Nickel-Catalyzed Tetramerization of Alkynes: Synthesis and Structure of Octatetraenes[†]
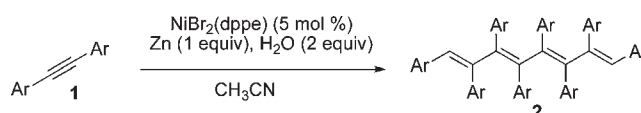
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ABSTRACT

In the presence of a catalytic system comprised of NiBr$_2$(dppe) and Zn, arylacetylenes undergo tetramerization to form linear octatetraenes, generally in good to excellent yields. The structure of the coupling products was verified by X-ray crystallography.

Alkynes are ideal building blocks and synthons for a variety of interesting and important π-conjugated molecules. The unique reactivity of the *sp*-hybridized carbon provides an essential method for the construction of carbon−carbon bonds.[1] One such method for carbon−carbon bond construction is the metal-catalyzed self-reaction of alkynes. Transition-metal catalysts are used in these reactions to increase the efficiency of alkyne coupling. There are numerous examples of reactions of this type, including (cyclo)dimerization,[2] (cyclo)trimerization,[3] and cyclotetramerization.[4] In contrast to these reactions, we recently observed that linear tetraenes **2** can be directly generated from alkynes **1** using nickel catalysts. Compounds **2** should be suitable precursors for the synthesis of polycyclic aromatic hydrocarbons, and these linearly conjugated oligoenes could possess interesting properties in material science.[5] Herein, this study investigates the scope and limitations of this reaction and analyzes the structures of the coupling products.

Heating diphenylacetylene (**1a**) in acetonitrile with a mixture of NiBr$_2$(dppe) and Zn gave octatetraene **2a** in low yield (entry 1 in Table 1).[6] Systematic studies of the reaction conditions have revealed that a nickel catalyst, water, solvent, and temperature all crucially affect

[†] Metal-Catalyzed Reactions of Alkynes. Part XI. Part X: Hsu, S.-F.; Ko, C.-W.; Wu, Y.-T. *Adv. Synth. Catal.* **2011**, *353*, 1756.

(1) (a) *Acetylene Chemistry: Chemistry, Biology, and Material Science*; Stang, P. J., Tykwinski, R. R., Diederich, F., Eds.; Wiley-VCH: Weinheim, 2005. (b) *Carbon-Rich Compounds: From Molecules to Materials*; Haley, M. M., Tykwinski, R. R., Eds.; Wiley-VCH: Weinheim, 2006.

(2) For dimerization of internal alkynes, see: (a) Sakabe, K.; Tsurugi, H.; Hirano, K.; Satoh, T.; Miura, M. *Chem.—Eur. J.* **2010**, *16*, 445. (b) Eisch, J. J.; Adeosun, A. A.; Birmingham, J. M. *Eur. J. Inorg. Chem.* **2007**, 39. (c) Jaroschik, F.; Nief, F.; Le Goff, X.-F.; Ricard, L. *Organometallics* **2007**, *26*, 1123. For cyclobutadiene complex, see:(d) Wolf, R.; Schnoeckelborg, E.-M. *Chem. Commun.* **2010**, 2832. For dimerization of terminal alkynes forming enynes, see:(e) Trost, B. M.; Sorum, M. T.; Chan, C.; Harms, A. E.; Rühter, G. *J. Am. Chem. Soc.* **1997**, *119*, 698 and references therein.

(3) For recent reviews for formal [2 + 2 + 2] cyclotrimerizations, see: (a) Tanaka, K. *Chem.—Asian J.* **2009**, *4*, 508. (b) Chopade, P. R.; Louie, J. *Adv. Synth. Catal.* **2006**, *348*, 2307. For a rare cycloisomerization, see: (c) Wu, Y.-T.; Kuo, M.-Y.; Chang, Y.-T.; Shin, C.-C.; Wu, T.-C.; Tai, C.-C.; Cheng, T.-H.; Liu, W.-S. *Angew. Chem., Int. Ed.* **2008**, *47*, 9891. Linear and angular trimerization of terminal alkynes forms dienynes, see:(d) Wu, Y.-T.; Lin, W.-C.; Liu, C.-J.; Wu, C.-I. *Adv. Synth. Catal.* **2008**, *350*, 1841 and references therein.

