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## Cobalt-catalyzed homocoupling of terminal alkynes: synthesis of 1,3-diynes

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Abstract—Homocoupling of terminal alkynes proceeds using  $Co_2(CO)_8$  pretreated with phenanthroline to give good yields of 1,3-diynes under mild conditions. © 2001 Elsevier Science Ltd. All rights reserved.

Formation of substituted 1,3-divnes via coupling between sp hybridized atoms<sup>1</sup> represents one class of coupling reactions which yields polyfunctionalized molecules. The most commonly used metal salts for alkyne-alkyne coupling are Cu(+1) or Cu(+2) salts under either catalytic or stoichiometric conditions. The Glaser<sup>1-3</sup> and Eglington<sup>1,4–7</sup> procedures for direct coupling of terminal alkynes, or the Chodkiewicz-Cadiot procedure1,8-10 for coupling of a terminal alkyne with a halo alkyne, and modifications thereof represent the most widely used alkyne coupling reactions for the synthesis of 1,3-diynes. To a lesser extent complexes of palladium,<sup>11</sup> nickel,<sup>12</sup> cobalt<sup>13</sup> and Rieke copper<sup>14</sup> have been shown to mediate homo- or heterocoupling of terminal alkynes. Phase transfer catalysis has been shown by Alper to give alkyne homocoupling products.<sup>15</sup> Recently, heterogeneous coupling of phenylethyne over Cu-Mg-Al mixed oxides has been demonstrated.<sup>16</sup> Alkyne coupling reactions to form both symmetrical and unsymmetrical 1,3-diynes have been used to generate polymers and monomers,<sup>17,18</sup> functional host molecules<sup>19</sup> and intermediates for the total synthesis of natural products.3,5,9,20

Dicobalt octacarbonyl is known to be an efficient catalyst for the Pauson–Khand reaction as well as for hydroformylations.<sup>21</sup> A variety of cobalt complexes can also be prepared from  $Co_2(CO)_8$  by ligand exchange or disproportionation reactions. In the presence of Lewis bases,  $Co_2(CO)_8$  undergoes disproportionation to *homonuclear ion-pairs* (HNIP).<sup>22</sup> The disproportionation patterns are dependent on the bases and polarity of solvents. Generally, amines or alcohols tend to form Co(II) salts [LnCo][Co(CO)\_4]\_2 (Ln = neutral ligand) and isonitriles or phosphines form Co(I) salts [LnCo][Co(CO)\_4] when the reaction is conducted in polar solvents. The reactivity of these species has been well-studied with respect to hydroformylation chemistry. Fachinetti reported that  $[Py_6Co][Co(CO)_4]_2$  reacts with hydrogen at ambient temperature under CO/H<sub>2</sub> (1:1) atmosphere to give  $[Py_2H][Co(CO)_4]_2$ .<sup>23</sup> Under the same conditions  $[Py_6Co]-[Co(CO)_4]_2$  reacts with alkenes to give  $[RCOCo]-[Co(CO)_4]_2$ .<sup>24</sup>

During the course of our studies on the role of amines in the catalytic Pauson-Khand reaction<sup>25</sup> we investigated the in situ formation of different amine-ligated cobalt carbonyl complexes and their subsequent reactions with enynes. Much to our surprise we discovered that reaction of 20% of 2,2'-dipyridyl (dipy) with 10% of Co<sub>2</sub>(CO)<sub>8</sub> for 30 min at ambient temperature followed by the addition of enyne 1 and warming to 70°C for 18 h gave rise only to 1,3-divne 2 in 33% yield. Homocoupling of the terminal alkyne had apparently occurred (Eq. (1)) and none of the normal Pauson-Khand product 3 was isolated.<sup>26</sup> Consequently, we assumed that  $Co_2(CO)_8$  had been converted to a HNIP via disproportionation with dipy and the resulting HNIP was therefore responsible for the observed coupling. Herein we describe subsequent modifications of the reaction conditions and the development of an alkyne coupling using a cobalt HNIP as the catalyst.



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We attempted to optimize the yield of the coupling product by screening a series of ligands which would form HNIPs in the reaction with  $Co_2(CO)_8$ . Reaction of enyne 1 with 10 mol% of Co<sub>2</sub>(CO)<sub>8</sub> pre-treated for 30 min with a variety of ligands gave diyne 2 and starting envne 1 in varying yields (Table 1, Eq. (2)). Reactions with phosphines and aliphatic amines led to the formation of metal deposits upon prolonged heating and resulted only in the recovery of the starting material (entries 1–4). The conjugated aromatic diamines were found to be good ligands, with 1,10-phenanthroline (phen) giving the best results. Since no Pauson-Khand product was formed it seemed evident that pre-treatment of  $Co_2(CO)_8$  with phenanthroline in acetonitrile was giving rise to a new complex which was inactive as a catalyst for the Pauson-Khand cycloaddition.

