Highly Efficient Regio- and Stereoselective Dimerization of (Hetero)aromatic Terminal Alkynes by Organo Rare-Earth Metal Catalysts

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*Summary: The yttrium dialkyl complex [(**L**)Y(CH_2SiMe_3)$_2$] (**1**, L = 1,4,6-trimethyl-N-(2-pyrrolidin-1-ylethyl)-1,4-diazepan-6-amine), activated by [$PhNMe_2H$][$B(C_6F_5)_4$], catalytically dimerizes a range of (hetero)aromatic alkynes to Z-enynes with 100% selectivity and high rates. Catalyst turnovers up to 2000 were readily achieved in preparative scale (5–10 mmol) reactions. For comparison, the related E-enynes were produced with a permethyl lanthanocene catalyst.*

Catalytic coupling of terminal alkynes is the most conceptually straightforward and atom-efficient way to synthesize conjugated enyne motifs, which can be found in a variety of biologically active compounds[1] and synthetic conjugated polymers developed for optoelectronic applications.[2] Many organometallic catalysts, employing early[3] or late transition[4] metals or rare-earth metals,[5] have been reported to catalyze this reaction. Nevertheless, it is difficult to find catalysts that can combine high catalyst activity, selectivity, and substrate scope. Rare-earth metal catalysts show good activities,[5a,b,g] but heteroatom-containing substrates have barely been studied.[6] Although these metals are hard Lewis acids, their high kinetic lability provides interesting opportunities for the conversion of functionalized substrates.[7] Here we report a new and highly efficient cationic yttrium catalyst for the head-to-head dimerization of (hetero)aromatic alkynes to *Z*-enynes. The corresponding *E*-enynes were prepared with the known permethyl lanthanocene $Cp^*_2LaCH(SiMe_3)_2$ (**2**).[8]

The new tetradentate ancillary ligand 1,4,6-trimethyl-*N*-(2-pyrrolidin-1-ylethyl)-1,4-diazepan-6-amine (H**L**) is derived from the tridentate 1,4,6-trimethyl-1,4-diazepan-6-amine ligand moiety recently employed by us on Sc and Y organometallics.[9] It is prepared from 6-amino-1,4,6-trimethyl-1,4-diazepine in three steps (Scheme 1). 2-Chloro-*N*-(1,4,6-trimethyl-1,4-diazepin-6-yl)acetamide (**A**) was prepared by the reaction of 6-amino-1,4,6-trimethyl-1,4-diazepine with chloroacetyl chloride under basic conditions. Reaction of **A** with pyrrolidine and a catalytic amount of NaI yielded 2-pyrrolidin-1-yl-*N*-(1,4,6-trimethyl-1,4-diazepin-6-yl)acetamide (**B**). This was reduced by $LiAlH_4$ in di-*n*-butyl ether followed by aqueous workup to give H**L** as a colorless oil in 81% yield after Kugelrohr distillation.

Yttrium complex **1** was obtained in 72% yield by reacting H**L** with $Y(CH_2SiMe_3)_3(THF)_2$ in toluene (Scheme 1) followed by recrystallization from *n*-hexane. The pendant pyrrolidinyl group in **1** is coordinated to the metal, even in the Lewis basic solvent THF-d_8, as its α-H resonances are diastereotopic at ambient temperature, as are the alkyl methylene protons. Reaction of **1** with [$PhNMe_2H$][$B(C_6X_5)_4$] (X = H, F) in the same solvent cleanly generates the corresponding monoalkyl cation (^{13}C NMR Y-CH_2: δ 28.9 ppm, J_{CH} = 97.8 Hz, J_{YC} = 38.8 Hz vs **1**: δ 27.9 ppm, J_{CH} = 100.6 Hz, J_{YC} = 36.2 Hz).

The ionic catalyst system **1**/[$PhNMe_2H$][$B(C_6F_5)_4$] in the weakly coordinating polar solvent bromobenzene proved to be highly effective for the *Z*-selective head-to-head alkyne dimer-

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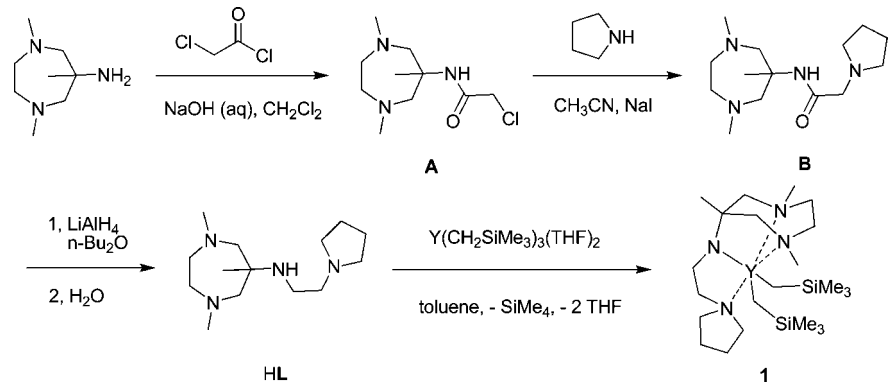
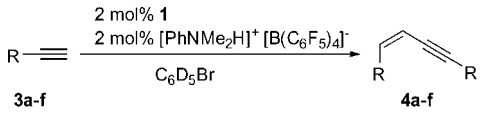
Scheme 1



