

Rhodium-Catalyzed Intramolecular Hydroacylation of 5- and 6-Alkynals: Convenient Synthesis of α -Alkylidenecycloalkanones and Cycloalkenones

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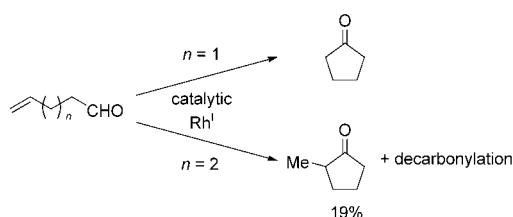
Abstract: A novel intramolecular hydroacylation of 5- and 6-alkynals leading to α -alkylidenecycloalkanones was accomplished by using cationic a rhodium(I)/BINAP complex. For all cyclizations described, a single (*E*)-olefin isomer was obtained. At elevated temperature, hydroacylation and double bond migration of 5- and 6-alkynals proceeded in a one-pot reaction to give cycloalkenones. An intramolecular hydroacylation of a 7-alkynal was unsuccessful. This method represents an attractive new route to highly functionalized α -alkylidenecycloalkanones and cycloalkenones.

Keywords: aldehydes • alkynes • cyclization • hydroacylation • rhodium

Introduction

Rhodium-catalyzed intramolecular hydroacylation of 4-alkenals is a well established method for the preparation of cyclopentanones.^[1–3] However, hydroacylation of alkenals to cycloalkanones is limited to 4-alkenals: it is not applicable to 5-alkenals. In fact, Larock et al. noted that 5-hexenal furnishes 2-methylcyclopentanone in only 19% yield and a significant amount of decarbonylation occurs (Scheme 1).^[2b]

Only one report for the intramolecular hydroacylation of 5-alkenal to generate cyclohexanone was reported, though it turned out to be sensitive to substitution of the alkene



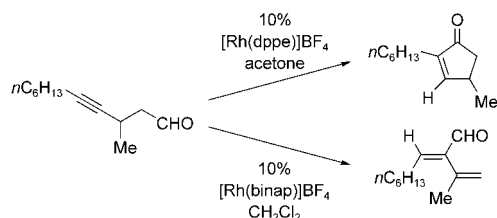
Scheme 1. Rhodium-catalyzed intramolecular hydroacylation of 4- and 5-alkenals.

moiety because of alternative reactivity of these substrates.^[4] Extension of this method to the synthesis of larger cyclic compounds was accomplished by the use of 4,6-dienals or cyclopropyl-4-alkenals as reaction substrates.^[5,6] Synthesis of cycloheptenones was carried out by rhodium-catalyzed intramolecular hydroacylation of 4,6-dienals;^[5a] the synthesis of cyclooctenones was carried out by rhodium-catalyzed intramolecular hydroacylation of 5-cyclopropyl-4-alkenals.^[5b]

The corresponding reaction of 4-alkynals to generate cyclopentenones is an attractive route for their synthesis. Recently, intramolecular *trans* hydroacylation of 4-alkynals was developed by using a cationic rhodium(I)/dppe complex (Scheme 2).^[7,8] This result prompted our investigation into whether the intramolecular hydroacylation of 5-alkynals can proceed using cationic rhodium(I) complex. As one example of an intramolecular hydroacylation of 5-alkynals, Nicolaou et al. observed an unexpected intramolecular hydroacylation of a tricyclic 5-alkynal to generate a tetracyclic cyclohexenone (78% yield based on 50% conversion) while attempting to decarbonylate an aldehyde with stoichiometric amount of $[\text{RhCl}(\text{PPh}_3)_3]$.^[9] Murai et al. observed formation of an ethylidenecyclopentanone as a by-product (13% yield) while attempting cyclocarbonylation of a 5-heptynal to a bicyclic α,β -unsaturated γ -butyrolactone with CO and catalytic amounts of $[\text{Ru}_3(\text{CO})_{12}]$.^[10] Narasaka et al. also accomplished the synthesis of α -alkylidenecycloalkanones by rhodium(I)-catalyzed acylation of alkynes with acylsilanes.^[11] However, no general method for intramolecular hydroacylation of 5-alkynals has been developed to date. This paper describes the general protocol for intramolecular *cis*-hydroacylation of 5- and 6-alkynals, which leads to α -alkylidenecycloalkanones using a cationic rhodium(I)/BINAP complex.

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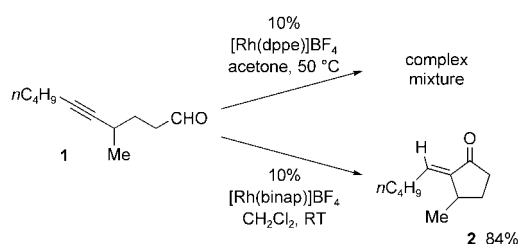
Supporting information for this article is available on the WWW under <http://www.chemeurj.org/> or from the author: selected ¹H NMR spectra.



Scheme 2. Rhodium-catalyzed intramolecular hydroacylation of 4-alkynals.

Results and Discussion

We first examined the reaction of 4-methyl-5-decynal (**1**) in the presence of 10% $[\text{Rh}(\text{dppe})]\text{BF}_4$ in acetone at room temperature, which currently appears to be the best condition for the intramolecular hydroacylation of 4-alkynals (Scheme 2),^[7] although the reaction was extremely sluggish. The increase in reaction temperature (50°C) led to an unidentified complex mixture, which included decarbonylated by-products. Although the reaction was sluggish, the use of CH_2Cl_2 as a solvent suppressed the formation of decarbonylated by-products (Scheme 3). Moreover, very small amounts of a cyclized product, 3-methyl-2-pentylidenecyclopentanone (**2**), were detected. When 4-alkynals were treated with $[\text{Rh}(\text{dppe})]\text{BF}_4$ in CH_2Cl_2 , self [4+2] annulation to generate cyclohexenones proceeded in high yields. The use of coordinating solvents such as acetone and CH_3CN efficiently suppressed undesired self-coupling.^[12] After examining various phosphine ligands, we discovered that the same reaction conducted in the presence of 10% $[\text{Rh}(\text{binap})]\text{BF}_4$ in CH_2Cl_2 at room temperature cleanly furnished the cyclized product **2** in 84% yield (Scheme 3). This result contrasts with the reaction of 4-alkynals with $[\text{Rh}(\text{binap})]\text{BF}_4$ in CH_2Cl_2 , which furnishes dienals via carbonyl migration (Scheme 2).^[13] No reaction was observed by using neutral rhodium(i) complexes, while alkyne **1** was recovered unchanged.



Scheme 3. Rhodium-catalyzed intramolecular hydroacylation of 5-alkynals.

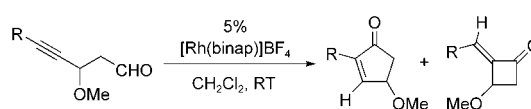
A series of 5-alkynals was subjected to the above optimal reaction conditions (see also Table 1). Both 6-aryl and 6-alkyl-5-alkynals cleanly afforded the corresponding α -alkylidenecyclopentanones in high yields (entries 1–3). The reaction tolerates substituents at the 3 and 4 positions (entries 4 and 5). The cyclization of the labile secondary propargylic ethers also proceeded (entries 6 and 7). This result contrasts the reaction of 3-methoxy-4-alkynals with $[\text{Rh}(\text{binap})]\text{BF}_4$,

Table 1. Cationic rhodium(i)/BINAP complex-catalyzed intramolecular hydroacylation of 5-alkynals.

Entry	5-Alkynal	Product	Yield [%] ^[a]
1			78
2			75
3			94
4			84
5			82
6			57
7			56
			10

[a] Isolated yield.

which furnishes cyclopentenones and cyclobutanones (Scheme 4).^[8b] In all cyclizations a single (*E*)-olefin isomer was produced; however, 6-alkyl propargylic ether furnished cyclopentenone as a by-product.

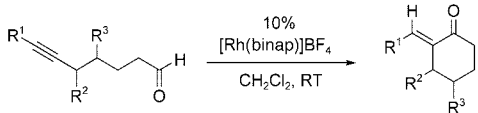


Scheme 4. Reaction of 3-methoxy-4-alkynals with $[\text{Rh}(\text{binap})]\text{BF}_4$.

Not only 5-alkynals, but also 6-alkynals (Table 2) afforded the corresponding α -alkylidenecyclohexanones in high yields with single (*E*)-olefin isomer. Both 6-aryl and 6-alkyl-6-alkynals afforded the corresponding α -alkylidenecyclopentanones (entries 1 and 2). The substitution at the 4 and 5 positions were tolerated (entries 3 and 4). The cyclohexenone was obtained as a by-product in the case of 7-phenyl-6-alkynal.