To determine the structure of catalyst 4 generated in situ from  $Co_2(CO)_8$  and phenanthroline, we carried out

Table 1.

Co <sub>2</sub> (CO) <sub>8</sub> + ligand	CH <sub>3</sub> CN	[LnCo][Co(CO) <sub>4</sub> ] <sub>2</sub>	
	reflux	n=3,6	(2)
		<b>4</b> : L = phen, n=3 <b>5</b> : L = dipy, n=3	

Entry	Ligand	(%)	2 (%)	1 (%)
1	Ph <sub>3</sub> P	30	0	100
2	DPPE	15	0	100
3	Triethylamine	40	0	100
4	TMEDA	20	0	100
5	Pyridine	40	Trace	$\sim 100$
6	Dipyridyl	20	33	59
7	Phenanthroline	20	45	45
8	Dimethyl-phen <sup>a</sup>	20	0	87

<sup>a</sup> 2,9-Dimethyl-4,7-diphenyl-1,10-phenanthroline.

Table 2. Optimization of general reaction conditions<sup>a</sup>

several spectroscopic experiments. The structure of 4, which was prepared from 2 equiv. of phenanthroline and 1 equiv. of Co<sub>2</sub>(CO)<sub>8</sub>, was predicted to be  $[phen_3Co][Co(CO)_4]_2$  based on the previous reports.<sup>27,28</sup> The <sup>1</sup>H NMR spectrum in CD<sub>3</sub>CN showed four broad signals of equal intensity ( $\delta$  17.2, 32.9, 49.5, 106.5 ppm). These strong downfield shifts clearly suggest the formation of a paramagnetic Co(II) species and the symmetry of ligands suggest three ligands associated with the metal center. The <sup>13</sup>C NMR spectrum of 4 showed three downfield carbons (200.2, 389.5, 686.6 ppm) and one highly upfield carbon (-182.9 ppm) for phen (two quaternary carbons were not observed) and eight CO carbons between 200 and 230 ppm for a pair of  $[Co(CO)_4]$  anions. These spectra are consistent with the expected structure, [phen<sub>3</sub>Co][Co(CO)<sub>4</sub>]<sub>2</sub>. The IR spectrum for 4 showed only one CO absorption at 1892  $cm^{-1}$  which is typical for the isolated [Co(CO)<sub>4</sub><sup>-</sup>]. The <sup>1</sup>H NMR spectrum of the analogous complex 5, which was prepared from 1 equiv. of  $Co_2(CO)_8$  and 2 equiv. of dipy, also showed chemical shifts similar to 4 in the downfield region ( $\delta$  14.5, 46.0, 83.7, 87.8 ppm), suggesting the formation of  $[dipy_3Co][Co(CO)_4]_2$ . These complexes were easily isolated by removal of the solvent in vacuo.<sup>28</sup> The resulting solid was moderately stable under air and could be stored in the freezer for a week with little observable decomposition. The reactivity of the isolated solid was essentially the same as the catalyst that was generated in situ. Additional support for the presence of Co(+2) was provided by magnetic susceptibility measurements over the wide temperature range -269 to 25°C, using a SQUID magnetometer. The measured susceptibility yielded a magnetic moment of 4.8 BM, which is well within the range 4.7-5.2 for distorted octahedral complexes of Co(+2).<sup>29</sup>

Further optimization of the reaction conditions involved a change in temperature, solvent, atmosphere, amount of catalyst and concentration (Table 2). Similar

