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Increased Activity of in Situ Catalysts for Alkyne Metathesis

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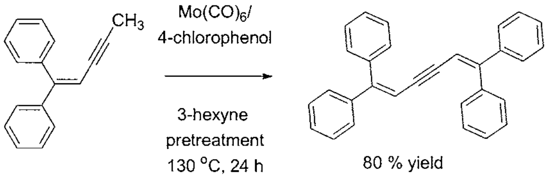
ABSTRACT

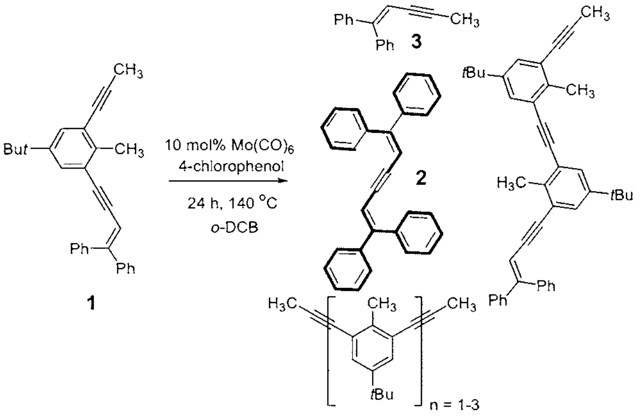


Reaction of an enyne (1,1-diphenyl-pent-1-ene-3-yne) with a preheated mixture of $Mo(CO)_6$/4-chlorophenol/3-hexyne at 130 °C furnished 1,1,6,6-tetraphenylhex-1,5-diene-3-yne in an 80% yield. If the starting material was heated with a mixture of $Mo(CO)_6$ and 4-chlorophenol under identical conditions, no reaction was observed.

We have developed an efficient protocol to perform alkyne metathesis utilizing simple catalyst systems formed from Mo(CO)$_6$ and 4-chlorophenol at elevated temperatures (130−150 °C).[1] Propynylated alkylbenzenes, styrenes, and stilbenes all undergo metathesis or ADIMET polymerization smoothly and afford the desired products in high yield and purity. However, the in situ catalysts fail if propynylated alkenes (enynes) or *ortho*-alkoxy-substituted benzene derivatives are treated under these conditions.[1] Starting materials were always reisolated in quantitative yield, and none of the desired products formed. To access oligomers that at least incorporate the enediyne motif, we prepared the monomer **1**, which we subjected to standard alkyne metathesis conditions in the expectation to obtain its dimer (Scheme 1). Workup showed that a series of compounds, inseparable by standard chromatographic techniques, had formed. The mass spectrometric analysis of the reaction mixture suggested that random metathesis had occurred, and the compounds shown in Scheme 1 were identified by their molecular ions.

The significance of the experiment lies in the unexpected detection of the "excised" dimer **2** that suggests that "in situ" alkyne metathesis of propynylated olefins is possible under the correct experimental conditions. It seems that once the system is activated, productive alkyne metathesis of otherwise sluggishly reacting substrates commences, albeit at the (unacceptable) price of the formation of all cross dimers. If the catalyst system could be independently "preactivated", it should be feasible to perform alkyne metathesis of enynes. Consequently, the catalytic mixture of Mo(CO)$_6$ and 4-chlorophenol in *o*-DCB (*o*-dichlorobenzene) was placed in a high-pressure tube, an excess of 3-hexyne (bp 81 °C) added to

Scheme 1. Mass Spectroscopic Analysis of Alkyne Metathesis of **1**



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[1] (a) Kloppenburg, L.; Song, D.; Bunz, U. H. F. *J. Am. Chem. Soc.* **1998**, *120*, 7973. (b) Bunz, U. H. F.; Kloppenburg, L. *Angew. Chem.* **1999**, *38*, 478. (c) Pschirer, N. G.; Bunz, U. H. F. *Tetrahedron Lett.* **1999**, *40*, 2481. (d) Brizius, G.; Pschirer, N. G.; Steffen, W.; Stitzer, K.; zur Loye, H. C.; Bunz U. H. F. *J. Am. Chem. Soc.* **2000**, *122*, 12435. (e) Bunz, U. H. F. *Acc. Chem. Res.* **2001**, *34*, 998.

