple hydrocarbon substrates.

Phenylpropyne **1a** was treated under the modified conditions mentioned above (pre-activation step, DPE, MS)



Scheme 1. Structural correlation of the ether additive and solvent effects on the metathesis efficiency.⁸ Phenylpropyne substrate at 50 °C, after pre-activation at 135 °C, in the presence of 4 Å MS. Top: in chlorobenzene; bottom: with diphenoxyethane as the co-ligand.

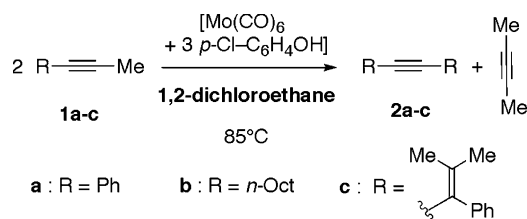
Keywords: Alkyne metathesis; *In situ* catalyst; Molybdenum; Solvent effect; DFT models.

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in 1,2-dichloroethane (DCE). Since the pre-activation step cannot be run at a temperature higher than the solvent boiling point, the whole sequence was uniformly run at 85 °C. We found that the kinetics of the metathesis reaction is strongly accelerated, and that DCE is indeed the missing link (Scheme 1). Encouraged by this result, we decided to check whether either of the three (complicating) modifications were still required in DCE instead of chlorobenzene as solvent.

- (i) *Precatalyst generation step*: We were here inspired by Bunz et al., who proposed a methodological improvement for difficult substrates by adding an auxiliary alkyne to efficiently generate the alkyldi-yne-Mo active species.¹⁰ In the simplest version, the phenylpropyne substrate itself was added as the ‘suicide’ alkyne, and we observed that the reaction starts to proceed rapidly. A separated pre-activation step is thus no longer required.
- (ii) *Co-ligand addition*: In the absence of any ether additive, the catalysis proceeded with the same efficiency, and even slightly faster. Speculations about a possible role of DCE as a weak co-ligand of molybdenum are inviting (see below), but the main point here is the simplification of the catalytic mixture.
- (iii) *Molecular sieves addition*: In the absence of molecular sieves, the use of distilled DCE resulted in the same activity. The simplification of the procedure is now extreme: no reaction takes place in the strict absence of Mo(CO)₆ or *p*-chlorophenol (Scheme 2).

A blank experiment using freshly distilled chlorobenzene at 85 °C, in one step and in the absence of any additive,



Scheme 2. Simple Mo-catalyzed alkyne metathesis procedure.

confirmed the specific accelerating effect of DCE: after 9 h, the metathesis yield reaches 95% in DCE, while it remains below 5% in chlorobenzene (Fig. 1).

Nevertheless, the reaction then accelerates in chlorobenzene, and smoothly reaches 60% after 24 h while the concentration of the tolane product has remained stationary in DCE. These results were established for a *p*-chlorophenol/[Mo] ratio of 3.1:1. No reaction occurs in the absence of *p*-chlorophenol, but lowering this ratio to 2:1 or 1:1, did not markedly affect the initial catalytic activity. After 7 h, the tolane yield (85%) is almost equal to the conversion (90%), but then the diphenylacetylene product (tolan) starts to degrade. Thus, in the absence of sufficient amount of *p*-chlorophenol ligand, as the catalytic species is less and less involved in the metathesis process, the Lewis acidity of the unsaturated molybdenum centers starts to promote some oligo/polymerization processes.

Since 3 or 1 catalytic equivalents of *p*-chlorophenol trigger metathesis at the same rate, an efficient Mo active species might involve a single *p*-chlorophenolate ligand (instead of three, as it has long been assumed).^{2–4} Assuming that this species is a Mo(VI)-carbyne complex,⁵ the missing X ligands could reasonably be chloride ligands, which are potentially abundant in our system and in most related systems based on the Mortreux’ catalyst.^{2–4} The above results suggest that DCE could be an optimal chlorine donor.¹¹ Before speculating about the nature of the putative chlorinated species (see below), the scope of the optimization was tested in more details concerning the working temperature, the catalytic ratio, and the substrate compatibility.

