Ether-induced rate enhancement of Mo-catalyzed alkyne metathesis under mild conditions

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A "user-friendly" catalyst system generated *in situ* in the absence of alkyne from Mo(CO)$_6$, *p*-chlorophenol and a polyether over a bed of molecular sieves, is seen to achieve the metathesis of phenylpropyne at 50 °C with a significant rate enhancement depending on the nature of the ether, with 1,2-diphenoxyethane exhibiting the highest efficiency.

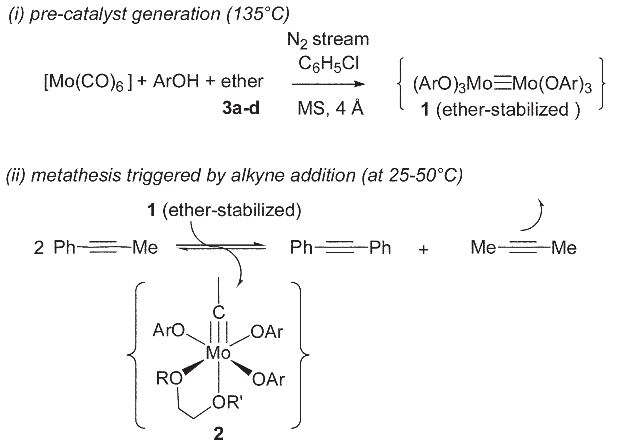
Whereas a range of well-defined and highly efficient alkyne metathesis catalysts have been proposed by Schrock[1] and Fürstner[2] and their collaborators, their preparation and handling often remain the specialist's domain, due to their extreme sensitivity to air and moisture. More readily accessible in view of its simplicity, the "instant catalyst" originally generated *in situ* by Mortreux *et al.* from Mo(CO)$_6$–*p*-chlorophenol is of high practical interest,[3] as evidenced by a number of valuable applications developed by the groups of Bunz[4] and Fürstner.[2]

In attempts to find new synthetic strategies for ring carbomer molecules[5] using "skipped" 1,4-diynes as the substrates, we were primarily led to devise modifications of the Mortreux system so as to bring about catalysis of alkyne metathesis under mild conditions. The modified procedure disclosed here (Scheme 1) was optimized with phenylpropyne as the alkyne prototype.

First, given that the active species in the Mortreux system are mononuclear alkylidyne complexes [R–C≡Mo(OAr)$_3$], as previously suggested by Schrock *et al.*,[6] these should be prone to work under moderate conditions. Thus, a logical improvement is to separate the reaction into two consecutive steps, namely (i) *pre-catalyst generation* at high temperature and (ii) *metathesis reaction* at low temperature. During the course of the present work, such a pre-activation principle was also independently introduced by Brizius and Bunz.[7]

Second, in order to ensure a rigorous dehydration, it may be better to run the whole one-pot reaction in the presence of molecular sieves, in a way used earlier by Sharpless *et al.*[8]

Third, we propose to introduce a controlled amount of ether as a co-ligand in the starting mixture. Such a simple trick was inspired by a literature survey indicating that a number of metathesis-active carbyne complexes are trappable as adducts with a bidentate ether ligand, such as dimethoxyethane (DME).[9] In fact, we discovered that the addition of ether is highly beneficial in both steps (i) and (ii) (Scheme 1). In the initial step, a stoichiometric amount of ether (1.2 equiv.) reduces the decarbonylation time of Mo(CO)$_6$ from 16 h to 10 h (and down to 3 h when 10 equiv. of ether are used), leading to a very deep orange solution exhibiting no ν(CO) absorption. In the second step, as shown in Fig. 1, the presence of the ether is seen *to accelerate the rate of alkyne metathesis.*[10] The bidentate ether, 1,2-diphenoxyethane, when used as the



Scheme 1 Modified one-pot procedure for the metathesis of alkynes. ArOH = *p*-chlorophenol. Additives: **3a** = 1,2-dimethoxyethane; **3b** = 1,2-diphenoxyethane; **3c** = anisole; **3d** = diglyme.

