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# Synthesis of substituted 6-imino-2-piperidinones by Rh-catalyzed [4+2] annulation of 4-alkynals with carbodiimides

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ABSTRACT

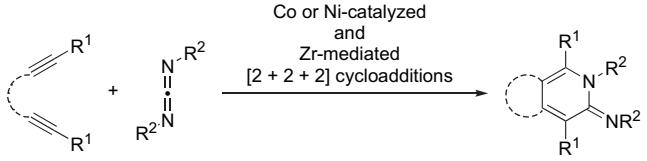
Synthesis of substituted 6-imino-2-piperidinones has been achieved by cationic rhodium(I)/dppp complex-catalyzed [4+2] annulations of various 4-alkynals with carbodiimides at room temperature. The reactions of benzene-linked 4-alkynals (2-alkynylbenzaldehydes) and carbodiimides also proceeded at room temperature, affording the corresponding 6-imino-2-piperidinones.



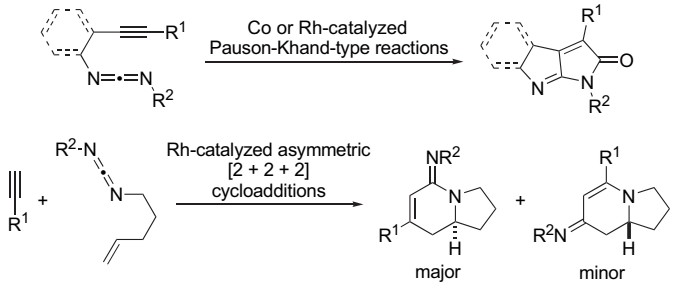
## 1. Introduction

Transition-metal-catalyzed cycloadditions are powerful synthetic methods for the construction of cyclic frameworks because of their atom economical and convergent nature.[1] For the synthesis of six-membered carbonyl compounds, [4+2] cycloadditions of five-membered acylmetal intermediates with unsaturated compounds have been developed.[2,3] Such five-membered acylmetal intermediates can be generated through the reactions of transition-metal carbonyl complexes with alkynes[4] and carbon–carbon bond cleavage of cyclobutenones[5–7] or cyclobutanones.[8,9] An alternative, more convenient generation of five-membered acylmetal intermediates was realized by intramolecular cis addition of a rhodium acyl hydride to a metal-bound triple bond of 4-alkynals, which react intermoleculaly with alkynes,[10] alkenes,[11] or carbonyl compounds[12] to form substituted cyclohexenones,[10] cyclohexanones,[11] or 2-pyranones,[12] respectively.[13]

On the other hand, transition-metal-catalyzed or mediated cycloadditions involving heterocumulenes have been widely examined for the synthesis of heterocycles.[14] In particular, cycloadditions utilizing isocyanates are efficient methods for the synthesis of nitrogen heterocycles.[15–19] For example, a number of transition-metal-catalyzed [2+2+2] cycloadditions of alkynes with isocyanates to form substituted 2-pyridones have been reported using Co,[15] Ni,[16] Ru,[17] and Rh[18] catalysts. On the contrary, transition-metal-catalyzed or mediated cycloadditions involving carbodiimides have been reported in a few number of examples.[15b,e,19a,20–22] A cobalt or nickel-complex[15b,e,20] and a zirconium complex[19a] are able to catalyze or mediate [2+2+2] cycloadditions of alkynes with untethered carbodiimides (Scheme 1). Cobalt or rhodium-catalyzed Pauson–Khand-type reactions of tethered alkyne-carbodiimides with carbon monoxide[21] and rhodium-catalyzed asymmetric [2+2+2] cycloadditions of tethered alkene-carbodiimides with alkynes[22] have been reported (Scheme 2). However, successful transition-metal-catalyzed cycloadditions involving untethered carbodiimides are limited to the above cobalt or nickel-catalyzed [2+2+2] cycloadditions.[15b,e,20]




**Scheme 1.** Transition-metal-catalyzed or mediated cycloadditions involving untethered carbodiimides.




**Scheme 2.** Transition-metal-catalyzed cycloadditions involving tethered carbodiimides.

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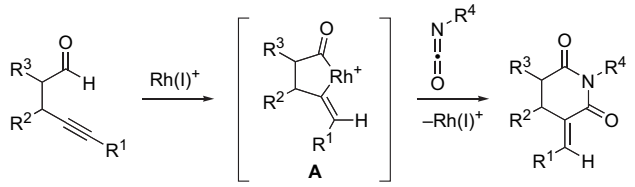
For the synthesis of nitrogen-containing six-membered carbonyl compounds, we have recently developed rhodium-catalyzed intermolecular cross-[4+2] annulations of 4-alkynals including 2-alkynylbenzaldehydes with isocyanates, leading to substituted glutarimides, presumably through five-membered acylrhodium intermediate **A** (Scheme 3).[23] The use of an isocyanate as a cycloaddition partner efficiently suppressed the formation of the undesired homo-[4+2] annulation products (Fig. 1). In this paper, we describe the successful use of carbodiimides instead of isocyanates in the above cross-[4+2] annulation, which furnishes substituted 6-imino-2-piperidinones presumably through the same acylrhodium intermediate **A** (Scheme 4).




**Scheme 3.** Rhodium-catalyzed [4+2] annulations of 4-alkynals with isocyanates.

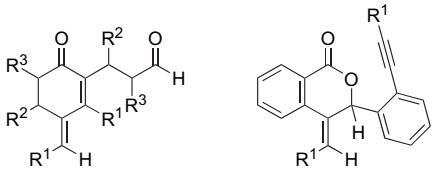
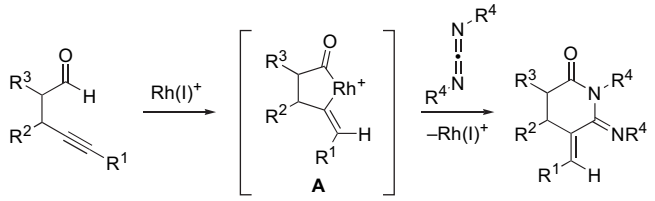


**Figure 1.** Structures of homo-[4+2] annulation products.




**Scheme 4.** Rhodium-catalyzed [4+2] annulations of 4-alkynals with carbodiimides.

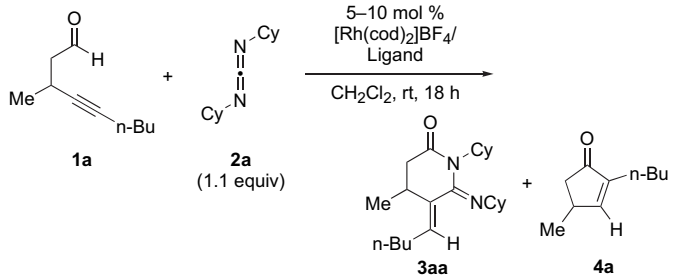
## 2. Results and discussion

### 2.1. Rhodium-catalyzed [4+2] annulations of 4-alkynals with carbodiimides

We first examined the reaction of 3-methyl-4-nonynal (**1a**) with dicyclohexyl carbodiimide (**2a**) in the presence of a cationic rhodium(I)/dppe complex (10 mol %) at room temperature. However, the reaction was sluggish and the expected 6-imino-2-piperidinone **3aa** was obtained in very low yield (Table 1, entry 1). Screening of various bisphosphine ligands (Fig. 2) revealed that the use of ligands having the large P-M-P natural bite angles (dppp, dppb, dppf, and *rac*-BINAP, entries 2–5) improved the conversion of **1a**, and furnished the desired 6-imino-2-piperidinone **3aa** along with cyclopentenone **4a**.[24] The highest yield of **3aa** was achieved with dppp (entry 2), and the catalyst loading could be reduced to 5 mol % without erosion of the product yield (entry 6).

