CHEMISTRY
A EUROPEAN JOURNAL

Rhodium-Catalyzed Asymmetric Aqueous Pauson–Khand-Type Reaction

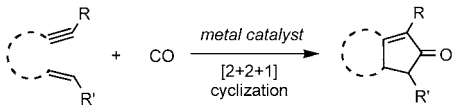
Fuk Yee Kwong,*[a] Yue Ming Li,[a] Wai Har Lam,[a] Liqin Qiu,[a] Hang Wai Lee,[a] Chi Hung Yeung,[a] Kin Shing Chan,[b] and Albert S. C. Chan*[a]

Abstract: An interesting rhodium-catalyzed asymmetric aqueous Pauson–Khand-type reaction was developed. A chiral atropisomeric dipyridyldiphosphane ligand was found to be highly effective in this system. This operationally simple protocol allows both catalyst and reactants to be handled under air without precautions. Various enynes were transformed to the corresponding bicyclic cyclopentenones in good yield and enantiomeric excess (up to 95% *ee*). A study of the electronic effects of the enyne substrates revealed a correlation between the electronic properties of the substrates and the *ee* value obtained in the product of the Pauson–Khand-type reaction. A linear free-energy relationship was observed from a Hammett study.

Keywords: asymmetric catalysis · cyclization · Pauson–Khand reactions · phosphane ligands · rhodium

Introduction

Transition-metal-catalyzed/mediated [2+2+1] carbonylative cycloaddition of an alkene and an alkyne (called the Pauson–Khand-type reaction or PKR)[1] represents one of the most versatile methods for the preparation of various scientifically useful and biologically interesting carbocycles.[2] Conventionally, the PKR requires a stoichiometric amount of $[Co_2(CO)_8]$ (obtained by heating a $[Co_2(CO)_6$(alkyne)] complex with excess alkene). However, the development of the catalytic PKR has prospered recently because of the apparent advantages [Eq. (1)].[3]



(1)

[a] Dr. F. Y. Kwong, Dr. Y. M. Li, Dr. W. H. Lam, Dr. L. Qiu, H. W. Lee, Dr. C. H. Yeung, Prof. Dr. A. S. C. Chan
Open Laboratory of Chirotechnology of the Institute of Molecular Technology for Drug Discovery and Synthesis
Department of Applied Biology and Chemical Technology
The Hong Kong Polytechnic University, Hung Hom (Hong Kong)
Fax: (+852) 23-649-932
E-mail: bcfyk@inet.polyu.edu.hk
bcachan@polyu.edu.hk

[b] Prof. Dr. K. S. Chan
Department of Chemistry
The Chinese University of Hong Kong, Shatin, New Territories (Hong Kong)

The first example of the cobalt-catalyzed PKR was reported in 1973 by Pauson, Khand, and co-workers [Eq. (1)].[4] Several other research groups also attempted to perform this interesting catalytic reaction in 1980s.[5] In early 1990s, a successful and practical intramolecular PKR of enynes by using $[Co_2(CO)_8]$ with $P(OPh)_3$ ligands was reported by Jeong et al.[6] Apart from the cobalt-catalyzed PKR,[7] the use of other transition metals, especially in the corresponding chiral catalysts, for this enantioselective carbonylative cyclization is currently of high interest. Recent examples have shown that chiral titanium,[8] rhodium,[9] and iridium[10] complexes are effective in the asymmetric PKR. Although major improvements have been shown, the use of highly toxic gaseous carbon monoxide signifies a drawback to these procedures. Recently, two independent groups led by Morimoto/Kakiuchi and Shibata reported notable accomplishments in the investigation of aldehydes as CO surrogates.[11,12] These findings enable us to use a nontoxic "carbon monoxide" like reagent for carbonylation reactions.