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the mixture, and the closed pressure tube heated to 130 °C for 1 h. After the pressure cap was removed, it was replaced with a septum and purged for 1 h with nitrogen at 130 °C to remove any excess of hexyne. After that time the monomer **3** was added to the reaction mixture and stirred under N_2 for another 24 h at 130 °C. Workup furnished the title compound **2** in 80% yield as a colorless crystalline material. Single-crystal analysis (Figure 1) assured that metathesis had succeeded.

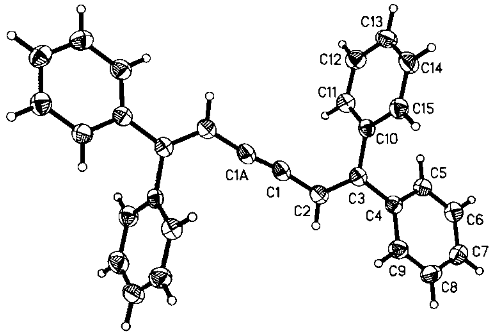
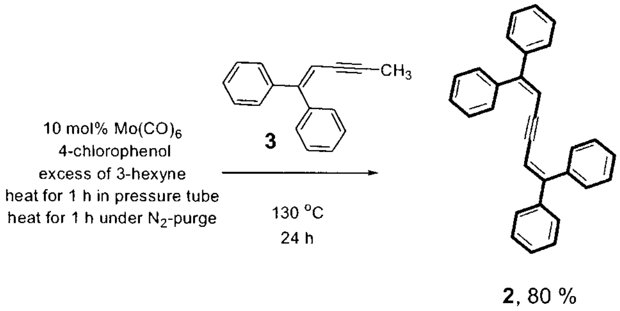


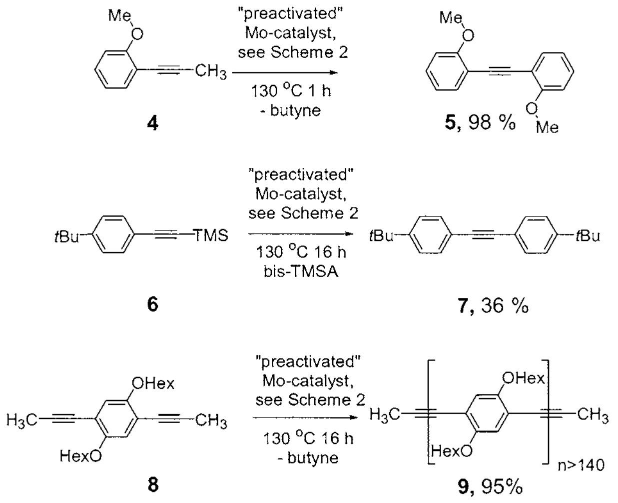
Figure 1. ORTEP representation of **2**.

With this method available we turned our attention to the problem of the dimerization of *ortho*-methoxypropynylbenzene **4** with the in situ catalysts. While this type of ether-containing substrate is easily metathesized with the Fürstner-type Mo catalysts[2] and probably as well with the Schrock-type tungsten carbynes,[3] the simple in situ approach did not work well, despite the one example of a low molecular weight dialkoxy-substituted poly(*para*-phenyleneethynylene) formed by in situ ADIMET.[1a] With the pretreated catalyst system (Scheme 3), dimerization of **4** occurs at 130 °C in 3 h to give the alkyne **5** in almost quantitative yield after workup.[1c] It was possible to lower the reaction temperature to 75 °C after an initial pretreatment at 130 °C, but then the yield of the dimer **5** dropped from 98 to 36% after a reaction time of 24 h.

