

Novel Z-Selective Head-to-Head Dimerization of Terminal Alkynes Catalyzed by Lanthanide Half-Metallocene Complexes

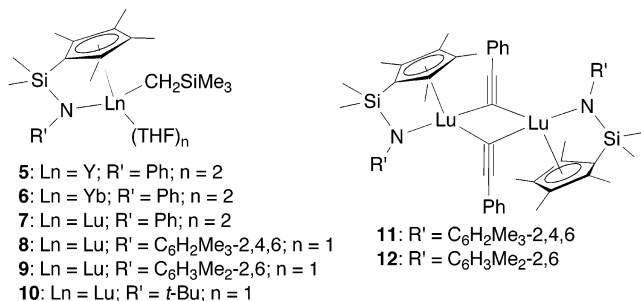
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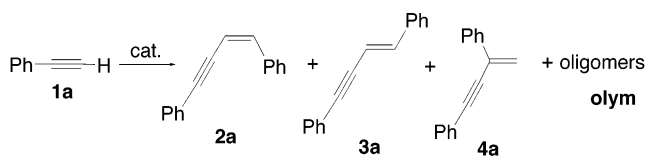
Catalytic dimerization of terminal alkynes is an atom economic and straightforward method for the synthesis of conjugated enynes, which are important building blocks for organic synthesis and significant components in various biologically active compounds.¹ In particular, the regio- and stereoselective head-to-head (*Z*)-dimerization of terminal alkynes is of special importance and interest, because the resulting (*Z*)-enynes are key units found in a variety of naturally occurring anticancer antibiotics.^{1b} Although various transition metal² and f-element catalysts³ are known to catalyze the dimerization of terminal alkynes, in most cases a mixture of regio (head-to-head vs head-to-tail)- and stereo (*E/Z*-head-to-head)-isomers was obtained, while (*Z*)-selective head-to-head dimerization of terminal alkynes has hardly been achieved.^{2–4} None of the previously reported catalyst systems were found to be recyclable. We report here a novel organolanthanide catalyst system for the regio- and stereoselective head-to-head (*Z*)-dimerization of terminal alkynes. In addition to its excellent selectivity, this catalyst system can be recovered and reused.

In the course of our studies on lanthanide half-metallocene complexes,^{5,6} we examined the reactivity of a series of half-metallocene alkyl complexes such as **5–10** toward phenylacetylene (Table 1).⁷ In sharp contrast with the previously reported catalyst systems,^{2,3} these complexes, in particular, the lutetium anilido complexes **7–9**, showed extremely high head-to-head (*Z*)-selectivity for the dimerization of phenylacetylene, which yielded solely the (*Z*)-dimer **2a** (entries 3–5, Table 1). As far as we are aware, this is the first example of exclusive formation of a (*Z*)-enyne compound in the dimerization of an aromatic alkyne.^{2–4}



Complex **8** was then chosen as a catalyst to examine the dimerization of various terminal alkynes. Some of the representative results are summarized in Table 2. The aromatic C–Cl (entries 5 and 8), C–Br (entries 6 and 9), and C–I bonds (entry 7), which are known to be extremely susceptible to reductive cleavage by transition metals, survived in the present reactions to afford exclusively the corresponding (*Z*)-enynes **2e–i**, a new class of enyne

Table 1. Dimerization of Phenylacetylene Catalyzed by Lanthanide Half-Metallocene Complexes^a



| entry | cat. | time/h | conversion/% ^b | product distribution ^b 2a:3a:4a:olym |
|-------|-----------|--------|---------------------------|--|
| 1 | 5 | 20 | 85 | 89:0:6:5 |
| 2 | 6 | 18 | 69 | 92:0:0:8 |
| 3 | 7 | 18 | >99 | 100:0:0:0 |
| 4 | 8 | 5 | >99 | 100:0:0:0 |
| 5 | 9 | 5 | >99 | 100:0:0:0 |
| 6 | 10 | 17 | 89 | 72:0:13:15 |

^a Conditions: phenylacetylene (1 mmol), cat. (0.02 mmol), in C₆D₆ (0.45 mL) at 80 °C. ^b Determined by ¹H NMR and GC-MS.

