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Alkyne Metathesis with Simple Catalyst Systems: High Yield Dimerization of Propynylated Aromatics; Scope and Limitations

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Abstract: High yield dimerization of propynylated benzenes and propynylnaphthalene by a mixture of $Mo(CO)_6$ and 4-chlorophenol at 140 °C in 1,2-dichlorobenzene is reported to give the corresponding disubstituted alkynes. The scope and limitation of the reaction and the influence of substitution pattern and substitution type are discussed. Oxygen or nitrogen carrying substrates metathesize in moderate to good yields and *ortho*-alkyl substituted examples form the respective tolanes very efficiently. © 1999 Elsevier Science Ltd. All rights reserved.

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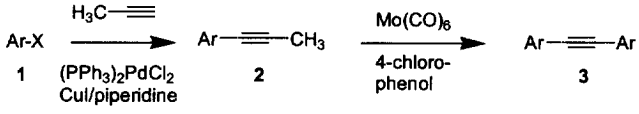
In this communication we wish to report upon the metathesis of propynylated benzenes utilizing the "instant" catalysts formed *in situ* from $Mo(CO)_6$ and 4-chlorophenol at 140 °C. A series of substituted diarylalkynes is obtained in yields up to 96 % under these conditions.

In the past, alkyne metathesis has attracted much less attention in comparison to olefin metathesis, which developed into a powerful tool in organic synthesis as well as in polymer chemistry.[1] The recent commercial availability of active and robust catalysts for alkene metathesis (Schrock, Mo-;[2] Grubbs, Ru-based[3]) has additionally increased the popularity of this reaction. Contrary to that, the field of alkyne metathesis was clearly dominated by mechanistic organometallic research.[4] Applications were rare and restricted to metathetic ring opening of cycloalkynes with defined tungsten or molybdenum carbyne complexes.[5,6] Recently, Schrock's tungsten carbyne $(t\text{BuO})_3\text{W}{\equiv}\text{C}\text{-}t\text{Bu}$ (**A**) was used to access poly(*p*-phenyleneethynylene)s by the acyclic diyne metathesis[7] and Fürstner[8] performed ring-closures utilizing alkyne metathesis. While the carbyne **A**[9] is a superbly active catalyst, and metathesizes internal alkynes readily at temperatures around 80 °C, it is very sensitive towards air and moisture, and not commercially available.



The first homogeneous catalysts for alkyne metathesis, developed by Mortreux, consisted of $Mo(CO)_6$ with a phenolic additive forming the active species *in situ*.[10] The nature of this species is not known but assumed to be a Schrock-type carbyne complex. In 1995 Mori[11] reported an application of a similar catalyst system consisting of $Mo(CO)_6$ and 4-chlorophenol for the synthesis of unsymmetrically substituted alkynes. Only few examples with mostly unimpressive yields were reported. The archaic catalyst system however is intriguing in its

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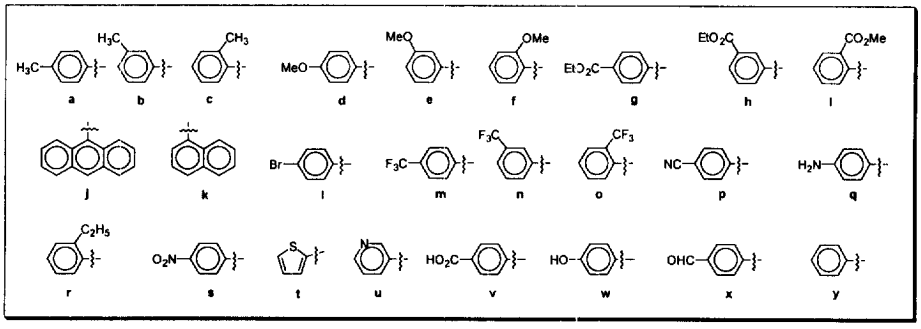
simplicity and ease of application: it forms *in situ* from commercially available reagents in off-the-shelf solvents without prior drying or other purification steps.[12] If it would be possible to optimize the reaction conditions and improve the yields, alkyne metathesis with "instant" catalysts could easily develop into an established synthetic tool.

It was found that an increase in the reaction temperature to 140 °C, employing 1,2-dichlorobenzene as solvent and consequent removal of the formed butyne by introducing a steady stream of pure N_2 into the reaction vessel considerably enhanced the efficiency of the alkyne metathesis.[12] The reaction temperature, 140 °C, and the introduction of pure N_2 led to an anhydrous environment, explaining why off-the-shelf solvents can here be used without decreasing the catalyst efficiency.

