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Intramolecular Cyclotrimerization of Triynes Catalyzed by N-Heterocyclic Carbene–$CoCl_2$/Zn or –$FeCl_3$/Zn

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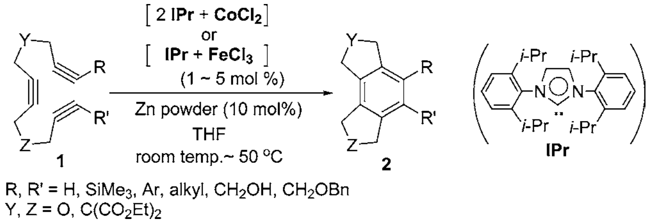
ABSTRACT



Triynes 1 could effectively be cyclotrimerized to annulated benzenes 2 by treatment with a catalytic amount of zinc powder, N-heterocyclic carbene, and $CoCl_2$ or $FeCl_3$.

Catalytic [2 + 2 + 2] cyclotrimerization of alkynes is a valuable means for synthesis of highly substituted and/or annulated benzenes.[1,2] Transformations of this variety are attractive by virtue of their intrinsic atom economy,[3] as well as the importance of benzenes as synthetic intermediates. Complexes of many transition metals (e.g., Co, Rh, Ir, Ru, Ni, Pd, and Ti) have been shown to be effective catalysts for this process. Among them, CpCo complexes (Cp = cyclopentadienyl) such as $CpCo(CO)_2$ have been used most widely, numerous applications of which have been reported for preparation of natural products, pharmaceutically important molecules, and functional materials.[4] Recently, Chiusoli,[5] and Malacria[6] reported CoX_2/Mn and CoX_2/PR_3/Mn reagents, respectively, as a catalyst system for the cyclotrimerization,[7] the CO-free characteristic of which contributed to easy initiation of the catalysis under relatively milder reaction conditions compared to those with $CpCo(CO)_2$; however, further study of the reactions and their application have not been explored. Herein we describe a novel Cp- and CO-free system for cyclotrimerization of triynes which is catalyzed by a $CoCl_2$−imidazolium carbene[8] reagent in the presence of Zn powder, and we also found that an $FeCl_3$−imidazolium carbene reagent in the presence of Zn powder can effectively catalyze cyclotrimerization.

First, we investigated the catalytic ability of several transition metal salts for cycloisomerization in the presence

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(5) Chiusoli, G. P.; Costa, M.; Reverberi, S.; Terenghi, M. G. *Transition Met. Chem.* **1989**, *14*, 238. Chiusoli, G. P.; Terenghi, G. *Transition Met. Chem.* **1984**, *9*, 360.

(6) Slowinski, F.; Aubert, C.; Malacria, M. *Adv. Synth. Catal.* **2001**, *343*, 64.

(7) The CoI_2/Zn-catalyzed cycloaddition of norbornadiene and alkynes has been reported: Duan, I.-F.; Cheng, C.-H.; Shaw, F.-S.; Cheng, S. S.; Liou, K. F. *J. Chem. Soc., Chem. Commun.* **1991**, 1347. Pardigon, O.; Tenaglia, A.; Buono, G. *J. Org. Chem.* **1995**, *60*, 1868.

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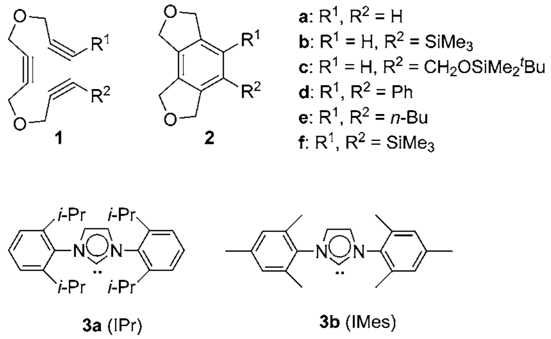
of an imidazolium carbene and zinc powder as a reducing agent. Thus, a 1:1 or 2:1 mixture of imidazolium carbene **3**[9] (Figure 1) and transition metal salts (1−5 mol %) such as $FeCl_2$, $FeCl_3$, $CoCl_2$, CoI_2, $Co(acac)_2$, $NiCl_2$, and $PdCl_2$ in THF was mixed with triyne **1a** and a zinc powder (10 mol %), and the resulting mixture was stirred at room temperature or 50 °C.