		A 1111 (0/)	G . 1	T (0C)	C	<b>X</b> <sup>2</sup> , <b>11</b> , (0/)	
Entry	Catalyst (%)	Additive (%)	Solvent	Temp. (°C)	Conc. (mol/l)	Y leid (%)	KSM (%)
1	Co <sub>2</sub> (CO) <sub>8</sub> (10)	o-phen (20)	CH <sub>3</sub> CN	60	0.067	10	80
2	$Co_2(CO)_8$ (10)	o-phen (20)	CH <sub>3</sub> CN	70	0.067	45	45
3	$Co_2(CO)_8$ (10)	o-phen (20)	CH <sub>3</sub> CN	80	0.067	77	5
4	$Co_2(CO)_8$ (10)	o-phen (20)	CH <sub>3</sub> CN	80	0.067	70	12
5	$Co_2(CO)_8$ (10)	o-phen (14)	CH <sub>3</sub> CN	80	0.067	72	9
6	4 (7)		CH <sub>3</sub> CN	80	0.02	45	54
7	4 (7)		CH <sub>3</sub> CN	80	0.067	74	20
8	<b>4</b> (10)		CH <sub>3</sub> CN	80	0.067	82	18
9 <sup>b</sup>	4 (10)		CH <sub>3</sub> CN	80	0.067	3	87
10	<b>4</b> (7)		CH <sub>3</sub> CN	80	0.1	85	11
11	4 (10)		CH <sub>3</sub> CN	80	0.1	86	0
12	<b>4</b> (7)		CH <sub>3</sub> CN	80	0.2	71	10
13	4 (3)		C <sub>2</sub> H <sub>5</sub> CN	80	0.067	22	67
14	<b>4</b> (7)		C <sub>2</sub> H <sub>5</sub> CN	97	0.067	0	100
15	4 (7)		CH <sub>3</sub> NO <sub>2</sub>	80	0.067	0	100
16	4 (7)		DMF	80	0.067	6	83
17	4 (7)		C <sub>2</sub> H <sub>5</sub> OH	80	0.067	33	56

<sup>a</sup> All reactions carried out under a blanket of CO except entry 4 in which argon was used.

<sup>b</sup> Reaction was carried out in a sealed tube.

results were obtained whether the catalytic species was prepared in situ (entries 1–5) or pre-formed and stored in a freezer (compare entry 3 with entries 7 and 10). The catalyst showed a narrow temperature range over which it was active, 60–80°C, (entries 1–3) with the best results obtained at 80°C in most cases.

Acetonitrile proved to be the solvent of choice for the coupling reaction (entries 11, 14–17). The cobalt salts are insoluble in ethereal solvents such as  $Et_2O$ , 1,2-dimethoxyethane or 1,4-dioxane regardless of whether they are prepared in situ or pre-made and stored in a freezer. Reactions performed under an atmosphere of carbon monoxide gave the highest yields. It seems plausible that the carbon monoxide atmosphere enhances the catalyst lifetime although the coupling proceeded under an argon atmosphere (entry 4). Interestingly, diyne formation was almost completely suppressed when the reaction was performed in a sealed tube. To demonstrate the generality of the coupling process, a series of terminal alkynes was subjected to the optimized conditions (Table 3).

In an attempt to understand the mechanism of the coupling and the role of the two cobalt ions, we examined the reaction of alkyne 1 with different cobalt salts which have only one cobalt ion in the complex (Table 4). Complexes [phen<sub>3</sub>Co][ClO<sub>4</sub>]<sub>2</sub> and PPNCo(CO)<sub>4</sub> did not show any catalytic activity for the coupling reaction when they were used independently (entries 1 and 2). Interestingly, the mixture of [phen<sub>3</sub>Co][ClO<sub>4</sub>]<sub>2</sub> and [PPN][Co(CO)<sub>4</sub>] catalyzed the coupling reaction to give

## Table 3.

	СО, 1 10-20%	atm catalyst <sup>a</sup> –		
$R \longrightarrow H \xrightarrow{f} CH_3CN, 18h$				
Entry	R	Temp. (°C)	Yield 2 (%)	
1	Ph	70	88	
2	$n - C_{10} H_{21}$	80	91	
3	1-Cyclohexenyl	70	75	
4	PhCO <sub>2</sub> (CH <sub>2</sub> ) <sub>3</sub>	80	53 (19) <sup>b</sup>	
5	$TBSO(CH_2)_2$	80	71	
6	TBSO(CH <sub>2</sub> ) <sub>3</sub>	80	79	
7	$TBSO(CH_2)_4$	80	79	
8	THPO(CH <sub>2</sub> ) <sub>3</sub>	80	81	
9	$BnO(CH_2)_3$	80	71°	
10	E CH2 <sup>d</sup>	80	86	
11	E' CH <sub>2</sub> <sup>e</sup>	80	81	

<sup>a</sup> The catalyst was prepared in situ or pre-made.

- <sup>b</sup> Yield of monodebenzylated diyne.
- ° 24 h.
- <sup>d</sup>  $E = CO_2Et$ .

 $^{e}$  E' = CO<sub>2</sub>Me.

Table 4.



PPN, bis(triphenylphosphoranylidene)ammonium.

diyne **2** in 56% yield (entry 3). These results suggest that both of the ions phen<sub>3</sub>Co(II) and  $[Co(CO)_4^-]$  are involved in the catalytic cycle for the alkyne–alkyne coupling, however, their specific role is still unclear at this point. Further work on elucidating the mechanistic pathway is underway.

In summary, we have described a new cobalt-catalyzed terminal alkyne homocoupling to generate substituted 1,3-diynes under mild conditions.<sup>30</sup>

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