

## Catalytic Nitrile-Alkyne Cross-Metathesis

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The development of well-understood, efficient, controllable catalysts for olefin and alkyne metathesis (AM) reactions has revolutionized organic and polymer synthesis.<sup>1</sup> Because of the ease with which the nitrile functionality can be incorporated into a molecule compared to the alkyne moiety,<sup>2,3</sup> the ability to convert a nitrile into an alkyne cleanly and efficiently has great potential to facilitate the synthesis of complex molecules and materials. We now report catalytic nitrile-alkyne cross-metathesis (NACM), a specific example of which is depicted in Scheme 1, via the reversible formation of a terminal alkylidyne complex from the corresponding nitride species. In the current system, a “sacrificial” alkyne is required as the acceptor for the two N atoms formally released when two RC≡N molecules are coupled to generate the desired alkyne RC≡CR (i.e., N≡N is not formed as the N-containing byproduct). Three readily synthesized tungsten nitrido complexes catalyze this process.

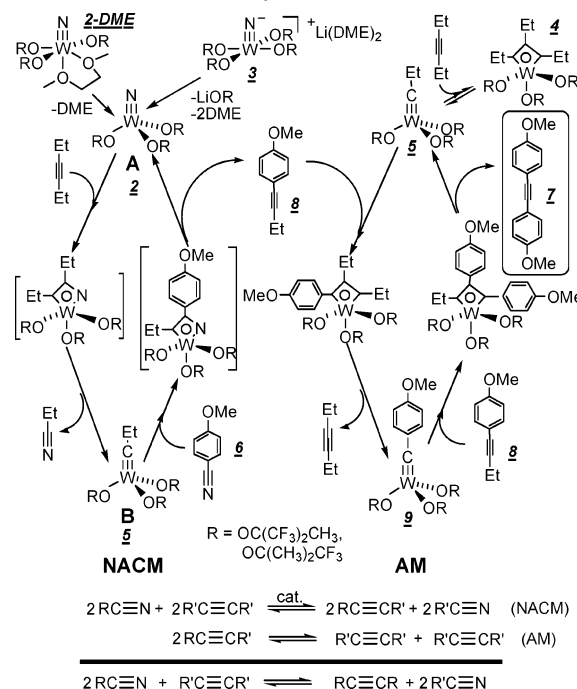
The right half of the NACM cycle, **B** → **A**, is known to occur readily for several tungsten alkylidyne species **B**, which release alkyne and form the corresponding nitride complexes **A** upon treatment with nitriles.<sup>4–8</sup> Accordingly, we probed several nitride complexes to access the left half of the NACM cycle. Metathesis of N≡Mo(OC(CF<sub>3</sub>)<sub>2</sub>CH<sub>3</sub>)<sub>3</sub><sup>9</sup> with 3-hexyne led to slow irreversible formation of EtC≡Mo(OC(CF<sub>3</sub>)<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>.<sup>10</sup> The nitride had been destabilized too greatly relative to the alkylidyne, thus accessing the left half of the NACM cycle but not the right half.

Consequently, we examined tungsten complexes that contain alkoxide ligands of the form OC(CH<sub>3</sub>)<sub>3–n</sub>(CF<sub>3</sub>)<sub>n</sub> (*n* = 1,2). Increased fluorination of the ligands was expected to facilitate the desired cycle in two ways. First, by stabilizing the alkylidyne complex relative to the nitride, the necessary reformation of **B** from **A** would become more energetically feasible.<sup>11</sup> Second, experimental<sup>12,13</sup> and computational<sup>14</sup> studies reveal that AM becomes more favorable as the degree of fluorination of the *tert*-butoxide ligands increases, owing to stabilization of the transition state for metalacyclobutadiene formation. The same effect is seen in Mo- and W-catalyzed degenerate N-atom exchange between nitriles.<sup>9,15</sup> Hence, we expected diminished rates of reaction with N≡W(OC(CH<sub>3</sub>)<sub>2</sub>CF<sub>3</sub>)<sub>3</sub> (**1**) compared to N≡W(OC(CF<sub>3</sub>)<sub>2</sub>CH<sub>3</sub>)<sub>3</sub> (**2**)

Treatment of [N≡WCl<sub>3</sub>]<sub>4</sub>·1.1DCE<sup>16</sup> (DCE = 1,2-dichloroethane) with 16 equiv of LiOC(CF<sub>3</sub>)<sub>2</sub>CH<sub>3</sub> and 8.2 equiv of 1,2-dimethoxyethane (DME) in toluene affords [Li(DME)<sub>2</sub>][N≡W(OC(CF<sub>3</sub>)<sub>2</sub>CH<sub>3</sub>)<sub>4</sub>] (**3**) in 63% yield. The DME adduct of **2**, **2-DME**, is then prepared from **3** in 78% yield upon treatment with CF<sub>3</sub>SO<sub>3</sub>H in diethyl ether at low temperature. Both **2-DME** and **3**, which are pale yellow in solution and colorless in the crystalline state, serve as sources of **2** (Scheme 1).