Scheme 2. Synthesis of **2** from **3**



Scheme 3. Synthesis of **5**, **7**, and **9** by Alkyne Metathesis



The pretreated catalyst system was used to make a dihexoxy-PPE **9** in high yields (95%) and with a degree of polymerization (P_n) of 140 repeating units.[1a,c] This polymer was obtained after a metathesis time of 16 h. Gel permeation chromatography (GPC) of aliquots taken during the reaction show a greatly enhanced activity over the traditional Mo-$(CO)_6$/4-chlorophenol system. The increased activity of the catalyst system led us to try the dimerization of the TMS-substituted alkyne **6**. Here, the corresponding dimer **7** was isolated in 36% yield after successful but somewhat more sluggish reaction. The decreased reactivity must be due to the significantly increased steric hindrance that the TMS group imparts upon the monomer. The only other compound that could be isolated from the reaction mixture was unreacted starting material, and increasing the temperature/duration did not improve the yield of the reaction.

Ring-closing alkyne metathesis is a fascinating and important reaction that has found applications both in the synthesis of novel natural products as well as in the preparation of cyclophane- and dehydroannulene-type rings.[4] With the successful dimerization of **4** into **5**, a series of dipropynyls **11a**−**c** was prepared (Scheme 4) and their metathesis reaction was investigated. Subjecting either **11a** or **11c** to the conditions of alkyne metathesis furnished (after multiple chromatographies) the cycles **12a**,**c** but in relatively disappointing yields (Scheme 4). In the case of **11c**, a dimeric cycle, **13c**, is isolated, but in lower yield. If the bispropyne

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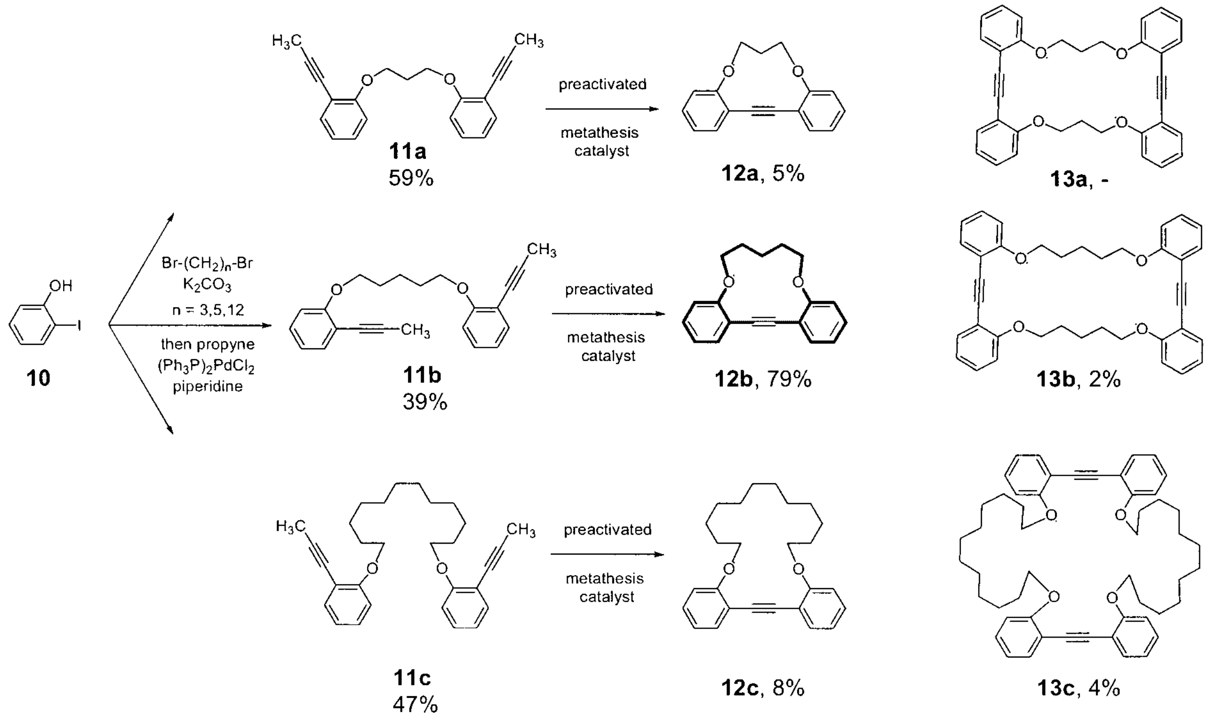
(2) (a) Fürstner, A.; Mathes, C.; Lehmann, C. W. *Chem.*−*Eur. J.* **2001**, *7*, 5299. Fürstner, A.; Mathes, C.; Lehmann, C. W. *J. Am. Chem. Soc.* **1999**, *121*, 9453. (b) Tsai, Y.-C.; Diaconescu, P. L.; Cummins, C. C. *Organometallics* **2000**, *19*, 5260.