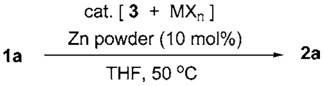
1 **2** **3a** (IPr) **3b** (IMes)

Figure 1.

The results summarized in Table 1 show that these transition metal salts could catalyze the transformation of **1a** to **2a** in the presence of imidazolium carbene IPr (**3a**) and zinc powder. Among them, a 2:1 mixture of **3a** and $CoCl_2$ (entries 2 and 3) and a 2:1 or 1:1 mixture of **3a** and $FeCl_3$ (entries 9 and 10) were found to be effective catalyst precursors, where the reaction provided **2a** in a quantitative yield. The results shown in entry 2 indicate that an active species could be generated at room temperature, and an increase of the reaction temperature to 50 °C accelerated the reaction rate (entry 3). IPr (**3a**) was better than IMes (**3b**) as a ligand for these processes (entries 5 and 11). The reaction of **1a** with a 2:1 mixture of **3a** and $CoCl_2$ in the presence of a metal powder other than Zn, such as Al, Mg, and Mn, did not proceed. Imidazolium carbene−$NiCl_2$ and −$PdCl_2$ were also candidates as catalyst precursors for the reaction.[10]

With these results in hand, we next carried out the reaction of 1,4-diprop-2-ynyloxybut-2-yne derivatives **1b**−**f** with a [2 × **3a** + $CoCl_2$] or [**3a** + $FeCl_3$] reagent as a catalyst precursor under the reaction conditions shown in Table 2. In all cases the cyclotrimerized product **2** was provided. Triynes **1** having a terminal alkyne moiety could effectively be transformed to the corresponding **2** by both cobalt- and iron-based reagents at 50 °C (entries 1−3 and 7−9). Although the reaction of disubstituted triynes **1d**−**f** at 50 °C resulted in a low yield of **2** probably due to their steric hindrance, an increase of temperature to reflux improved the yields of fully substituted benzenes **1e** and **1f** (entries 5, 6, 11, and 12).

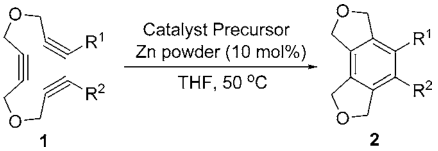
Table 1.



entry	metal salt (mol %)	3 (mol %)	time, h	yield of **2a**,[a] %
1	$CoCl_2$ (1)		24	trace
2	$CoCl_2$ (1)	**3a** (2)	12 (room temp)	74
3[b]	$CoCl_2$ (1)	**3a** (2)	12	~100
4	$CoCl_2$ (1)	**3a** (1)	24	trace
5	$CoCl_2$ (1)	**3b** (2)	24	trace
6	CoI_2 (1)	**3a** (2)	12	12
7	$Co(acac)_2$ (2)	**3a** (4)	24	16
8	$FeCl_2$ (5)	**3a** (10)	24	49
9	$FeCl_3$ (2)	**3a** (4)	48	~100
10	$FeCl_3$ (2)	**3a** (2)	24	91
11	$FeCl_3$ (5)	**3b** (10)	24	58
12	$NiCl_2$ (5)	**3a** (10)	24	68
13	$PdCl_2$ (2)	**3a** (4)	48	16

[a] Determined by ^{1}H NMR analysis using an internal standard. The crude mixture consisted of **2a** and recovered **1a**. [b] Use of powder of other metals powder such as Mn, Al, Mg, instead of Zn did not yield **2a**.