Dissolution of **2-DME** in a toluene-*d*<sub>8</sub> solution containing 2 equiv of 3-hexyne leads after 20 h at 28 °C to an equilibrium mixture containing 5 mol % tungstenacyclobutadiene complex W(C<sub>3</sub>Et<sub>3</sub>)-(OC(CF<sub>3</sub>)<sub>2</sub>CH<sub>3</sub>)<sub>3</sub> (**4**)<sup>13</sup> and 95 mol % propylidyne complex EtC≡W(OC(CF<sub>3</sub>)<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>(DME) (**5-DME**).<sup>13</sup> The organic byproduct of the formation of **4** and **5-DME**, propionitrile, is also observed.

Scheme 1. NACM and AM Cycles<sup>a</sup>



<sup>a</sup> Unobserved intermediates are bracketed. All steps are in principle reversible. Numbered metal complexes are those for which R = OC(CF<sub>3</sub>)<sub>2</sub>CH<sub>3</sub>.

Having thus shown that the alkylidyne complex **5-DME** is formed from the nitrido complex **2-DME** under mild conditions, we next examined reversibility of this process by searching for exchange of the R and R' groups of a nitrile (RC≡N) and an alkyne (R'C≡CR') in the presence of **2-DME**. Upon heating a mixture of *p*-methoxybenzonitrile (**6**) (R = 4-C<sub>6</sub>H<sub>4</sub>OMe) and 0.5 equiv of 3-hexyne (R' = Et) with 5 mol % **2-DME** (based on **6**) for 21 h at 95 °C, <sup>1</sup>H NMR spectroscopy indicated conversion to 1,2-bis(4-methoxyphenyl)acetylene (**7**, 77%) and 1-(4-methoxyphenyl)-1-butyne (**8**, 15%), with **6** (8%) remaining. Propionitrile was formed as the N-containing byproduct.

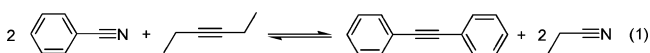
There are two potential mechanisms for the formation of the symmetrical diarylalkyne **7**. Following the NACM cycle in Scheme 1, **7** can result from the replacement of 3-hexyne by the unsymmetrical alkyne **8** in the catalytic cycle. Alternatively, AM of **8** mediated by **5-DME** and its substituted benzylidyne analogue **9** could afford **7** (Scheme 1).<sup>13</sup> Under the conditions employed, AM is much more rapid than NACM, a fact that helps account for the majority of the **7** that is formed. In a reaction between 3,5-dimethylbenzonitrile and a mixture of 3-hexyne (0.5 equiv) and **7** (0.5 equiv), AM affords a statistical mixture of 3-hexyne, **7**, and **8** rapidly (within 20 min) compared to the rate at which NACM occurred (hours). However, there is also a thermodynamic contribution to the product selectivity. The model reaction shown in eq 1 is enthalpically favored in the gas phase: Δ*H*<sup>o</sup> = −13.2 kcal

**Table 1.** Alkyne Formation at 95 °C (5 mol % Catalyst)

substrate R-CN, R =	catalyst	3-hexyne equiv	t (h)	RCCEt (%)	RCCR (%)
4-MeOC <sub>6</sub> H <sub>4</sub> -	2-DME	0.5	8	11	81
	1	0.5	31	18	61
4-BrC <sub>6</sub> H <sub>4</sub> -	2-DME	1	15	0	100
4-MeC(OCH <sub>2</sub> CH <sub>2</sub> O)C <sub>6</sub> H <sub>4</sub> - <sup>a</sup>	2-DME	0.5	11	19	23
	1	0.5	25	58	12
4-MeOCOC <sub>6</sub> H <sub>4</sub> -	2-DME	1.5	24	76	24
2-C <sub>4</sub> H <sub>4</sub> S-CH <sub>2</sub> -	2-DME	1	22	0	75
2-C <sub>4</sub> H <sub>4</sub> S-	2-DME	1	11	19	41
3,5-CF <sub>3</sub> C <sub>6</sub> H <sub>4</sub> -	2-DME	1	25	5	95
3,5-MeC <sub>6</sub> H <sub>4</sub> -	2-DME	1	24	<5	>95
I(CH <sub>2</sub> ) <sub>2</sub> - <sup>a</sup>	2-DME	1	6	40	33
4-H <sub>2</sub> C=CHC <sub>6</sub> H <sub>4</sub> -	2-DME	0.8	13	34	64
4-tBuO <sub>2</sub> CC <sub>6</sub> H <sub>4</sub> -	1	1	20	43	6