Because the cycloalkenones were obtained as by-products, we anticipated that tandem hydroacylation/double-bond migration would occur at elevated temperature. Indeed, when the reactions of 5-alkynals were conducted at 80°C , the cyclopentenones were obtained in good yield via tandem hy-

Table 2. Cationic rhodium(I)/BINAP complex-catalyzed intramolecular hydroacylation of 6-alkynals.

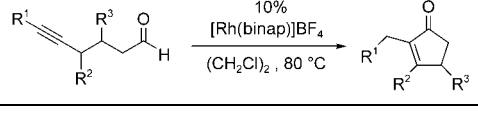


Entry	6-Alkynal	Product	Yield [%] ^[a]
1			56
			5
2			74
3			77
4			91

[a] Isolated yield.

hydroacylation/double-bond migration (Table 3). This reaction enabled the synthesis of α,β -disubstituted cyclopentenones (entries 4, 6, and 7), such as dihydrojasmonone (entry 4).

Table 3. Cationic rhodium(I)/BINAP complex-catalyzed intramolecular tandem hydroacylation/double-bond migration of 5-alkynals.

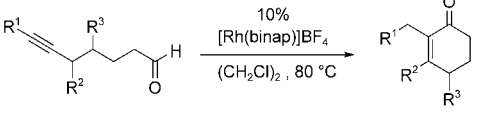


Entry	5-Alkynal	Product	Yield [%] ^[a]
1			60
2			59
3			84
4			83
5			58
6			39
7			62 ^[b]

[a] Isolated yield. [b] At 50 °C.

The double-bond migration of 6-alkynals also proceeded (Table 4), but the presence of substituents at the 4 and 5 positions prohibited the double-bond migration (entries 3 and 4).

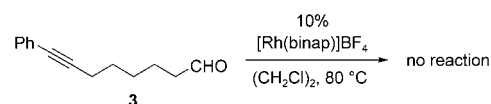
Table 4. Cationic rhodium(I)/BINAP complex-catalyzed intramolecular tandem hydroacylation/double bond migration of 6-alkynals.



Entry	6-Alkynal	Product	Yield [%] ^[a]
1			41
2			76
3			0
4			0

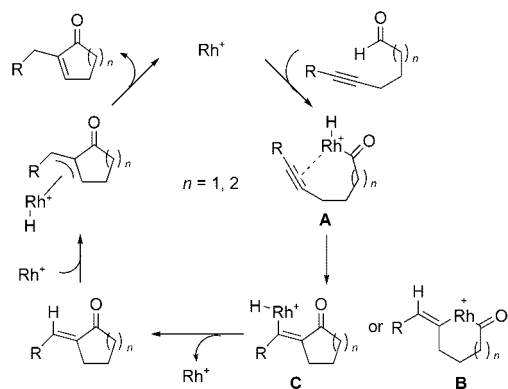
[a] Isolated yield.

Although the reaction of 7-alkynal **3** was also investigated, no reaction was observed even at 80 °C and the alkynal **3** was recovered unchanged (Scheme 5).

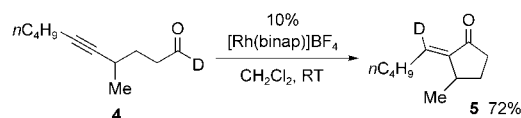
Scheme 5. Reaction of 7-alkynal with rhodium(I)⁺/BINAP complex.

Scheme 6 depicts a plausible mechanism of this novel cyclization.^[14,15] We believe that the rhodium(I) catalyst oxidatively inserts into the aldehyde C–H bond, affording a rhodium acyl hydride **A**. *cis*-Addition of the rhodium hydride to the metal-bound alkyne then provides the rhodium metal-lacycle **B**. Reductive elimination furnishes the α -alkylidene-cycloalkanones and regenerates the rhodium(I) catalyst. Alternatively, the catalytic cycle can be elucidated as the following: a *cis* addition of the acyl rhodium to the alkyne provides the rhodium vinyl hydride **C** followed by reductive elimination. Murai et al. proposed the formation of the ethylidene cyclopentanone via a reductive elimination from a ruthenium–vinyl hydride.^[10] At elevated temperature, rhodium-catalyzed double bond migration of the α -alkylidenecycloalkanones proceeded to give cycloalkenones.

Consistent with these pathways, reaction of a deuterium-labeled 5-alkynal **4** led to stereospecific incorporation of deuterium in the β position of the α -alkylidenecyclopentanone **5** (Scheme 7), and rhodium catalyst is essential for the double-bond migration (Scheme 8). Although the transfor-

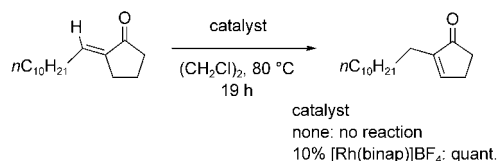


Scheme 6. Proposed reaction mechanism for formation of α -alkyldenecycloalkanones and cycloalkanones.



Scheme 7. Deuterium labeling study.

mation of α -alkyldenecycloalkanones to cycloalkanones was already reported using a stoichiometric amount of $[\text{RhCl}(\text{PPh}_3)_3]$ in the presence of a catalytic amount of triethylsilane,^[15] the present method enables this transformation using a catalytic amount of rhodium(I) complex.



Scheme 8. Rhodium-catalyzed double bond migration of α -alkyldenecyclopentanones to cyclopentenones.

Conclusion

In summary, we have established that a cationic rhodium(I)/BINAP complex catalyzes a novel intramolecular hydroacylation of 5- and 6-alkynals leading to α -alkyldenecycloalkanones. In addition, hydroacylation and double-bond migration of 5- and 6-alkynals proceeded in a one-pot reaction at elevated temperature to give cycloalkanones. Hydroacylation of alkenals to cycloalkanones is limited to 4-alkenals, but hydroacylation of alkynals is not limited to 4-alkynals: it is applicable to 5- and 6-alkynals. Although the reaction of a 7-alkynal was investigated, no reaction was observed. We believe that this method represents an attractive new route to produce highly functionalized α -alkyldenecycloalkanones and cycloalkanones. The *endo*-intramolecular hydroacylation of 5- and 6-alkynals leading to medium-sized cycloalkanones (cyclohexenones and cycloheptenones) is currently underway in our laboratory.

Experimental Section

General: ^1H NMR spectra were recorded on either 300 MHz (JEOL AL 300) or 400 MHz (JEOL AL 400) at 25 °C and are referenced to residual solvent downfield from tetramethylsilane (see Supporting Information). ^{13}C NMR spectra were obtained with complete proton decoupling on either 75 MHz (JEOL AL 300) or 100 MHz (JEOL AL 400) at 25 °C. ^2H NMR spectra were obtained with complete proton decoupling on 61 MHz (JEOL AL 400) at 25 °C. Infrared spectra were obtained on a JASCO A-302 IR. HRMS were collected on JEOL JMS 700. Anhydrous CH_2Cl_2 was obtained from Aldrich (No. 27099-7) and used as received. Anhydrous $(\text{CH}_2\text{Cl})_2$ was obtained from Alrich (No. 28450-5) and used as received. THF and CH_2Cl_2 was dried over $\text{MS } 4 \text{ \AA}$ for the synthesis of substrates. CuI (99.999 %, Aldrich) was used as received. All other reagents and solvents were obtained from commercial sources, and used as received. All reactions were carried out under an atmosphere of nitrogen or argon in oven-dried glassware with magnetic stirring, unless otherwise indicated.

General procedure 1—Preparation of 4-alkynals: *n*BuLi (1.58 M in hexane, 15.0 mL, 23.7 mmol) was added to a stirred solution of 1-dodecyne (5.2 mL, 24.3 mmol) in THF (63 mL) at -10°C , and the resulting mixture was stirred at -10°C for 30 min. CuI (99.999 %, 5.02 g, 26.4 mmol) was added, and the resulting mixture was stirred at -10°C for 1.5 h. After cooling to -78°C , TMSI (3.4 mL, 23.9 mmol) was added, and the resulting mixture was stirred at -78°C for 5 min. Acrolein (1.6 mL, 23.9 mmol) was added at -78°C , and the resulting mixture was stirred at -45°C for 2 h, and then stirred at RT overnight. The reaction was quenched by the addition of saturated aqueous NH_4Cl and extracted with Et_2O . The organic layer was washed with 5 % $\text{Na}_2\text{S}_2\text{O}_3$ and brine, dried over Na_2SO_4 , and concentrated. To complete hydrolysis, a solution of the residue in THF (250 mL) was treated with aqueous 10 % HCl (56 mL) at RT for 1 h. Saturated aqueous NaHCO_3 was added slowly to neutralize acid and then extracted with Et_2O . The combined organic extracts were washed with 5 % $\text{Na}_2\text{S}_2\text{O}_3$ and brine, dried over Na_2SO_4 , and concentrated. The residue was purified by silica gel chromatography (hexane/ EtOAc 50:1), which furnished pentadec-4-ynal (3.84 g, 17.3 mmol, 72 %, not optimized) as a colorless oil.

