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Multidentate Triphenolsilane-Based Alkyne Metathesis Catalysts

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Abstract: A series of triphenolsilane-coordinated molybdenum(VI) propylidyne catalysts has been developed, which are resistant to small alkyne polymerization and compatible with various functional groups (including phenol substrates). The catalysts remain active in solution for days at room temperature (months at −30 °C). The catalysts are also compatible with 5 Å molecular sieves (small alkyne scavengers), and have enabled the homodimerization of small alkyne substrates at 40–70 °C in a closed system, with dimer products being obtained in 76–96% yields. A shape-persistent aryleneethynylene macrocycle (**11**) was also prepared on a gram scale with 0.5 mol% catalyst loading, in almost quantitative yield.

Keywords: alkyne metathesis; macrocycle synthesis; multidentate ligands

Alkyne metathesis represents an emerging organic transformation that has attracted significant research interest. It has been utilized in efficient syntheses of a variety of organic compounds and materials,[1] including natural products,[2] organic polymers[3], shape-persistent 2D macrocycles[4] and rigid 3D covalent organic polyhedrons (COPs, i.e., molecular cages).[5] In the past two decades, numerous well-defined catalytic systems based on Schrock-type molybdenum(VI) and tungsten(VI) alkylidyne complexes have been developed, consisting of various monodentate ligands, such as alkoxide,[6] aryloxide,[4j,k,7] amido,[4f,8] imidazolin-2-iminato,[9] phosphoraneiminato,[10] or silanolate ligands.[11] Recently, our group reported a multidentate molybdenum(VI) carbyne catalyst (**2a**, Figure 1).[4j] The properties of this multidentate catalyst surpass those of many existing monodentate alkyne metathesis catalysts (e.g., **1**), showing high catalytic activity, improved functional group tolerance, longer lifetime, and complete inhibition of the undesired polymerization of the 2-butyne by-product.[4j] Highlights of its applications include the syntheses of shape-persistent 2D macrocycles, 3D molecular cages, as well as conjugated polymers (1D molecular wires).[4j,k,5b] However, there exists a potential drawback with such triphenolamine-based catalysts: strong coordination of the ligand nitrogen to molybdenum, which lowers its Lewis acidity, thus the catalyst activity (no activity observed without the nitro substituents, i.e., **2b**).[4k] Although methylation of the nitrogen atom in the ligand prevents its metal coordination and restores the catalyst activity (**2c**, Figure 1), the synthetic difficulty (time-consuming, low-yielding synthesis) and poor solubility of the charged triphenolammonium ligand represent big disadvantages.[4k] Herein, we report the design and synthesis of a series of multidentate catalysts (**3a**–**3c**) consisting of triphenolsilane ligands (**L1**, **L2** and **L3**, Scheme 1), which are readily accessible

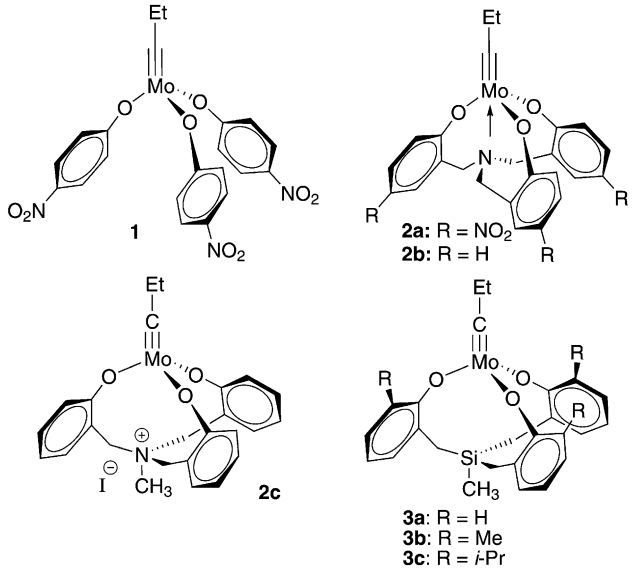
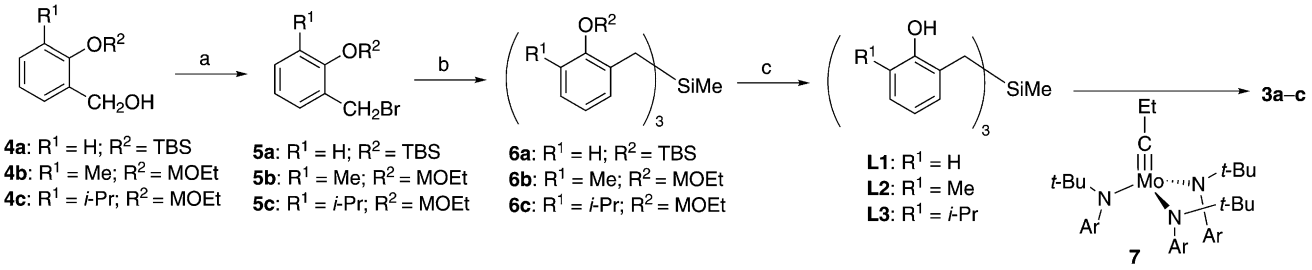


