Pauson–Khand Reaction of Dienynes

The Dienyl Pauson–Khand Reaction**

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Studies in our organometallic subgroup are aimed at the design and development of new catalytic reactions, with an emphasis on processes that, in the absence of catalysts, would be forbidden or would require harsh conditions.[1,2] These studies have thus far produced the first examples of transition-metal-catalyzed [4+4] cycloadditions of bisdienes,[3] [4+2] cycloadditions of dienynes (and diene allenes),[4] [5+2] cycloadditions of vinylcyclopropanes and π systems,[5] and [6+2] cycloadditions of vinylcyclobutanones and π systems.[6] Recently, we started to investigate whether these and other two-component [*m*+*n*] cycloadditions could be converted into multicomponent [*m*+*n*+*o*…+*x*)] processes through trapping of the organometallic intermediates with additional components.[7] These investigations have thus far led to the first metal-catalyzed, three-component [5+2+1] cycloaddition reactions based on trapping of an intermediate in the [5+2] cycloaddition reaction with CO.[8] The current study was directed at determining whether intermediates in the [4+2] cycloaddition of dienynes could be similarly trapped with CO.

Outlined in Scheme 1 are three competing metal-catalyzed cycloaddition pathways available for a dienyne in the

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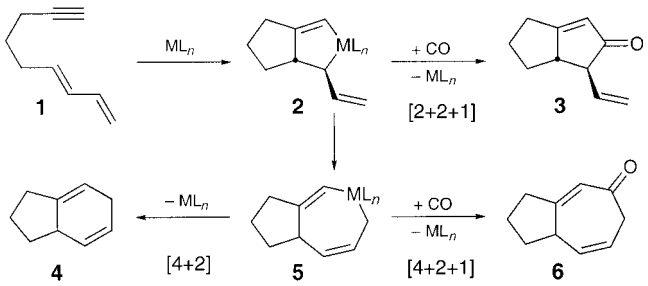
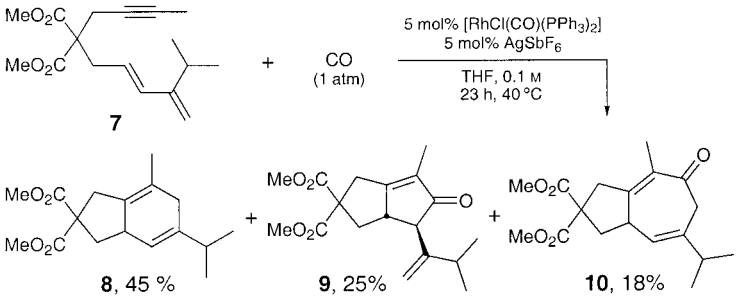


Scheme 1. Possible competing cycloaddition pathways.

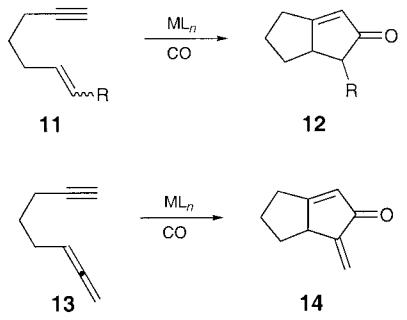
presence of CO: an intramolecular [4+2] cycloaddition (**1**→**4**), an unexplored version of the Pauson–Khand [2+2+1] cycloaddition (**1**→**3**), and an unprecedented [4+2+1] cycloaddition (**1**→**6**). Consistent with these possibilities, the reaction of dienyne **7** in THF in the presence of $[RhCl(CO)(PPh_3)_2]$, $AgSbF_6$, and CO produces a mixture of cycloadducts **8**, **9**, and **10** (Scheme 2). In the absence of CO,



Scheme 2. Representative cycloaddition reaction with CO.

only the [4+2] cycloadduct **8** is obtained in 63% yield (60°C, 30 min). The formation of cycloheptadienone **10** represents a new [4+2+1] cycloaddition reaction for the construction of seven-membered rings, while the formation of alkenylcyclopentenone **9**, the focus of the current study, represents a new class of the Pauson–Khand reaction, employing a diene rather than an alkene or an allene.

The conventional Pauson–Khand reaction is based on the coupling of an alkyne and CO with an alkene,[9,10] which is typically substituted with H, alkyl, aryl, or OR′ groups (Scheme 3, **11**→**12**). While originally mediated by cobalt,[11]



Scheme 3. Pauson–Khand reactions of alkenes and allenes.

several transition metals have been shown to catalyze the reaction.[12] Recently, Brummond and co-workers have greatly enhanced the synthetic utility of this process through the use of allenes in place of alkenes (Scheme 3, **13**→**14**).[13] In view of the potential synthetic utility of the diene version of the Pauson–Khand reaction, our attention focused on whether the reaction of dienes such as **7** could be made selective for the [2+2+1] pathway (**7**→**9**).

