A Rhodium(I)-Catalyzed Formal Allenic Alder Ene Reaction for the Rapid and Stereoselective Assembly of Cross-Conjugated Trienes

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Transition metal catalyzed carbon−carbon bond-forming processes have revolutionized strategies used to increase molecular complexity. Recently, Trost,[1] Buchwald[2] and Zhang[3] have demonstrated the feasibility of a transition metal-catalyzed formal Alder ene reaction by effecting the formation of five-membered rings possessing a 1,4-diene moiety from enynes. An analogous intramolecular allenic Alder ene reaction has received less attention due to its requiring a regioselective reaction with the distal π-bond of the allene.[4] Malacria[5] and Sato[6] have both effected intramolecular allenic Alder ene reactions, but the substrate-controlled constitutional group selectivity is limiting. Furthermore, Livinghouse and Oh have both observed cross-conjugated trienes in low yields during transition metal-catalyzed reactions of alkynyl allenes, but no follow-up studies have been reported.[7] A cross-conjugated triene is an interesting building block since it can participate in a variety of tandem carbon−carbon bond-forming processes, such as Diels−Alder reactions.[8] It would seem then that the cross-conjugated substructure would be ubiquitous, but in fact, few strategies are available for its preparation with the majority of them relying on classical synthetic methods.[9]

Recently, while screening transition metals to mediate the allenic Pauson−Khand reaction under milder conditions with higher stereoselectivity, we discovered that 5 mol % rhodium biscarbonyl chloride dimer [Rh(CO)$_2$Cl]$_2$ gave only the 4-alkylidene cyclopentenones, resulting from selective reaction with the distal double bond of the allene, independent of the allene substitution pattern (Scheme 1).[10] Typically strategies used to control allene constitu-

Scheme 1
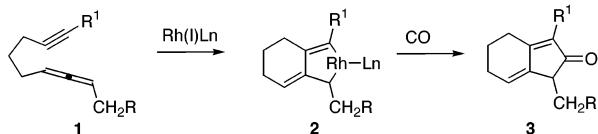
tional group selectivity involve (1) differential substitution of the allene termini, (2) intramolecularization, and (3) incorporation of directing functional groups on the carbon adjacent to the allene. This result constitutes a rare example of transition metal-directed constitutional group selectivity of an allene and incentive for further investigations involving other interesting carbon−carbon bond-forming reactions.[11]

Since metallocycle **2** is an intermediate in the formation of the 4-alkylidene cyclopentenone **3** from alkynyl allene **1**, it was postulated that metallocycle **2** could serve as a diverging point for other metal-catalyzed processes (Scheme 1). On the basis of this hypothesis, reaction conditions were then adjusted to eliminate the possibility of carbon monoxide insertion. To our delight, treatment of alkynyl allene **4** to the standard Rh(I) conditions [2 mol % [Rh-

(CO)$_2$Cl]$_2$] but substitution of the carbon monoxide atmosphere with nitrogen resulted in formation of cross-conjugated triene **5** in 72% yield (eq 1). The exocyclic olefin (vinyl silane) was obtained as the *E* isomer exclusively evidenced by the observed nOe of 4.5% between H^1 and H^2. The appending olefin was obtained as a mixture of *E:Z* isomers (5:1) as determined by ^{1}H NMR.
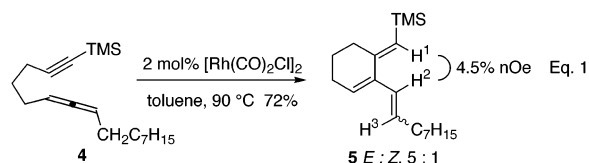
The mechanism most likely involves β-hydride elimination of the intermediate rhodium metallocycle to afford the appending olefin of **5**, followed by a reductive elimination of a metallo−hydride species to give the exocyclic olefin. The exclusive *E*-stereochemistry of the *exocyclic* olefin supports this mechanism. Furthermore, the deuterated allenyne **6** affords triene **7** in 63% yield with complete transfer of the deuterium (eq 2). A crossover experiment was performed where a 1:1 mixture of **6** and **8** were subjected to [Rh(CO)$_2$Cl]$_2$ in toluene at 90 °C and only trienes **7** and **9** were obtained with no evidence of deuterium scrambling. An nOe of 1.3% was observed between X^1 = H and the CH$_3$ on the appending olefin.
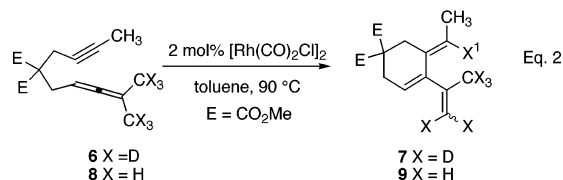
The scope and limitations of this new method are currently being investigated, and the results obtained to date are summarized in Table 1. Treatment of allenyne **11** with 2 mol % [Rh(CO)$_2$Cl]$_2$ at 90 °C provided compound **12** in 80% yield with a 3:1, *E:Z* ratio (entry 1, Table 1). Similarly, allenyne **13** possessing only a methyl group on the distal position of the allene gave only triene **14** in 71% yield (entry 2, Table 1). Rh(COD)$_2$Cl can also be used to effect the allenic Alder ene in much faster reaction times, but this catalyst does require an additive (entry 3, Table 1). Replacement of the terminal alkyne with a TMS-alkyne also gives the trienes but in somewhat lower yields (entries 4 and 5, Table 1). The sulfonamide functionality is compatible with this method based upon the conversion of allenynes **19**, **21**, and **23** to **20**, **22**, and **24**, respectively (entries 6−9, Table 1). Performing this reaction at room temperature gives a higher yield of triene **20** with a slight increase in *E:Z* selectivity (compare entries 6 and 7, Table 1). Ether-tethered allenyne **25** gives only the triene **26** in 74% yield (entry 10, Table