General procedure 2—Preparation of 4-alkynals: *n*BuLi (1.58 M in hexane, 15.2 mL, 24.0 mmol) was added to a stirred solution of 1-octyne (3.5 mL, 23.7 mmol) in THF (63 mL) at -10°C , and the resulting mixture was stirred at -10°C for 20 min. CuI (99.999 %, 5.03 g, 26.5 mmol) was added, and the resulting mixture was stirred at -10°C for 1 h. After cooling to -78°C , TMSI (3.4 mL, 23.9 mmol) was added, and the resulting mixture was stirred at -78°C for 5 min. 2-Methyl-2-propenal (2.0 mL, 24.2 mmol) was added at -78°C , and the resulting mixture was stirred at -45°C for 2 h, and then stirred at RT overnight. The reaction was quenched by the addition of saturated aqueous NH_4Cl and extracted with Et_2O . The organic layer was washed once with 5 % $\text{Na}_2\text{S}_2\text{O}_3$ and brine, dried over Na_2SO_4 , and concentrated. The residue was purified by silica gel chromatography (hexane/ EtOAc 50:1), which furnished 2-methylundec-4-ynal (2.60 g, 14.4 mmol, 61 %, not optimized) as a colorless oil.

General procedure 3—Preparation of 5- and 6-alkynals: A lithium diisopropylamine solution consisting of *n*BuLi (1.58 M in hexane, 5.5 mL, 8.7 mmol) and diisopropylamine (1.3 mL, 9.3 mmol) in THF (15 mL) was added under argon atmosphere to a cooled (-10°C), stirred suspension of (methoxymethyl)triphenylphosphonium chloride (3.09 g, 9.03 mmol) in THF (15 mL). To the deep red solution was added a solution of pentadec-4-ynal (1.01 g, 4.50 mmol) in THF (15 mL). The resulting solution was kept at -10°C for 1 h and then diluted with saturated aqueous NaHCO_3 (45 mL). After extraction with Et_2O , the combined organic layers were dried over Na_2SO_4 , filtered, and concentrated. The crude 1-methoxy-1-hexadecen-5-yne was used without purification in the next step.

A solution of the 1-methoxy-1-hexadecen-5-yne in THF (30 mL) was treated with aqueous HCl (12 mL, 10 %) at RT for 24 h. Saturated aqueous NaHCO_3 was added slowly to neutralize acid and then extracted with Et_2O . The combined organic extracts were washed with brine, dried over Na_2SO_4 , concentrated, and purified by silica gel chromatography (hexane/ EtOAc 50:1), which furnished hexadec-5-ynal (0.86 g, 3.64 mmol, 81 %, not optimized) as a colorless oil.

Hexadec-5-ynal (Table 1, entry 3): The title compound was prepared according to the GP 1 and 3. ^1H NMR (CDCl_3 , 300 MHz): δ = 9.81 (t, J = 1.2 Hz, 1H), 2.57 (dt, J = 6.9, 1.2 Hz, 2H), 2.23 (tt, J = 6.9, 2.4 Hz, 2H), 2.13 (tt, J = 6.9, 2.4 Hz, 2H), 1.81 (quint, J = 6.9 Hz, 2H), 1.56–1.18 (m, 16H), 0.88 (t, J = 7.2 Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz): δ = 202.1, 81.7, 78.6, 42.8, 31.9, 29.6, 29.5, 29.3, 29.1, 29.0, 28.9, 22.7, 21.6, 18.7, 18.2, 14.1; IR (neat): $\tilde{\nu}$ = 2920, 2860, 1720, 1440 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{16}\text{H}_{28}\text{O}$: 236.2140, found 236.2124 [M] $^+$.

4-Methyldec-5-ynal (1) (Table 1, entry 4): The title compound was prepared as a colorless oil in 51% isolated yield (not optimized) from 3-methylnon-4-ynal according to the GP 3. 3-Methylnon-4-ynal was prepared as colorless oil in 39% isolated yield (not optimized) from crotonaldehyde according to the GP 1. ^1H NMR (CDCl_3 , 300 MHz): δ = 9.81 (t, J = 1.8 Hz, 1H), 2.65–2.54 (m, 2H), 2.54–2.38 (m, 1H), 2.14 (dt, J = 6.9, 2.1 Hz, 2H), 1.87–1.55 (m, 2H), 1.52–1.31 (m, 4H), 1.17 (d, J = 6.9 Hz, 3H), 0.91 (t, J = 7.2 Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz): δ = 202.4, 83.3, 81.6, 42.0, 31.1, 29.4, 25.5, 21.9, 21.4, 18.3, 13.6; IR (neat): $\tilde{\nu}$ = 2860, 2720, 1715, 1370, 1320 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{11}\text{H}_{18}\text{O}$: 166.1358, found 166.1323 [M] $^+$.

3-Methyldec-5-ynal (Table 1, entry 5): The title compound was prepared as a colorless oil in 80% isolated yield (not optimized) from 2-methylundec-4-ynal according to the GP 3. 2-Methylundec-4-ynal was prepared according to the GP 2 to yield a colorless oil. ^1H NMR (CDCl_3 , 300 MHz): δ = 9.79 (t, J = 2.4 Hz, 1H), 2.77–2.50 (m, 1H), 2.37–2.06 (m, 6H), 1.57–1.21 (m, 8H), 1.04 (d, J = 6.3 Hz, 3H), 0.89 (t, J = 7.2 Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz): δ = 202.3, 82.5, 77.4, 49.8, 31.3, 29.0, 28.5, 28.0, 26.0, 22.5, 19.7, 18.7, 14.0; IR (neat): $\tilde{\nu}$ = 2920, 2870, 1720, 1375, 910, 730 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{13}\text{H}_{22}\text{O}$: 194.1671, found 194.1665 [M] $^+$.

6-Phenylhex-5-ynal (Table 1, entry 1):^[17] A solution of DMSO (3.3 mL, 46.5 mmol) in CH_2Cl_2 (20 mL) was added at -78°C to a solution of $(\text{COCl})_2$ (3.1 mL, 23.1 mmol) in CH_2Cl_2 (45 mL). The resulting mixture was stirred at -78°C for 15 min, and then a solution of the 6-phenylhex-5-ynol^[18] (3.06 g, 17.6 mmol) in CH_2Cl_2 (45 mL) was added at -78°C . The mixture was stirred at -78°C for 1 h, and Et_3N (18.3 mL) was added after stirring at RT for 1 h. The reaction was quenched by the addition of water and extracted with CH_2Cl_2 . The organic layer was washed with saturated aqueous NH_4Cl , dried over Na_2SO_4 , concentrated, and purified by silica gel chromatography (hexane/ EtOAc 50:1), which furnished 6-phenylhex-5-ynal (2.42 g, 14.1 mmol, 80%, unoptimized) as a yellow oil. ^1H NMR (CDCl_3 , 300 MHz): δ = 9.85 (t, J = 1.2 Hz, 1H), 7.46–7.34 (m, 2H), 7.33–7.21 (m, 3H), 2.66 (dt, J = 7.2, 1.2 Hz, 2H), 2.50 (t, J = 7.2 Hz, 2H), 1.94 (quint, J = 7.2 Hz, 2H); ^{13}C NMR (CDCl_3 , 75 MHz): δ = 201.9, 131.5, 128.2, 127.7, 123.5, 88.9, 81.7, 42.8, 21.2, 18.8.

6-*o*-Tolylhex-5-ynal (Table 1, entry 2): [$\text{PdCl}_2(\text{PPh}_3)_2$] (0.35 g, 0.50 mmol) was added to a solution of 2-iodotoluene (3.2 mL, 25.0 mmol) and 5-hexyn-1-ol (3.3 mL, 29.9 mmol) in Et_3N (100 mL). The mixture was stirred for 5 min, and CuI (70 mg, 0.37 mmol) was added. The resulting mixture was heated under a nitrogen atmosphere at 50°C for 2 h and stirred overnight at RT. The resulting mixture was filtered, concentrated, and purified by silica gel chromatography (hexane/ EtOAc 20:1), which furnished 6-*o*-tolylhex-5-ynol (4.50 g, 23.9 mmol, 96%, not optimized) as a yellow oil.