We envisioned, as a prerequisite, an attractive and convenient protocol for a reaction that should be operationally simple, in particular, a reaction that can be carried out in less harmful solvents. Recently, tremendous attention has been given to aqueous transition-metal-catalyzed reactions.[13] However, no catalytic asymmetric systems that enable the use of water as the only solvent, without a surfactant, in the PKR have been developed yet.[14] To further improve the PKR, the use of an aqueous solvent in this catalytic reaction would be a good direction to take. We herein describe this approach for a catalytic and enantioselective

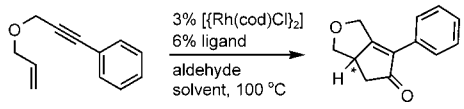
DOI: 10.1002/chem.200401237

aqueous Pauson–Khand-type reaction of enynes in the presence of aldehydes as the source of carbon monoxide. This attractive protocol uses a catalyst and reactants that can be handled under air without special precautions.[15]

Results and Discussion

We first examined the reaction of enynes with aldehydes in conventional organic solvents, such as toluene, dioxane, and *N*,*N*-dimethylformamide (DMF; see Table 1, entries 1–3). However, moderate chemical yields and *ee* values were obtained. To our delight, we observed that an increase in the concentration of the reaction would give a higher reactivity in the PKR (data not shown). These significant findings offer us a good way in which to improve this reaction. An interesting angle in this direction is the application of the aqueous micellar concept to the reaction, to increase the effective concentration of the reactants and thereby accelerate the reaction.[16] It is noteworthy that when water was used as the sole solvent in the PKR, the highest activity of the reaction was observed in our case (Table 1, entry 4). These results prompted us to use water as the prototypical solvent for further ligand screening. BINAP-class ligands showed poor conversion with a moderate *ee* value for the bicyclic cyclopentenone (Table 1, entries 5,6). Et-DUPHOS, PHANEPHOS, and Et-FerroTANE gave a sluggish reaction rate during the reaction and a poor yield (Table 1, entries 7–9).[17] In contrast, the atropisomeric dipyridyldiphosphane ligand (*S*)-P-Phos[18] (see Table 2 for formula) was found to be the best ligand among those screened (Table 1, entries 4–7).

Table 1. Effects of solvent, ligand, and aldehyde combinations in the enantioselective Pauson–Khand-type reaction.[a]



Entry	Ligand	Aldehyde	Solvent	Yield[b] [%]	*ee*[c] [%]
1	P-Phos	cinnamylaldehyde	toluene	65	80
2	P-Phos	cinnamylaldehyde	dioxane	63	74
3	P-Phos	cinnamylaldehyde	DMF	6	0
4	P-Phos	cinnamylaldehyde	water	82	84
5	BINAP[17]	cinnamylaldehyde	water	23	61
6	tol-BINAP[17]	cinnamylaldehyde	water	33	79
7	Et-DuPHOS[17]	cinnamylaldehyde	water	5	22
8	PHANEPHOS[17]	cinnamylaldehyde	water	6	15
9	FerroTANE[17]	cinnamylaldehyde	water	21	30
10	P-Phos	benzaldehyde	water	82	63
11	P-Phos	*p*-OMe-benzaldehyde	water	19	71
12	P-Phos	*p*-Cl-benzaldehyde	water	83	80
13	P-Phos	*n*-nonylaldehyde	water	45	81

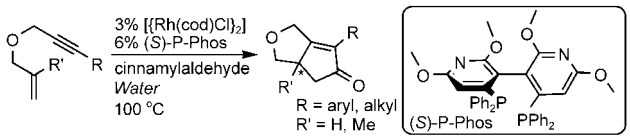
[a] Reaction conditions: [{Rh(cod)Cl}$_2$] (3 mol%), ligand (6 mol%), enyne (0.3 mmol), and aldehyde (0.45 mmol) were charged to a screw-cap flask at RT under air. Solvent (0.2 mL; concentration of enyne 1.5 M) was added under nitrogen and the reaction was stirred at 100 °C for 36 h. [b] Yield of isolated product. [c] Average of two runs from chiral HPLC analysis.