The effect of the solvent on the reaction of **7** was studied first (Table 1). In the presence of $[RhCl(CO)(PPh_3)_2]$, AgOTf, and CO in TFE, dienyne **7** afforded the [4+2] cycloadduct **8** in 44% yield and the [2+2+1] cycloadduct **9** in 48% yield. The use of $AgSbF_6$ instead of AgOTf in TFE gave a higher selectivity for the formation of the cycloadduct **9** (Table 1, entry 1). An enhanced yield of **9** was also seen with dioxane and DCE. Importantly, when the reaction was carried out at room temperature in DCE, **9** was obtained in 82% yield with only 11% of **8** (Table 1, entry 6).

Table 1: Effect of solvent variation on the reaction of **7**.[a]

Entry	Solvent[b]	T [°C]	t [h]	Yield [%][c]	
				8	**9**
1	TFE	40	48	20	63
2	dioxane	40	23	9	69
3	*n*-BuOH	40	48	no reaction	
4	toluene	40	22	no reaction	
5	DCE	40	4	23	49
6	DCE	RT	12	11	82

[a] $[RhCl(CO)(PPh_3)_2]$ (5 mol%), $AgSbF_6$ (5 mol%), 0.1 M, CO (1 atm). [b] TFE = 2,2,2-trifluoroethanol, DCE = 1,2-dichloroethane. [c] Yield determined by GC; less than 5% of **10** was observed by GC.

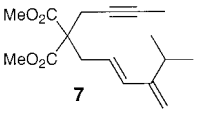
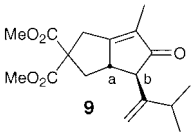
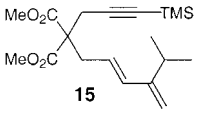
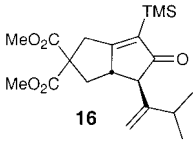
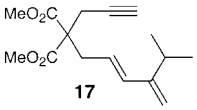
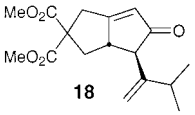
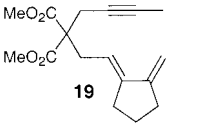
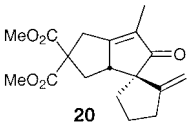
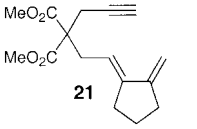
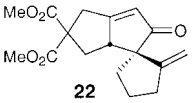
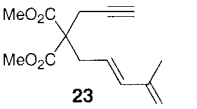
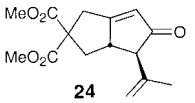
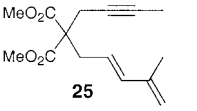
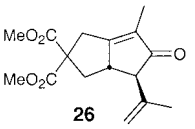
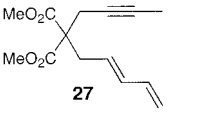
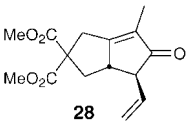
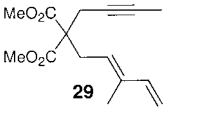
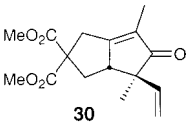
Further optimization of the reaction of **7** was realized through an investigation of variations in substrate concentration, catalyst loading, and CO pressure (cf. Table 1, entry 6 and Table 2). In these studies, the reaction efficiency was found to decrease with substrate concentrations above 0.1M (Table 2, entries 1 and 2). In contrast, an increase in CO pressure modestly enhanced the yield (Table 2, entries 4 and 5). Importantly, when the catalyst loading was decreased to 1 mol%, the reaction proceeded efficiently under 1 atmosphere of CO at room temperature, and the cycloadduct **9** was isolated in 89% yield (Table 2, entry 6).

Table 2: Effects of concentration, catalyst loading, and CO pressure variations on the reaction of **7**.[a]

Entry	c [M]	Cat. [mol%][a]	CO [atm]	t [h]	Yield [%][b]	
					8	**9**
1	0.5	5	1	20	21	51
2	0.2	5	1	26	12	63
3	0.01	5	1	26	8	82
4	0.1	5	2	26	6	87
5	0.1	5	4	18	6	86 (89)
6	0.1	1	1	14	7	88 (89)

[a] $[RhCl(CO)(PPh_3)_2]$ (x mol%), $AgSbF_6$ (x mol%), room temperature, DCE. [b] Yield determined by GC (yield of isolated product is given in parentheses); less than 5% of **10** was observed by GC.