A solution of DMSO (1.7 mL, 24.0 mmol) in CH_2Cl_2 (25 mL) was added at -78°C to a solution of $(\text{COCl})_2$ (3.2 mL, 23.9 mmol) in CH_2Cl_2 (50 mL). The resulting mixture was stirred at -78°C for 15 min, and then a solution of the 6-*o*-tolylhex-5-ynol (3.12 g, 16.6 mmol) in CH_2Cl_2 (50 mL) was added at -78°C . The mixture was stirred at -78°C for 1 h, and Et_3N (12.0 mL) was added after stirring at RT for 1 h, the reaction was quenched by the addition of water and extracted with CH_2Cl_2 . The organic layer was washed with saturated aqueous NH_4Cl , dried over Na_2SO_4 , concentrated, and purified by silica gel chromatography (hexane/ EtOAc 50:1), which furnished 6-*o*-tolylhex-5-ynal (2.74 g, 14.7 mmol, 89%, unoptimized) as a yellow oil. ^1H NMR (CDCl_3 , 300 MHz): δ = 9.84 (t, J = 1.2 Hz, 1H), 7.39–7.32 (m, 1H), 7.20–7.15 (m, 2H), 7.15–7.05 (m, 1H), 2.68 (dt, J = 6.9, 1.2 Hz, 2H), 2.54 (t, J = 6.9 Hz, 2H), 2.41 (s, 3H), 1.95 (quint, J = 6.9 Hz, 2H); ^{13}C NMR (CDCl_3 , 75 MHz): δ = 201.9, 139.9, 131.8, 129.3, 127.7, 125.5, 123.3, 92.6, 80.5, 42.8, 21.3, 20.7, 19.0; IR (neat): $\tilde{\nu}$ = 3230, 2890, 1705, 755 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{13}\text{H}_{14}\text{O}$: 186.1045, found 186.1039 [M] $^+$.

4-Methoxy-6-phenylhex-5-ynal (Table 1, entry 6): DIBAL (0.95 M in *n*-hexane, 24.4 mL, 23.2 mmol) was added a solution of 3-cyanopropionaldehyde dimethyl acetal (3.02 mL, 23.2 mmol) in CH_2Cl_2 (120 mL) at -78°C and the resulting mixture was stirred for 1 h. The resulting mixture was warmed slowly to RT, and treated with excess saturated aqueous NH_4Cl . The reaction mixture was then diluted with water and extracted with CH_2Cl_2 . The organic layer was washed with water, dried over Na_2SO_4 , dried over Mg_2SO_4 , and concentrated, which afforded crude 4,4-dimethoxybutyraldehyde (2.6 g, 19.6 mmol, 84%) as a pale yellow oil.

*n*BuLi (1.58 M in *n*-hexane, 14.4 mL, 22.8 mmol) was added a solution of phenylacetylene (3.13 mL, 28.5 mmol) in THF (64 mL) at 0°C and the resulting mixture was stirred for 0.5 h. A solution of crude 4,4-dimethoxybutyraldehyde (2.51 g, 19.0 mmol) in THF (16.0 mmol) was added, and the mixture was stirred for 0.5 h. MeI (5.92 mL, 95.0 mmol) and DMSO (56 mL) were added, and the resulting mixture was heated under reflux at 80°C for 1 h. The reaction mixture was then diluted with water and extracted with ether. The organic layer was washed with water and brine, dried over Na_2SO_4 , and concentrated. To the residue was added water (17 mL) and AcOH (51 mL), and the resulting mixture was stirred at 80°C for 1 h. The reaction mixture was diluted with water and extracted with Et_2O . The organic layer was washed with water and saturated aqueous NaHCO_3 , dried over Na_2SO_4 , concentrated, and purified by chromatography (hexane/ EtOAc 10:1), which afforded 4-methoxydodec-5-ynal (1.13 g, 5.56 mmol, 29%, not optimized) as a pale yellow oil. ^1H NMR (CDCl_3 , 300 MHz): δ = 9.82 (t, J = 1.5 Hz, 1H), 7.48–7.38 (m, 2H), 7.35–7.28 (m, 3H), 4.26 (t, J = 6.0 Hz, 1H), 3.46 (s, 3H), 2.69 (dt, J = 7.1, 1.5 Hz, 2H), 2.15 (dt, J = 7.1, 6.0 Hz, 2H); ^{13}C NMR (CDCl_3 , 75 MHz): δ = 201.8, 131.7, 128.5, 128.30, 128.29, 98.9, 86.9, 70.5, 56.6, 39.7, 28.3; IR (neat): $\tilde{\nu}$ = 3300, 2900, 1720, 1100, 760, 690 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{13}\text{H}_{14}\text{O}_2$: 202.0994, found 202.0919 [M] $^+$.

4-Methoxydodec-5-ynal (Table 1, entry 7): The title compound was prepared as a pale yellow oil in 6% isolated yield (not optimized) from 1-octyne according to the procedure for 4-methoxy-6-phenylhex-5-ynal. ^1H NMR (CDCl_3 , 300 MHz): δ = 9.79 (t, J = 1.8 Hz, 1H), 4.00 (tt, J = 6.0, 1.8 Hz, 1H), 3.37 (s, 3H), 2.61 (dt, J = 7.3, 1.8 Hz, 2H), 2.22 (dt, J = 6.9, 1.8 Hz, 2H), 2.02 (dt, J = 7.3, 6.0 Hz, 2H), 1.65–1.15 (m, 8H), 0.89 (t, J = 6.9 Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz): δ = 202.0, 87.4, 77.8, 70.2, 56.2, 39.7, 31.2, 28.6, 28.47, 28.46, 22.5, 18.6, 14.0; IR (neat): $\tilde{\nu}$ = 2900, 1720, 1440, 1330, 1100 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{12}\text{H}_{18}\text{O}$: 178.1358, found 178.1334 [$M - \text{CH}_3\text{OH}$] $^+$.

7-Phenylhept-6-ynal (Table 2, entry 1): The title compound was prepared as a yellow oil in 49% isolated yield (not optimized) from 6-phenylhex-5-ynal according to the GP 3. ^1H NMR (CDCl_3 , 300 MHz): δ = 9.80 (t, J = 1.8 Hz, 1H), 7.42–7.35 (m, 2H), 7.34–7.24 (m, 3H), 2.51 (dt, J = 7.2, 1.8 Hz, 2H), 2.45 (t, J = 6.9 Hz, 2H), 1.88–1.77 (m, 2H), 1.73–1.60 (m, 2H); ^{13}C NMR (CDCl_3 , 75 MHz): δ = 202.3, 131.5, 128.2, 127.6, 123.8, 89.4, 81.1, 43.4, 28.1, 21.3, 19.2; IR (neat): $\tilde{\nu}$ = 3260, 2920, 2710, 1720, 1600, 1490, 1440, 1070, 755, 695 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{13}\text{H}_{14}\text{O}$: 186.1045, found 186.1048 [M] $^+$.

Heptadec-6-ynal (Table 2, entry 2): The title compound was prepared as a colorless oil in 95% isolated yield (not optimized) from hexadec-5-ynal according to the GP 3. ^1H NMR (CDCl_3 , 300 MHz): δ = 9.77 (t, J = 1.8 Hz, 1H), 2.46 (dt, J = 7.5, 1.8 Hz, 2H), 2.26–2.05 (m, 4H), 1.83–1.66 (m, 2H), 1.60–1.15 (m, 18H), 0.88 (t, J = 7.2 Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz): δ = 202.4, 80.9, 79.2, 43.4, 31.9, 29.6, 29.5, 29.3, 29.12, 29.07, 28.9, 28.4, 22.6, 21.2, 18.7, 18.5, 14.1; IR (neat): $\tilde{\nu}$ = 2850, 2710, 1715, 1430 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{17}\text{H}_{30}\text{O}$: 250.2297, found 250.2278 [M] $^+$.

5-Methylundec-6-ynal (Table 2, entry 3): The title compound was prepared as a pale yellow oil in 88% isolated yield (not optimized) from 4-methyldec-5-ynal according to the GP 3. ^1H NMR (CDCl_3 , 300 MHz): δ = 9.70 (t, J = 2.1 Hz, 1H), 2.42–2.27 (m, 3H), 2.08 (dt, J = 6.6, 2.1 Hz, 2H), 1.84–1.56 (m, 2H), 1.45–1.25 (m, 6H), 1.07 (d, J = 6.9 Hz, 3H), 0.84 (t, J = 6.9 Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz): δ = 202.6, 83.9, 80.9, 43.6, 36.6, 31.2, 25.8, 21.9, 21.5, 20.0, 18.4, 13.6; IR (neat): $\tilde{\nu}$ = 2920, 2710, 1720, 1440, 1330, 1250, 1095, 790, 740 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{12}\text{H}_{20}\text{O}$: 180.1514, found 180.1480 [M] $^+$.