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Table 1. Examining the Scope of the Allenic Alder Ene Reaction[a]

entry	allenyne	triene	temp(°C)	time	E : Z	yield
1	11 R = C_5H_{11}, R^1 = H	12	90	1h	3 : 1	80%
2	13 R = H, R^1 = H	14	90	1h	--	71%
3*	13	14	rt	15min	--	74%
4	15 R = C_5H_{11}, R^1 = TMS	16	rt	3h	3 : 1	60%
5	17 R = H, R^1 = TMS	18	rt	3h	--	45%
6	19 R = C_5H_{11}, R^1 = H	20	90	1h	4 : 1	64%
7	19	20	rt	6h	6 : 1	90%
8	21 R = H, R^1 = H	22	rt	3h	--	93%
9	23 R = C_5H_{11}, R^1 = TMS	24	rt	5h	5 : 1	85%
10	25	26	90	1h	6 : 1	74%
11	27 R = C_5H_{11}	28	rt	6	2 : 1	80%±
12	29 R = H	30	rt	3	--	80%±
13	31 R = C_5H_{11}, R^1 = TMS	32	rt	6	3 : 1	69%±

[a] Conditions: 2 mol % $[Rh(CO)_2Cl]_2$, toluene, N_2. *5 mol $[Rh(COD)Cl]_2$, 10 mol % $AgSbF_6$. ± Reactions were run in CH_2Cl_2 or DCE; toluene gave, on average, yields that were 15% lower.

Table 2. Stereochemistry of Olefinic Side Chain[a]

entry	allenyne	triene	conditions	E/Z	yield (%)
1	4	5	A	5:1	72
2	4	5	B[b]	13:1	67
3	4	5	C[b]	4:1	46
4	4	5	D	>20:1	57
5	15	16	D	180:1[c]	67
6	23	24	D	>20:1	62
7	31	32	D	>99:1[c]	74

[a] Conditions: (A) 2 mol % $[Rh(CO)_2Cl]_2$, toluene, N_2, 90 °C, 1 h. (B) 5 mol % $[Rh(COD)Cl]_2$, 10 mol % $AgSbF_6$, DCE, rt, 15 min. (C) 5 mol % $[Rh(CH_2CH_2)_2Cl]_2$, 10 mol % $AgSbF_6$, DCE, rt, 15 min. (D) 10 mol % $[Ir(COD)Cl]_2$, 20 mol % $AgBF_4$, DCE, 60 °C, 5 min. [b] Under these conditions the silyl group was completely removed from the exocyclic olefin. [c] E/Z ratio determined by GC analysis.

compound **25** and the substrates possessing terminal alkynes to these iridium conditions gave only decomposition by crude NMR. In the terminal alkyne case, the iridium most likely reacts with the acidic alkyne proton to form a metal acetylide. Further studies from our laboratory will be forthcoming which will elucidate the scope of this stereoselective iridium allenic Alder ene reaction.

In conclusion, we have discovered a rhodium(I)-catalyzed allenic Alder ene reaction that provides cross conjugated trienes in very good yields. This method shows enticing functional group compatibility, and progress has been made to increase the stereoselectivity of the olefinic side chain via iridium(I) catalysis. We have subsequently shown that these trienes can be used in tandem Diels−Alder reactions, and these results will be reported on soon.

Supporting Information Available: Experimental details and ¹H and ¹³C NMR spectra of all new compounds are available (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

1). Finally, an unprotected hydroxymethyl group is well-tolerated in the rhodium-catalyzed Alder ene reaction. Allenynes **27**, **29**, and **31** give high yields of the corresponding trienes **28**, **30**, and **32** (entries 11−13).

The ability to control the stereochemistry of the olefinic side chain is important if this method is to be applicable to target-oriented synthesis and to gain a better understanding of the transition metal-catalyzed Alder ene reaction. Allenyne **4** and $[Rh(CO)_2Cl]_2$ give triene **5** with an E:Z selectivity of 5:1 (entry 1, Table 2). Allenyne **4** and $[Rh(COD)Cl]_2$ along with 10 mol % of $AgSbF_6$ additive provided the desilylated triene **5** in 67% yield with an E:Z ratio of 13:1 (entry 2, Table 2). In contrast to the example in entry 1, this reaction was very fast at room temperature. Treatment of allenyne **4** to 5 mol % $[Rh(CH_2CH_2)_2Cl]_2$ and 10 mol % $AgSbF_6$ gave a 46% yield of desilylated triene **5** in an E:Z ratio of 4:1 (entry 3, Table 2). Moving down the periodic column to iridium enhanced the selectivity, since subjecting allenyne **4** to 10 mol % $[Ir(COD)Cl]_2$ along with 20 mol % of $AgBF_4$ additive provided the triene **5** in 57% yield with an E:Z ratio of >20:1 as measured by ¹H NMR (entry 4, Table 1). Using these same iridium conditions, compounds **15**, **23**, and **31** all afforded good yields of the trienes with very high E:Z selectivities (entries 5, 6, and 7, Table 2). In addition to the very high E:Z selectivities, this represents the first iridium-catalyzed Alder ene reaction. However, treatment of

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