Figure 1. Molybdenum(VI) carbyne catalysts with phenol ligands.



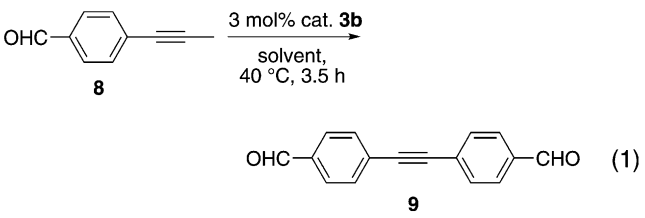
Scheme 1. Syntheses of multidentate ligands (**L1**–**L3**) and their coordinated molybdenum(VI) propylidyne catalysts. *Conditions:* a) PPh_3, Br_2, imidazole, CH_3CN, Et_2O (67%) for **4a**; NBS, PPh_3, CH_2Cl_2 (77–86%) for **4b** and **4c**; b) Mg, THF, room temperature, then $MeSiCl_3$ (72–90%); c) $Et_3N{\cdot}HF$, THF (39%) for **L1**; PPTS, *i*-PrOH (63%–66%) for **L2** and **L3**.

and compatible with various substrates. The catalysts remain active in solution phase for days at room temperature (months at −30 °C). Such catalysts also enabled the metathesis of challenging phenol-based substrates in good yield. A gram-scale preparation of a phenyleneethynylene macrocycle was also accomplished starting from simple dipropynyl-substituted monomers in a closed system.

Triphenolsilane ligands (**L1**–**L3**) were prepared from the protected salicyclic alcohols (**4a**–**c**). In order to study the steric effect on catalytic activity, we designed and synthesized ligands with different *ortho* substituents (H, Me, *i*-Pr). Conversion of benzylic alcohols (**4a**–**c**) to benzylic bromides (**5a**–**c**), generation of Grignard reagents, followed by coupling with $MeSiCl_3$ and subsequent deprotection provided ligands **L1**–**L3**. The active catalysts **3a**–**3c** were generated by mixing the molybdenum(VI) trisamide precursor (**7**) with a triphenolic silane ligand in 1:1 ratio in carbon tetrachloride. The complete displacement of the amine ligands with the multidentate ligand **L2** was confirmed by ^{1}H NMR analysis (see the Supporting Information, Figure S1). Further ^{13}C NMR characterization clearly showed the downfield shift of the carbyne carbon from 302.3 ppm to 310.1 ppm upon ligand exchange, indicating the formation of the multidentate catalyst **3b** (see the Supporting Information, Figure S2 and Figure S3).