(3) Schrock, R. R. *J. Chem. Soc.* **2001**, 2541. Krouse, S. A.; Schrock, R. R. *Macromolecules* **1989**, *22*, 2569. Zhang, X. P.; Bazan, G. C. *Macromolecules* **1994**, *27*, 4627. Weiss, K.; Michel, A.; Auth, E. M.; Bunz, U. H. F.; Mangel, T.; Müllen, K. *Angew. Chem.* **1997**, *36*, 506. Fürstner, A.; Guth, O.; Rumbo, A.; Seidel, G. *J. Am. Chem. Soc.* **1999**, *121*, 11108.

(4) (a) Pschirer, N. G.; Fu, W.; Adams, R. D.; Bunz, U. H. F. *Chem. Commun.* **2000**, 87. Ge, P. H.; Fu, W.; Herrmann, W. A.; Herdtweck, E.; Campana, C.; Adams, R. D.; Bunz, U. H. F. *Angew. Chem.* **2000**, *39*, 3607. (b) Fürstner, A.; Grela, K. *Angew. Chem.* **2000**, *39*, 1234. Fürstner, A.; Seidel, G. *Angew. Chem.* **1998**, *37*, 1734.

Scheme 4. Ring-Closing Metathesis of the Dipropynylarenes **11a−c**



11b is submitted to the conditions of the alkyne metathesis, the cycle **12b** is isolated in 79% yield, indicating a correlation between linker chain length and yield of obtained cycles. Here as well, some of the dimer **13b** forms, but only in low yield. While the NMR spectra of monomeric and dimeric cycles are very similar, the molecular ion peaks in the mass spectra ensure that the assignment was correct.

In conclusion, we have developed an improved version of the instant catalysts formed from molybdenum hexacarbonyl and phenols first reported by Mortreux,[5] used by Mori,[6] and optimized by us.[1] The latest generation of the in situ catalyst described herein is capable of dimerizing enyne substrates as well as *ortho*-alkoxy-substituted propynylbenzenes unreactive under the regular in situ conditions. We have used the expanded scope of this reaction to make a series of novel bridged tolane cyclophanes.[7] In the future, we will investigate the use of this catalytic system for the synthesis of enyne-containing oligomers and cycles.

See ref 8 for experimental details for the synthesis of compounds **2** and **12b**.

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Supporting Information Available: Detailed descriptions of experimental procedures and characterization of all new compounds and syntheses of the metathesis substrates. This material is available free of charge via the Internet at http://pubs.acs.org.

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(5) (a) Mortreux, A.; Blanchard, M. *Chem. Commun.* **1974**, 786. (b) See also: Villemin, D.; Heroux, M.; Blot, V. *Tetrahedron Lett.* **2001**, *42*, 3701.

(6) Kaneta, N.; Hirai, T.; Mori, M. *Chem. Lett.* **1995**, 1055. Nishida, M.; Shiga, H.; Mori, M. *J. Org. Chem.* **1998**, *63*, 8606.