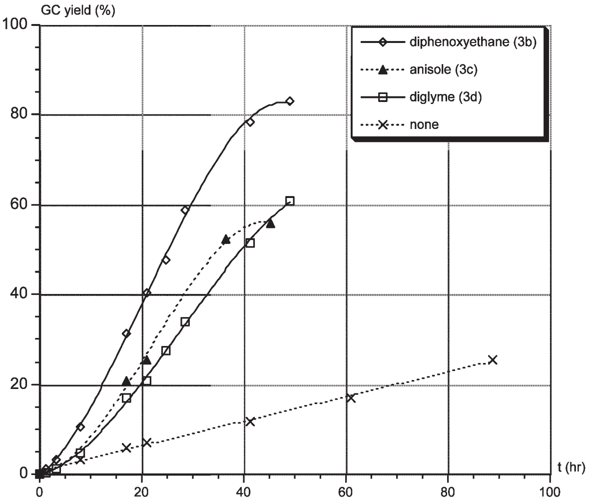


Fig. 1 Effect of the presence of an ether on the kinetics of the metathesis reaction run under a regulated nitrogen flow. Conditions: substrate/catalyst ratio = 10, [PhCCMe] : [Mo(CO)$_6$] : [ArOH] : = 10 : 1 : 11.4, [Mo(CO)$_6$] : **3b**/**3d** = 1.2, [Mo(CO)$_6$] : **3c** = 2.4, MS 4 Å, chlorobenzene, decaline as internal standard, 50 °C. Though **3a** (DME) is as efficient as **3b**, its volatility precludes a rigorous control of its concentration *vs.* time.

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ancillary ligand led to the highest rate enhancement. The monoether anisole (2.4 equiv.) or the triether-like diglyme were found to exhibit a somewhat lower efficiency.

At 50 °C, diphenylacetylene was reproducibly obtained in yields exceeding 95% after 72 h. Under such conditions, only traces of the cyclotrimeric side product $[(C_6H_5)CC(CH_3)]_3$ (two isomers, $m/z = 348$) were detectable by GC/MS.

The presence of 4 Å molecular sieves appears essential to obtain reproducibility in the yields. Keeping in mind that silanol ligands were used earlier as phenol substitutes,[3e] the possibility of a heterogeneous reaction that might be due to an adsorption of Mo complexes onto the sieves was considered, but was unambiguously ruled out by a negative test experiment carried out in the absence of *p*-chlorophenol.

The present system can be used with a *p*-chlorophenol : Mo ratio close to the theoretical 3 : 1 stoichiometry of the expected active species. Indeed, an experiment carried out at 50 °C with a 4 : 1 *p*-chlorophenol : Mo ratio produced pure diphenylacetylene in a net (weighted) 90% yield.

At the present stage of our investigation, the interpretation of the effects of the ether is still speculative.[10] One might reasonably propose that the oxidative decarbonylation of $Mo(CO)_6$ in the absence of alkyne generates a dimolybdenum hexaaryloxide species, $(ArO)_3Mo{\equiv}Mo(OAr)_3$, possibly stabilized by the ether. Pioneering studies by Schrock *et al.* have provided experimental evidence for the reaction of such complexes with alkynes on the way to the formation of alkylidyne species.[1,11] Furthermore, Chisholm and co-workers[12] have disclosed the existence of equilibria between μ-alkyne and alkylidyne complexes of tungsten alkoxides, in some cases with possible mediation by ancillary pyridine ligands. Thus, the effect of the ether might be partly rationalized in terms of pioneering observations, by Schrock and collaborators,[11] that *addition of a base-like pyridine assists the splitting of the transient bis-alkylidyne dimer to provide mononuclear alkylidyne species incorporating the basic ligand.*

Globally, combined beneficial effects of the ether would include (i) an electronic tuning of the affinity of Mo centers for C≡C bonds, (ii) prevention of the formation of inactive aggregates (these representing a thermodynamic sink), and (iii) a hemi-labile behavior providing a low activation energy pathway for coordination of the incoming alkyne, thereby favoring the metathesis step.[10]