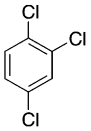
Triphenolic silane ligands share similar geometrical features with our previous multidentate triphenolamine ligands, in which the effective coordination of the three phenol moieties to molybdenum forms a cage-shaped metal center and blocks the extra substrate-binding site. However, unlike nitrogen, which can easily coordinate to molybdenum and reduce its Lewis acidity, the silicon atom has no lone pair available for the metal-ligand coordination. We therefore expected catalysts **3a–3c** to possess the advantages of robust multidentate catalysts without sacrificing their catalytic activity. A well-known relatively inert compound, 4-nitropropynylbenzene, was used as the substrate to test the activity. As expected, under the typical alkyne metathesis condition (3 mol% cat. loading, 40 °C, ~10 h, dynamic vacuum), the reactions catalyzed by triphenolic silane-based catalysts **3a–3c** all showed good yields (54%, 58%, and 54%, respectively). It is interesting to note that the catalytic activity of this new family of catalysts (**3a–3c**) seems not to be sensitive to the sterics of the ligands. Since catalysts **3a–3c** exhibit similar activity, we used **3b** as the catalyst in the catalysis studies described below.

Next, we explored the solvent effect on the catalyst activity. The pre-generated catalyst **3b** in carbon tetrachloride (20 vol%) was used in this study. We used 4-formylpropynylbenzene (**8**) as the substrate and the reaction was carried out at 40 °C with 3 mol% catalyst loading [Eq. (1)]. It should be noted that propynylated benzaldehyde (e.g., **8**) derivatives are reported to be difficult substrates to metathesize, destroying some alkyne metathesis catalysts, such as monodentate siloxy-based molybdenum catalyst.[11c] To our great delight, the multidentate triphenolsilane catalyst showed 60–74% substrate conversion as well as good solubility in a variety of commonly used solvents as shown in Table 1. Considerably lower conversions in THF and hexane were observed, presumably due to the coordinating nature of THF and lower solubility of the catalyst in hexane. It appears that carbon tetrachloride is a preferred solvent for the generation of the catalyst, which could be a potential disadvantage of this catalyst system. We attempted to generate the catalyst in other solvents, such as toluene. However, we observed reduced catalytic activity (conversion 73% *vs.* 65%).



It is well-known that the polymerization of the 2-butyne by-product, one of the commonly-observed

Table 1. Metathesis reactions in various solvents.

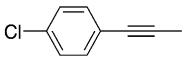
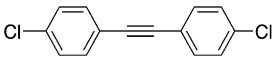
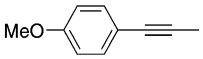
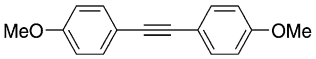
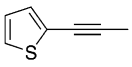
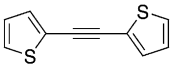
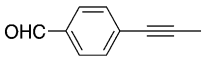
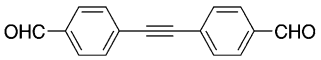
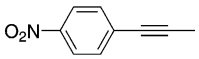
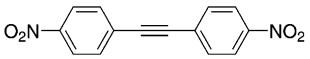
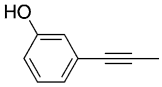
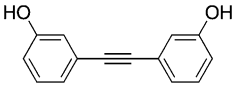
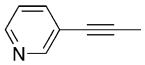
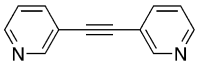
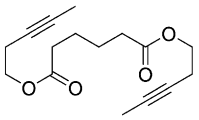
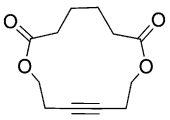
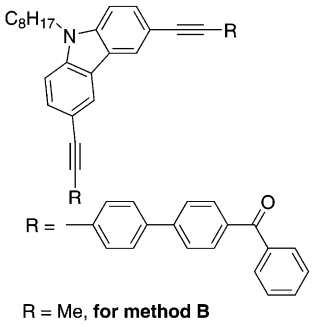
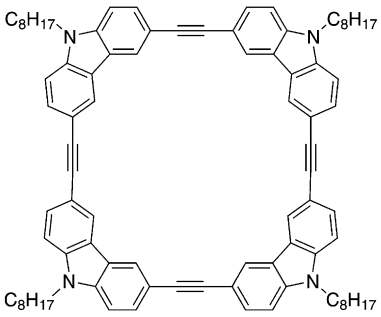
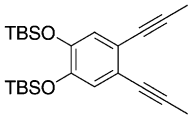
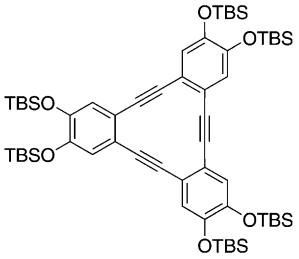
Solvent	Conversion [%]	Solvent	Conversion [%]
n-C_6H_{14}	26	chlorobenzene	70
t-BuOMe	69	dichloroethane	74
THF	50		66
CH_2Cl_2	61		71
$CHCl_3$	63	CCl_4	79
toluene	73 (65)		