4-Methyltridec-6-ynal (Table 2, entry 4): The title compound was prepared as a colorless oil in 33% isolated yield (not optimized) from 3-methylundec-5-ynal according to the GP 3. ^1H NMR (CDCl_3 , 400 MHz):

δ = 9.77 (t, J = 1.6 Hz, 1H), 2.49–2.42 (m, 2H), 2.18–2.09 (m, 5H), 1.83–1.60 (m, 2H), 1.59–1.22 (m, 8H), 0.98 (d, J = 6.8 Hz, 3H), 0.89 (t, J = 6.8 Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz): δ = 202.4, 81.8, 77.8, 41.7, 32.4, 31.4, 29.1, 28.6, 27.9, 25.9, 22.6, 19.4, 18.8, 14.1; IR (neat): $\tilde{\nu}$ = 2900, 2860, 2720, 1720, 1440, 1380 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{14}\text{H}_{24}\text{O}$: 208.1827, found 208.1813 [M] $^{+}$.

8-Phenylhept-7-ynal (3) (Scheme 5): The title compound was prepared as a yellow oil in 31% isolated yield (not optimized) from 7-phenylhept-6-ynal according to the GP 3. ^1H NMR (CDCl_3 , 300 MHz): δ = 9.78 (t, J = 1.8 Hz, 1H), 7.46–7.34 (m, 2H), 7.34–7.20 (m, 3H), 2.46 (dt, J = 6.9, 1.8 Hz, 2H), 2.42 (t, J = 6.9 Hz, 2H), 1.76–1.41 (m, 6H); ^{13}C NMR (CDCl_3 , 75 MHz): δ = 202.6, 131.5, 128.2, 127.5, 123.9, 89.8, 80.8, 43.7, 28.4, 28.3, 21.6, 19.2; IR (neat): $\tilde{\nu}$ = 3210, 2910, 2850, 1705, 760, 695 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{14}\text{H}_{16}\text{O}$: 200.1201, found 200.1176 [M] $^{+}$.

1-Deuterio-4-methyldec-5-ynal (4) (Scheme 7): Jones reagent (1.5 M; 3.1 mL, 4.7 mmol) was added at 0°C to a solution of 4-methyldec-5-ynal (700 mg, 4.21 mmol) in acetone (15 mL). The resulting mixture was stirred at 0°C for 15 min, and then the reaction was quenched by the addition of 2-PrOH (3.8 mL) at 0°C. The mixture was stirred at RT for 10 min and then concentrated. The resulting residue was diluted with water and extracted with Et_2O . The organic layer was concentrated, and the product was purified by silica gel chromatography (hexane/EtOAc 10:1), which furnished 4-methyldec-5-ynoic acid (706 mg, 3.87 mmol, 92%, not optimized) as a colorless oil.

A solution of 4-methyldec-5-ynoic acid (706 mg, 3.87 mmol) in THF (4.0 mL) was added at 0°C to a stirred mixture of LiAlD_4 (316 mg, 7.53 mmol) in THF (17 mL). The resulting mixture was stirred at reflux for 45 min and then cooled to 0°C. The reaction was then quenched by the addition of water (1.0 mL), followed by stirring at 0°C for 10 min. The solution was dried over MgSO_4 , filtered through Celite, and concentrated to give the crude alcohol (375 mg) as a colorless oil.

A solution of DMSO (0.35 mL, 4.9 mmol) in CH_2Cl_2 (3.0 mL) was added at -78°C to a solution of $(\text{COCl})_2$ (0.22 mL, 2.6 mmol) in CH_2Cl_2 (7.0 mL). The resulting mixture was stirred at -78°C for 20 min, and then a solution of the crude alcohol (375 mg) in CH_2Cl_2 (7.0 mL) was added at -78°C . The mixture was stirred at -78°C for 1.5 h, and Et_3N (1.0 mL) was added. After 1 h of stirring RT, the reaction was quenched by the addition of water and extracted with CH_2Cl_2 . The organic layer was washed with saturated aqueous NH_4Cl , dried over Na_2SO_4 , concentrated, and purified by silica gel chromatography (hexane/EtOAc 50:1), which furnished 1-deuterio-4-methyldec-5-ynal (110 mg, 0.66 mmol, 30%, not optimized) as a colorless oil. ^1H NMR (CDCl_3 , 300 MHz): δ = 2.71–2.54 (m, 2H), 2.54–2.37 (m, 1H), 2.14 (dt, J = 6.9, 2.1 Hz, 2H), 1.88–1.72 (m, 1H), 1.72–1.56 (m, 1H), 1.53–1.30 (m, 4H), 1.17 (d, J = 6.9 Hz, 3H), 0.91 (t, J = 6.9 Hz, 3H); ^2H NMR (CDCl_3 , 61 MHz): δ = 9.78 (s).

General procedure 4—Intramolecular hydroacylation of 5- and 6-alkynals: Under an Ar atmosphere, BINAP (31.3 mg, 0.050 mmol) and $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (20.4 mg, 0.050 mmol) were dissolved in CH_2Cl_2 (2.0 mL) and the mixture was stirred for 15 min. H_2 was introduced to the resulting solution in Schlenk tube. After stirring for 1 h at RT, the resulting solution was concentrated to dryness and dissolved in CH_2Cl_2 (1.5 mL). The residue was added to a solution of 6-phenylhex-5-ynal (86.1 mg, 0.500 mmol) in CH_2Cl_2 (0.5 mL). The mixture was stirred at RT for 13 h. The resulting solution was concentrated and purified by silica gel chromatography (hexane/EtOAc 20:1), which furnished (*E*)-2-benzylidenecyclopentanone (67.3 mg, 0.391 mmol, 78%) as a yellow solid.

(*E*)-2-Benzylidenecyclopentanone (Table 1, entry 1):^[19] m.p. 60–62°C; ^1H NMR (CDCl_3 , 300 MHz): δ = 7.59–7.50 (m, 2H), 7.48–7.31 (m, 4H), 2.98 (dt, J = 7.5, 2.7 Hz, 2H), 2.41 (t, J = 7.5 Hz, 2H), 2.03 (quint, J = 7.5 Hz, 2H); ^{13}C NMR (CDCl_3 , 75 MHz): δ = 208.0, 136.0, 135.5, 132.2, 130.4, 129.3, 128.6, 37.7, 29.3, 20.1.

(*E*)-2-(2-Methylbenzylidene)cyclopentanone (Table 1, entry 2): The title compound was prepared as a yellow solid in 75% isolated yield from 6-*o*-tolylhex-5-ynal (93.2 mg, 0.500 mmol), BINAP (31.3 mg, 0.050 mmol), and $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (20.4 mg, 0.050 mmol) according to the GP 4; reaction time: 17 h. M.p. 67–68°C; ^1H NMR (CDCl_3 , 300 MHz): δ = 7.61 (t, J = 2.7 Hz, 1H), 7.47–7.40 (m, 1H), 7.30–7.18 (m, 3H), 2.90 (dt, J = 7.5, 2.7 Hz, 2H), 2.42 (t, J = 7.5 Hz, 2H), 2.41 (s, 3H), 1.99 (quint, J = 7.5 Hz, 2H); ^{13}C NMR (CDCl_3 , 75 MHz): δ = 208.0, 138.9, 136.8, 134.3, 130.5,

129.8, 129.1, 128.6, 125.7, 38.0, 29.4, 20.5, 20.0; IR (neat): $\tilde{\nu}$ = 3400, 2920, 1700, 1620, 1600, 1460, 1400, 1200, 1180, 760 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{13}\text{H}_{14}\text{O}$: 186.1045, found 186.1044 [M] $^{+}$.

(*E*)-2-Undecylidenecyclopentanone (Table 1, entry 3):^[20] The title compound was prepared as a pale yellow oil in 94% isolated yield from hexadec-5-ynal (118.5 mg, 0.501 mmol), BINAP (31.5 mg, 0.051 mmol) and $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (20.5 mg, 0.050 mmol) according to the GP 4; reaction time: 40 min. ^1H NMR (CDCl_3 , 300 MHz): δ = 6.55 (tt, J = 7.5, 2.7, 1H), 2.65–2.51 (m, 2H), 2.33 (t, J = 7.5, 2H), 2.21–2.07 (m, 2H), 1.93 (quint, J = 7.5 Hz, 2H), 1.53–1.16 (m, 16H), 0.88 (t, J = 6.9 Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz): δ = 207.0, 137.0, 136.2, 38.5, 31.8, 29.54, 29.46, 29.4, 29.32, 29.26, 29.2, 28.3, 26.6, 22.5, 19.7, 14.0.