<sup>a</sup> 10 mol % catalyst loading

mol<sup>-1</sup>.<sup>17</sup> Solvation effects are unlikely to overcome this preference, given the similarity of the compounds involved.



Having demonstrated catalytic NACM, we studied the effect of catalyst identity. Complexes **1**, **2-DME**, and **3** catalyze this process in toluene. Under otherwise identical conditions, an initial assay demonstrated more rapid reaction and greater conversion with **2-DME** than with **1** or **3**. Accordingly, we focused on **2-DME** in optimization studies. The complete consumption of 3-hexyne under conditions in which **6** was incompletely converted to **7** and **8** suggested that poly(3-hexyne) was forming. Alkyne polymerization is known to compete with AM in some systems.<sup>18–20</sup> Examination of the effect of catalyst on the competition between these metathesis and polymerization processes revealed that a catalyst concentration of 6.0 mM maximizes the formation rate and yield of metathesis products.

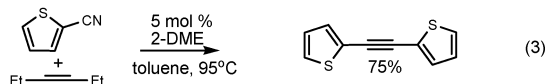
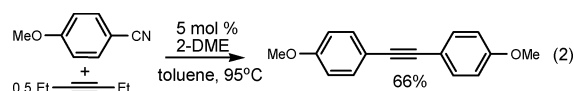
A study of the effects of catalyst loading, 3-hexyne loading, and temperature on the reaction rate and yield led to the adoption of standard reaction conditions of 5 mol % **2-DME** and 95 °C; extra 3-hexyne was used for nitrile substrates that reacted sluggishly. However, when >0.5 equiv of 3-hexyne (relative to nitrile) is used, fast AM affords a mixture of symmetrical and unsymmetrical alkyne products. Simple removal of the volatiles from the system, followed by heating in toluene often allows the unsymmetrical alkyne to be metathesized into the symmetrical alkyne and 3-hexyne. The latter alkyne is then removed from the system by polymerization or evacuation.<sup>21</sup>

As Table 1 shows, **2-DME** (5 mol %) at 95 °C catalyzes NACM in good yields for substrates containing alkyl, alkyl halide, vinyl, and several substituted aryl groups. However, aldehydes and ketones deactivate the catalyst, although methyl esters are tolerated. Acetals and ketals are poor substrates. Other functional groups that are incompatible with this catalyst are those that can coordinate strongly to W, contain acidic protons, or are bulky.

Replacement of the catalyst **2-DME** by **1** permits the use of *tert*-butyl esters and improves the results with ketals. The NACM activity of both **1** and **2-DME**, despite the large difference in p*K*<sub>a</sub> between HOC(CF<sub>3</sub>)<sub>2</sub>CH<sub>3</sub> and HOC(CH<sub>3</sub>)<sub>2</sub>CF<sub>3</sub>,<sup>22</sup> suggests that numerous complexes are likely to be active NACM catalysts, which bodes well for the tuning of activity and substrate tolerance.

Reactions conducted on a larger scale (eq 2 and 3) reveal the synthetic utility of NACM. Compatibility of **2-DME**/**5-DME** with

thiophene-containing nitriles and alkynes is important because of the potential applications of poly(2,5-thienyleneethynylene)s as conjugated polymers.<sup>23</sup>



Our work establishes a new catalytic method for the preparation of alkynes: cross-metathesis of nitriles with a readily available “sacrificial” alkyne. Tungsten nitrido complexes **1**, **2-DME**, and **3** are suitable catalysts for NACM in toluene. Kinetic and computational investigations of the NACM mechanism are currently underway. We are also pursuing synthetic studies aimed at improving catalyst activity and functional group tolerance.

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**Supporting Information Available:** Characterization data for new compounds; all synthetic information. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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