Thus, we explored the scope of this process by using 1.1 equiv of carbodiimides and 5 mol % of the cationic rhodium(I)/dppp complex at room temperature as shown in Table 2. With respect to carbodiimides, not only dicyclohexyl carbodiimide (**2a**, entry 1) but also diisopropyl carbodiimide (**2b**, entry 2) could participate in this reaction giving the corresponding cycloadduct **3ab**, although its yield was lower than that of **3aa**. Unfortunately, aromatic carbodiimide **2c** failed to react with **1a** (entry 3). With respect to 4-alkynals, a variety of 5-substituted-4-alkynals could be subjected to this process. Alkyl- (**1a** and **1b**, entries 1, 4, and 5), chloropropyl- (**1c**, entry 6), trimethylsilyl- (**1d**, entry 7), and alkenyl-substituted 4-alkynals (**1e**, entry 8) reacted with **2a** to afford the corresponding 6-imino-2-piperidinones in moderate to good yields. 4-Alkynal **1f** bearing no substituent at the 3-position could also participate in this reaction (entry 9). Importantly, a single olefin isomer, described in Table 2, was produced for all of these annulations.

**Table 1**
Screening of ligands for cationic rhodium(I) complex-catalyzed [4+2] annulation of 4-alkynal **1a** with carbodiimide **2a**[a]




| Entry | Ligand | Catalyst (%) | Convn[b] (%) | Yield (%) | |
|---|---|---|---|---|---|
| | | | | **3aa**[c] | **4a**[b] |
| 1 | dppe | 10 | <5 | <5 | <1 |
| 2 | dppp | 10 | 83 | 55 | <1 |
| 3 | dppb | 10 | 90 | 18 | 7 |
| 4 | dppf | 10 | 42 | 9 | 22 |
| 5 | *rac*-BINAP | 10 | 74 | 7 | 6 |
| 6[d] | dppp | 5 | 94 | 58 | <1 |

[a] $[Rh(cod)_2]BF_4$ (0.0050–0.010 mmol), ligand (0.0050–0.010 mmol), **1a** (0.10 mmol), **2a** (0.11 mmol), and $CH_2Cl_2$ (1.0 mL) were used.
[b] Determined by $^1H$ NMR.
[c] Isolated yield.
[d] For 48 h.

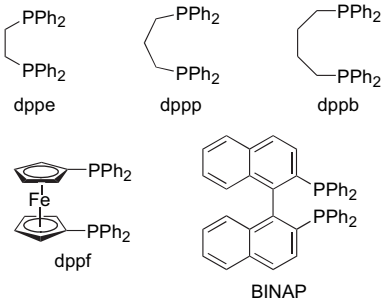
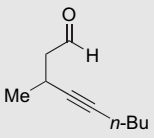
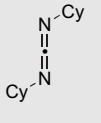
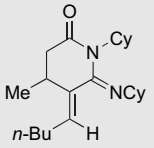
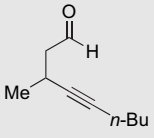
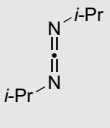
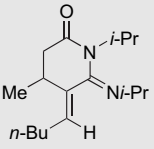
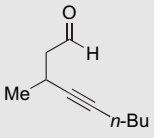
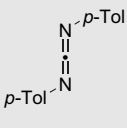
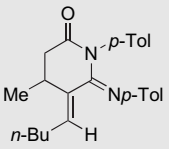
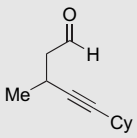
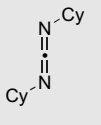
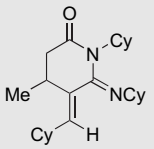
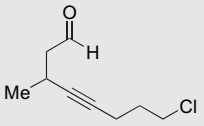
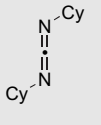
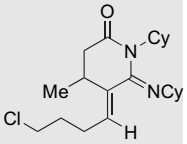
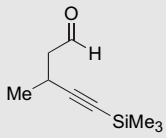
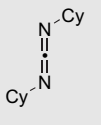
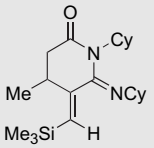
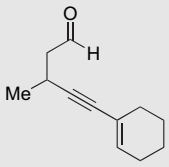
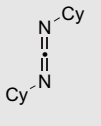
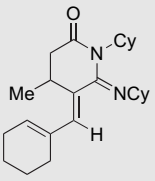
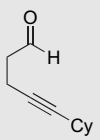
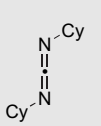
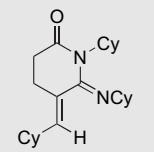



**Figure 2.** Structures of bisphosphine ligands.

### 2.2. Rhodium-catalyzed [4+2] annulations of 2-alkynylbenzaldehydes with carbodiimides

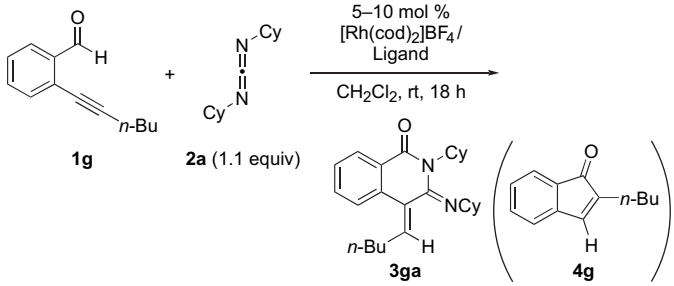
Having succeeded the intermolecular [4+2] annulations of 4-alkynals with carbodiimides, we turned our attention to rhodium-catalyzed intermolecular [4+2] annulations of benzene-linked 4-alkynals (2-alkynylbenzaldehydes) with carbodiimides. After screening of bisphosphine ligands (Table 3, entries 1–5) in the reaction of 2-hexynylbenzaldehyde (**1g**) and dicyclohexyl

**Table 2**
Cationic rhodium(I)/dppp complex-catalyzed [4+2] annulations of 4-alkynals **1a–f** with carbodiimides **2a–c**[a]

| Entry | 1 | 2 | 3/% yield[b] |
|---|---|---|---|
| 1 |  |  |  |
| | **1a** | **2a** | **3aa**/58 |
| 2 |  |  |  |
| | **1a** | **2b** | **3ab**/30 |
| 3 |  |  |  |
| | **1a** | **2c** | **3ac**/0[c] |
| |  |  |  |
| 4[d] | **1b** | **2a** | **3ba**/64 |
| 5[d,e] | **1b** | **2a** | **3ba**/75 |
| 6 |  |  |  |
| | **1c** | **2a** | **3ca**/79 |
| 7 |  |  |  |
| | **1d** | **2a** | **3da**/39 |
| 8 |  |  |  |
| | **1e** | **2a** | **3ea**/44 |
| 9 |  |  |  |
| | **1f** | **2a** | **3fa**/53 |

[a] Reactions were conducted using $[Rh(cod)_2]BF_4$ (0.010 mmol), dppp (0.010 mmol), **1a–f** (0.20 mmol), **2a–c** (0.22 mmol), and $CH_2Cl_2$ (2.0 mL) at room temperature for 24 h.
[b] Isolated yield.
[c] No reaction was observed.
[d] For 72 h.
[e] Catalyst: 10 mol %.