Table 1

Ar =	**a**	**b**	**c**	**d**	**e**	**f**	**g**	**h**	**i**	**j**	**k**	**l**	**m**
Yield **2** (%)	83	86	86	79	71	99	81	70	65	5	94	21	12
Yield **3** (%)	**78**	**93**	**96**	**72**	**54**	--	**53**[a]	**53**	--	**10**	**95**	**36**	**49**
Ar =	**n**	**o**	**p**	**q**	**r**	**s**	**t**	**u**	**v**	**w**	**x**	**y**	
Yield **2** (%)	53	16	26	57	78	75	60	40	22	60	87	com	
Yield **3** (%)	**14**	**25**	**15**	**6**[b]	**90**	--	--	--	--	**69**	--	**82**	

[a] $Ti\text{-}(OiPr)_4$ added to reaction [b] 4-aminopropiophenone forms by hydration [c] aryl bromide used for coupling



Synthesis of the propynylated precursors: Utilizing Pd-catalyzed couplings,[13] the precursor propynyls **2** were synthesized by treatment of the iodinated or brominated benzene derivatives **1** with a measured quantity of propyne gas in piperidine and $(PPh_3)_2PdCl_2/CuI$ at 24 °C.[13,14] The reaction was shaken for 4-16 h, and heated in the cases of aryl bromides.[14] Most of these couplings gave high yields of the desired product **2**, (**1**→**2**, Table 1). As of the technical aspect of the propynylation, the amount of starting material **1** applied is calculated according to the exact volume (and thus the exact amount of gaseous propyne introduced) of the Schlenk flask selected. This ensures an economical use of propyne.

Alkyne metathesis with $Mo(CO)_6$/4-chlorophenol or 4-trifluoromethylphenol catalyst system:[15] In a first experiment we subjected the commercially available propynyl benzene (**2y**) to the mixture of $Mo(CO)_6$ and either 4-trifluoromethylphenol or 4-chlorophenol. The maximum coupling yield in this case never exceeded 82% regardless of the used conditions, i.e. variation of the temperature, catalyst amount and reaction time. A similar result was obtained with 4-methylpropynylbenzene (**2a**) which yielded the corresponding 4,4'-dimethyltolane (**3a**) in 78%. The optimum reaction conditions for this coupling are the use of 5 mol% of $Mo(CO)_6$, and 30 mol% of 4-chlorophenol at 140 °C for 12-16 h.[15] In Table 1 the results for the dimerization of propynylated arenes under these conditions are shown.

- *Alkyl substitution:* Treatment of **2c** under the conditions described in the preceding paragraph furnished the corresponding 2,2'-(dimethyldiphenyl)acetylene (**3c**) in 96 % yield after aqueous workup and chromatography. Other 2- and 3-alkyl substituted benzenes and 1-propynylnaphthalene likewise metathesize in almost quantitative yields (see entries **b**, **c**, **k**, and **r**), significantly higher than the unsubstituted propynyl benzene. The slight steric shielding of the propynyl group by the *o*-alkyl groups seems to suppress side reactions efficiently and may protect the formed product.

- *Alkoxy, hydroxy, and carboxy substitution:* Methoxy and ester substituents are tolerated in the alkyne metathesis if positioned in the *p*- or the *m*- position with regard to the propynyl group (entry **d**, **e**, **g**, and **h**). Hydroxy functions in the *p*- position are also amenable to metathesis (entry **w**). The formation of dimers is not quantitative but proceeds in synthetically useful yields. In entry **g** (*p*-carbethoxy) the coupling yield is 36 % but can be increased by addition of 1.0 equivalent of $Ti(OiPr)_4$ to 51 %.[16] When positioned *o*- to the propynyl group, both alkoxy and ester groups shut down the metathesis completely, probably due to internal coordination of the active Mo-containing species.

- *Miscellaneous:* We have as well tested some other substrates for coupling activity and find that propynylated arenes **2** with free electron pairs generally give lower and often unsatisfying yields. A *p*-nitro substituent (**2g**) prevents the metathesis. Likewise, the electron accepting CF_3 groups (entrys **m**, **n**, **and o**) lead to decreased coupling efficiency. An interesting case is the amino-substituted **2q**, which suffers hydration to 4-aminopropiophenone under the reaction conditions and furnishes the dimer **3q** only in trace amounts. Heterocyclic or aldehyde-carrying substrates do not undergo the reaction at all but lead to isolation of starting material.