major side reactions in alkyne metathesis, could poison the metathesis catalyst through the "ring-expansion" mechanism.[7b] Previously, we demonstrated that triphenolamine-based catalyst (**2a**), with the N–Mo coordination, can completely inhibit the small alkyne polymerization,[4j] Now without an Si–Mo bonding interaction, the question arises as to whether such a multidentate silane-based catalyst can still inhibit small alkyne polymerization. As a model study, the efficiency of catalyst **3b** on inhibiting alkyne polymerization was tested with a large excess of 2-butyne (>100 equiv.). Catalyst **3b** showed no polymerization even after 24 h. Furthermore, the catalyst **3b**, with or without 2-butyne treatment, showed similar metathesis activity even after exposure to 2-butyne for one week (4-formylpropynylbenzene **8** as the substrate). This result further supports the notion that the catalyst with multidentate ligands can completely inhibit the small alkyne polymerization, presumably because the cage-shaped catalyst effectively blocks the access of butyne to the extra open binding site on the Mo(VI) center.

Another complication with alkyne metathesis is the efficient removal of one of the alkyne products in order to drive the reaction to completion. Since the most widely used common substrates contain methyl-substituted alkynes, a typical alkyne metathesis reaction is driven to completion by the removal of the 2-butyne by-product. Continuous dynamic vacuum is commonly applied to remove 2-butyne. However, such an approach usually requires solvent refill, and often does not work well for catalysts that are highly sensitive to air and moisture. Although the later development of precipitation-driven alkyne metathesis by Moore et al. significantly improved shape-persistent macrocycle synthesis, such an approach requires more synthetic efforts (e.g., installment of large aromatic end groups) and generates a large amount of diarylacetylene by-product, thus it is not atom-economic.[12] Recently Fürstner showed that 5 Å molecular sieves can be used as an efficient small alkyne scavenger.[11c] However, only few catalysts have been reported to be effective for catalytic alkyne metathesis reactions in the presence of 5 Å molecular sieves.[10,11c,13] To further improve the efficiency and the synthetic utility of our newly developed multidentate triphenolsilane catalysts, and make them more user-friendly, we explored the feasibility of conducting metathesis reactions in a closed system by using 5 Å molecular sieves. To our delight, comparable or much improved conversions of metathesis reactions catalyzed by this class of silane-based catalysts were observed in the presence of 5 Å molecular sieves. Such conditions work particularly well for those challenging substrates (e.g., 4-nitropropynylbenzene) which usually require longer reaction time and higher catalyst loading under conventional dynamic vacuum conditions. In entry 5 (Table 2), the conversion was improved from 49% to 86% when 5 Å molecular sieves were used as 2-butyne scavenger. Such closed system conditions can also be applied to the synthesis of shape-persistent macrocycles in almost quantitative yields on a multigram scale (2.6 g, entry 10). It should also be noted that for the same multigram macrocycle synthesis (entry 10), the catalyst loading could be reduced to as little as 0.5 mol% without sacrificing the yield, at slightly elevated temperature (55 °C, 4.31 g, 98%). The carbazole-based cyclic tetramer was also prepared in one step from a simple propynyl-substituted monomer in quantitative yield (entry 9). Thus our catalyst system holds promise for the convenient access to shape-persistent 2D or 3D molecular architectures which have been recognized as important building blocks for the future of nanotechnology.