**Table 3**
Screening of ligands for cationic rhodium(I) complex-catalyzed [4+2] annulation of 2-alkynylbenzaldehyde **1g** with carbodiimide **2a**[a]




| Entry | Ligand | Catalyst (%) | Convn[b] (%) | Yield (%) | |
|---|---|---|---|---|---|
| | | | | 3ga[c] | 4g[b] |
| 1 | dppe | 10 | <5 | <1 | 0 |
| 2 | dppp | 10 | 93 | 41 | 0 |
| 3 | dppb | 10 | 98 | 12 | 0 |
| 4 | dppf | 10 | 0 | 0 | 0 |
| 5 | *rac*-BINAP | 10 | 0 | 0 | 0 |
| 6 | dppp | 5 | <5 | <5 | 0 |

[a] $[Rh(cod)_2]BF_4$ (0.0050–0.010 mmol), ligand (0.0050–0.010 mmol), **1g** (0.10 mmol), **2a** (0.11 mmol), and $CH_2Cl_2$ (1.0 mL) were used.
[b] Determined by $^1H$ NMR.
[c] Isolated yield.

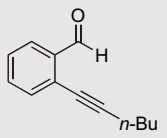
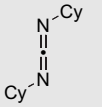
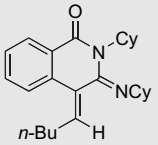
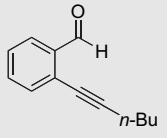
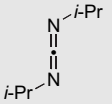
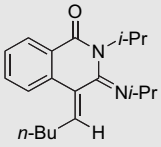
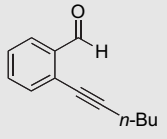
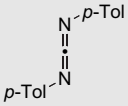
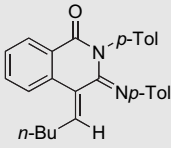
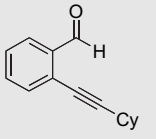
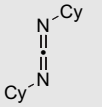
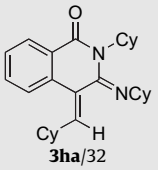
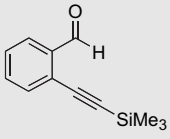
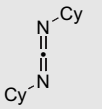
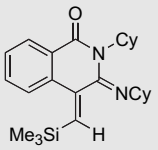
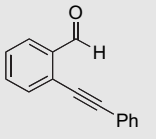
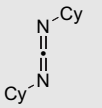
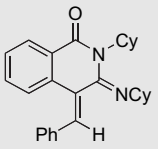
carbodiimide (**2a**) at room temperature, we were pleased to find that the desired 6-imino-2-piperidinone **3ga** was obtained in moderate yield by using dppp as a ligand (entry 2). In these reactions, intramolecular hydroacylation product **4g** was not generated at all. Unfortunately, decreasing the catalyst loading to 5 mol % significantly lowered the catalytic activity (entry 6).

Under the above optimized reaction conditions, the scope of carbodiimides and 2-alkynylbenzaldehydes was examined as shown in Table 4. The use of diisopropyl carbodiimide (**2b**, entry 2) instead of dicyclohexyl carbodiimide (**2a**, entry 1) decreased the yield of the corresponding cycloadduct. Interestingly, aromatic carbodiimide **2c** (entry 3) could also participate in this reaction, although the reaction was sluggish. As the product 6-imino-2-piperidinone **3gc** was gradually decomposed to unidentified mixture of products under the above reaction conditions, prolonged reaction time did not increase the product yield. Alkyl- (**1g** and **1h**, entries 1 and 4), trimethylsilyl- (**1i**, entry 5) and phenyl-substituted 2-ethynylbenzaldehydes (**1j**, entry 6) could react with **2a** to afford the corresponding 6-imino-2-piperidinones. These [4+2] annulations using 2-alkynylbenzaldehydes also produced a single olefin isomer described in Table 4.

### 2.3. Mechanistic consideration regarding rhodium-catalyzed [4+2] annulations of 4-alkynals with carbodiimides

Scheme 5 shows a plausible mechanism for the rhodium-catalyzed [4+2] annulation of 4-alkynal **1** with carbodiimide **2**. The rhodium catalyst oxidatively inserts into the aldehyde C–H bond of **1**, affording rhodium acyl hydride **B**. The cis addition of the rhodium hydride to the metal-bound alkyne then provides five-membered acylrhodium intermediate **A**. Complexation of carbodiimide **2** is followed by insertion to form rhodacycle **C**. Reductive elimination furnishes 6-imino-2-piperidinone **3** and regenerates the rhodium catalyst. The homo-[4+2] annulations of **1** (Fig. 1), which are the major side-reactions, also proceed presumably through the same rhodacycle **A**.[10,12] Cyclopentenone **4** can be obtained by the

**Table 4**
Cationic rhodium(I)/dppp complex-catalyzed [4+2] annulations of 2-alkynylbenzaldehydes **1g–j** with carbodiimides **2a–c**[a]

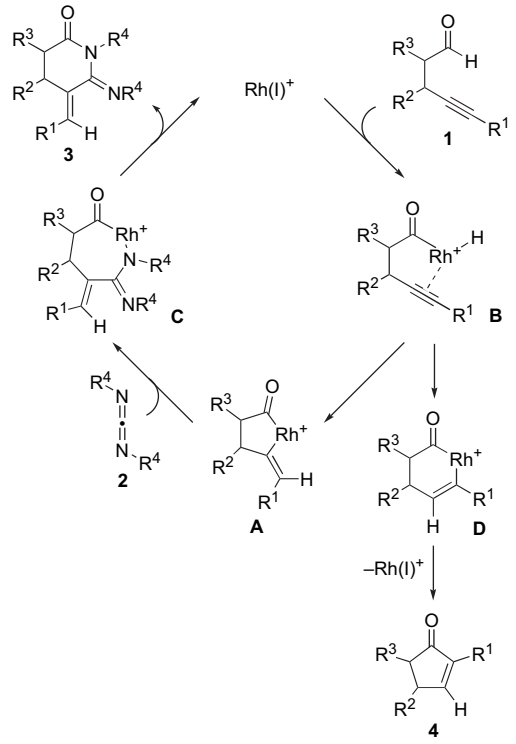
| Entry | 1 | 2 | 3/% yield[b] |
|---|---|---|---|
| 1 |  **1g** |  **2a** |  **3ga**/46 |
| 2 |  **1g** |  **2b** |  **3gb**/36 |
| 3 |  **1g** |  **2c** |  **3gc**/23[c] |
| 4 |  **1h** |  **2a** |  **3ha**/32 |
| 5 |  **1i** |  **2a** |  **3ia**/34 |
| 6 |  **1j** |  **2a** |  **3ja**/53 |