(4) For Ni-catalyzed protocols, see: (a) Wender, P. A.; Christy, J. P.; Lesser, A. B.; Gieseler, M. T. *Angew. Chem., Int. Ed.* **2009**, *48*, 7687 and references therein. (b) Goswami, A.; Ito, T.; Saino, N.; Kase, K.; Matsunoa, Okamoto, S. *Chem. Commun.* **2009**, 439. For review, see: (c) Saito, S. In *Modern Organonickel Chemistry*; Tamaru, Y., Ed.; Wiley-VCH: Weinheim, 2005; p 171. For copper-mediated examples, see: (d) Yamamoto, Y.; Ohno, T.; Itoh, K. *Chem.—Eur. J.* **2002**, *8*, 4734. (e) Takahashi, T.; Sun, W.; Nakajima, K. *Chem. Commun.* **1999**, 1595. For review, see:(f) Takahashi, T.; Li, Y. In *Titanium and Zirconium in Organic Synthesis*; Marek, I., Ed.; Wiley-VCH: Weinheim, 2002, p 50.

(5) Reviews for applications of oligoenes in material science, see: (a) Dalton, L. R.; Sullivan, P. A.; Bale, D. H. *Chem. Rev.* **2010**, *110*, 25. (b) Meier, H. *Angew. Chem., Int. Ed.* **2005**, *44*, 2482. (c) Schwab, P. F. H.; Smith, J. R.; Michl, J. *Chem. Rev.* **2005**, *105*, 1197. (d) Martin, R. E.; Diederich, F. *Angew. Chem., Int. Ed.* **1999**, *38*, 1350. (e) *Electronic Materials: The Oligomer Approach*; Müllen, K., Wegner, G., Eds.; Wiley-VCH: Weinheim, 1998.

(6) The catalytic system comprised of NiBr$_2$(dppe), and Zn is also used in the cocyclotrimerization of alkynes; see: (a) Hsieh, J. C.; Cheng, C. H. *Chem. Commun.* **2008**, 2992. (b) Hsieh, J. C.; Cheng, C. H. *Chem. Commun.* **2005**, 2459. (c) Jeevanandam, A.; Korivi, R. P.; Huang, I. W.; Cheng, C. H. *Org. Lett.* **2002**, *4*, 807.

this reaction. Adding 2 equiv of water dramatically increased the yield of octatetraene **2a**, whereas its absence or large excess inhibited the reaction (entries 1−3 in Table 1). Unlike other solvents, such as methanol, o-xylene,

Table 1. Optimization of Reaction Conditions for Preparing **2a**[a]
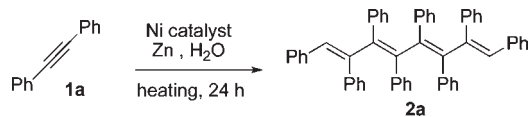
| entry	catalyst	solvent	temp [°C]	conv (%)	yield (%)[b]
1	NiBr₂(dppe)	CH₃CN	130	40	22[c]
2	NiBr₂(dppe)	CH₃CN	130	100	79
3	NiBr₂(dppe)	CH₃CN	130	78	66[d]
4	NiBr₂(dppe)	CH₃CN	110	100	82
5	NiBr₂(dppe)	CH₃CN	80	65	61
6	NiBr₂(dppe)	CH₃OH	80	0	0
7	NiBr₂(dppe)	o-xylene	110	49	6
8	NiBr₂(dppe)	dioxane	110	54	19
9	NiBr₂(dppe)	DMF	110	86	13
10	NiBr₂·3H₂O	CH₃CN	110	23	14
11	NiCl₂(PPh₃)₂	CH₃CN	110	89	65[e]
12	NiCl₂(acac)₂	CH₃CN	110	0	0
13	NiBr₂(dme)	CH₃CN	110	40	10
14	NiCl₂(dppp)	CH₃CN	110	51	31
15	NiCl₂(dppe)	CH₃CN	110	60	29

[a] A mixture of alkyne **1a** (1.0 mmol), Ni catalyst (5 mol %), Zn (1.0 mmol), and water (2.0 mmol) in a solvent (2.5 mL) was heated for 24 h. acac = acetylacetone. The conversion of **1a** was determined by GC MS. [b] Isolated yield for **2a**. [c] No additional water was added. [d] Water (40 mmol) was used. [e] Hexaphenylbenzene (21%) was obtained.