Table 2.



entry	catalyst		1	time, h	yield of **2**,[a] %
1	[2 × **3a** + $CoCl_2$]	(1 mol %)	**1a**	12	98
2		(2 mol %)	**1b**	48	96
3		(2 mol %)	**1c**	24	90
4		(3 mol %)	**1d**	40	5[b,c]
5		(2 mol %)	**1e**	48	57[c] (95)[d]
6		(3 mol %)	**1f**	40	20[b,c] (86)[d]
7	[**3a** + $FeCl_3$]	(2 mol %)	**1a**	24	91
8		(2 mol %)	**1b**	48	98
9		(2 mol %)	**1c**	48	85[c]
10		(2 mol %)	**1d**	48	90
11		(2 mol %)	**1e**	48	69[c] (98)[d]
12		(2 mol %)	**1f**	48	31[b,c] (66)[d]

[a] Isolated yield unless otherwise indicated. [b] Determined by ^{1}H NMR analysis using an internal standard. [c] The crude mixture consisted of **2** and recovered **1**. [d] The mixture was refluxed for 48 h.

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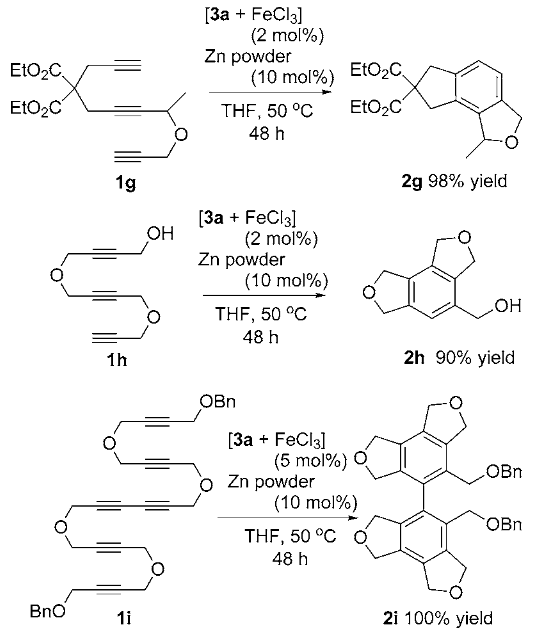
(9) Imidazolium carbenes **3** were prepared as a THF solution from the corresponding imidazolium chloride and n-BuLi prior to use (see Supporting Information). These imidazolium chlorides, IPr−HCl and IMes−HCl, are commercially available from Strem Chemicals, Inc.

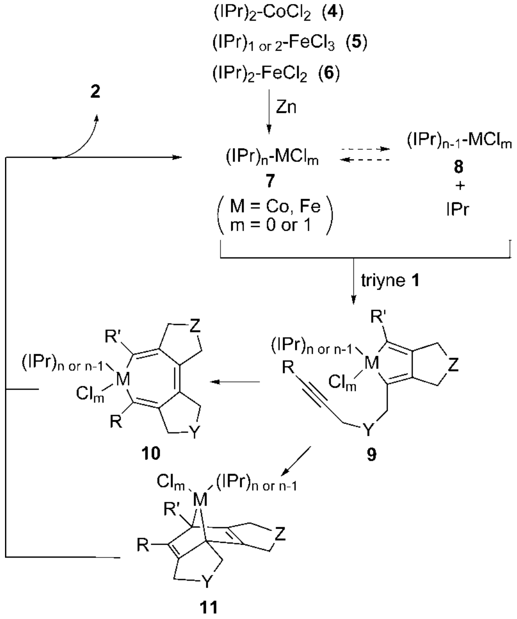
Scheme 1 illustrates other representative examples of the present benzene-formation reaction with a catalytic amount of a [**3a** + $FeCl_3$] reagent and zinc powder in THF, the results of which feature the following characteristics: The reaction was compatible with functional groups such as ester, hydroxy, and benzyloxy moieties.[11] The formation of carbocyclic as well as O-heterocyclic compounds was possible. Double cyclotrimerization of hexaynes to biaryl compounds could effectively be carried out.

Scheme 1



Although confirmation of the reaction mechanism must await further study, as illustrated in Scheme 2 we postulate the reaction course based on those proposed for reported metal-catalyzed reactions.[2] Thus, in the solution prepared by mixing MCl_{m+2} (M = Co or Fe, $m = 0$ or 1) and IPr (**3a**), the imidazolium carbene complexes $(IPr)_n{-}MCl_{m+2}$ **4**, **5** or **6** may be generated.[12,13] They can readily be reduced by Zn powder to give the corresponding low valent complexes **7**, which may be in equilibrium with IPr-dissociated complex **8** (when $n = 2$). These complexes may be metastable and can quickly react with triynes **1** to give metallacyclopentadienes **9**,[14] which may further be cyclized to **10** and/or **11** through an insertion or [4 + 2]-cycloaddition pathway, respectively. Reductive elimination reaction of **10** and/or **11** yields annulated benzenes **2** and regenerates the low valent complexes **7** and/or **8**.