[a] Reactions were conducted using $[Rh(cod)_2]BF_4$ (0.020 mmol), dppp (0.020 mmol), **1g–j** (0.20 mmol), **2a–c** (0.22 mmol), and $CH_2Cl_2$ (2.0 mL) at room temperature for 24 h.
[b] Isolated yield.
[c] Convn of **1g** was ca. 40%.

rhodium-catalyzed trans hydroacylation of **1** through six-membered acylrhodium intermediate **D**.[24]

## 3. Conclusions

In conclusion, we have determined that a cationic rhodium(I)/dppp complex catalyzes [4+2] annulations of various 4-alkynals including 2-alkynylbenzaldehydes with carbodiimides at room temperature, giving substituted 6-imino-2-piperidinones. Although product yields using carbodiimides are lower than those using isocyanates, this catalysis represents a successful new example of scarcely reported transition-metal-catalyzed cycloadditions involving untethered carbodiimides. Furthermore, this method serves as an attractive new route to substituted 6-imino-2-piperidinones in view of the one-step access of 4-alkynals starting from readily available terminal alkynes.




**Scheme 5.** Possible mechanism for rhodium-catalyzed [4+2] annulation of 4-alkynal **1** with carbodiimide **2**.

## 4. Experimental

### 4.1. General

$^1H$ NMR spectra were recorded on 300 MHz (JEOL AL 300). $^{13}C$ NMR spectra were obtained with complete proton decoupling on 75 MHz (JEOL AL 300). HRMS data were obtained on a Bruker micrOTOF Focus II. Infrared spectra were obtained on a JASCO FT/IR-4100. All reactions were carried out under an atmosphere of argon in oven-dried glassware with magnetic stirring.

### 4.2. Materials

Anhydrous $CH_2Cl_2$ (No. 27,099-7) was obtained from Aldrich and used as received. 4-Alkynals **1a**,[23] **1b**,[23] **1c**, **1d**,[23] **1e**,[23] and **1f**[25] were prepared by 1,4-addition reactions of the corresponding terminal alkynes and alkenylaldehydes.[26] 2-Alkynylbenzaldehydes **1g**,[12] **1h**,[12] and **1j**[12] were prepared by Sonogashira couplings of 2-bromobenzaldehyde and the corresponding terminal alkynes. All other reagents were obtained from commercial sources and used as received.

### 4.3. 8-Chloro-3-methyloct-4-ynal (1c)

*n*-BuLi (1.59 M in hexane, 12.6 mL, 20.0 mmol) was added to a stirred solution of 5-chloro-1-pentyne (2.05 g, 20.0 mmol) in THF (40 mL) at −10 °C, and the resulting mixture was stirred at −10 °C for 30 min. CuI (3.8 g, 20.0 mmol) was added, and the resulting mixture was stirred at −10 °C for 5 min. After cooling to −78 °C, TMSI (2.8 mL, 20.0 mmol) was added. Crotonaldehyde (1.40 g, 20.0 mmol) was added at −78 °C, and the resulting mixture was stirred at −78 °C for 5 h. The reaction was quenched by the addition of saturated aqueous $NH_4Cl$. After stirring for 30 min, 37% HCl (2.0 g) was added. Aftter stirring for another 30 min, the reaction was extracted with $Et_2O$. The organic layer was washed with 5%

$Na_2S_2O_3$ and brine, dried over $Na_2SO_4$, and concentrated. The residue was purified by a silica gel column chromatography (hexane/EtOAc=20:1), which furnished **1c** (2.66 g, 15.4 mmol, 77% yield) as a yellow oil. IR (neat) 2968, 2933, 1726, 1442, 1332 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ 9.77 (t, $J$=2.1 Hz, 1H), 3.61 (t, $J$=6.9 Hz, 2H), 2.96 (tsext, $J$=6.9, 2.1 Hz, 1H), 2.54 (ddd, $J$=16.5, 6.9, 2.1 Hz, 1H), 2.46 (ddd, $J$=16.5, 6.9, 2.1 Hz, 1H), 2.34 (dt, $J$=6.9, 2.1 Hz, 2H), 1.92 (quint, $J$=6.9 Hz, 2H), 1.20 (d, $J$=6.9 Hz, 3H); $^{13}C$ NMR ($CDCl_3$, 75 MHz) $\delta$ 201.3, 83.7, 79.6, 50.2, 43.7, 31.5, 21.2, 20.6, 16.0; HRMS (ESI) calcd for $C_9H_{13}ClONa$ $[M+Na]^+$ 195.0547, found 195.0539.

### 4.4. Representative procedure for rhodium-catalyzed [4+2] annulations of 4-alkynals 1 with carbodiimides 2 (Table 2, entry 1)

A $CH_2Cl_2$ (0.2 mL) solution of dppp (4.1 mg, 0.010 mmol) was added to a $CH_2Cl_2$ (0.2 mL) solution of $[Rh(cod)_2]BF_4$ (4.1 mg, 0.010 mmol) and the mixture was stirred at room temperature for 30 min. $H_2$ was introduced to the resulting solution in a Schlenk tube. After stirring at room temperature for 2 h, the resulting solution was concentrated to dryness and dissolved in $CH_2Cl_2$ (0.5 mL). To this solution was added a $CH_2Cl_2$ (1.5 mL) solution of **1a** (30.4 mg, 0.200 mmol) and **2a** (45.4 mg, 0.220 mmol). The mixture was stirred at room temperature for 24 h. The resulting solution was concentrated and purified by a preparative TLC (hexane/EtOAc=7:1, then $CH_2Cl_2$), which furnished **3aa** (41.6 mg, 0.116 mmol, 58% yield) as a pale yellow oil.

#### *4.4.1. (4E)-1-Cyclohexyl-6-cyclohexylimino-4-methyl-5-pentylidenepiperidin-2-one (**3aa**)*

Pale yellow oil; IR (neat) 2927, 2853, 1682, 1632, 1197 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ 5.40 (t, $J$=7.5 Hz, 1H), 4.68 (tt, $J$=12.3, 3.6 Hz, 1H), 3.53 (tt, $J$=8.4, 4.2 Hz, 1H), 2.95 (dquint, $J$=6.6, 2.1 Hz, 1H), 2.62 (dd, $J$=16.8, 6.6 Hz, 1H), 2.44 (dq, $J$=12.3, 3.6 Hz, 1H), 2.39 (dd, $J$=16.8, 2.1 Hz, 1H), 2.33 (dq, $J$=12.3, 3.6 Hz, 1H), 2.17 (q, $J$=7.5 Hz, 1H), 2.09 (q, $J$=7.5 Hz, 1H), 1.87–1.05 (m, 22H), 0.99 (d, $J$=6.6 Hz, 3H), 0.91 (t, $J$=7.2 Hz, 3H); $^{13}C$ NMR ($CDCl_3$, 75 MHz) $\delta$ 170.4, 150.8, 131.7, 130.2, 58.4, 53.9, 41.9, 35.0, 34.6, 31.6, 30.1, 28.3, 26.82, 26.76, 26.7, 26.5, 25.9, 25.7, 24.3, 24.2, 22.3, 18.6, 13.9; HRMS (ESI) calcd for $C_{23}H_{39}N_2O$ $[M+H]^+$ 359.3057, found 359.3049.

