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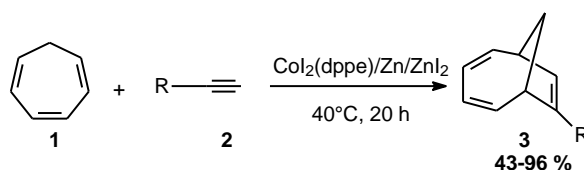
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First Cobalt(I)-catalyzed [6+2] Cycloadditions of Cycloheptatriene with Alkynes

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The $\text{CoI}_2(\text{dppe})/\text{Zn}/\text{ZnI}_2$ system effectively catalyzes the [6+2] cycloaddition of cycloheptatriene with terminal alkynes to afford 7-alkyl-bicyclo[4.2.1]nona-2,4,7-trienes in fair to excellent yields. The catalyst proved tolerant towards functional groups such as ketone, sulfone, ester, ketal, ether, alcohol, imide, and nitrile. The enantioselective cycloaddition of CHT and phenylacetylene with BINOL phosphoramidite ligand 4 afforded the cycloadduct 3a (R= Ph) in 91% yield and 74% ee.

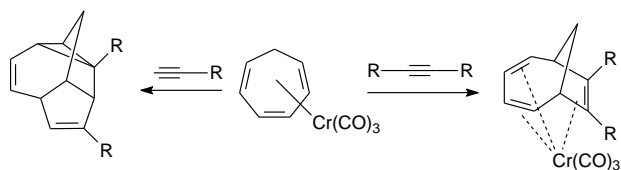
Transition metal-mediated higher order cycloadditions are important synthetic tools for the construction of medium-sized ring compounds.¹ The photoinduced [6+2] cycloaddition of cycloheptatriene (CHT) with internal alkynes was reported first by Pettit² using a tricarbonyl(η^4 -cycloheptatriene)iron(0) complex to afford bicyclo[4.2.1]nonatriene adducts as tricarbonyl(η^4 -triene)iron(0) complexes. A related chromium(0)-mediated [6+2] cycloaddition with tricarbonyl(η^6 -cycloheptatriene)chromium(0) was demonstrated later by Grevels³ and thoroughly investigated by Sheridan.⁴ In between, Turecek reported the first catalytic procedure with Ziegler catalyst ($\text{TiCl}_4/\text{Et}_2\text{AlCl}$) but the cycloaddition suffered from the competitive cyclotrimerization of the alkyne.⁵ Recent efforts focused on the development of $\text{Cr}(\text{CO})_n\text{L}_{6-n}$ ($n = 2, 3$) complexes bearing labile ligands to perform catalytic processes.⁶

With terminal alkynes the chromium(0)-promoted cycloadditions are difficult to arrest at the 1:1 alkyne:CHT cycloadduct stage; instead tetra- and pentacyclic 2:1 alkyne:CHT adducts are produced (Scheme 1).⁷ These multicomponent reactions are believed to occur through a stepwise [6+2] cycloaddition-*homo*[6+2] cycloaddition sequence.⁷⁻⁸ To date, the chromium(0)-promoted [6+2] cycloadditions with alkynes remains confined to internal alkynes.

In continuation of studies into metal promoted cycloadditions,⁹ we have addressed the possibility of effecting a [6+2] cycloaddition of cycloheptatriene 1 with terminal alkynes 2 and we report in this letter the first cobalt(I)-catalyzed [6+2] cycloaddition which gives 7-alkyl-bicyclo[4.2.1]nona-2,4,7-trienes 3.

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Scheme 1. Cycloadditions of $[(\eta^6\text{-CHT})\text{Cr}(\text{CO})_3]$ and Alkynes

From the outset, we judged that the makeup of Co-based complexes offered an attractive opportunity for the design, synthesis and development of effective cycloaddition catalysts. The following cobalt catalytic systems (**A-D**) combining CoI_2 , 1,2-bis(diphenylphosphino)ethane (dppe) and tetrabutylammonium borohydride or zinc metal as reducing agent with or without ZnI_2 in 1,2-dichloroethane (DCE) were selected to test the cycloaddition of **1** with phenylethyne **2a** (Table 1):

Catalyst **A**: CoI_2 / dppe / Bu_4NBH_4 / ZnI_2

Catalyst **B**: CoI_2 / dppe / Zn

Catalyst **C**: CoI_2 / dppe / ZnI_2

Catalyst **D**: CoI_2 / dppe / Zn / ZnI_2

These catalysts revealed effective in homo-Diels Alder cycloadditions (**A**, **B** and **C**),⁹⁻¹³ [4+2+2] cycloaddition of functionalized norbornadienes and butadiene (catalysts **A-D**),¹⁴ Diels-Alder type reactions of 1,3-dienes with terminal or internal alkynes (catalysts **A** and **D**),^{10, 15} and 1,4-hydrovinylation reactions of 1,3-dienes with functionalized terminal alkenes (catalysts **A** and **D**).¹⁶