As shown in Fig. 2, a DFT model analysis of the elusive alkylidyne complex **2** using DME as the model ancillary ligand was found to be consistent with the above hypothesis. The observation of a negative atoms-in-molecules (AIM) charge on the carbynic carbon (−0.42 e) is indeed expected for a Schrock-type nucleophilic Mo carbyne.[13]

As indicated above, our original goal was to achieve the sequential metathesis of dipropynylsilanes $Ph_2Si(C{\equiv}CMe)_2$ (**4**) to sila-pericyclynes. While no metathesis reaction was observed with the unmodified Mortreux system, 40% conversion of the above substrate was obtained with the present ether-doped system, albeit requiring a high temperature of 135 °C, giving the $(MeC{\equiv}C)(Ph)_2Si–(C{\equiv}C)–Si(Ph)_2(C{\equiv}CMe)$ (**5a**) dimer in 10% isolated yield (Scheme 2), along with MS evidence for the corresponding trimeric **5b** ($[M + NH_4]^+ = 690$) and tetrameric **5c** ($[M + NH_4]^+ = 897$) products. The relatively low efficiency of the system in the specific case of 1,4-diynes (probably one of the most difficult challenges in alkyne metathesis) may be ascribed to the formation of stable chelates whose displacement from the metal center requires thermal activation.

In the current rush to the construction of more and more sophisticated carbon-rich architectures, we believe that "user-friendly" procedures like the present one will become valuable on a laboratory scale. The specific booster effect of the ether observed here may even be beneficial in the case of well-defined catalyst precursors. It is certainly not unique[10] and future research will probably broaden the scope of ancillary ligands exhibiting similar properties. Notably, the important recent discovery by Grela and Ignatowska[14] that the use of 2-fluorophenol leads to a spectacular enhancement of the performance of the Mortreux system may be rationalized in terms of a comparable effect of the fluoride ligand in the outer coordination sphere of molybdenum.

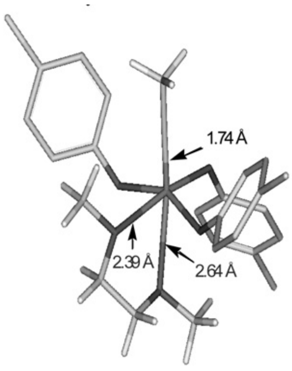


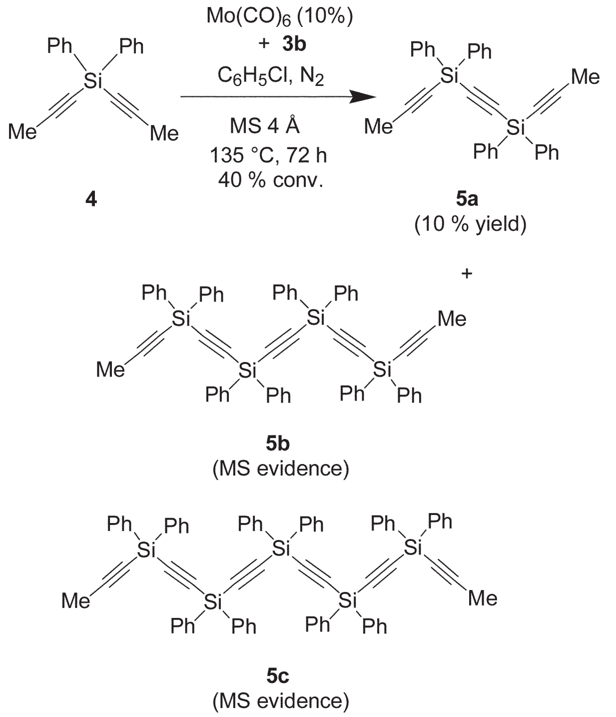
Fig. 2 Optimized geometry of the putative Mo-carbyne complex **2** at the B3LYP/6-31G*/LANL2DZ(Mo) level. The *mer* isomer shown here is more stable than the *fac* one by 21 kcal mol^{-1}.