Table 2. Dimerization of Terminal Alkynes Catalyzed by **8**^a

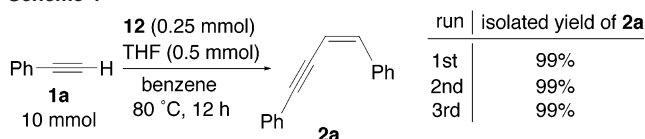
| entry | R | solvent ^b | temp (°C) | time (h) | convn ^c (%) | select ^c (%) |
|-------|--|---|-----------|----------|------------------------|-------------------------|
| 1 | Ph (a) | C ₆ D ₆ | 80 | 5 | >99 | >99 |
| 2 | 4-MeC ₆ H ₄ (b) | toluene- <i>d</i> ₈ | 110 | 2 | >99 | >99 |
| 3 | 4-MeOC ₆ H ₄ (c) | toluene- <i>d</i> ₈ + THF ^d | 110 | 2 | >99 | >99 |
| 4 | 4-CF ₃ C ₆ H ₄ (d) | toluene- <i>d</i> ₈ | 110 | 2 | 97 | 95 ^e |
| 5 | 4-ClC ₆ H ₄ (e) | C ₆ D ₆ | 80 | 2 | >99 | >99 |
| 6 | 4-BrC ₆ H ₄ (f) | C ₆ D ₆ | 80 | 2 | >99 | >99 |
| 7 | 4-IC ₆ H ₄ (g) | C ₆ D ₆ | 80 | 2 | >99 | >99 |
| 8 | 2-ClC ₆ H ₄ (h) | C ₆ D ₆ | 80 | 3 | >99 | >99 |
| 9 | 2-BrC ₆ H ₄ (i) | C ₆ D ₆ | 80 | 3 | >99 | >99 |
| 10 | <i>n</i> -C ₆ H ₁₃ (j) | THF- <i>d</i> ₈ | 100 | 14 | >99 | 95 ^f |

^a Conditions: substrate (1 mmol), **8** (0.02–0.05 mmol). ^b 0.45 mL. ^c Determined by ¹H NMR and GC-MS. ^d THF: 5 equiv per **8**. In THF-free toluene, 2,4-bis(4-methoxyphenyl)but-1-ene-3-yne (33%, head-to-tail dimer) was also formed. ^e 1,4,6-Tris[4-(trifluoromethyl)phenyl]hex-1-yne-3,5-diene (5%) was also formed. ^f 2-Hexyldec-1-ene-3-yne (5%, head-to-tail dimer) was also formed.

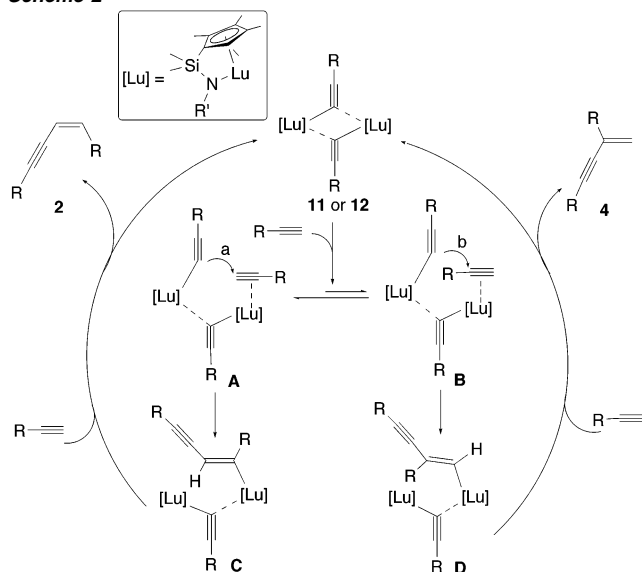
building blocks that would be useful for the architecture of further large molecules. A novel solvent effect on the regioselectivity was also observed. The dimerization of 4-methoxyphenylacetylene (**1c**) in pure toluene gave a 67:33 mixture of the head-to-head and head-to-tail dimers, whereas that in the presence of a small amount of THF (ca. 5 equiv per **8**) yielded solely the head-to-head (*Z*)-dimer **2c** (entry 3, Table 2). Similarly, the dimerization of 1-octyne (**1j**) in toluene-*d*₈ gave the head-to-tail dimer in 76% yield, while that

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Scheme 1



Scheme 2



in THF- d_8 afforded the head-to-head *Z*-dimer (**2j**) in 95% yield (entry 10, Table 2).