#### *4.4.2. (4E)-1-Isopropyl-6-isopropylimino-4-methyl-5-pentylidenepiperidin-2-one (**3ab**)*

Pale yellow oil; IR (neat) 2963, 2928, 1682, 1632, 1242 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ 5.45 (t, $J$=7.2 Hz, 1H), 5.11 (sept, $J$=6.9 Hz, 1H), 3.84 (sept, $J$=6.0 Hz, 1H), 2.97 (dquint, $J$=6.6, 1.8 Hz, 1H), 2.62 (dd, $J$=17.1, 6.6 Hz, 1H), 2.41 (dd, $J$=17.1, 1.8 Hz, 1H), 2.18 (quint, $J$=7.2 Hz, 1H), 2.13 (quint, $J$=7.2 Hz, 1H), 1.46–1.22 (m, 4H), 1.40 (d, $J$=6.9 Hz, 3H), 1.34 (d, $J$=6.9 Hz, 3H), 1.18 (d, $J$=6.0 Hz, 3H), 1.03 (d, $J$=6.0 Hz, 3H), 1.00 (d, $J$=6.6 Hz, 3H), 0.92 (t, $J$=7.2 Hz, 3H); $^{13}C$ NMR ($CDCl_3$, 75 MHz) $\delta$ 170.3, 150.6, 131.6, 130.4, 50.4, 45.1, 41.9, 31.6, 26.9, 26.7, 25.1, 24.6, 22.4, 20.5, 19.0, 18.4, 13.9; HRMS (ESI) calcd for $C_{17}H_{31}N_2O$ $[M+H]^+$ 279.2431, found 279.2423.

#### *4.4.3. (4E)-1-Cyclohexyl-6-cyclohexylimino-5-cyclohexylmethylene-4-methylpiperidin-2-one (**3ba**)*

Pale yellow oil; IR (neat) 2925, 2852, 1681, 1630, 1197 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ 5.26 (d, $J$=9.6 Hz, 1H), 4.69 (tt, $J$=12.3, 3.6 Hz, 1H), 3.53 (tt, $J$=8.4, 4.2 Hz, 1H), 2.96 (dquint, $J$=6.6, 1.8 Hz, 1H), 2.62 (dd, $J$=17.1, 6.6 Hz, 1H), 2.53–2.22 (m, 1H), 2.46 (dq, $J$=12.3, 3.6 Hz, 1H), 2.41 (dd, $J$=17.1, 2.0 Hz, 1H), 2.34 (dq, $J$=12.3, 3.6 Hz, 1H), 1.87–1.06 (m, 28H), 0.99 (d, $J$=6.6 Hz, 3H); $^{13}C$ NMR ($CDCl_3$, 75 MHz) $\delta$ 170.4, 150.7, 135.9, 129.6, 58.5, 53.8, 42.3, 36.4, 35.0, 34.7, 33.6, 32.7, 30.0, 28.3, 27.1, 26.7, 26.5, 25.9, 25.7, 25.6, 25.5, 24.3, 18.7; HRMS (ESI) calcd for $C_{25}H_{41}N_2O$ $[M+H]^+$ 385.3213, found 385.3239.

#### *4.4.4. (4E)-5-(4-Chlorobutylidene)-1-cyclohexyl-6-cyclohexylimino-4-methylpiperidin-2-one (**3ca**)*

Pale yellow oil; IR (neat) 2927, 1852, 1679, 1632, 1197 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ 5.35 (t, $J$=7.5 Hz, 1H), 4.66 (tt, $J$=12.0, 3.6 Hz, 1H), 3.55 (t, $J$=6.3 Hz, 2H), 3.48 (tt, $J$=8.4, 4.2 Hz, 1H), 2.99 (dquint, $J$=6.6, 2.4 Hz, 1H), 2.63 (dd, $J$=17.1, 6.6 Hz, 1H), 2.52–2.22 (m, 3H), 2.42 (dq, $J$=12.0, 3.6 Hz, 1H), 2.40 (dd, $J$=17.1, 2.4 Hz, 1H), 1.88 (quint, $J$=6.3 Hz, 2H), 1.80–1.15 (m, 18H), 1.00 (d, $J$=6.6 Hz, 3H); $^{13}C$ NMR ($CDCl_3$, 75 MHz) $\delta$ 170.1, 150.4, 133.4, 127.7, 58.4, 53.9, 44.0, 41.8, 34.9, 34.6, 31.8, 30.0, 28.2, 26.74, 26.71, 26.4, 25.8, 25.7, 24.2, 24.15, 24.08, 18.6; HRMS (ESI) calcd for $C_{22}H_{36}ClN_2O$ $[M+H]^+$ 389.2511, found 379.2516.

#### *4.4.5. (4E)-1-Cyclohexyl-6-cyclohexylimino-4-methyl-5-trimethylsilanylmethylenepiperidin-2-one (**3da**)*

Colorless solid; mp 77–79 °C; IR (KBr) 2925, 2853, 1682, 1627, 1195 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ 5.41 (s, 1H), 4.69 (tt, $J$=12.3, 3.6 Hz, 1H), 3.47 (tt, $J$=8.4, 4.2 Hz, 1H), 2.83 (dquint, $J$=6.6, 1.5 Hz, 1H), 2.67 (dd, $J$=17.1, 6.6 Hz, 1H), 2.48 (dq, $J$=12.3, 3.6 Hz, 1H), 2.47 (dd, $J$=17.1, 1.5 Hz, 1H), 2.35 (dq, $J$=12.3, 3.6 Hz, 1H), 1.87–1.12 (m, 18H), 1.02 (d, $J$=6.6 Hz, 3H), 0.17 (s, 9H); $^{13}C$ NMR ($CDCl_3$, 75 MHz) $\delta$ 170.0, 151.1, 147.2, 129.5, 58.5, 53.9, 42.2, 34.9, 34.5, 32.5, 29.9, 28.1, 26.8, 26.5, 25.9, 25.7, 24.1, 18.4, 0.0; HRMS (ESI) calcd for $C_{22}H_{39}N_2OSi$ $[M+H]^+$ 375.2826, found 375.2825.

#### *4.4.6. (4E)-5-Cyclohex-1-enylmethylene-1-cyclohexyl-6-cyclohexylimino-4-methylpiperidin-2-one (**3ea**)*

Yellow oil; IR (neat) 2928, 1853, 1678, 1628, 1198 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ 5.76 (s, 1H), 5.71–5.64 (m, 1H), 4.73 (tt, $J$=12.0, 3.6 Hz, 1H), 3.57 (tt, $J$=8.4, 4.2 Hz, 1H), 3.26 (dquint, $J$=6.6, 1.5 Hz, 1H), 2.66 (dd, $J$=17.1, 6.6 Hz, 1H), 2.49 (dq, $J$=12.0, 3.6 Hz, 1H), 2.40 (dd, $J$=17.1, 1.5, 1H), 2.37 (dq, $J$=12.0, 3.6 Hz, 1H), 2.24–1.19 (m, 4H), 1.88–1.13 (m, 22H), 1.02 (d, $J$=6.6 Hz, 3H); $^{13}C$ NMR ($CDCl_3$, 75 MHz) $\delta$ 170.4, 150.9, 133.5, 132.0, 130.3, 129.2, 58.0, 53.9, 42.1, 35.0, 34.5, 30.0, 28.8, 28.3, 27.6, 26.8, 26.5, 26.0, 25.7, 25.5, 24.2, 24.0, 22.6, 21.8, 18.9; HRMS (ESI) calcd for $C_{25}H_{39}N_2O$ $[M+H]^+$ 383.3057, found 383.3065.