Given these encouraging findings, we next investigated their substrate scope. The reactions were performed either under dynamic vacuum or in the presence of 5 Å molecular sieves. Table 2 summarizes reactions of different substrates catalyzed by *in situ* generated catalyst **3b**. Catalyst **3b** is compatible with all the different substrates tested, providing the corresponding products in good to excellent yields. The substrates include: (i) compounds containing electron-donating/electron-withdrawing substituents, (ii) heterocyclic molecules, (iii) the ring closing alkyne metathesis (RCAM) of diyne to cycloalkyne, (iv) compounds containing free phenolic hydroxy groups (entry 6), and (v) the precipitation-driven cyclooligomerization reaction of the carbazole diyne substrate (entry 9). Even those challenging substrates, containing nitro or aldehyde functional groups are compatible with our conditions to give the corresponding dimers (86–96%). Half-lives of less than 1 hour were generally observed for those reactions, even at 40 °C with a catalyst loading as low as 3 mol% (based on Mo). It should be noted that the metathesis reaction works surprisingly well with the phenol substrate

Table 2. Homodimerization, RCAM and cyclooligomerization reactions of propynyl substrates.[a,b]

Entry	Substrate	Product	Method A or B	Temperature [°C]	Time [h]	Yield [%]
1			A	40	4.5	91
2			A	40	5	94
3			A	40	5	92
4			A B B	40 40 40	5 16 16	79 94 96[c]
5			A B	40 40	5 (15) 20	47 (49) 86
6			A B	70 70	19 20	64 76
7			A B B	70 70 70	4 4 (7) 4	84 84 (88) 90[c]
8			A	40	3.5	95
9			B	20 40	0.5 5	93[d] >99
10			B	40	16	>99

[a] Catalyst **3b** and solvent CCl_4 were used unless stated otherwise.
[b] 3 mol% catalyst loading for entries 1–5 and 7–10; 10 mol% for entry 6.
[c] Catalyst **3c** was used.
[d] Precipitation-driven cyclooligomerization. Method A: vacuum with 30 min-interval without the addition of molecular sieves. Method B: 150 mg MS 5 Å/0.1 mmol for entries 4–7 and 300 mg MS 5 Å/0.1 mmol for entries 9 and 10.

(entry 6), which, to the best of our knowledge, represents the first successful alkyne metathesis of a substrate containing free phenolic hydroxy groups.[14] This finding would enable the synthesis and applications of other phenol-based substrates, including shape-persistent macrocycles.

Compared to olefin metathesis that has become a powerful tool in organic synthesis and has been widely used by chemists in various disciplines, the analogous alkyne metathesis lags far behind in popularity. A significant disadvantage of alkyne metathesis is the availability of a user-friendly catalyst. Previous catalysts for alkyne metathesis are usually generated *in situ* from relatively more stable precatalysts, and the catalytically active species possess very limited lifetimes in solution. For example, as shown in Fig-

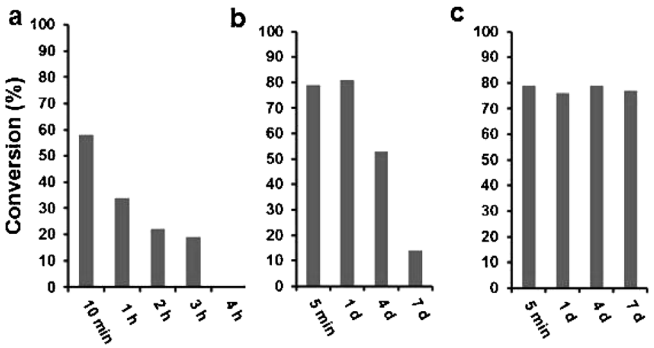
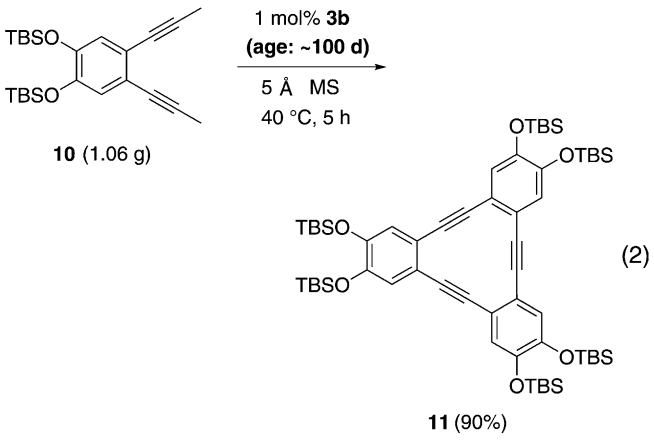