Beyond aryl-propyne **1a**, an alkyl-propyne **1b** (undeca-2-yne) has been submitted to the novel metathesis conditions using 3 catalytic equivalents of *p*-chlorophenol (Table 1). After overnight reaction, the GC yield of the known octadeca-9-yne **2b** is almost quantitative (96%).¹² Finally, a third kind of hydrocarbon propyne derivative, that is an alkenyl-propyne, has been tested from enyne **1c**. The use of 3 catalytic equivalents of *p*-chlorophenol allows to stabilize the known diyne product **2c**,¹³ which is produced in 96% GC yield after 24 h. Let us notice that metathesis of a similar enyne substrate under Mortreux–Bunz’ conditions in *o*-dichlo-

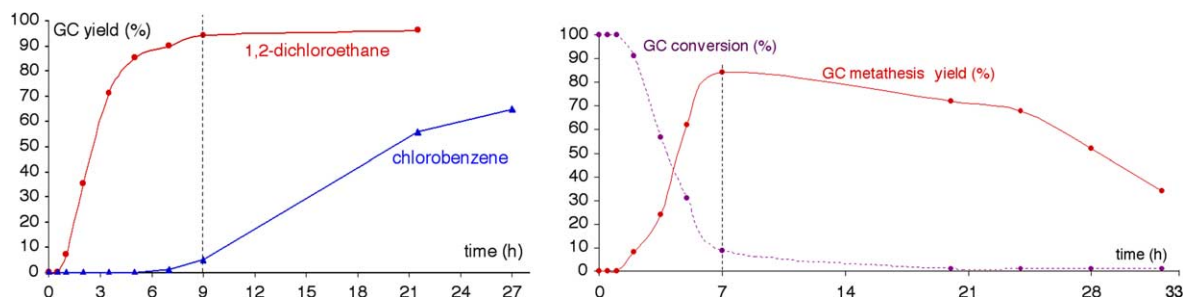


Figure 1. Kinetics of phenylpropyne metathesis. Left: Compared kinetic solvent effect of DCE and chlorobenzene, for a ratio *p*-chlorophenol/[Mo] = 3:1. Right: Conversion and metathesis yield curves in DCE for a ratio *p*-chlorophenol/[Mo] = 1:1. In the three experiments, the simplified procedure is used (direct mixing of reaction components at 85 °C, catalytic ratio **1a**/[Mo] = 1:0.1).

Table 1. Alkyne metathesis of substrates **1a–c** in 1,2-dichloroethane at 85 °C

Entry	Substrate	Time (h)	Conversion (%)	GC yield (%) ^a	Isolated yield (%) ^b
1	1a	9	95	94	96 ^c
2	1b	15	96	96	91
3	1c	24	97	96	93

Conditions: **1**/Mo(CO)₆/*p*-chlorophenol = 10:1:3.1, DCE, 85 °C.

^a Decaline was introduced as the internal standard.

^b After column chromatography over silicagel.

^c 99% GC yield after 15 h.

robenezene required both high temperature (130 °C) and a pre-activation step by 3-hexyne.¹⁰ The DCE trick allows to run the reaction under much milder and simpler conditions.

Beyond a simple solvent effect, a specific ‘chlorine effect’ is supported by the fact that the catalytic activity on substrate **1a** is totally suppressed by switching to non-chlorinated polar solvents (DMF, benzonitrile, nitrobenzene, methylbenzoate, ...), and in particular to the isostructural 1,2-dibromoethane ($\epsilon = 4.75$). Along the same line, we also observed that upon reflux, a colorless DCE solution of Mo(CO)₆ and phenylpropyne **1a** turned to brown-red after a few hours. The corresponding species (possibly quite diluted) could not be characterized, but it might result from an oxidation of the Mo(0) centers by the chlorinated solvent. In a closely related prospect, Fürstner and Moore reported on selective chlorination processes of a molybdenum complexes in CH₂Cl₂ solution, which afforded efficient catalysts for alkyne metathesis.¹⁴ Likewise, photochemical chlorination of W(CO)₆ in CCl₄ solution was also shown to provide polymerization catalysts.¹⁵ In the present case, several catalyst structures can thus be envisaged. Although only partial decarbonylation cannot be ruled out (residual IR CO absorption bands were detected after the metathesis has started), we may reasonably consider tetracoordinate Cl_{*n*}(ArO)_{3–*n*}Mo≡C–R cores, possibly boosted or stabilized by weak coligands (L = DME, DPE, or DCE). The case *n* = 2 is not only supported by our observations (see above), but also by literature reports on the catalytic activity of di- and tri-chloro molybdenum(III) moieties.¹⁶

To gain insight into the stability and the structure of the putative chlorinated active species (see above), DFT calculations were carried out at the B3LYP/6-31G*/