Table 3: [2+2+1] Reaction of tethered dienynes.[a]

Entry	Substrate	*T* [°C]	CO [atm]	Cat.[a] [mol%]	*t* [h]	Product	Yield[b] [%]
1	 **7**	RT	1	1	14	 **9**	89
2	 **15**	RT	2	2	12	 **16**	85
3	 **17**	RT	1	1	40	 **18**	43
4	 **19**	RT	1	1	24	 **20**	96
5	 **21**	RT	1	5	32	 **22**	45
6	 **23**	RT	1	1	30	 **24**	42
7	 **25**	40	2	2.5	12	 **26**	86
8	 **27**	40	1	2.5	12	 **28**	90
9	 **29**	40	1	2.5	10	 **30**	96

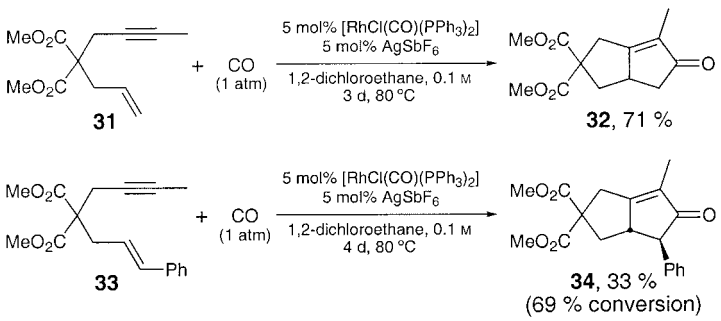
[a] $[RhCl(CO)(PPh_3)_2]$ (*x* mol%), $AgSbF_6$ (*x* mol%), 0.1 M, DCE. [b] Yield of isolated product.

To study the generality of this new class of Pauson–Khand reaction, we examined the reaction of eight other substrates, which differed in the substitution of the alkyne and diene (Table 3). Internal alkynes gave excellent yields of the [2+2+1] cycloadducts (85–96% yield), whereas terminal alkynes reacted less efficiently. Substitution at the 2- or 3-position of the diene was also well tolerated. The *syn* relationship between the angular hydrogen atom at C(a) and the alkenyl substituent at C(b) in the cycloadducts was determined by NOE experiments and indicates that the geometry of the alkene is conserved during the transformation (Table 3, entry 1). Cycloadducts **20** and **30**, which contain a quaternary center, were obtained in excellent yields from dienynes **19** and **29**, respectively.

In addition to its synthetic value, the diene serves to facilitate the cycloaddition reaction relative to that of an alkene (Scheme 4). For example, whereas the reactions of dienes **7**, **25**, and **27** are all complete within 14 h at room temperature or 40 °C with 1–2.5 mol% catalyst (Table 3, entries 1, 7, 8), the reaction of the corresponding enyne **31** requires 3 days and much harsher conditions (80 °C, 5 mol% catalyst). Significantly, conjugation alone is not sufficient to facilitate the reaction, as under these same conditions the reaction of styrene substrate **33** is even more sluggish, requiring 4 days to reach 69% completion.

The substituent on the diene also has a significant effect on the reaction rate. The *i*Pr-substituted substrate **7** and bisalkylidene cyclopentane substrate **19**, for example, undergo [2+2+1] cycloaddition within 24 h at room temperature, whereas Me-substituted and unsubstituted analogues (**25** and **27**) give no conversion at room temperature after 12 h. However, efficient transformations are achieved in these cases at 40 °C with 2.5 mol% catalyst.

In summary, a new class of the Pauson–Khand reaction based on dienes is reported. In the case of internal alkynes, alkenylcyclopentenones are produced in excellent yields under mild conditions and low catalyst loadings (1–2.5 mol%). Substitution of the diene is well tolerated and allows the facile diastereoselective construction of quaternary centers (**20** and **30**). Further studies on this novel [2+2+1] pro-



Scheme 4. Reaction of enynes using our catalyst system.

cess and the new [4+2+1] carbonylative cycloaddition reaction are in progress.

Experimental Section

Characterization data for compounds **9**, **10**, **16**, **18**, **20**, **22**, **24**, **26**, **28**, and **30** are given in the Supporting Information.

General procedure: $[RhCl(CO)PPh_3)_2]$ (0.039 g, 0.056 mmol), $AgSbF_6$ (0.020 g, 0.058 mmol), and DCE (5.6 mL, 0.01M) were added into an oven-dried borosilicate glass test tube equipped with a stirrer bar and capped with a rubber septum. The resulting suspension was stirred for 1 h under a balloon of CO, vented through a bubbler. Dienyne **7** (0.035 g, 0.1197 mmol) was dissolved in DCE (1.08 mL, 0.11M) in a separate oven-dried borosilicate glass test tube equipped with a stirrer bar and capped with a rubber septum. This solution was stirred under a balloon of CO, vented through a bubbler, for 15 min. The catalyst solution (0.12 mL) was added to the solution of **7** and the resulting mixture was stirred vigorously under CO (1 atm) for 14 h. The mixture was purified by flash-column chromatography on silica gel (gradient elution: 0→10% ethyl acetate in pentane). Product-containing fractions were concentrated to give **9** in 89% yield as a colorless oil.

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Keywords: cycloaddition · dienes · homogeneous catalysis · Pauson–Khand reaction · rhodium

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[9] Dienyne **7** reacts under conventional Pauson–Khand conditions ($[Co_2(CO)_8]$ (1.1 equiv) and CO (1 atm) in THF at 55°C) to give **9** in 39% yield.

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