Figure 2. The conversion of 4-formylpropynylbenzene in the catalytic runs (3 mol% loading, 40 °C) at different time intervals after the generation of the catalysts. (a): catalyst **1**, stored at room temperature after its generation; (b): catalyst **3b**, stored at room temperature after its generation; (c) catalyst **3b**, stored at −30 °C after its generation.

ure 2a, the catalyst **1** with monodentate ligands, in the absence of any alkyne substrates, shows a progressive measurable decrease in the catalytic activity, and is completely inactive after 4 h of the generation under argon at room temperature. In great contrast, catalyst **3b** showed good stability in solution. Its metathesis activity at different time intervals after its generation (in the absence of any alkyne substrates) was tested, using the 4-formylpropynylbenzene (**8**) as the model compound. Complex **3b** showed no loss in catalytic activity after 24 h storage at room temperature and remained active even after one week at room temperature. When stored in solution at −30 °C, catalyst **3b** did not show any noticeable decrease in activity for a period of more than 3 months. The presence of only 1 mol% of 100-day aged catalyst **3b** was sufficient to catalyze the cyclooligomerization of monomer **10** to form macrocycle **11** in 5 h at 40 °C in 90% yield [Eq. (2)]. Our findings here represent one step forward for commercializing a user-friendly stable alkyne metathesis catalyst. Such a long lifetime is desired particularly for the alkyne metathesis of tough substrates, and also for industrial processes where catalyst stability is often of paramount importance.



In summary, a class of triphenolsilane-based, uncharged, multidentate alkyne metathesis catalysts has been developed. The good functional group tolerance, fast reaction rate and long lifetime (remaining active in solution for months) represent major advantages. These catalysts are compatible with 5 Å molecular sieves that serve as small alkyne by-product scavengers. A variety of tough substrates (e.g., pyridine, phenol, benzaldehyde, nitrobenzene) were successfully cross-metathesized. Moreover, shape-persistent aryleneethynylene macrocycles were prepared in almost quantitative yields on a multi-gram scale in a closed system, highlighting the feasibility of achieving a convenient access to a variety of novel 2D and also 3D molecular architectures targeting various potential applications (e.g., carbon capture, artificial photosynthesis, catalysis, etc.).

Experimental Section

General Procedure for Alkyne Metathesis Reactions listed in Table 2

The ligand (**L1**, **L2** or **L3**) (0.003 mmol) and the precursor **7** (2.0 mg, 0.003 mmol) were premixed in dry carbon tetrachloride (3 mL for all entries except for entry 8, Table 2, where the solvent volume was doubled to ensure intramolecular alkyne metathesis) and stirred for 5 min to generate the catalyst *in situ*. Subsequently, the substrate (0.1 mmol) and 5 Å molecular sieves (for removing 2-butyne by-product) were added, and the stirring was continued with regular monitoring of the reaction by NMR. For the vacuum-driven alkyne metathesis reactions, the solution was exposed to vacuum with 30 min intervals to remove the metathesis by-product 2-butyne and the loss of solvent during the application of vacuum was compensated by adding fresh solvent each time. The yields were determined with ^{1}H NMR by using 1,4-dimethoxybenzene as an internal standard.

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