LANL2DZ*(Mo) level.¹⁷ The coordinating properties of DCE were investigated either in the gas phase or in the solvent ($\epsilon = 10.36$) through PCM calculations.¹⁸ The geometry of the various isomers of [Cl_{*n*}(OAr)_{3–*n*}Mo≡C–Me](L) complexes (*n* = 1, 2) were first optimized in the gas phase.¹⁹ All but one converged toward flattened four-coordinate Mo complexes resulting from the decoordination of the DCE ligand. The latter remains in the vicinity of the Mo-ethynylidyne moiety through weak hydrogen interactions (H₂CH···Cl = 2.7–2.9 Å, C–H···Cl = 167–170°). In the case of a *mer* starting structure bearing a single chlorine ligand, DCE was found to be retained as a *very weak* monodentate ligand *trans* to the carbyne ligand (Mo···ClCH₂CH₂Cl = 3.40 Å) (Fig. 2a), while the geometry of the Mo-carbyne moiety remains classical.²⁰ The corresponding five-coordinate structure is however isoenergetic with a four-coordinate structure in the non-bonding vicinity of DCE. In this and all other cases, PCM calculations yielded only four-coordinate Mo-carbyne species.

These results rule out a significant role of DCE through Mo-coordination or simple dielectric constant effect. They support experimental suggestions of its chlorinating effect, and propound that the catalytic precursor might involve a four-coordinate/two-chloride Mo complex (Fig. 2b).

In conclusion, mild chemical and thermal conditions were found to give reproducible results for the catalytic metathesis of all kinds of hydrocarbon alkynes with alkyl, aryl, or alkenyl substituents. The dramatic effect of the DCE solvent has been investigated through control experiments and DFT calculations. It seems that the main effect could actually be chemical in nature, and that an efficient catalytic species might be a dichloro(monoaryloxy)molybdenum carbyne complex. This hypothesis of course requires confirmation by experimental evidences, but calculations are in progress to compare the reactivity of Cl_{*n*}(OAr)_{3–*n*}Mo≡C–Me species toward alkynes. We indeed considered the resting state of the catalytic species, but DCE might also play a decisive role in the stabilization of the transition state. A more practical prospect is the scope of the substrate compatibility of the DCE system. Aware of the preliminary character of the reported results, we are now focussing on more challenging substrates such as functional alkynes and/or alkadiynes. According to our latest investigations, however, the case of functional alkylpropynes is more problematic. While single metathesis

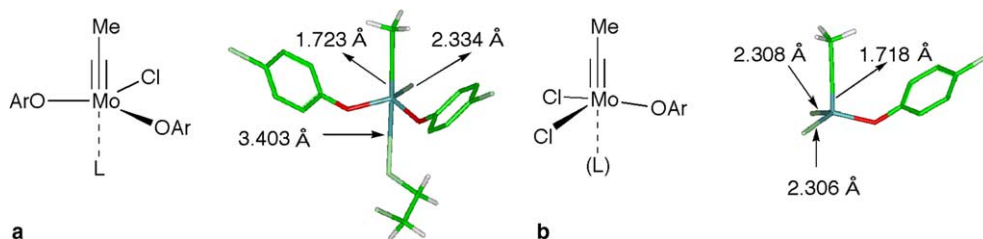


Figure 2. DFT-optimized geometries of (a) monochlorinated Mo-carbyne complex weakly retaining a DCE ligand; (b) free dichlorinated Mo-carbyne complex (see text).

of classical ω -diynes to medium-size cycloalkynes (RCAM) has been widely exemplified with other catalytic systems,^{1a} we are specifically interested in exploring the possibility of sequential metathesis of β -diynes for the synthesis of ring carbo-mers.²¹ Sequential metathesis of non-functional β -diynes $X(C\equiv CMe)_2$ (X = alkylidene, alkenylidene), the feasibility of which has been illustrated for $X = Ph_2Si$ with the Mo/MS/diether system,⁴ is being currently investigated with the DCE system. The results will be communicated in the near future.

2. Typical metathesis procedure

A 25 mL round-bottom flask equipped with a reflux condenser is filled with $Mo(CO)_6$ (0.100 g, 0.38 mmol), *p*-chlorophenol (0.155 g, 1.21 mmol), the substrate (3.8 mmol), decalin as the internal standard for GPC (0.3 mL), and 12 mL of distilled DCE. The solution is stirred under a stream of argon at 85 °C (gentle reflux). The metathesis is monitored by gas chromatography. At the end of the reaction, the solvent is removed under vacuum and the metathesis product is purified by silica gel chromatography.

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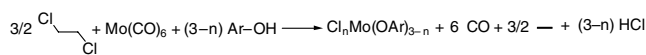
Supplementary data

GC analyses of the final reaction products corresponding to entries 1–3 in Table 1, preparation and ¹³C and ¹H NMR spectra of substrate **1c**, cartesian coordinates and total energy of optimized structures a and b are shown in Figure 2. Supplementary data associated with this article can be found, in the online version at doi:10.1016/j.tetlet.2006.01.120.

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