#### *4.4.7. (4E)-1-Cyclohexyl-6-cyclohexylimino-5-cyclohexylmethylenepiperidin-2-one (**3fa**)*

Pale yellow oil; IR (neat) 2925, 2852, 1682, 1631, 1187 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ 5.38 (d, $J$=9.3 Hz, 1H), 4.64 (tt, $J$=12.0, 3.6 Hz, 1H), 3.57 (tt, $J$=9.0, 4.2 Hz, 1H), 2.535 (t, $J$=7.2, 1H), 2.533 (t, $J$=6.6, 1H), 2.48–2.15 (m, 3H), 2.40 (dd, $J$=7.2, 6.6 Hz, 2H), 1.88–1.04 (m, 28H); $^{13}C$ NMR ($CDCl_3$, 75 MHz) $\delta$ 171.1, 151.7, 137.1, 124.9, 58.3, 54.0, 36.6, 34.83, 34.79, 32.9, 29.3, 26.6, 25.9, 25.8, 25.7, 25.5, 24.3, 22.5; HRMS (ESI) calcd for $C_{24}H_{39}N_2O$ $[M+H]^+$ 371.3057, found 371.3088.

### 4.5. Representative procedure for rhodium-catalyzed [4+2] annulations of 2-alkynylbenzaldehydes 1 with carbodiimides 2 (Table 4, entry 1)

A $CH_2Cl_2$ (0.2 mL) solution of dppp (8.2 mg, 0.020 mmol) was added to a $CH_2Cl_2$ (0.2 mL) solution of $[Rh(cod)_2]BF_4$ (8.1 mg, 0.020 mmol) and the mixture was stirred at room temperature for 30 min. $H_2$ was introduced to the resulting solution in a Schlenk tube. After stirring at room temperature for 2 h, the resulting solution was concentrated to dryness and dissolved in $CH_2Cl_2$ (0.5 mL). To this solution was added a $CH_2Cl_2$ (1.5 mL) solution of **1g** (37.2 mg, 0.200 mmol) and **2a** (45.4 mg, 0.220 mmol). The mixture was stirred at room temperature for 24 h. The resulting solution was concentrated and purified by a preparative TLC (hexane/toluene/EtOAc/triethylamine=10:6:1:1), which furnished **3ga** (36.4 mg, 0.093 mmol, 46% yield) as a yellow oil.

*4.5.1. (4E)-2-Cyclohexyl-3-cyclohexylimino-4-pentylidene-3,4-dihydro-2H-isoquinolin-1-one (**3ga**)*

Yellow oil; IR (neat) 2928, 1854, 1673, 1637, 1357 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ 8.16–8.09 (m, 1H), 7.51 (dt, $J$=7.5, 1.5 Hz, 1H), 7.45–7.35 (m, 2H), 5.83 (t, $J$=7.5 Hz, 1H), 4.64 (tt, $J$=12.0, 3.6 Hz, 1H), 3.75 (tt, $J$=8.4, 4.2 Hz, 1H), 2.55–2.33 (m, 2H), 2.42 (q, $J$=7.5 Hz, 2H), 1.87–1.08 (m, 22H), 0.92 (t, $J$=7.5 Hz, 3H); $^{13}C$ NMR ($CDCl_3$, 75 MHz) $\delta$ 164.0, 151.3, 136.1, 133.3, 131.1, 128.8, 128.5, 127.8, 126.3, 126.0, 57.6, 55.8, 34.6, 31.8, 28.1, 26.6, 25.9, 25.8, 24.1, 22.4, 13.9; HRMS (ESI) calcd for $C_{26}H_{37}N_2O$ $[M+H]^+$ 393.2900, found 393.2932.

*4.5.2. (4E)-2-Isopropyl-3-isopropylimino-4-pentylidene-3,4-dihydro-2H-isoquinolin-1-one (**3gb**)*

Pale yellow oil; IR (neat) 2964, 2928, 1675, 1356, 1247 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ 8.14 (dd, $J$=7.5, 1.5 Hz, 1H), 7.51 (dt, $J$=7.5, 1.5 Hz, 1H), 7.41 (dt, $J$=7.5, 1.5 Hz, 1H), 7.40 (dd, $J$=7.5, 1.5 Hz, 1H), 5.86 (t, $J$=7.5 Hz, 1H), 5.05 (sept, $J$=6.9, 1H), 4.06 (sept, $J$=6.3, 1H), 2.43 (q, $J$=7.5 Hz, 2H), 1.57–1.43 (m, 2H), 1.49 (d, $J$=6.9 Hz, 6H), 1.42–1.25 (m, 2H), 1.16 (d, $J$=6.3 Hz, 6H), 0.91 (t, $J$=7.2 Hz, 3H); $^{13}C$ NMR ($CDCl_3$, 75 MHz) $\delta$ 163.9, 151.3, 136.6, 133.3, 131.2, 128.8, 128.4, 127.8, 126.2, 126.1, 49.9, 47.2, 31.9, 28.2, 24.8, 22.4, 20.3, 13.9; HRMS (ESI) calcd for $C_{20}H_{29}N_2O$ $[M+H]^+$ 313.2274, found 313.2267.

*4.5.3. (4E)-4-Pentylidene-2-p-tolyl-3-p-tolylimino-3,4-dihydro-2H-isoquinolin-1-one (**3gc**)*

Yellow solid; mp 115–116 °C; IR (KBr) 2954, 2925, 2869, 1640, 1361 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ 8.23 (dd, $J$=7.5, 1.5 Hz, 1H), 7.61 (dt, $J$=7.5, 1.5 Hz, 1H), 7.50 (dt, $J$=7.5, 1.5 Hz, 1H), 7.46 (d, $J$=7.5 Hz, 1H), 7.36–7.17 (m, 4H), 7.07–6.96 (m, 2H), 6.67–6.55 (m, 2H), 6.00 (t, $J$=7.8 Hz, 1H), 2.40 (s, 3H), 2.27 (s, 3H), 2.23 (q, $J$=7.8 Hz, 2H), 1.30–1.16 (m, 2H), 1.16–1.01 (m, 2H), 0.80 (t, $J$=7.2 Hz, 3H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 164.5, 146.3, 143.8, 137.4, 135.2, 133.5, 132.2, 132.1, 129.7, 129.4, 128.7, 128.6, 128.1, 127.9, 126.2, 122.5, 120.9, 31.1, 28.4, 22.0, 21.2, 20.7, 13.8; HRMS (ESI) calcd for $C_{28}H_{29}N_2O$ $[M+H]^+$ 409.2274, found 409.2274.