1,4-dioxane, and DMF, acetonitrile yielded excellent results (entries 6−9 in Table 1). Catalyst NiBr₂(dppe) was found to absolutely outperform the other catalysts listed in Table 1. NiCl₂(PPh₃)₂ formed a significant amount of hexaphenylbenzene as a byproduct. Apparently, reactions that were conducted at 110 °C were better than those run at 80 or 130 °C (entries 2, 4, and 5 in Table 1). Under the optimal conditions, **2a** was obtained in 82% yield and a large-scale synthesis gave a slightly low yield (73%, entry 1 in Table 2). Although the ¹H NMR spectrum of **2a** has been reported elsewhere, the small difference between the data in the literature[7] and the analytical data obtained herein motivated us to further reanalyze its structure by X-ray crystallography.[8] Octatetraene **2a** can also be generated by oxidative addition of 2,3,4,5-tetraphenyl-1-ziconacyclopentadiene,[7] but the protocol developed herein is more efficient and convenient. The protons at positions C1 and C8 in **2a** mainly (>91%) come from the added water, according

(7) Takahashi, T.; Liu, Y.; Iesato, A.; Chaki, S.; Nakajima, K.; Kanno, K.-i. *J. Am. Chem. Soc.* **2005**, *127*, 11928.

(8) X-ray crystallographic data for compounds **2a** (CCDC-823434), **3n** (CCDC-823438), **4** (CCDC-823439), *syn*-**6b** (CCDC-823436), and *anti*-**6b** (CCDC-823437) can be obtained from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/const/retrieving.html.

to the results of an isotopic experiment that was performed with deuterium oxide.

The reactivity of many alkynes **1** was investigated (Table 2). Most of them generated the corresponding cycloadducts **2** in moderate to good yields. Sterically congested and/or electron-deficient substituents strongly reduced the reaction efficiency and gave diarylalkenes and/or tetraarylbutadienes as byproducts in considerable quantities (entries 5, 7, and 10 in Table 2). Unlike other

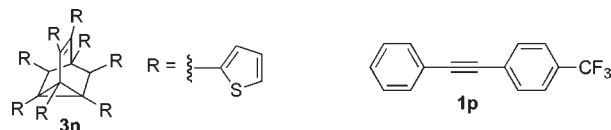**Table 2.** Preparation of Octatetraenes **2** from Alkynes **1**[a]
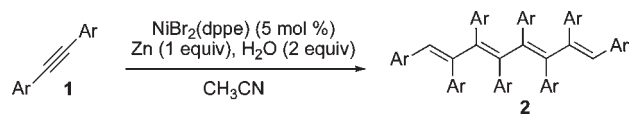
entry	alkyne	Ar	temp [°C]/ time [h]	conv (%)	product (yield, %[b])
1	1a	Ph	110/24	100	2a (82, 73[c])
2	1b	4-OCH₃-C₆H₄	110/24	100	2b (85[d])
3	1c	4-CH₃-C₆H₄	110/24	100	2c (84)
4	1d	4-tBu-C₆H₄	110/24	100	2d (82)
5	1e	4-F-C₆H₄	110/24	100	2e (60)
6	1f	4-Cl-C₆H₄	130/24	100	2f (57)
7	1g	4-CF₃-C₆H₄	110/24	31	2g (17)
8	1h	3-OCH₃-C₆H₄	110/24	100	2h (87)
9	1i	3-CH₃-C₆H₄	110/24	100	2i (84)
10	1j	2-CH₃-C₆H₄	130/60	25	2j (trace[e])
11	1k	3,5-(OCH₃)₂-C₆H₃	110/24	100	2k (86)
12	1l	3,5-(CH₃)₂-C₆H₃	110/24	100	2l (85)
13	1m		110/24	92	2m (74)
14	1n	2-thiophenyl	130/24	100	2n (trace[f])

[a] Reaction scale: alkyne **1** (1.0 mmol). The conversion of **1** was determined by GC MS. [b] Isolated yield for **2**. [c] Reaction was conducted with 10 mmol of **1a**. [d] Containing an inseparable byproduct (approximately 5%). [e] The reaction was conducted with NiBr₂(dppe) (10 mol %) and Zn (3.0 mmol). [f] **3n** was isolated in 74% yield.

examples, di(2-thiophenyl)ethyne (**1n**) produced tricyclo-[3.2.1.0²,⁷]oct-3-ene **3n** (entry 14 in Table 2).[8] This undesired product should be produced from a octatetraene derivative (see below). Notably, 4-octyne and phenylacetylene cannot be used in this reaction because they mainly furnished benzene derivatives by formal [2 + 2 + 2] cyclotrimerization.