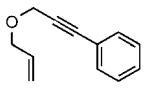
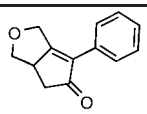
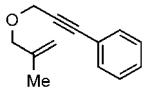
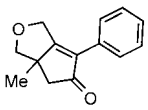
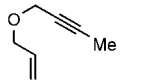
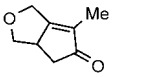
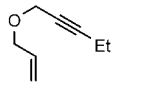
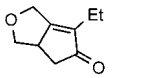
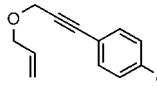
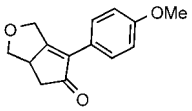
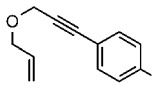
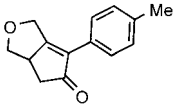
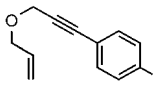
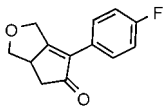
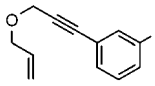
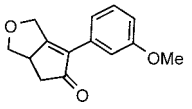
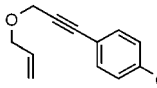
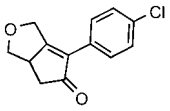
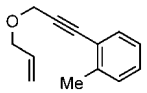
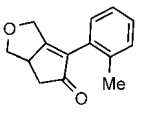
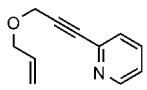
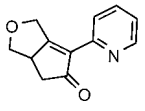
A variety of aldehydes were examined as CO surrogates. Cinnamylaldehyde gave the best results in both optical and chemical yields (Table 1, entry 4). Electron-donating *p*-methoxybenzaldehyde gave a complicated reaction mixture with poor product yield, while electron-deficient *p*-chlorobenzaldehyde furnished the desired product in both good yield and enantioselectivity (Table 1, entries 11,12). It is particularly noteworthy that we found the electronic properties of the aromatic aldehydes were responsible for both the enantioselectivity and yield of the corresponding substituted-cyclopentenone products (Table 1, entries 10–12). Additionally, the aliphatic aldehyde also gave a high *ee* value in the product with moderate chemical yield (Table 1, entry 13). The amount of aldehyde added was further optimized. When we used an equivalent of aldehyde in these cooperative processes (decarbonylation/Pauson–Khand cyclization), it gave a moderate yield with good enantioselectivity.[19] To our delight, when the amount of cinnamylaldehyde was increased to 1.5 equivalents, optimal yield and enantioselevtivity were both obtained (Table 1, entry 4). Further increase of the aldehyde loading from 1.5 to 10 equivalents had no significant beneficial effect. The effectiveness of cationic [Rh(cod)$_2$]BF$_4$ and [Rh(cod)$_2$]OTf complexes as the metal source was also examined (Tf = trifluoromethanesulfonyl); however, we found that the neutral complex [{Rh(cod)Cl}$_2$] gave the best results.

These relatively mild and optimized conditions were applied to the Pauson–Khand-type cyclization of different oxygen-tethered substrates. An enyne with a 1,1-disubstituted alkene reacted smoothly to give high enantioselectivity (90% *ee*) in the chiral quaternary-carbon center of the bicyclic cyclopentenone (Table 2, entry 2). Alkyl-substituted alkynes gave excellent enantioselectivities (95% *ee*) in the corresponding products (Table 2, entries 3,4). In order to further explore this Pauson–Khand-type reaction, we performed an electronic effect investigation. Various new aromatic enynes with different electronic properties were prepared and subjected to carbonylative cyclizations. Interestingly, the electronic effect study showed that electron-donating aromatic enynes provided higher enantioselectivity of the product, while enynes with electron-withdrawing substituents afforded relatively lower *ee* values in the bicyclic cyclopentenones (Table 2, entries 5–9).

Particularly noteworthy is the fact that this unprecedented correlation of the product *ee* value and the electronic properties of the substrates in Pauson–Khand-type cyclizations can be demonstrated from a Hammett Plot (Figure 1).[20] A linear free-energy relationship was obeyed for substrates

Table 2. Catalytic and enantioselective aqueous Pauson–Khand-type reactions.[a]



Entry	Substrate	Product	Yield[b] [%]	*ee* [%]
1			82	84
2			71	90
3			82	95
4			60	95
5			93	93
6			92	88
7			90	82
8			88	81
9			91	77
10			49	74
11			no reaction	n.d.[c]