In conclusion we have been able to show that the catalyst system formed from $Mo(CO)_6$ and 4-chlorophenol in 1,2-dichlorobenzene efficiently catalyzes the dimerization of propynylated arenes. While pure hydrocarbon and *p*-alkoxy and carbethoxy substituted substrates give good to excellent yields in these dimerizations, *o*-positioned donors such as *o*-methoxy, or *o*-carbethoxy as well as heterocyclic substrates, shut down this reaction completely.

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Table 2: ^{1}H and ^{13}C NMR data of the newly synthesized compounds 2 and 3

2a. ^{1}H NMR: δ 7.47 (2H, d), 7.19 (2H, d), 2.35 (3H, s), 2.07 (3H, s); ^{13}C NMR: δ 137.4, 131.3, 128.9, 120.9, 84.9, 79.8, 21.5, 4.5. **2b.** ^{1}H NMR: δ 7.22-7.16 (3H, m), 7.09 (1H, d), 2.30 (3H, s), 2.03 (3H, s); ^{13}C NMR: δ 137.7, 132.0, 128.4, 128.3, 128.0, 123.7, 85.3, 79.8, 21.3, 4.4. **2c.** ^{1}H NMR: δ 7.37 (1H, d), 7.18-7.16 (1H, m), 7.14-7.08 (2H, m), 2.43 (3H, s), 2.10 (3H, s); ^{13}C NMR: δ 139.9, 131.9, 129.3, 127.5, 125.4, 123.8, 89.6, 78.6, 20.6, 4.3. **2d.** ^{1}H NMR: δ 7.33 (2H d), 6.80 (2H, d), 3.76 (3H, s), 2.02 (3H, s); ^{13}C-NMR: δ 158.8, 132.6, 116.1, 113.7, 84.0, 79.4, 55.2, 4.3. **2e.** ^{1}H NMR: δ 7.20-7.16 (1H, t), 7.00-6.98 (1H, d), 6.94-6.93 (1H, t), 6.84-6.81 (1H, m), 3.78 (3H, s), 2.05 (3H, s); ^{13}C-NMR: δ 159.1, 129.1, 124.9, 123.9, 116.3, 114.0, 85.6, 79.6, 55.1, 4.3. **2f.** ^{1}H NMR: δ 7.36 (1H, dd), 7.25-7.19 (1H, m), 6.89-6.82 (2H, m), 3.86 (3H, s), 2.10 (3H, s); ^{13}C NMR: δ 159.8, 133.6, 128.9, 120.4, 113.0, 110.5, 90.0, 77.5, 55.8, 4.8. **2g.** ^{1}H NMR: δ 7.93 (2H, d), 7.41 (2H, d), 4.34 (2H, q, *J*=7.1), 2.04 (3H, s), 1.35 (3H, t, *J*=7.1); ^{13}C NMR: δ 166.1, 131.3, 129.3, 129.2, 128.7, 89.2, 79.3, 61.0, 14.3, 4.4. **2h.** ^{1}H NMR: δ 8.03 (1H, s), 7.91-7.89 (1H, m), 7.52-7.50 (1H, m), 7.33-7.23 (1H, m), 4.33 (2H, q, *J*=7.1), 2.02 (3H, s), 1.36 (3H, t, *J*=7.1); ^{13}C NMR: δ 165.7, 135.3, 132.4, 130.4, 128.3, 128.1, 124.2, 86.7, 78.8, 61.0, 14.3, 4.3. **2i.** ^{1}H NMR: δ 7.83 (1H, dd), 7.47-7.44 (1H, m), 7.36 (1H, ddd), 7.27-7.22 (1H, m), 3.86 (3H, s), 2.07 (3H, s); ^{13}C NMR: δ 166.7, 134.2, 131.8, 131.5, 130.1, 127.1, 124.6, 92.5, 78.3, 52.1, 4.7. **2j.** ^{1}H NMR: δ 8.54 (2H, d), 8.35 (1H, s), 7.97 (2H, d), 7.56-7.43 (4H, m), 2.38 (3H, s). **2k.** ^{1}H NMR: δ 8.36 (1H, d), 7.85-7.76 (2H, m), 7.63 (1H, d), 7.59-7.47 (2H, m), 7.42-7.37 (1H, m), 2.22 (3H, s); ^{13}C NMR: δ 133.4, 133.1, 129.8, 128.0, 127.8, 126.3, 126.2, 126.1, 125.1, 121.7, 90.7, 77.8, 4.7. **2l.** ^{1}H NMR: δ 7.39 (2H, d), 7.23 (2H, d), 2.01 (3H, s); ^{13}C NMR: δ 132.9, 131.5, 123.0, 121.6, 87.2, 78.8, 4.4. **2m.** ^{1}H NMR: δ 7.54 (2H, d), 7.50 (2H, d), 2.07 (3H, s); ^{13}C NMR: δ 131.7, 129.2 (q, *J*=32), 127.9, 125.0 (m), 124.0 (q, *J*=271), 88.7, 78.7, 4.4. **2n.** ^{1}H NMR: δ 7.54 (2H, d), 7.50 (2H, d), 2.07 (3H, s). **2o.** ^{1}H NMR: δ 7.63 (1H, d), 7.55 (1H, d), 7.45-7.42 (1H, m), 7.33 (1H, t), 2.10 (3H, s); ^{13}C NMR: δ 134.0, 131.2 (m), 127.2, 124.0 (q, *J*=33), 92.1, 75.9, 4.5. **2p.** ^{1}H NMR: δ 7.54 (2H, d), 7.43 (2H, d), 2.07 (3H, s); ^{13}C NMR 131.9, 131.8, 128.9, 118.5, 110.7, 91.0, 78.5, 4.5. **2q.** ^{1}H NMR: δ 7.17 (2H, d), 6.55 (2H, d), 3.70 (2H, bs), 2.00 (3H, s); ^{13}C NMR: δ 145.8, 132.5, 117.4, 114.6, 83.1, 79.9, 4.4. **2r.** ^{1}H NMR: δ 7.37 (1H, d), 7.24-7.17 (2H, m), 7.13-7.08 (1H, m), 2.79 (2H, q, *J*=7.6),