When CHT and phenylethyne **2a** were mixed in the presence of CoI_2/dppe (5/5 mol%) or preformed $\text{CoI}_2(\text{dppe})$ ¹⁷ in DCE at 40°C for 20 h no reaction occurred (not shown in Table 1). Catalyst **B** and **C** afforded the desired cycloadduct **3a** in low yields (entry 1-2). The association of a reducing agent and a Lewis acid, (catalyst **D**) proved beneficial and improved the yield to 75 % (entry 6). Ligands such as PPh_3 , $\text{P}(\text{OPh})_3$ or dppp were less effective (entries 3, 4, 8). Interestingly, the monodentate phosphoramidite ligand proved satisfactory affording **3a** in 61 % yield (entry 5). The cycloaddition was also observed by changing CoI_2 to CoBr_2 giving the cycloadduct in lower yield (entry 7). The efficiency of the cycloaddition was also demonstrated by using Bu_4NBH_4 as the reducing agent (catalyst **A**) (entry 9). Although the

Table 1. Cobalt catalysts tested for the [6+2] cycloaddition of cycloheptatriene **1** with phenylethyne **2a** to form **3a**^a

entry	catalyst (molar ratio)	yield (%) ^c
1	$\text{CoI}_2/\text{dppe}/\text{Zn}$ (1/1/5)	39
2	$\text{CoI}_2/\text{dppe}/\text{ZnI}_2$ (1/1/5)	5
3	$\text{CoI}_2/\text{PPh}_3/\text{Zn}/\text{ZnI}_2$ (1/2/3/2)	35
4	$\text{CoI}_2/\text{P}(\text{OPh})_3/\text{Zn}/\text{ZnI}_2$ (1/2/3/2)	25
5	$\text{CoI}_2/\text{L}/\text{Zn}/\text{ZnI}_2$ (1/2/3/2)	61
	L=	
6	$\text{CoI}_2(\text{dppe})/\text{Zn}/\text{ZnI}_2$ (1/3/2)	75
7	$\text{CoBr}_2(\text{dppe})/\text{Zn}/\text{ZnI}_2$ (1/3/2)	40
8	$\text{CoI}_2(\text{dppp})/\text{Zn}/\text{ZnI}_2$ (1/3/2) ^b	45
9	$\text{CoI}_2(\text{dppe})/\text{Bu}_4\text{NBH}_4/\text{ZnI}_2$ (1/1/2)	74

^a All reactions were carried out at 0.3 M concentration in DCE at 40 °C for 20 h in a Schlenk tube under nitrogen atmosphere with CHT **1/2a**/[Co] in 1.2/1/0.05 molar ratio. ^b dppp is for 1,3-bis(diphenylphosphino)propane. ^c Yields of isolated **3a**.

catalysts **A** and **D** were similarly effective to promote the [6+2] cycloaddition, the catalyst **D** which would be expected to be more tolerant to the functional groups of the trienophile **2** was selected for further studies. The choice of solvent was critical: use of DCE (75%), trifluoroethanol (TFE) (55%) and toluene (53%) are acceptable; MeCN, THF, dioxane or DMF afforded none or trace amount of **3a**.

The scope of the [6+2] cycloaddition using catalyst **D** was further extended to other terminal alkynes (Table 2). This catalytic system tolerates functional groups of **2** such as ketone, sulfone, ester, ketal, ether, alcohol, imide and nitrile which are of interest for further transformations. For instance, cycloadducts featuring a vinyltrimethylsilane (**3c**, 92%) or allyltrimethylsilane (**3d**, 65%) (entries 3-4) can be involved in a range of reactions of organosilicon compounds.¹⁸ The yields observed depend on both the nature and the position of the

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Table 2. Cobalt-catalyzed [6+2] Cycloaddition of Cycloheptatriene with Terminal Alkynes^a

Entry	alkyne	R	product	yield (%) ^{b,c}
1	2a	Ph	3a	75 (86)
2	2b	<i>n</i> -Bu	3b	74 (95)
3	2c	SiMe ₃	3c	92
4	2d	CH ₂ SiMe ₃	3d	65
5	2e		3e	43 (68)
6	2f	CH ₂ SO ₂ Ph	3f	50
7	2g	CH ₂ CH(CO ₂ Me) ₂	3g	55 (83)
8	2h	CH ₂ C(Me) ₂ CH ₂ Ac	3h	96
9	2i	CO ₂ Me	3i	21 (43 ^d)
10	2j	CH(OEt) ₂	3j	43 (59)
11	2k	CH ₂ OH	3k	19
12	"	"	"	60 ^d
13	2l	CH ₂ CH ₂ OH	3l	67 ^d
14	2m	CH ₂ CH ₂ OAc	3m	83
15	2n		3n	82
16	2o	(CH ₂) ₃ CN	3o	90