Scheme 2



Scheme 3

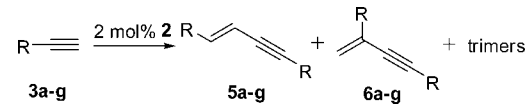


Table 1. Head-to-Head Z-Dimerization of (Hetero)aromatic Terminal Alkynes by Cationic Yttrium Complex[a]

Entry (substrate)	R	Time (min)	Conversion (%)[b]	Product selectivity (%)[b]
1 (**3a**)		<5	100	100
2 (**3b**)		30	100	100
3 (**3c**)		10	100	100
4 (**3d**)		<5	100	100
5 (**3e**)		<5	100	100
6 (**3f**)		40	100	100
7 (**3g**)		60	--	--

[a] Reaction conditions: catalyst **1** (10 μmol), [PhMe$_2$NH][B(C$_6$F$_5$)$_4$] (10 μmol), [Y] = 18.2 mM, substrate (0.5 mmol), solvent: C$_6$D$_5$Br, 80 °C. [b]Determined by in situ ^{1}H NMR spectroscopy.

Table 2. Dimerization of (Hetero)aromatic Terminal Alkynes by Lanthanocene Complex 2[a]

Entry	R	Time (min)	Conversion (%)[b]	Product selectivity (%)[b] 5	6	trimers
1 (**3a**)		<10	100	98	--	2
2 (**3b**)		60	100	93	5	2
3 (**3c**)		150	100	63	37	--
4 (**3d**)		<10	100	99	--	1
5 (**3e**)		<10	100	98	2	--
6 (**3f**)		<10	100	99	--	1
7 (**3g**)		60	95	100	--	--

[a] Reaction conditions: [**2**] = 4.1–4.4 mM, substrate (50 equiv), solvent: C$_6$D$_6$, 25 °C. [b]Determined by in situ ^{1}H NMR spectroscopy.

ization, with a high tolerance to heteroatom functionalities (Scheme 2). A range of (hetero)aromatic terminal alkynes were tested as substrates, and the results are summarized in Table 1. For substrates **3a**−**f** the reactions essentially go to completion with full selectivity for the *Z*-enyne, and the Lewis basic anisyl or thienyl groups pose no problems. Only the use of **3g**, with the 2-pyridyl substituent, results in complete deactivation of the catalyst. Deprotonation reactions and insertion reactions of pyridines with organo rare-earth compounds are known[10] and might lead to catalyst deactivation.

The kinetics of the dimerization of **3a** and **3e** was studied, revealing zero-order dependence in substrate concentration (see Supporting Information). In a 10 mmol scale reaction, 2000 equiv of phenylacetylene (**3a**) was converted within 2.5 h to give 99% isolated yield of pure 1,1′-(1*Z*)-but-1-en-3-yne-1,4-diyldibenzene (**4a**). In a 5 mmol scale reaction, 1000 equiv of 3-ethynylthiophene (**3e**) was converted within 4 h to give pure 3,3′-(1*Z*)-but-1-en-3-yne-1,4-diyldithiophene (**4e**) as bright yellow crystals in 94% isolated yield after recrystallization from methanol. Thus **1**/[PhNMe$_2$H][B(C$_6$F$_5$)$_4$] is a catalyst that provides *Z*-selective alkyne dimerization capability at TONs that would allow practical application in synthesis.

The lanthanocene alkyl complex Cp*$_2$LaCH(SiMe$_3$)$_2$ (**2**) is known to catalyze the oligomerization of alkynes to form *E*-dimers as the dominant products.[5g] We have applied this catalyst to the (hetero)aromatic alkyne substrates **3a**−**g** (Scheme 3), and the results are summarized in Table 2. For all the substrates, the main products formed are the *E*-enynes, but side products are present. Apart from the *ortho*-substituted substrates (which form significant amounts of the head-to-tail dimer, especially for the anisyl derivative **3c**), the selectivity for the *E*-enynes is >97%. Remarkably, the 2-pyridyl-substituted substrate **3g** readily forms the *E*-enyne **5g** with perfect selectivity. With this neutral catalyst, the pyridyl group only slows down the catalysis relative to the less strongly basic substrates.

Because in the alkyne dimerizations with the lanthanocene catalyst a certain amount of trimer is formed,[5f,g] the scaling up of these reactions should take this side-product formation into account. For the *E*-selective dimerization of phenylacetylene

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(**3a**), an increase in substrate concentration from 0.2 to 1.6 M leads to an increased trimer formation (from 2% to 11%). Nevertheless, dimerization of **3a** on a 5 mmol scale (500 equiv) in 0.5 mL of solvent could be performed with 97% selectivity for 1,1′-(1*E*)-but-1-en-3-yne-1,4-diyldibenzene (**5a**) when the substrate was added dropwise over a period of 30 min.

In conclusion, a new, highly efficient cationic yttrium catalyst for the head-to-head dimerization of (hetero)aromatic alkynes to *Z*-enynes has been found. It shows significantly higher turnover frequencies (up to 800 TO h^{-1}) than other catalysts for this transformation and was successfully applied on a preparative scale with proven turnover numbers up to 2000. The complementary *E*-enyne producs can be prepared using the permethyl lanthanocene catalyst. As the reaction route leading to *Z*-enyne products is still not well-established (the most recent proposal involves a dimeric catalytic species[5b]), we are currently addressing the mechanistic issues that determine the selectivity for *Z*- or *E*-products.

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Supporting Information Available: Text giving detailed experimental procedures and characterization data of the enynes. This material is available free of charge via Internet at http://pubs.acs.org.

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