(*E*)-3-Methyl-2-pentylidenecyclopentanone (2) (Table 1, entry 4):^[21] The title compound was prepared as a colorless oil in 84% isolated yield from 4-methyldec-5-ynal (83.1 mg, 0.500 mmol), BINAP (31.3 mg, 0.050 mmol) and $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (20.4 mg, 0.050 mmol) according to the GP 4; reaction time: 1 h. ^1H NMR (CDCl_3 , 300 MHz): δ = 6.51 (dt, J = 2.0, 7.7 Hz, 1H), 3.15–2.98 (m, 1H), 2.50–2.11 (m, 4H), 1.93–2.19 (m, 1H), 1.78–1.62 (m, 1H), 1.51–1.28 (m, 4H), 1.15 (d, J = 7.1 Hz, 3H), 0.91 (t, J = 7.1 Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz): δ = 207.4, 142.3, 136.7, 36.1, 33.0, 30.8, 28.7, 27.7, 22.5, 20.4, 13.8.

(*E*)-2-Heptylidene-4-methylcyclopentanone (Table 1, entry 5): The title compound was prepared as a yellow oil in 82% isolated yield from 3-methyldodec-5-ynal (97.4 mg, 0.501 mmol), BINAP (31.2 mg, 0.050 mmol) and $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (20.4 mg, 0.050 mmol) according to the GP 4; reaction time: 2 h. ^1H NMR (CDCl_3 , 300 MHz): δ = 6.59–6.49 (m, 1H), 2.84–2.71 (m, 1H), 2.49 (dd, J = 17.4, 7.2 Hz, 1H), 2.37–2.04 (m, 4H), 1.98 (dd, J = 17.4, 8.4 Hz, 1H), 1.52–1.18 (m, 8H), 1.12 (d, J = 6.3 Hz, 3H), 0.88 (t, J = 6.9 Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz): δ = 206.9, 137.6, 136.3, 47.1, 35.2, 31.6, 29.6, 29.0, 28.4, 28.3, 22.6, 21.0, 14.0; IR (neat): $\tilde{\nu}$ = 2950, 2900, 1720, 1650, 1440, 1180 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{13}\text{H}_{22}\text{O}$: 194.1671, found 194.1640 [M] $^{+}$.

(*E*)-2-Benzylidene-3-methoxycyclopentanone (Table 1, entry 6): The title compound was prepared as a pale yellow oil in 57% isolated yield from 4-methoxy-6-phenylhex-5-ynal (101.1 mg, 0.500 mmol), BINAP (31.1 mg, 0.050 mmol) and $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (20.3 mg, 0.050 mmol) according to the GP 4; reaction time: 15 h; reaction temperature: 25°C. ^1H NMR (CDCl_3 , 300 MHz): δ = 7.72–7.53 (m, 2H), 7.52–7.34 (m, 3H), 4.76–4.66 (m, 1H), 3.46 (s, 3H), 2.62 (ddd, J = 9.3, 12.3, 18.6 Hz, 1H), 2.47–2.22 (m, 2H), 2.04–1.80 (m, 1H); ^{13}C NMR (CDCl_3 , 75 MHz): δ = 206.4, 138.1, 136.1, 134.5, 131.0, 130.2, 128.8, 77.9, 55.3, 35.1, 25.0; IR (neat): $\tilde{\nu}$ = 2900, 1700, 1620, 1180, 1080, 760, 700 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{13}\text{H}_{14}\text{O}_2$: 202.0994, found 202.0966 [M] $^{+}$.

(*E*)-2-Heptylidene-3-methoxycyclopentanone (Table 1, entry 7): The title compound was prepared as a pale yellow oil in 56% isolated yield from 4-methoxydodec-5-ynal (63.1 mg, 0.300 mmol), BINAP (18.7 mg, 0.030 mmol) and $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (12.2 mg, 0.030 mmol) according to the GP 4; reaction time: 20 min; reaction temperature: 25°C. 2-Heptyl-3-methoxycyclopent-2-enone was also obtained in 10% isolated yield. ^1H NMR (CDCl_3 , 300 MHz): δ = 6.79 (dt, J = 8.1, 1.5 Hz, 1H), 4.56–4.48 (m, 1H), 3.31 (s, 3H), 2.53 (ddd, J = 9.0, 11.1, 18.3 Hz, 1H), 2.41–2.06 (m, 4H), 2.06–1.81 (m, 1H), 1.60–1.15 (m, 8H), 0.89 (t, J = 6.9 Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz): δ = 205.7, 142.3, 137.4, 76.9, 55.7, 35.5, 31.5, 29.5, 29.0, 28.5, 26.6, 22.4, 14.0; IR (neat): $\tilde{\nu}$ = 2900, 1720, 1640, 1460, 1180, 1080, 880 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{13}\text{H}_{22}\text{O}_2$: 210.1620, found 210.1643 [M] $^{+}$.

(*E*)-2-Benzylidenecyclohexanone (Table 2, entry 1):^[22] The title compound was prepared as a yellow solid in 56% isolated yield from 7-phenylhept-6-ynal (93.1 mg, 0.500 mmol), BINAP (31.2 mg, 0.050 mmol) and $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (20.5 mg, 0.050 mmol) according to the GP 4; reaction time: 66 h. 2-Benzylcyclohex-2-enone was also obtained in 5% yield. M.p. 36–39°C; ^1H NMR (CDCl_3 , 300 MHz): δ = 7.50 (t, J = 2.1 Hz, 1H), 7.44–7.23 (m, 5H), 2.84 (dt, J = 7.2, 2.1 Hz, 2H), 2.54 (t, J = 6.9 Hz, 2H), 2.02–1.86 (m, 2H), 1.82–1.70 (m, 2H); ^{13}C NMR (CDCl_3 , 75 MHz): δ = 201.8, 136.6, 135.5, 130.2, 129.1, 128.5, 128.3, 40.3, 28.9, 23.8, 23.3.

(*E*)-2-Undecylidenecyclohexanone (Table 2, entry 2): The title compound was prepared as a colorless oil in 74% isolated yield from heptadec-6-ynal (125.1 mg, 0.500 mmol), BINAP (31.2 mg, 0.050 mmol) and $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (20.4 mg, 0.050 mmol) according to the GP 4; reaction time: 4 h. ^1H NMR (CDCl_3 , 300 MHz): δ = 6.63 (tt, J = 7.5, 2.4 Hz, 1H),

2.53–2.38 (m, 4H), 2.14–2.03 (m, 2H), 1.91–1.68 (m, 4H), 1.51–1.18 (m, 16H), 0.88 (t, $J=7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz): δ = 201.1, 139.8, 136.0, 40.1, 31.8, 29.54, 29.51, 29.4, 29.3, 28.4, 27.7, 26.6, 23.6, 23.3, 22.6, 14.1; IR (neat): $\tilde{\nu}$ = 2950, 2880, 1685, 1615, 1450, 1250, 1140 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{17}\text{H}_{30}\text{O}$: 250.2297, found 250.2303 [M] $^{+}$.

(E)-3-Methyl-2-pentylidenecyclohexanone (Table 2, entry 3):^[23] The title compound was prepared as a colorless oil in 77% isolated yield from 5-methylundec-6-ynal (90.3 mg, 0.501 mmol), BINAP (31.2 mg, 0.050 mmol) and $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (20.5 mg, 0.050 mmol) according to the GP 4; reaction time: 3 h. ^1H NMR (CDCl_3 , 300 MHz): δ = 6.46 (dt, $J=7.8$, 0.9 Hz, 1H), 3.20–3.00 (m, 1H), 2.58–2.43 (m, 1H), 2.37–2.21 (m, 1H), 2.21–2.04 (m, 2H), 2.04–1.74 (m, 3H), 1.74–1.58 (m, 1H), 1.49–1.27 (m, 4H), 1.04 (d, $J=7.2$ Hz, 3H), 0.91 (t, $J=7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz): δ = 202.3, 141.7, 138.9, 40.3, 30.9, 30.6, 30.3, 27.2, 22.5, 20.4, 18.7, 13.9.

