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Direct Michael Addition of Alkenes via a Cobalt-Dinitrosyl Mediated Vinylic C−H Functionalization Reaction

Chen Zhao, F. Dean Toste,* and Robert G. Bergman*

Department of Chemistry, University of California, Berkeley, California 94720, United States

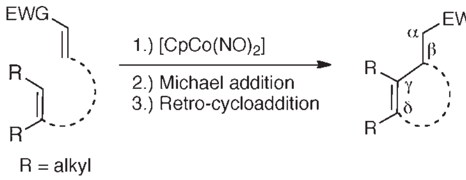
S *Supporting Information*

ABSTRACT: We report a one-pot, direct C−H functionalization reaction of alkenes mediated by [CpCo(NO)$_2$]. All intermediates in the proposed reaction sequence have been characterized. A variety of Michael acceptors can be utilized with the one-pot procedure to give the desired cyclic tetra-alkyl-substituted, γ,δ-unsaturated compounds in good yields. We also provide a preliminary result for catalytic turnover in both base and [CpCo(NO)$_2$].

The Michael addition of vinyl anion synthons to enones is a powerful synthetic transformation that forms new carbon−carbon (C−C) bonds and produces γ,δ-unsaturated ketones. While these compounds have traditionally been accessed by the stoichiometric addition of vinyl organometallic reagents, such as organocuprates, to Michael acceptors,[1] the need for improved substrate scope and functional group tolerance has provided impetus for the development of other methods. Over the past two decades, 1,4-addition of alkenes,[2] alkynes,[3] and allenes[4] to enones have been reported; however, intramolecular addition of alkenyl nucleophiles to enones remains challenging, as the organometallic moiety has to be generated in the presence of the reactive Michael acceptor.[5] This problem could be circumvented by the chemoselective generation of a nucleophile directly from a vinylic C−H bond,[6] followed by its conjugate addition to the enone. We now report the application of our recently developed C−H functionalization reaction of the sp^2-carbons of simple olefins mediated by [CpCo(NO)$_2$] (Scheme 1)[7,8] to a one-pot, direct vinylic C−H funtionalization reaction of alkenes.

We envisioned the cyclization reaction summarized in Scheme 1 and began by studying the individual steps of this overall transformation. It has previously been reported that upon heating, cobalt complex **1**[9] is in equilibrium with the free olefin and the reactive intermediate [CpCo(NO)$_2$] at 75 °C. This latter species can be trapped by a different alkene to give the corresponding cobalt dinitrosoalkane complex.[10,11] Thus, when complex **1** and 10 equiv of **2a** were heated in toluene, complex **3** was obtained in 65% yield (Scheme 2).

Scheme 1. Vinylic C−H Functionalization Reaction of Alkenes Mediated by [CpCo(NO)$_2$]



Scheme 2. Cycloaddition of 2a to [CpCo(NO)$_2$]

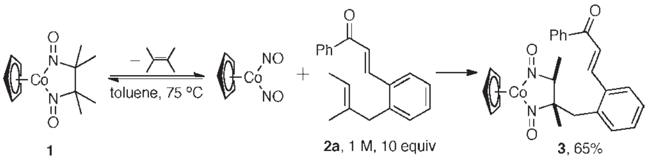
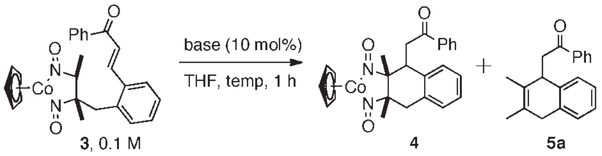
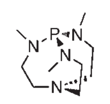


Table 1. Reaction Conditions for the Cyclization of Cobalt Complex 3 to Give Complex 4 and/or 5a



entry	base	temp (°C)	yield of 4	yield of 5a
1	Verkade's	- 78	25%	26%
2	Verkade's	25	25%	25%
3	Verkade's	75	-	81%
4	*t*BuOK	75	-	80%

Verkade's Base



Treatment of **3** with 10 mol % of Verkade's base at room temperature not only led to the corresponding cyclized cobalt complex **4** but also gave the desired organic product **5a** (Table 1, entry 2). While repeating the cyclization at −78 °C had no effect on this product distribution, when complex **3** was heated in the presence of 10 mol % of either Verkade's base or *t*-BuOK, **5a** was obtained exclusively in much improved yields (entries 3 and 4). Furthermore, when complex **4** was heated with 10 mol % of Verkade's base, **5a** was also obtained in 83% yield. The lability of the [CpCo(NO)$_2$] fragment in **4** has precedent in our previous studies and, due to their thermal instability, cobalt dinitrosoalkane complexes of cyclohexene have previously only been generated and studied *in situ*.[10] Further support was provided by a control experiment, in which heating complex **4** in THF for 30 min at 75 °C gave **5a** in 93% yield.