2.09 (3H, s), 1.24 (3H, t, *J*=7.6); ^{13}C NMR: δ 145.8, 132.0, 127.7, 127.6, 125.4, 123.0, 89.1, 78.3, 27.7, 14.9, 4.6. **2s.** ^{1}H NMR: δ 8.13 (2H, d), 7.49 (2H, d), 2.08 (3H, s); ^{13}C NMR: δ 132.2, 131.1, 127.2, 123.5, 92.8, 78.5, 4.5. **2t.** ^{1}H NMR: δ 7.17-7.12 (2H, m), 6.95-6.92 (1H, m), 2.08 (3H, s); ^{13}C NMR: δ 130.7, 126.6, 125.7, 124.0, 89.9, 77.3, 4.6. **2u.** ^{1}H NMR: δ 8.53 (1H, s), 8.38 (1H, d), 7.55 (1H, m), 7.09 (1H, m), 1.96 (3H, s); ^{13}C NMR: δ 151.8, 147.4, 137.9, 122.5, 120.7, 89.2, 76.2, 4.1. **2v.** ^{1}H NMR: δ 8.00 (2H, d), 7.45 (2H, d), 2.07 (3H, s); ^{13}C NMR: δ 167.2, 132.4, 130.6, 130.5, 129.8, 90.2, 79.9, 4.2. **2w.** ^{1}H NMR: δ 7.27 (2H, d), 6.73 (2H, d), 5.13 (1H, s), 2.02 (3H, s); ^{13}C NMR: δ 154.7, 132.9, 116.3, 115.2, 84.2, 79.3, 4.4. **2x.** ^{1}H NMR: δ 9.97 (1H, s), 7.78 (2H, d), 7.39 (2H, d), 2.08 (3H, s); ^{13}C NMR: δ 191.2, 134.9, 131.9, 130.4, 129.4, 90.6, 79.2, 4.6.