(E)-2-Heptylidene-4-methylcyclohexanone (Table 2, entry 4): The title compound was prepared as a colorless oil in 91% isolated yield from 4-methyltridec-6-ynal (104.2 mg, 0.500 mmol), BINAP (31.2 mg, 0.050 mmol) and $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (20.3 mg, 0.050 mmol) according to the GP 4. Reaction time: 24 h. ^1H NMR (CDCl_3 , 300 MHz): δ = 6.66–6.56 (m, 1H), 2.75–2.64 (m, 1H), 2.54 (ddd, $J=18.0$, 5.1, 3.3 Hz, 1H), 2.34 (ddd, $J=18.0$, 11.7, and 6.0 Hz, 1H), 2.19–1.75 (m, 5H), 1.57–1.16 (m, 9H), 1.06 (d, $J=6.3$ Hz, 3H), 0.88 (t, $J=7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz): δ = 201.1, 139.9, 135.4, 39.0, 35.1, 31.6, 31.2, 29.8, 29.1, 28.4, 27.7, 22.5, 21.6, 14.0; IR (neat): $\tilde{\nu}$ = 2880, 1685, 1615, 1450, 1295, 1250, 1120 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{14}\text{H}_{24}\text{O}$: 208.1827, found 208.1822 [M] $^{+}$.

(E)-3-Methyl-2-(1-deuteriopentylidene)cyclopentanone (5) (Scheme 7): The title compound was prepared as a colorless oil in 72% isolated yield from 1-deuterio-4-methyldec-5-ynal (50.4 mg, 0.301 mmol), BINAP (18.7 mg, 0.030 mmol) and $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (12.3 mg, 0.030 mmol) according to the GP 4; reaction time: 19 h. ^1H NMR (CDCl_3 , 300 MHz): δ = 3.15–3.00 (m, 1H), 2.50–2.12 (m, 4H), 2.10–1.94 (m, 1H), 1.74–1.61 (m, 1H), 1.52–1.27 (m, 4H), 1.15 (dd, $J=6.9$, 0.6 Hz, 3H), 0.91 (t, $J=6.9$ Hz, 3H); ^2H NMR (CDCl_3 , 61 MHz): δ = 6.56 (s).

2-Benzylcyclopent-2-enone (Table 3, entry 1):^[24] The title compound was prepared as a yellow oil in 60% isolated yield from 6-phenylhex-5-ynal (86.1 mg, 0.500 mmol), BINAP (31.1 mg, 0.050 mmol) and $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (20.3 mg, 0.050 mmol) according to the GP 4; reaction time: 45.5 h; reaction temperature: 80°C in $(\text{CH}_2\text{Cl})_2$. ^1H NMR (CDCl_3 , 300 MHz): δ = 7.39–7.08 (m, 6H), 3.49 (s, 2H), 2.62–2.48 (m, 2H), 2.48–2.35 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz): δ = 208.9, 158.7, 145.9, 138.7, 128.8, 128.4, 126.2, 34.6, 31.3, 26.5.

2-(2-Methylbenzyl)cyclopent-2-enone (Table 3, entry 2): The title compound was prepared as a yellow oil in 59% isolated yield from 6-*o*-tolylhex-5-ynal (93.1 mg, 0.500 mmol), BINAP (62.3 mg, 0.100 mmol) and $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (40.6 mg, 0.100 mmol) according to the GP 4; reaction time: 44.5 h; reaction temperature: 80°C in $(\text{CH}_2\text{Cl})_2$. ^1H NMR (CDCl_3 , 300 MHz): δ = 7.18–7.08 (m, 4H), 6.97–6.92 (m, 1H), 3.49–3.43 (m, 2H), 2.58–2.39 (m, 4H), 2.23 (s, 3H); ^{13}C NMR (CDCl_3 , 75 MHz): δ = 209.2, 158.6, 145.2, 137.0, 136.2, 130.2, 129.7, 126.5, 126.0, 34.6, 28.9, 26.4, 19.3; IR (neat): $\tilde{\nu}$ = 2910, 1609, 740 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{13}\text{H}_{14}\text{O}$: 186.1045, found 186.0998 [M] $^{+}$.

2-Undecylcyclopent-2-enone (Table 3, entry 3): The title compound was prepared as a pale yellow oil in 84% isolated yield from hexadec-5-ynal (118.3 mg, 0.500 mmol), BINAP (31.1 mg, 0.050 mmol) and $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (20.4 mg, 0.050 mmol) according to the GP 4; reaction time: 19 h; reaction temperature: 80°C in $(\text{CH}_2\text{Cl})_2$. ^1H NMR (CDCl_3 , 300 MHz): δ = 7.36–7.27 (m, 1H), 2.64–2.49 (m, 2H), 2.46–2.32 (m, 2H), 2.24–2.10 (m, 2H), 1.56–1.18 (m, 18H), 0.88 (t, $J=6.9$ Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz): δ = 210.0, 157.2, 146.5, 34.5, 31.9, 29.59, 29.56, 29.5, 29.37, 29.36, 29.3, 27.7, 26.4, 24.7, 22.6, 14.1; IR (neat): 2900, 2850, 1670, 1440, 1370 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{16}\text{H}_{28}\text{O}$: 236.2140 found 236.2110 [M] $^{+}$.

3-Methyl-2-pentylcyclopent-2-enone (dihydrojasnone, Table 3, entry 4):^[25] The title compound was prepared as a yellow oil in 83% isolated yield from 4-methyldec-5-ynal (83.1 mg, 0.500 mmol), BINAP (31.1 mg, 0.050 mmol) and $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (20.3 mg, 0.050 mmol) according to the GP 4. Reaction time: 72 h. Reaction temperature: 80°C in $(\text{CH}_2\text{Cl})_2$. ^1H NMR (CDCl_3 , 400 MHz): δ = 2.55–2.45 (m, 2H), 2.41–2.30

(m, 2H), 2.16 (t, $J=7.6$ Hz, 2H), 2.05 (s, 3H), 1.44–1.18 (m, 6H), 0.87 (t, $J=7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz): δ = 209.4, 169.8, 140.6, 34.3, 31.8, 31.5, 28.1, 23.0, 22.5, 17.2, 14.0.

2-Heptyl-4-methylcyclopent-2-enone (Table 3, entry 5): The title compound was prepared as a pale yellow oil in 58% isolated yield from 3-methylundec-5-ynal (96.9 mg, 0.499 mmol), BINAP (31.2 mg, 0.050 mmol) and $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (20.3 mg, 0.050 mmol) according to the GP 4; reaction time: 72 h; reaction temperature: 80°C in $(\text{CH}_2\text{Cl})_2$. ^1H NMR (CDCl_3 , 400 MHz): δ = 7.16 (s, 1H), 2.94–2.81 (m, 1H), 2.62 (dd, $J=18.8$, 6.4 Hz, 1H), 2.19–2.08 (m, 2H), 1.96 (dd, $J=18.8$, 2.0 Hz, 1H), 1.54–1.38 (m, 2H), 1.36–1.19 (m, 8H), 1.16 (d, $J=7.2$ Hz, 3H), 0.88 (t, $J=6.8$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz): δ = 209.6, 162.4, 145.3, 43.3, 33.3, 31.8, 29.4, 29.1, 27.7, 24.6, 22.7, 20.4, 14.1; IR (neat): $\tilde{\nu}$ = 2920, 2860, 1700, 1450 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{13}\text{H}_{22}\text{O}$: 194.1671 found 194.1667 [M] $^{+}$.

2-Benzyl-3-methoxycyclopent-2-enone (Table 3, entry 6): The title compound was prepared as a pale yellow oil in 39% isolated yield from 4-methoxy-6-phenylhex-5-ynal (101.1 mg, 0.500 mmol), BINAP (31.1 mg, 0.050 mmol) and $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (20.3 mg, 0.05 mmol) according to the GP 4. The reaction was conducted in $(\text{CH}_2\text{Cl})_2$ at 50°C for 15 h, and then 80°C for 11 h. ^1H NMR (CDCl_3 , 300 MHz): δ = 7.30–7.10 (m, 5H), 3.94 (s, 3H), 3.46 (s, 2H), 2.75–2.59 (m, 2H), 2.56–2.37 (m, 2H); ^{13}C NMR (CDCl_3 , 75 MHz): δ = 204.1, 184.9, 140.2, 128.5, 128.2, 125.8, 120.0, 56.5, 33.4, 27.2, 24.6; IR (neat): $\tilde{\nu}$ = 3400, 2900, 1620, 1440, 1360, 1260, 1090, 720, 700 cm^{-1} ; HRMS (EI) calcd for $\text{C}_{13}\text{H}_{14}\text{O}_2$: 202.0994, found 202.0969 [M] $^{+}$.