Scheme 2



In summary, we have found that transition metal salts of Co, Fe, Pd, and Ni could catalyze intramolecular cyclotrimerization of triynes in the presence of imidazolium carbene and zinc powder. The reagent combinations of imidazolium carbene$-CoCl_2$ and $-FeCl_3$ were good catalyst precursors and could transform a variety of triynes to annulated benzenes in good to excellent yields. To our best knowledge, the latter is the first example of homogeneous iron-catalyzed cyclotrimerization of triynes.[15]

Supporting Information Available: Experimental procedures and characterization for compounds **2a**−**i**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) Further investigation of the NiX_2- and PdX_2-catalyzed cyclotrimerization in the presence of imidazolium carbene is underway in our laboratories. The [2 + 2 + 2] cycloaddition reactions of diynes with nitriles, isocyanates, CO_2, and aldehydes catalyzed by imidazolium and 4,5-dihydroimidazolium carbene/$Ni(cod)_2$ reagents have been reported: McCormick, M. M.; Duong, H. A.; Zuo, G.; Louie, J. *J. Am. Chem. Soc.* **2005**, *127*, 5030 and references therein.

(11) The reaction of **1g** with a [2 × **3a** + $CoCl_2$]/Zn reagent did not proceed.

(12) Attempts to isolate these complexes were unsuccessful. The THF solution of [2 × **3a** + $CoCl_2$] or [**3a** + $FeCl_3$] could be stored in a few days under inert atmosphere.

(13) For recent examples of imidazolium carbene−cobalt complexes, see: (a) Van Rensburg, H.; Tooze, R. P.; Foster, D. F.; Slawin, A. M. Z. *Inorg. Chem.* **2004**, *43*, 2468. (b) Fooladi, E.; Dalhus, B.; Tilset, M. *Dalton Trans.* **2004**, 3909. (c) Hu, X.; Meyer, K. *J. Am. Chem. Soc.* **2004**, *126*, 16322. (d) Hu, X.; Castro-Rodriguez, I.; Meyer, K. *J. Am. Chem. Soc.* **2004**, *126*, 13464. (e) Poulton, A. M.; Christie, S. D. R.; Fryatt, R.; Dale, S. H.; Elsegood, M. R. J.; Andrews, D. M. *Synlett* **2004**, 2103. (f) McGuinness, D. S.; Gibson, V. C.; Steed, J. W. *Organometallics* **2004**, *23*, 6288. (g) Danopoulos, A. A.; Wright, J. A.; Motherwell, W. B.; Ellwood, S. *Organometallics* **2004**, *23*, 4807−4810. For recent examples of imidazolium carbene−iron complexes, see: (h) Nehete, U. N.; Anantharaman, G.; Chandrasekhar, V.; Murugavel, R.; Walawalkar, M. G.; Roesky, H. W.; Vidovic, D.; Magull, J.; Samwer, K.; Sass, B. *Angew. Chem., Int. Ed. Engl.* **2004**, *43*, 3832. (i) Danopoulos, A. A.; Tsoureas, N.; Wright, J. A.; Light, M. E. *Organometallics* **2004**, *23*, 166. See also ref 13f.

(14) The active species should be generated in the presence of the triyne substrate. After mixing of [2 × **3a** + $CoCl_2$] or [**3a** + $FeCl_3$] with Zn powder in the absence of triyne **1a**, addition of **1a** to this mixture and the following stirring at 50 °C did not afford **2a**.

(15) Arene−iron complex catalyzed [2 + 2 + 2] pyridine formation from alkynes and nitrile has been reported: Schmidt, U.; Zenneck, U. *J. Organomet. Chem.* **1992**, *440*, 187. Knoch, F.; Kremer, F.; Schmidt, U.; Zenneck, U. *Organometallics* **1996**, *15*, 2713.