3a. ^{1}H NMR: δ 7.47 (4H, d), 7.19 (4H, d), 2.41 (6H, s); ^{13}C NMR: δ 138.0, 131.3, 128.9, 120.3, 88.8, 21.5. **3b.** m.p. 73-75; ^{1}H NMR δ 7.36 (4H, m), 7.25 (2H, m), 7.17 (2H, m), 2.36 (6H, s); ^{13}C NMR: δ 137.8, 132.1, 129.0, 128.6, 128.1, 123.1, 89.2, 21.3. **3c** see ref.[16]. **3d** see ref.[16] **3e.** ^{1}H NMR: δ 7.25 (2H, m), 7.14 (2H, m), 7.07 (2H, m), 6.89 (2H, m), 3.81 (6H, s); ^{13}C NMR: δ 159.1, 129.3, 124.1, 116.3, 114.9, 89.1, 55.3. **3g.** m.p. 146-148; ^{1}H NMR: δ 7.93 (4H, d), 7.41 (4H, d), 4.37 (4H, q, *J*=7.1), 1.39 (6H, t, *J*=7.1); ^{13}C NMR: δ 165.8, 131.5, 130.2, 129.4, 127.2, 91.3, 61.2, 14.4. **3h.** m.p. 72-74; ^{1}H NMR: δ 8.20-8.19 (2H, m), 8.01-7.98 (2H, m), 7.69-7.67 (2H, m), 7.43-7.39 (2H, m), 4.38 (4H, q, *J*=7.1), 1.39 (6H, t, *J*=7.1); ^{13}C NMR: δ 165.6, 135.4, 132.6, 130.7, 129.3, 128.3, 123.1, 89.1, 61.2, 14.4. **3j.** ^{1}H NMR: δ 8.54 (4H, d), 8.35 (2H, s), 7.97 (4H, d), 7.56-7.43 (8H, m). **3k.** m.p. 127-129; ^{1}H NMR. δ 8.56 (2H, d), 7.91-7.88 (6H, m), 7.66-7.62 (2H, m), 7.58-7.49 (4H, m); ^{13}C NMR: δ 133.4, 130.7, 128.9, 128.4, 127.0, 126.6, 126.4, 125.4, 121.2, 92.5. **3l.** m.p. 184-185; ^{1}H NMR: δ 7.48 (4H, d), 7.37 (4H, d); ^{13}C NMR: δ 132.9, 131.6, 122.7, 121.8, 89.4. **3m.** ^{1}H NMR: δ 7.63 (8H, m); ^{13}C NMR: δ 131.9, 125.3 (q, *J*=33), 126.3, 125.3 (m), 123.74 (q, *J*=271), 90.1. **3n.** ^{1}H NMR: δ 7.81 (2H, s), 7.71 (2H, m), 7.61 (2H, m), 7.50 (2H, m); ^{13}C NMR: δ 134.6, 131.0 (q, *J*=32), 128.9, 128.4 (m), 125.2 (m), 123.5, 123.6 (q, *J*=271), 89.2. **3o.** ^{1}H NMR δ 7.69 (4H, m), 7.54 (2H, m), 7.44 (2H, m); ^{13}C NMR δ 134.1, 131.4 (m), 128.4, 125.8 (m), 123.4 (q, *J*=273), 120.9, 90.6. **3p.** ^{1}H NMR: δ 7.66 (4H, dd), 7.62 (4H, dd); ^{13}C NMR: δ 132.1, 132.0, 126.9, 118.1, 112.3, 91.5. **3q.** ^{1}H NMR: δ 7.15 (4H, d), 6.75 (4H, d), 2.52 (4H, bs). **3r.** ^{1}H NMR: δ 7.54 (2H, d), 7.28 (4H, m), 7.20 (2H, m), 2.93, (4H, q, *J*=7.6), 1.33 (6H, t, *J*=7.5); ^{13}C NMR: δ 145.9, 132.1, 128.3, 127.9, 125.6, 122.6, 91.5, 28.0, 15.2. **3w** see ref.[11]

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14 Experimental: propynylation (1➞2) A 1000 mL flame-dried Schlenk flask containing the aryl iodide or aryl bromide (50.0 mmol), $Pd(PPh_3)_2Cl_2$ (1.75 g, 2.5 mmol), CuI (0.950 g, 5.0 mmol), and 40 mL piperidine (triethylamine for aryl bromides) is degassed and evacuated. After the addition of one atmosphere of propyne the clear green solution changes to yellow. The reaction mixture is shaken for 4-16 h. In the case of aryl bromides, additional heating to 65 °C overnight is necessary. Aqueous workup followed by evaporation of solvent yields a crude product which is purified *via* filtration through a silica gel column or vacuum distillation (0.1 Torr, ~75 °C).

Experimental: alkyne metathesis (2➞3) In a typical reaction, **2a** (1.0 g, 7.69 mmol) and the catalyst system consisting of $Mo(CO)_6$ (0.047 g, 0.19 mmol) and 4-chlorophenol (0.147g, 1.14 mmol) were dissolved in 10 mL of 1,2-dichlorobenzene and stirred at 140 °C for an average of 12-16 h, removing butyne by a slow stream of nitrogen. Aqueous workup followed by evaporation of solvent yields a crude product which is purified *via* filtration through a silica gel column.

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