(7) Crisp, G. T.; Bubner, T. P. *Tetrahedron* **1997**, *53*, 11881. Crisp, G. T.; Bubner, T. P. *Tetrahedron* **1997**, *53*, 11899.

(8) **Synthesis of Compound 2.** A 30 mL cylindrical high-pressure glass tube (Ace Glass, Inc.; dried overnight) was charged under N_2 with $Mo(CO)_6$, (30.0 mg, 0.114 mmol) freshly distilled 4-chlorophenol (147 mg, 1.14 mmol), and *o*-DCB (3 mL, dried over molecular sieves). 3-Hexyne (100 mg, 1.22 mmol) was added, and the tube was sealed with a Teflon cap. After the mixture was heated to 130 °C for 2 h, the cap was removed and replaced with an upside-down rubber septum, which was secured with copper wire. A 20 gauge syringe needle was placed in the septum to serve as a gas outlet, and a slow stream of N_2 was introduced via cannula. This mixture was heated at 130 °C for 1 h. Compound **3** (250 mg, 1.15 mmol, dissolved in 0.5 mL *o*-DCB) was added via syringe. Heating at 130 °C with continued N_2 purge gave a dark brown solution after 24 h. The mixture was cooled and diluted with $CHCl_3$. Washing with 10% NaOH, 10% HCl, and H_2O followed by removal of solvent in vacuo gave a mixture of **2** and **3**. Column chromatography (5% EtOAc/hexanes) followed by recrystallization (hexanes) gave **2** as a mildly fluorescent white solid (175 mg, 80%). ^1H NMR: δ 7.23−7.35 (m, 20H), 6.12 (s, 2H). ^{13}C NMR: δ 151.81, 141.62, 139.08, 129.94, 128.20, 128.14, 128.06, 127.85, 107.56, 93.26. IR (thin film, cm^{-1}): 3057, 3020, 2916, 2849, 2731, 2212, 1952, 1885, 1812, 1738, 1656, 1597, 1493, 1441, 1367, 1263, 1182, 1078, 1026, 915, 856, 767, 693, 633. MS: M^+ calcd, 382.1722; found, 382.1734. Mp: 129 °C. **Synthesis of Compound 12b.** A 250 mL cylindrical high-pressure glass tube (Ace Glass, Inc.; dried overnight) was charged under N_2 with $Mo(CO)_6$, (235 mg, 0.890 mmol) freshly distilled 4-chlorophenol (1.16 g, 9.02 mmol), and *o*-DCB (50 mL, dried over molecular sieves). 3-Hexyne (1.00 g, 12.2 mmol) was added, and the tube was sealed with a Teflon cap. After the mixture was heated to 130 °C for 2 h, the cap was removed and replaced with an upside-down rubber septum, which was secured with copper wire. A mild nitrogen purge was introduced as described above, and compound **11b** (3.00 g, 9.04 mmol) was added. Heating overnight at 130 °C followed by standard workup (as described above) yielded, after flash chromatography (10% EtOAc/hexanes), cycle **12b** as a colorless solid (1.98 g, 78.7%). ^1H NMR: δ 7.51−7.52 (m, 2H), 7.24−7.27 (m, 2H), 6.93−6.99 (m, 4H), 4.14−4.17 (t, 4H), 1.92 (m, 6H). ^{13}C NMR: δ 160.26, 132.15, 129.33, 121.09, 114.69, 114.49, 90.14, 69.52, 27.50, 21.93. IR (thin film, cm^{-1}): 3064, 3020, 2931, 2863, 2745, 2553, 2204, 1901, 1775, 1693, 1589, 1478, 1441, 1382, 1278, 1234, 1151, 1093, 1041, 982, 945, 829, 752. MS: M^+ calcd, 556.2614; found, 556.2604. MP: 82 °C. UV−vis ($CHCl_3$): 280 nm, 312 nm (λ_{max}). Fluorescence ($CHCl_3$): 358 nm (broad).