The steric effects rather than the electronic properties of substituents in asymmetric alkynes dominated the regioselectivity in the coupling reaction. For instance,
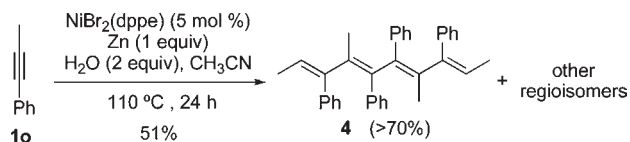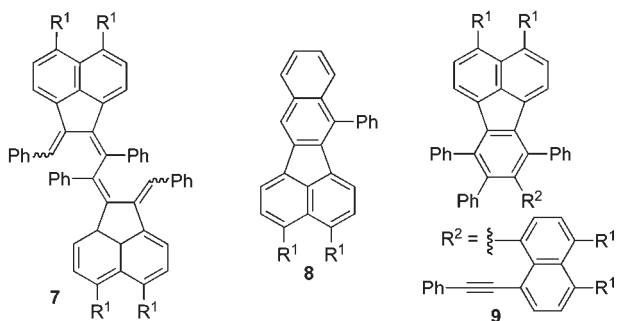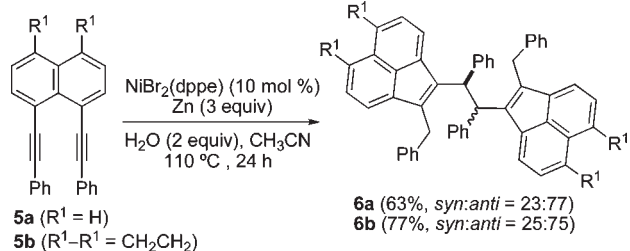

1-phenyl-1-propyne (**1o**) generated **4** as the major product (Scheme 1), whereas 1-(phenylethynyl)-4-(trifluoromethyl)-benzene (**1p**) gave complex regioisomers. Pure **4** was obtained by crystallization (see Supporting Information).[8]

Scheme 1. Reaction of 1-Phenyl-1-propyne (**1o**)

Under the optimal conditions developed herein, diyne **5b** produced a mixture of **8b** (13%) and **9b** (78%) by cyclization and formal [(2 + 2) + 2] cycloaddition,[9] respectively (Scheme 2). This undesired result can be improved by treating diynes **5** with more catalyst (10 mol %) and zinc (3 equiv), giving good yields of the coupling products **6**, accompanied by small amounts of **8** (approximately 10%). Compounds **6** were obtained in two stereoisomeric forms, which can only be distinguished by X-ray crystallography.[8] The *anti*-stereoisomers were determined to be the major products. Apparently, **6** should be generated from the expected products **7** through *in situ* reduction. An attempt was made to produce **7a** by oxidizing **6a** using DDQ (2, 3-dichloro-5,6-dicyanobenzoquinone). Interestingly, the reaction with excess DDQ at 110 °C formed compound **9a** in 81% yield.[10,11]

Scheme 2. Reaction of Diynes **5**

Scheme 3. Proposed Mechanism

Scheme 3 presents a putative reaction mechanism of the tetramerization of alkyne **1** based on the literature and the findings of the above experiments. Zinc reduces the precatalyst [Ni]X_2 to generate Ni(0), which undergoes oxidative cycloaddition with alkyne **1** to furnish 1-nickellacyclopentadiene **11**. As suggested by Eisch et al.,[12] the dimerization of **11** yields complex **12**,[13,14] which reacts with water to produce complex **14** via intermediate **13**. The crowded environment in **14** promotes the Ni-mediated *cis−trans* isomerization at positions C3−C6 to form **10**. The presence of **3n** perhaps supports isomerization (see below). Reductive elimination of **10** gives the desired product **2** and Ni(0) species. Notably, nickel oxide is the possible byproduct of this catalytic cycle, and it can eventually be transformed into the active Ni(0) complex by reduction with zinc. The selective formation of **4** should depend on the reactivity
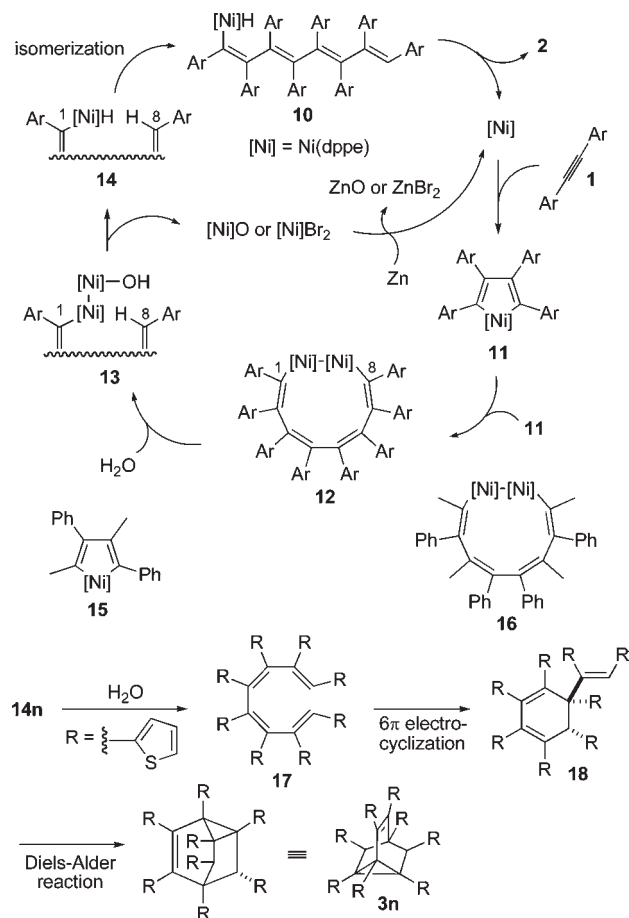
(9) For Rh-catalyzed [(2 + 2) + 2] cycloaddition of **5** with alkynes, see: (a) Wu, Y.-T.; Linden, A.; Siegel, J. S. *Org. Lett.* **2005**, *7*, 4353. (b) Wu, Y.-T.; Hayama, T.; Baldridge, K. K.; Linden, A.; Siegel, J. S. *J. Am. Chem. Soc.* **2006**, *128*, 6870.