All of these reactions were homogeneous at the reaction temperatures (80–110 °C). When the reaction mixtures were cooled to room temperature, however, the corresponding lutetium alkyne species precipitated as crystalline powders. In the case of phenylacetylene, single crystals of **11** were obtained, which adopted a dimeric structure via the phenylacetylide bridges as shown by an X-ray analysis.^{8,9} The activity and selectivity of **11** for the dimerization of phenylacetylene were almost the same as those of the alkyl complex **8** under similar conditions,¹⁰ which strongly suggests that the true catalysts in the present systems are alkyne species and more importantly the alkyne catalyst species can be recovered and reused. A much higher recovery yield for the less substituted (and thus less soluble) anilido complex **12** (93%) was achieved than for **11** (65%) by evaporation of the reaction solvent and hexane extraction of the residue. The recovered **11** or **12** was identical to that freshly prepared by the reaction of **8** or **9** with phenylacetylene, respectively, and could therefore be reused without loss of activity and selectivity (Scheme 1).¹⁰

A possible reaction mechanism is shown in Scheme 2. Acid–base reaction between an alkyl complex and a terminal alkyne should easily give a dimeric alkyne species such as **11** or **12**. Coordination of an alkyne to a metal center of the dimeric alkyne species could afford **A** or **B** by breaking one of the two alkyne bridges.¹¹ Attack of the terminal alkyne to the coordinated alkyne in **A** (path a) should give **C**, which upon deprotonation reaction with another molecule of alkyne would release the (*Z*)-enyne product **2** and regenerate the alkyne catalyst species. On the other hand, the addition of the terminal alkyne to the alkyne in **B** (path b) would give **D**, which upon reaction with another molecule of alkyne could yield the head-to-tail dimer **4** and regenerate the alkyne species similarly.¹² Apparently, a dimeric intermediate such as **A**, which leads to “intermolecular” addition of an alkyne to

an alkyne, must play a critically important role in the present (*Z*)-selective dimerization.^{9,11,12} This is in sharp contrast with the analogous reactions catalyzed by lanthanide metallocene or benzamidate-ligated catalysts, in which the addition of an alkyne to an alkyne took place in an “intramolecular” fashion at a monomeric alkyne/alkyne intermediate and thus always yielded the (*E*)-enyne products whenever the head-to-head reaction occurred.³

Supporting Information Available: Experimental details, X-ray data for **9** and **11** (CIF), and spectral data for all new compounds (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- (7) Complexes **5–9** (new compounds) were synthesized by the reactions of $\text{Ln}(\text{CH}_2\text{SiMe}_3)_3(\text{THF})_2$ with 1 equiv of $\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4\text{H})\text{NHR}'$, according to a procedure reported for the synthesis of **10**. See: Arndt, S.; Voth, P.; Spaniol, T. P.; Okuda, J. *Organometallics* **2000**, *19*, 4690.
- (8) See the Supporting Information for details.
- (9) The dimeric alkyne complexes **11** and **12** were very thermally stable, which remained unchanged after being heated at 150 °C in toluene- d_8 overnight in the absence of an alkyne. This is in striking contrast with what was observed previously in the case of the analogous metallocene or benzamidate-ligated lanthanide alkyne complexes, which rapidly decomposed or coupled into trienediyl derivatives upon heating.^{3a,c–e}
- (10) A small amount of THF (2 equiv per **11** or **12**) was required to achieve the exclusive head-to-head (*Z*)-dimerization of phenylacetylene, because **11** or **12** is a THF-free complex, while **8** or **9** bears a THF ligand. This result is in agreement with the THF effect observed above.
- (11) The ¹³C NMR spectrum of the analogous yttrium ($I = 1/2$) alkyne complex $[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)(\text{NPh})\text{Y}\{\mu\text{-CCC}_6\text{H}_4(\text{C}_5\text{H}_{11-n})\text{-4}\}(\text{THF})_2]$ in C_6D_6 (containing 1 equiv of THF per Y) showed a triplet at both 22 °C (δ 138.7, $^1J_{\text{YC}} = 23$ Hz) and 80 °C (δ 142.2, $^1J_{\text{YC}} = 23$ Hz) for the α -alkynide carbon, suggesting that the μ -alkynide-bridged dimeric structure in this type of complex is considerably strong. Addition of 2 equiv of 4-(*n*-pentyl)phenylacetylene to this solution at 80 °C afforded quantitatively the corresponding *Z*-dimerization product in 3 h, while the triplet for the α -alkynide carbon remained almost unchanged after the reaction.
- (12) Path a could be a sterically favored process, while path b might be electronically preferred especially when R is an alkyl or electron-donating group. In the presence of THF, A might be preferred to B because of crowdedness caused by the THF molecules (ligands) around the metal centers. Further studies are in progress to clarify the mechanism.

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