Experimental

General

$Mo(CO)_6$, phenylpropyne and *p*-chlorophenol were used as received. Nitrogen was dried over $CaCl_2$. Molecular sieves were dried under vacuum at 220 °C for 2 days.

GC analyses were carried out on an HP 4890 gas chromatograph equipped with an HP-5 column (5% Ph-Me-siloxane, 15 m × 0.53 mm). GC-MS: HP GC 6890, equipped with an HP-5MS column (5% Ph-Me-siloxane, 30 m × 0.25 mm, 250 μm); HP MSD 5973, EI 70 eV.



Scheme 2 Metathesis of diphenyl dipropynyl silane **4** giving **5a** (10% isolated yield), **5b** (MS evidence) and **5c** (MS evidence).

Typical metathesis procedure

A 50 ml Schlenk flask fitted with a reflux condenser was filled with *p*-chlorophenol (1.50 g, 11 mmol), diphenoxyethane (0.20 g, 0.93 mmol), decalin as internal standard (300 µL), freshly activated molecular sieves (6.00 g) and chlorobenzene (25 mL). The solution was refluxed for 3 h under nitrogen. Then, $Mo(CO)_6$ (0.2 g, 0.76 mmol) was added and the resulting colorless suspension was refluxed until complete disappearance of the characteristic ν(CO) IR absorption. The dark orange solution was then allowed to cool down to 50 °C and 8.33 mmol of phenylpropyne were added. The metathesis reaction was monitored by gas chromatography. After reaction completion, the solution was filtered through celite, which was then washed with THF. The organic filtrate was evaporated to dryness, giving a dark residue from which diphenylacetylene was isolated by column chromatography. The yield was determined after drying under vacuum to constant weight. The product was characterized by GC and GC/MS (based on comparison with authentic samples) and ^{1}H NMR spectroscopy.

Metathesis of $Ph_2Si(C{\equiv}CMe)_2$ (4)

(a) Preparation of $Ph_2Si(C{\equiv}CMe)_2$ (4). Ph_2SiCl_2 (0.81 mL, 3.84 mmol) was added to a solution of $MeC{\equiv}CMgBr$ (18 mL, 0.5 M, 9 mmol) in THF (50 mL). After stirring overnight, a white precipitate appeared and the mixture was treated with Et_2O–aq. NH_4Cl. The organic layer was separated and dried over $MgSO_4$. The residue was chromatographed over silical gel (eluent: pentane– CH_2Cl_2 10 : 1 to 10 : 3). The silane $Ph_2Si(C{\equiv}CMe)_2$ (**4**) was obtained as a white solid (1.05 g, quant.). MS (EI) *m/z*: 260 $[M]^+$, 245 $[M-CH_3]^+$, 183 $[M-Ph]^+$. ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 2.00 (s, 6 H); 7.37–7.40 (m, 6 H); 7.72–7.76 (m, 4 H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 5.39; 78.01; 107.20; 127.94; 129.98; 133.67; 134.74.

The molecular structure of $Ph_2Si(C{\equiv}CMe)_2$ (**4**) was confirmed by an X-ray structure analysis (unpublished result).

(b) Analytical data for the metathesis product $(MeC{\equiv}C)(Ph)_2Si\text{-}(C{\equiv}C)\text{-}Si(Ph)_2(C{\equiv}CMe)$ (5a). MS (EI) *m/z*: 466 $[M]^+$, 451 $[M-CH_3]^+$, 389 $[M-C_6H_5]^+$, 350 $[M-C_6H_5-CCCH_3]^+$, 245 $[M-Si(C_6H_5)_2-CCCH_3]^+$. ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 2.01 (s, 6 H); 7.24–7.41 (m; 6 H); 7.75–7.80 (m, 4 H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 5.19; 77.17; 107.97; 111.35; 121.11; 130.17; 132.28; 134.86.

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