*4.5.4. (4E)-2-Cyclohexyl-3-cyclohexylimino-4-cyclohexylmethylene-3,4-dihydro-2H-isoquinolin-1-one (**3ha**)*

Colorless solid; mp 142–143 °C; IR (KBr) 2926, 2853, 1675, 1638, 1344 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ 8.13 (dd, $J$=7.5, 1.2 Hz, 1H), 7.51 (dt, $J$=7.5, 1.5 Hz, 1H), 7.41 (dt, $J$=7.5, 1.2 Hz, 1H), 7.37 (d, $J$=7.5, 1H), 5.65 (d, $J$=10.5 Hz, 1H), 4.63 (tt, $J$=12.0, 3.3 Hz, 1H), 3.72 (tt, $J$=8.4, 4.2 Hz, 1H), 2.68–2.52 (m, 1H), 2.44 (dq, $J$=12.0, 3.3 Hz, 2H), 1.92–0.88 (m, 28H); $^{13}C$ NMR ($CDCl_3$, 75 MHz) $\delta$ 164.1, 151.6, 141.3, 133.5, 131.3, 128.9, 128.5, 127.8, 125.6, 124.1, 60.4, 57.8, 55.7, 36.7, 34.7, 32.9, 26.6, 25.9, 25.8, 25.7, 25.2, 24.2, 21.0, 14.2; HRMS (ESI) calcd for $C_{28}H_{39}N_2O$ $[M+H]^+$ 419.3057, found 419.3064.

*4.5.5. (4E)-2-Cyclohexyl-3-cyclohexylimino-4-trimethylsilanylmethylene-3,4-dihydro-2H-isoquinolin-1-one (**3ia**)*

Pale yellow solid; mp 125–126 °C; IR (KBr) 2928, 2852, 1638, 1216, 1096 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ 8.11–8.04 (m, 1H), 7.52–7.40 (m, 3H), 5.85 (s, 1H), 4.60 (tt, $J$=12.6, 3.3 Hz, 1H), 3.72 (tt, $J$=8.4, 4.2 Hz, 1H), 2.42 (dq, $J$=12.6, 3.3 Hz, 2H), 1.98–1.00 (m, 18H), 0.13 (s, 9H); $^{13}C$ NMR ($CDCl_3$, 75 MHz) $\delta$ 164.0, 152.3, 141.4, 135.9, 135.4, 131.0, 128.9, 128.7, 128.2, 125.4, 57.7, 55.9, 34.5, 29.8, 26.6, 25.9, 25.8, 24.0, 0.2; HRMS (ESI) calcd for $C_{25}H_{37}N_2OSi$ $[M+H]^+$ 409.2670, found 409.2685.

*4.5.6. (4E)-4-Benzylidene-2-cyclohexyl-3-cyclohexylimino-3,4-dihydro-2H-isoquinolin-1-one (**3ja**)*

Colorless solid; mp 65–66 °C; IR (KBr) 2928, 2852, 1674, 1638, 1344 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ 8.11 (d, $J$=7.8 Hz, 1H), 7.39–7.32 (m, 1H), 7.30–7.17 (m, 7H), 6.72 (s, 1H), 4.66 (tt, $J$=12.3, 3.0 Hz, 1H), 3.98 (tt, $J$=8.4, 4.2, 1H), 2.46 (dq, $J$=12.3, 3.0 Hz, 2H), 1.94–1.19 (m, 18H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 164.1, 150.8, 134.9, 132.6, 132.0, 130.8, 129.2, 128.54, 128.51, 128.4, 128.3, 126.9, 126.6, 60.4, 58.1, 56.0, 34.7, 30.0, 26.6, 25.9, 25.8, 24.2, 21.1, 14.2; HRMS (ESI) calcd for $C_{28}H_{32}N_2ONa$ $[M+Na]^+$ 435.2407, found 435.2412.