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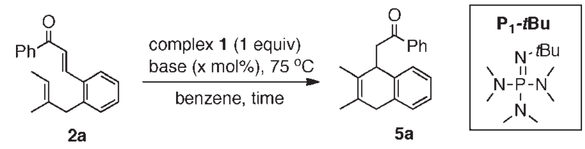
Table 2. Reaction Optimization of 2a to 5a Mediated by 1



entry	conc. of **2a** (M)	base	mol %	time (h)	yield of **5a**[a]
1	0.1	Verkade's	10	53	55%
2	0.2	Verkade's	10	72	70%
3	0.33	Verkade's	10	53	78%
4	0.33	LiCp	15	48	46%
5	0.33	P_1-*t*Bu	15	24	75%
6	**0.33**	**P_1-*t*Bu**	**20**	**24**	**85%**
7	0.33	P_1-*t*Bu	25	24	72%

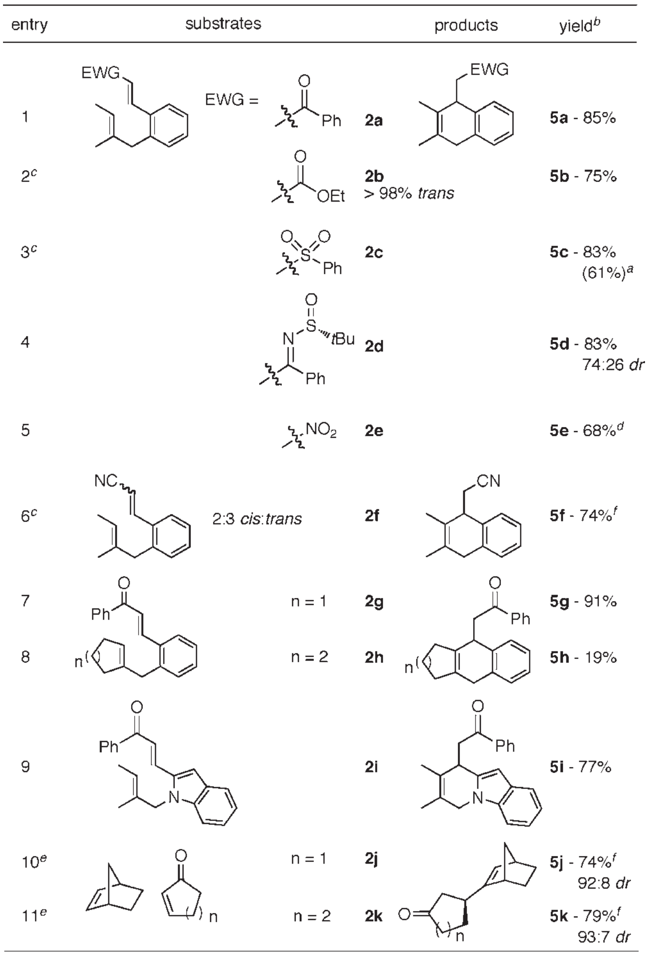
[a] Yields are determined by ^{1}H NMR spectroscopy with trimethoxybenzene as internal standard.

Having verified each step in the proposed reaction sequence outlined in Scheme 1, we envisioned effecting the overall transformation in one step. An initial reaction between stoichiometric amounts of **1** and **2a** in the presence of 10 mol % of Verkade's base at 75 °C led to a 55% yield of **5a** over 53 h (Table 2, entry 1). By increasing the concentration of **2a** and employing 20 mol % of P_1-*t*Bu phosphazene base, **5a** was obtained in 85% yield in 24 h (entry 6). Control experiments between **2a** and 20 mol % of either Verkade's or P_1-*t*Bu phosphazene base at 75 °C for 3 days led to no desired product and only recovered starting material.