2-Heptyl-3-methoxycyclopent-2-enone (Table 3, entry 7): The title compound was prepared as a pale yellow oil in 62% isolated yield from 4-methoxyundec-5-ynal (63.1 mg, 0.300 mmol), BINAP (18.7 mg, 0.030 mmol) and $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (12.2 mg, 0.03 mmol) according to the GP 4; reaction time: 20 h; reaction temperature: 50°C in $(\text{CH}_2\text{Cl})_2$. ^1H NMR (CDCl_3 , 300 MHz): δ = 3.94 (s, 3H), 2.75–2.56 (m, 2H), 2.52–2.35 (m, 2H), 2.11 (t, $J=7.2$ Hz, 2H), 1.46–1.15 (m, 10H), 0.87 (t, $J=6.6$ Hz, 3H); ^{13}C NMR (CDCl_3 , 75 Hz): δ = 204.9, 184.5, 121.0, 56.2, 33.4, 31.8, 29.5, 29.1, 28.0, 24.4, 22.6, 21.2, 14.0; IR (neat): $\tilde{\nu}$ = 2900, 1680, 1620, 1460, 1360, 1250, 1080 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{13}\text{H}_{22}\text{O}_2$: 210.1620, found 210.1644 [M] $^{+}$.

2-Benzylcyclohex-2-enone (Table 4, entry 1):^[24] The title compound was prepared as a yellow oil in 41% isolated yield from 7-phenylhept-6-ynal (93.3 mg, 0.501 mmol), BINAP (31.2 mg, 0.050 mmol) and $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (20.3 mg, 0.050 mmol) according to the GP 4; reaction time: 19 h; reaction temperature: 80°C in $(\text{CH}_2\text{Cl})_2$. ^1H NMR (CDCl_3 , 300 MHz): δ = 7.29–7.15 (m, 2H), 7.15–7.02 (m, 3H), 6.52–6.42 (m, 1H), 3.44 (s, 2H), 2.43–2.31 (m, 2H), 2.29–2.17 (m, 2H), 1.89 (quint, $J=8.0$ Hz, 2H); ^{13}C NMR (CDCl_3 , 75 MHz): δ = 198.9, 146.4, 139.6, 139.4, 129.1, 128.3, 126.0, 38.4, 35.3, 26.0, 23.0.

2-Undecylcyclohex-2-enone (Table 4, entry 2): The title compound was prepared as a pale yellow oil in 76% isolated yield from heptadec-6-ynal (125.3 mg, 0.500 mmol), BINAP (31.2 mg, 0.050 mmol) and $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (20.3 mg, 0.050 mmol) according to the GP 4; reaction time: 17.5 h; reaction temperature: 80°C in $(\text{CH}_2\text{Cl})_2$. ^1H NMR (CDCl_3 , 300 MHz): δ = 6.81–6.59 (m, 1H), 2.52–2.26 (m, 4H), 2.23–2.09 (m, 2H), 2.05–1.89 (m, 2H), 1.49–1.13 (m, 18H), 0.88 (t, $J=8.8$ Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz): δ = 199.5, 144.7, 139.9, 38.6, 31.9, 29.61, 29.57, 29.55, 29.5, 29.43, 29.38, 29.3, 28.5, 26.0, 23.1, 22.6, 14.1; IR (neat): $\tilde{\nu}$ = 2910, 2850, 1700, 1420 cm^{-1} ; HRMS (EI): m/z : calcd for $\text{C}_{17}\text{H}_{30}\text{O}$: 250.2297 found 250.2294 [M] $^{+}$.

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- [1] For pioneering work of intramolecular hydroacylation of 4-alkenals in the presence of stoichiometric amount of $[\text{RhCl}(\text{PPh}_3)_3]$, see: K. Sakai, J. Ide, N. Nakamura, *Tetrahedron Lett.* **1972**, 1287.

- [2] For examples of intramolecular hydroacylation of 4-alkenals in the presence of catalytic amounts of rhodium complexes, see: a) C. F. Lochow, R. G. Miller, *J. Am. Chem. Soc.* **1976**, *98*, 1281; b) R. C. Larock, K. Oertle, G. J. Potter, *J. Am. Chem. Soc.* **1980**, *102*, 190; c) K. Sakai, Y. Ishiguro, K. Funakoshi, K. Ueno, H. Suemune, *Tetrahedron Lett.* **1984**, 961; d) D. P. Fairlie, B. Bosnich, *Organometallics* **1988**, *7*, 936.
- [3] For examples of catalytic enantioselective intramolecular hydroacylation of 4-alkenals, see: a) B. R. James, C. G. Young, *J. Chem. Soc. Chem. Commun.* **1983**, 1215; B. R. James, C. G. Young, *J. Organomet. Chem.* **1985**, 285, 321; b) Y. Taura, M. Tanaka, K. Funakoshi, K. Sakai, *Tetrahedron Lett.* **1989**, *30*, 6349; M. Tanaka, M. Imai, M. Fujio, E. Sakamoto, M. Takahashi, Y. Eto-Kato, X.-M. Wu, K. Funakoshi, K. Sakai, H. Suemune, *J. Org. Chem.* **2000**, *65*, 5806; c) R. W. Barnhart, X. Wang, P. Noheda, S. H. Bergens, J. Whelan, B. Bosnich, *J. Am. Chem. Soc.* **1994**, *116*, 1821; B. Bosnich, *Acc. Chem. Res.* **1998**, *31*, 667.
- [4] K. P. Gable, G. A. Benz, *Tetrahedron Lett.* **1991**, *32*, 3473.
- [5] a) Y. Sato, Y. Oonishi, M. Mori, *Angew. Chem.* **2002**, *114*, 1266; *Angew. Chem. Int. Ed. Engl.* **2002**, *41*, 1218. b) A. D. Aloise, M. E. Layton, M. D. Shair, *J. Am. Chem. Soc.* **2000**, *122*, 12610.
- [6] Synthesis of medium ring sulfur heterocycles via chelation-assisted intramolecular hydroacylation, see: H. D. Bendorf, C. M. Colella, E. C. Dixon, M. Marchetti, A. N. Matukonis, J. D. Musselman, T. A. Tiley, *Tetrahedron Lett.* **2002**, *43*, 7031.
- [7] K. Tanaka, G. C. Fu, *J. Am. Chem. Soc.* **2001**, *123*, 11492.
- [8] For examples of catalytic enantioselective intramolecular hydroacylation of 4-alkynals, see: a) K. Tanaka, G. C. Fu, *J. Am. Chem. Soc.* **2002**, *124*, 10296; b) K. Tanaka, G. C. Fu, *J. Am. Chem. Soc.* **2003**, *125*, 8078.
- [9] K. C. Nicolaou, J. L. Gross, M. A. Kerr, *J. Heterocycl. Chem.* **1996**, *33*, 735.
- [10] N. Chatani, T. Morimoto, Y. Fukumoto, S. Murai, *J. Am. Chem. Soc.* **1998**, *120*, 5335.
- [11] M. Yamane, T. Amemiya, K. Narasaka, *Chem. Lett.* **2001**, 1210.
- [12] K. Tanaka, G. C. Fu, *Org. Lett.* **2002**, *4*, 933.
- [13] K. Tanaka, G. C. Fu, *Chem. Commun.* **2002**, 684.
- [14] For the mechanistic studies of the rhodium-catalyzed cyclization of 4-pentenals, see: a) R. E. Campbell Jr., R. G. Miller, *J. Organomet. Chem.* **1980**, *186*, C27; b) R. E. Campbell Jr., C. F. Lochow, K. P. Vora, R. G. Miller, *J. Am. Chem. Soc.* **1980**, *102*, 5824; c) D. P. Fairlie, B. Bosnich, *Organometallics* **1988**, *7*, 946.
- [15] For the isolation of *cis*-hydridopent-4-enoylrhodium(III) complex, see: D. Milstein, *J. Chem. Soc. Chem. Commun.* **1982**, 1357.
- [16] M. Tanaka, H. Mitsuhashi, M. Maruno, T. Wakamatsu, *Chem. Lett.* **1994**, 1455.
- [17] D. L. Boger, R. J. Mathvink, *J. Org. Chem.* **1992**, *57*, 1429.
- [18] K. R. Roesch, R. C. Larock, *J. Org. Chem.* **2001**, *66*, 412.
- [19] D. J. Coveney, V. F. Patel, G. Pattenden, D. M. Thompson, *J. Chem. Soc. Perkin Trans. 1* **1990**, 2721.
- [20] G. Lardelli, V. Lamberti, W. T. Weller, A. P. de Jonge, *Recueil Trav. Chim.* **1967**, *86*, 481.
- [21] D. Liotta, C. S. Barnum, M. Saindane, *J. Org. Chem.* **1981**, *46*, 4301.
- [22] E. J. Enholm, P. E. Whitley, Y. Xie, *J. Org. Chem.* **1996**, *61*, 5384.
- [23] F. E. Ziegler, M. A. Cady, *J. Org. Chem.* **1981**, *46*, 122.
- [24] K. Högenauer, J. Mulzer, *Org. Lett.* **2001**, *3*, 1495.
- [25] B. M. Trost, A. B. Pinkerton, *J. Org. Chem.* **2001**, *66*, 7714.

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