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## References and notes

1. For reviews of transition-metal-catalyzed cycloadditions, see: (a) Yet, L. *Chem. Rev.* **2000**, *100*, 2963; (b) Wender, P. A.; Love, J. A. *Advances in Cycloaddition*; JAI: Greenwich, 1999; Vol. 5; p 1; (c) Mehta, G.; Singh, V. *Chem. Rev.* **1999**, *99*, 881; (d) Ojima, I.; Tzamarioudaki, M.; Li, Z.; Donovan, R. J. *Chem. Rev.* **1996**, *96*, 635; (e) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49; (f) Schore, N. E. *Chem. Rev.* **1988**, *88*, 1081.
2. For a review of cycloadditions through five-membered acylmetal intermediates leading to six-membered carbonyl compounds, see: Tanaka, K. *Chim. Oggi* **2006**, *24*, 20.
3. For a review of rhodium-catalyzed [4+2] cycloadditions, see: Robinson, J. E. In *Modern Rhodium-Catalyzed Organic Reactions*; Evans, P. A., Ed.; Wiley-VCH: Weinheim, 2005; p 241.
4. (a) Reppe, W.; Vetter, H. *Justus Liebigs Ann. Chem.* **1953**, *582*, 133; (b) Maruyama, K.; Shio, T.; Yamamoto, Y. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1877; (c) Foust, D. F.; Rausch, M. D. *J. Organomet. Chem.* **1982**, *239*, 321; (d) Cabrera, A.; Mondragón, J.; Torres, F.; Gómez, L. J. *Rev. Soc. Quim. Mex.* **1983**, *27*, 311.
5. (a) Liebeskind, L. S.; Baysdon, S. L.; South, M. S. *J. Am. Chem. Soc.* **1980**, *102*, 7397; (b) Baysdon, S. L.; Liebeskind, L. S. *Organometallics* **1982**, *1*, 771; (c) South, M. S.; Liebeskind, L. S. *J. Org. Chem.* **1982**, *47*, 3815; (d) Liebeskind, L. S.; Baysdon, S. L. *Tetrahedron Lett.* **1984**, *25*, 1747; (e) South, M. S.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1984**, *106*, 4181; (f) Liebeskind, L. S.; Leeds, J. P.; Baysdon, S. L.; Iyer, S. *J. Am. Chem. Soc.* **1984**, *106*, 6451; (g) Liebeskind, L. S.; Baysdon, S. L.; South, M. S.; Iyer, S.; Leeds, J. P. *Tetrahedron* **1985**, *41*, 5839; (h) Liebeskind, L. S.; Baysdon, S. L.; Goedken, V.; Chidambaram, R. *Organometallics* **1986**, *5*, 1086; (i) Iyer, S.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1987**, *109*, 2759; (j) Huffman, M. A.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1991**, *113*, 2771.
6. (a) Kondo, T.; Taguchi, Y.; Kaneko, Y.; Niimi, M.; Mitsudo, T. *Angew. Chem., Int. Ed.* **2004**, *43*, 5369; (b) Kondo, T.; Niimi, M.; Nomura, M.; Wada, K.; Mitsudo, T. *Tetrahedron Lett.* **2007**, *48*, 2837.
7. For the synthesis of five-membered rings by rhodium-catalyzed [3+2] cycloadditions of cyclopropenones with alkynes, see: Wender, P. A.; Paxton, T. J.; Williams, T. J. *J. Am. Chem. Soc.* **2006**, *128*, 14814.
8. (a) Murakami, M.; Itahashi, T.; Ito, Y. *J. Am. Chem. Soc.* **2002**, *124*, 13976; (b) Matsuda, T.; Fujimoto, A.; Ishibashi, M.; Murakami, M. *Chem. Lett.* **2004**, *33*, 876.
9. For the synthesis of eight-membered rings from cyclobutanones, see: Wender, P. A.; Correa, A. G.; Sato, Y.; Sun, R. *J. Am. Chem. Soc.* **2000**, *122*, 7815.
10. Tanaka, K.; Fu, G. C. *Org. Lett.* **2002**, *4*, 933.
11. (a) Tanaka, K.; Hagiwara, Y.; Noguchi, K. *Angew. Chem., Int. Ed.* **2005**, *44*, 7260; (b) Tanaka, K.; Hagiwara, Y.; Hirano, M. *Eur. J. Org. Chem.* **2006**, 3582.
12. Hojo, D.; Noguchi, K.; Hirano, M.; Tanaka, K. *Angew. Chem., Int. Ed.* **2008**, *47*, 5820.
13. Rhodium-catalyzed [4+2] annulations of vinylarylaldehydes with alkenes and alkynes leading to substituted tetralones and 1-naphthols were also reported; see: (a) Tanaka, K.; Hojo, D.; Shoji, T.; Hagiwara, Y.; Hirano, M. *Org. Lett.* **2007**, *9*, 2059; For a rhodium-catalyzed homo-[4+2] annulation of vinylbenzaldehyde, see: (b) Kundu, K.; McCullagh, J. V.; Morehead, A. T., Jr. *J. Am. Chem. Soc.* **2005**, *127*, 16042.
14. For reviews, see: (a) Heller, B.; Hapke, M. *Chem. Soc. Rev.* **2007**, *36*, 1085; (b) Chopade, P. R.; Louie, J. *Adv. Synth. Catal.* **2006**, *348*, 2307; (c) Nakamura, I.; Yamamoto, Y. *Chem. Rev.* **2004**, *104*, 2127; (d) Varela, J. A.; Saà, C. *Chem. Rev.* **2003**, *103*, 3787.
15. (a) Hong, P.; Yamazaki, H. *Synthesis* **1977**, 50; (b) Hong, P.; Yamazaki, H. *Tetrahedron Lett.* **1977**, 1333; (c) Earl, R. A.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1983**, *105*, 6991; (d) Earl, R. A.; Vollhardt, K. P. C. *J. Org. Chem.* **1984**, *49*, 4786; (e) Diversi, P.; Ingrosso, G.; Lucherini, A.; Malquori, S. *J. Mol. Catal.* **1987**, *40*, 267; (f) Bonaga, L. V. R.; Zhang, H.-C.; Gauthier, D. A.; Reddy, I.; Maryanoff, B. E. *Org. Lett.* **2003**, *5*, 4537; (g) Bonaga, L. V. R.; Zhang, H.-C.; Moretto, A. F.; Ye, H.; Gauthier, D. A.; Li, J.; Leo, G. C.; Maryanoff, B. E. *J. Am. Chem. Soc.* **2005**, *127*, 3473.
16. (a) Hoberg, H.; Oster, B. W. *Synthesis* **1982**, 324; (b) Hoberg, H.; Oster, B. W. *J. Organomet. Chem.* **1982**, *234*, C35; (c) Hoberg, H.; Oster, B. W. *J. Organomet. Chem.* **1983**, *252*, 359; (d) Duong, H. A.; Cross, M. J.; Louie, J. *J. Am. Chem. Soc.* **2004**, *126*, 11438; (e) Duong, H. A.; Louie, J. *J. Organomet. Chem.* **2005**, *690*, 5098; (f) Duong, H. A.; Louie, J. *Tetrahedron* **2006**, *62*, 7552.
17. (a) Yamamoto, Y.; Takagishi, H.; Itoh, K. *Org. Lett.* **2001**, *3*, 2117; (b) Yamamoto, Y.; Kinpara, K.; Saigoku, T.; Takagishi, H.; Okuda, S.; Nishiyama, H.; Itoh, K. *J. Am. Chem. Soc.* **2005**, *127*, 605.
18. For cationic rhodium(I)/biaryl bisphosphine complex-catalyzed [2+2+2] cycloadditions of alkynes with isocyanates, see: (a) Tanaka, K.; Wada, A.; Noguchi, K. *Org. Lett.* **2005**, *7*, 4737; (b) Tanaka, K.; Takahashi, Y.; Suda, T.; Hirano, M. *Synlett* **2008**, 1724; For neutral rhodium(I) complex-catalyzed [2+2+2] cycloadditions of alkynes with isocyanates, see: (c) Flynn, S. T.; Hasso-Henderson, S. E.; Parkins, A. W. *J. Mol. Catal.* **1985**, *32*, 101; (d) Yu, R. T.; Rovis, T. *J. Am. Chem. Soc.* **2006**, *128*, 2782; (e) Kondo, T.; Nomura, M.; Ura, Y.; Wada, K.; Mitsudo, T. *Tetrahedron Lett.* **2006**, *47*, 7107; (f) Yu, R. T.; Rovis, T. *J. Am. Chem. Soc.* **2006**, *128*,

12370; (g) Lee, E. E.; Rovis, T. *Org. Lett.* **2008**, *10*, 1231; (h) Yu, R. T.; Lee, E. E.; Malik, G.; Rovis, T. *Angew. Chem., Int. Ed.* **2009**, *48*, 2379.
19. For examples using stoichiometric transition-metal complexes, see: (a) Takahashi, T.; Tsai, F.-Y.; Li, Y.; Wang, H.; Kondo, Y.; Yamanaka, M.; Nakajima, K.; Kotora, M. *J. Am. Chem. Soc.* **2002**, *124*, 5059; (b) Li, Y.; Matsumura, H.; Yamanaka, M.; Takahashi, T. *Tetrahedron* **2004**, *60*, 1393.
20. (a) Hoberg, H.; Burkhart, G. *Synthesis* **1979**, 525; (b) Young, D. D.; Deiters, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 5187.
21. (a) Mukai, C.; Yoshida, T.; Sorimachi, M.; Odani, A. *Org. Lett.* **2006**, *8*, 83; (b) Saito, T.; Sugizaki, K.; Otani, T.; Suyama, T. *Org. Lett.* **2007**, *9*, 1239; (c) Aburano, D.; Yoshida, T.; Miyakoshi, N.; Mukai, C. *J. Org. Chem.* **2007**, *72*, 6878.
22. Yu, R. T.; Rovis, T. *J. Am. Chem. Soc.* **2008**, *130*, 3262.
23. Tanaka, K.; Hagiwara, Y.; Noguchi, K. *Angew. Chem., Int. Ed.* **2006**, *45*, 2734.
24. Tanaka, K.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 11492.
25. Molander, G. A.; Retsch, W. H. *J. Org. Chem.* **1998**, *63*, 5507.
26. Eriksson, M.; Iliefski, T.; Nilsson, M.; Olsson, T. *J. Org. Chem.* **1997**, *62*, 182.