^a All reactions were carried out with CHT 1/Alkyne **2**/Co₂(dppe)/Zn/ZnI₂ in a 1.2/1/0.05/0.15/0.1 molar ratio in DCE at 40°C for 20h. ^b Yields of isolated products by column chromatography or distillation. ^c Yields in parentheses are for optimized conditions (slow addition of the alkyne (4h) using 2.5 mol% of CoI₂(dppe)). ^d TFE as solvent.

functional group on the alkyne. Alkynes **2h**, **2m**, **2n** and **2o** with the functional group remote from the triple bond afforded the cycloadducts in excellent yields (entries 8, 14, 15, 16) compared to alkynes **2d**, **2f**, or **2j** with the functionality at propargylic carbon atom (entries 4, 6, 10). TFE as solvent proved beneficial to promote the cycloaddition of propargyl and homopropargyl alcohols in quite good yields (entries 11-13). Electron-poor alkynes such as methyl propiolate **2i** afforded cycloadduct **3i** in only 21% yield (entry 9), this is likely due to a

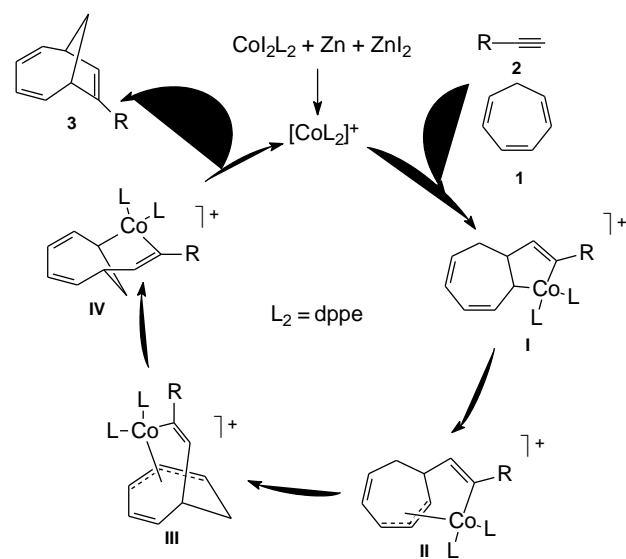
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Scheme 2. Proposed Mechanism for the Cobalt Catalyzed [6+2] Cycloaddition



marked preference of coordination of **2i** to the cobalt species triggering the cyclotrimerization. The efficiency of the cycloaddition was improved by using slow addition of the alkyne (syringe pump, 4 h) and lower catalyst loading (2.5 mol %) (entries 1, 2, 5, 7, 9, 10).

A plausible mechanism is depicted in Scheme 2. As suggested by Snyder, ZnI₂ accelerates the reduction of a CoL₂I₂ by zinc metal.^{14a} The coordination of the alkyne and cycloheptatriene to the cationic [Co(I)L₂]⁺ complex^{16c} is followed by an oxidative cyclometallation to give the cobaltacyclopentene **I**.¹⁹ The latter undergoes a 1,5-migration of the C(sp³)-Co bond through consecutive σ , π -allyl complexes (π -allyl complexes **II** and **III**) to form the bicyclo cobaltacycle **IV**. Subsequent reductive elimination of **IV** releases the cycloadduct **3** and regenerates the cationic [Co(I)L₂]⁺ species.

On the basis of the above results, a preliminary attempt was made to unravel the catalytic enantioselective [6+2] cycloaddition.²⁰ By using phosphoramidite ligand **4**²¹

(12) Catalyst **A** promoted the [2+2+2] cycloaddition of 1,6-heptadiynes with allenes: Wu, M. S.; Shanmugasundaram, M.; Cheng, C. H. *J. Chem. Soc., Chem. Commun.* **2003**, 718-719.

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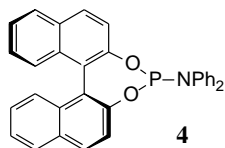
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Scheme 3. Phosphoramidite Ligand for the Enantioselective Cycloaddition



(Scheme 3), the cycloaddition^{20b} between CHT with **2a** gave rise to **3a** in excellent chemical yield (91%) and good enantioselectivity (74%).^{20c}

(20) (a) To the best of our knowledge the metal-catalyzed enantioselective [6+2] cycloaddition of CHT and alkynes has not yet been reported. (b) The reaction was performed at 40°C for 20h in DCE using 5 mol% CoI₂ and CoI₂/L/ZnI₂/Zn in 1/2/2/3 molar ratio. (c) Determined by HPLC: Chiracel OJ-H, n-hexane/2-propanol 97:3, 1mL/min, 25°C, t_r = 17.7 min and t_r = 19.2 min.

In conclusion, we have developed the first cobalt-catalyzed [6+2] cycloaddition of cycloheptatriene and functional terminal alkynes that proceeds with a non-carbonyl metal catalyst and without irradiation. The reaction proceeded under mild conditions and the catalyst tolerates a wide range of functional groups. Further optimisation of the enantioselectivity with chiral phosphoramidite ligands is underway in our laboratory.

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Supporting Information Available: Experimental procedures and characterization data for all unknown compounds (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>

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