(10) For examples for the DDQ-mediated dehydrogenative cross-coupling reaction, see: Zhang, Y.; Li, C.-J. *J. Am. Chem. Soc.* **2006**, *128*, 4242.

(11) The reaction should be through a radical-type cyclization, and the intermediate can be isolated in good yield (89%) when the reaction was conducted under mild conditions (50 °C); see Supporting Information.

(12) Eisch, J. J.; Piotrowski, A. M.; Han, K. I.; Krüger, C.; Tsay, Y. H. *Organometallics* **1985**, *4*, 224. For X-ray crystallographic structure of a 10-membered dinuclear nickellacycle, see: Ramakrishna., T. V. V.; Sharp, P. R. *Organometallics* **2004**, *23*, 3079.

(13) As shown in Scheme 2, a high loading of catalysts selectively yields compounds **6**, and this result may be evidence of the dimeric mechanism.

(14) For other proposed mechanism for the dimerization of 1-nickellacyclopentadienes, see: (a) Wilke, G. *Pure Appl. Chem.* **1978**, *50*, 677. (b) Lawrie, C. J.; Gable, K. P.; Carpenter, B. K. *Organometallics* **1989**, *8*, 2274.

and the stability of 1-nickellacyclopentadienes. Other regioisomers of **15** should also be generated, but they would easily form butadienes and [2 + 2] cycloadducts. Like other tetraaryl-substituted complexes, **15** undergoes dimerization to form **16**, and the carbon—carbon bond formation occurs at the carbon with the phenyl substituent, rather than the one with the methyl group.

The reaction of acyclic conjugated tetraenes in the literature provided very useful information for establishing a reasonable mechanism of the formation of the unusual product **3n**.[15] Based on careful analysis of the structure of **3n** determined by X-ray crystallography,[8] the key inter-

mediate of the cascade reaction should be tetraene **17**, which can be generated from **14n** by reductive elimination. Compound **17** undergoes 6π electrocyclization[15,16] and a subsequent intramolecular Diels—Alder reaction[17] to give **3n** via cyclohexadiene **18**.

In conclusion, this work provided a simple approach for generating octatetraenes **2** directly from alkynes **1**. Further studies of the physical properties of these molecules and their use in synthesizing new polycyclic aromatic hydrocarbons are currently underway.

Supporting Information Available. Experimental procedures and characterizations, NMR spectra, and crystal data. This material is available free of charge via the Internet at http://pubs.acs.org.

(15) (a) Skropetaa, D.; Rickards, R. W. *Tetrahedron Lett.* **2007**, *48*, 3281. (b) Marvell, E. N.; Seubert, J.; Vogt, G.; Zimmer, G.; Moy, G.; Siegmann, J. R. *Tetrahedron* **1978**, *34*, 1323.

(16) Tetraene **17** should not be generated from **2n** by thermolytic *trans—cis* isomerization. When a solution of **2a** in diphenyl ether was heated at 200 °C for 24 h, compound **3a** was not obtained.

(17) (a) Heimbach, P.; Ploner, K.-J.; Thornel, F. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 276. (b) Ng, S. M.; Beaudry, C. M.; Trauner, D. *Org. Lett.* **2003**, *5*, 1701. (c) Giomi, D.; Nesi, R.; Turchi, S.; Mura, E. *J. Org. Chem.* **2000**, *65*, 360.