We next surveyed the scope of the one-pot C—H functionalization reaction. As shown by Table 3, a variety of Michael acceptors can be utilized to give the corresponding tetra-alkyl-substituted alkene products in moderate to good yields (entries 1—6). In our initial reports,[7] α,β-unsaturated esters were ineffective as electrophiles for functionalization of cobalt dinitrosoalkane complexes; however, substrate **2b** (entry 2) cyclized to give the desired product in good yield. It is noteworthy that although substrate **2f** was synthesized as a mixture of *cis* and *trans* isomers (see Supporting Information), this mixture reacted readily to give **5f**. Substrates containing cyclic alkenyl groups can also give the desired tricyclic products (entries 7—8). We believe that the cyclopentyl group of **2g** is advantageous since strained alkenes bind [CpCo(NO)$_2$] much more effectively than simple, unstrained olefins.[11] This argument is exemplified by the low yield obtained with substrate **2h**. Furthermore, intermolecular coupling between norbornene and simple cyclic enones was achieved in one step to give the corresponding products in good yields and excellent *dr* (entries 10—11).[12]

While cobalt is an affordable and readily available transition metal, rendering the reaction outlined in Scheme 1 catalytic in [CpCo(NO)$_2$] would further improve upon the chemistry of this class of ligand-based C—H functionalization reaction. Although base-mediated decomposition of [CpCo(NO)$_2$] and the formation of a cobalt dimer **6**,[11] a stable and inactive species, have thus far limited catalytic turnover, substrate **2g** cyclized to give 60% yield of **5g** with 20 mol % of complex **1** (Scheme 3).

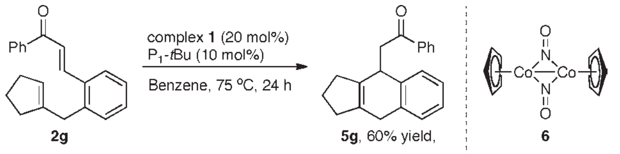
Table 3. Substrate Scope of the One-Pot C—H Functionalization Reaction Mediated by Complex 1[a]



entry	substrates		products	yield[b]
1		**2a**		**5a** - 85%
2[c]		**2b** > 98% *trans*		**5b** - 75%
3[c]		**2c**		**5c** - 83% (61%)[a]
4		**2d**		**5d** - 83% 74:26 *dr*
5		**2e**		**5e** - 68%[d]
6[c]	2:3 *cis*:*trans*	**2f**		**5f** - 74%[f]
7	n = 1	**2g**		**5g** - 91%
8	n = 2	**2h**		**5h** - 19%
9		**2i**		**5i** - 77%
10[e]	n = 1	**2j**		**5j** - 74%[f] 92:8 *dr*
11[e]	n = 2	**2k**		**5k** - 79%[f] 93:7 *dr*

[a] General condition: 1.2 equiv of **1**, P_1-*t*Bu (20 mol %), 75 °C, 24 h, benzene (0.33 M). [b] Yields are determined by ^{1}H NMR spectroscopy with trimethoxybenzene as an internal standard. [c] P_1-*t*Bu (100 mol %), second equiv of **1** added after 12 h of heating, followed by additional heating for 24 h. [d] 1.2 equiv of **1**, P_1-*t*Bu (10 mol %), 24 h. [e] 2 equiv of enone, 1.2 equiv of **1**, P_1-*t*Bu (10 mol %), 95 °C, 24 h. [f] Isolated yields.

Scheme 3. Catalytic Vinyl C—H Functionalization



In conclusion, we have developed a simple one-pot, C—H functionalization reaction of alkenes mediated by complex **1**. This methodology allows for the chemoselective generation of nuleophiles directly from vinyl C—H bonds, which can add to a variety of internal, and some external Michael acceptors in a 1,4-fashion. This strategy also gives rise to tri- and tetra-alkyl-substituted alkene products, where the olefin is γ,δ-unsaturated with respect to the electron-withdrawing functional groups. Efforts toward improving the catalytic reaction and extension to other transition metals are underway.

ASSOCIATED CONTENT

Supporting Information. Experimental procedures and full characterization for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author
fdtoste@berkeley.edu; rbergman@berkeley.edu

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(9) Complex **1** can be made on multigram scales and is bench stable. For experimental details, see Supporting Information.

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(12) The *dr* obtained is consistent with our previous studies; see ref 8.