[a] Reaction conditions: [{Rh(cod)Cl}$_2$] (3 mol%), (*S*)-P-Phos (6 mol%), enyne (0.3 mmol), and aldehyde (0.45 mmol) were charged to a screw-cap flask at RT under air. Solvent (0.2 mL; concentration of enyne 1.5 M) was added under nitrogen and the reaction was stirred at 100 °C for 36 h. [b] Yield of isolated product. [c] n.d. = not determined.

with *para* and *meta* substitutions (Figure 1).[21] However, sterically congested *ortho*-substituted enynes gave an *ee* value outside the trend (Table 2, entry 10). Presumably, the steric factor, instead of the electronic effect, plays the dominant role for this particular substrate. A proposed transition-state model can be used to account for this interesting electronic effect in asymmetric Pauson–Khand-type reaction (Figure 2). We suggest that, in the stereotransition state, the electron-rich enyne may coordinate more closely to the rhodium center by π interactions;[22] this would result in improved stereochemical communication and would thus give rise to a higher enantioselectivity (Figure 2, Model A). The electron-poor enyne may, however, coordinate to the metal center in a different mode, which is far away from the chiral environment in the transition state (Figure 2, Model B).[23] Therefore, a lower *ee* value is observed in the bicyclic cyclopentenone.

These attractive aqueous PKR conditions were also explored with other carbon- and nitrogen-tethered enynes. Excellent isolated yields were obtained for these substrates with good enantioselectivities (Table 3).

In conclusion, we have demonstrated an interesting catalytic and enantioselective aqueous Pauson–Khand-type cyclization. Although these aqueous reactions required organic solvents for product purification, this is a good start for the development of this chemistry with less environmental impact in the near future. In addition, the unprecedented electronic effect in the Pauson–Khand-type reaction is notable. To the best of our knowledge, this is the first example to show a correlation between enyne electronic properties and the *ee* value of the bicyclic cyclopentenones for the PKR in a Hammett study. Rationalization of these observations by full investigation of the stereodetermining/rhodacycle-forming step in the aqueous Pauson–Khand-type cyclization is currently underway.

Experimental Section

General considerations: Unless otherwise noted, all reagents were purchased from commercial suppliers and used without purification. All air-sensitive reactions were performed in Rotaflo (England) resealable screw-cap Schlenk flasks (approximately 10 mL volume) or screw-cap vials (approximately 2 mL volume). Toluene and tetrahydrofuran (THF) were distilled from sodium and sodium benzophenone ketyl, respectively, under nitrogen,.[24] Allylamine and triethylamine were distilled over CaH_2 prior to use. Aldehydes (liquid form at RT) were distilled under reduced pressure and stored in screw-cap vials. NaH (60% in mineral oil) was washed with dry hexane prior to use. (Caution: This procedure should be performed in a relatively dry atmosphere with adequate shielding.) [{Rh(cod)Cl}$_2$], as a shiny orange crystalline solid, was purchased from Strem Chemicals. Water was degassed and stored in a Schlenk flask. Thin-layer chromatography was performed on Merck precoated silica gel 60 F_{254} plates. Silica gel (Merck, 230–400 mesh) was used for flash column chromatography. Melting points were recorded on an uncorrected Büchi B-545 melting point instrument. ^{1}H NMR spectra were recorded on a Varian INOVA 500 spectrometer. Spectra were referenced internally to the residual proton resonance in $CDCl_3$ ($\delta = 7.26$ ppm) or to tetramethylsilane (TMS; $\delta = 0.00$ ppm) as the internal standard. Chemical shifts (δ) are reported as parts per million (ppm) on the δ scale downfield from TMS. ^{13}C NMR spectra were recorded on a Varian INOVA 500 spectrometer and referenced to $CDCl_3$ ($\delta = 77.0$ ppm). ^{31}P NMR spectra were recorded on a Varian INOVA 500 spectrometer and referenced externally to 85% H_3PO_4 ($\delta = 0.0$ ppm). Coupling constants (J) are reported in Hertz (Hz). Mass spectra (EI and FAB) were recorded on a Hewlett–Packard 5989B mass spectrometer. High-resolution mass spectra (HRMS) were obtained on a Brüker APEX 47e ESI FT-ICR mass spectrometer. HPLC analyses were performed on a Waters 600 instrument by using Chiralcel AS, AS-H, AD, AD-H, OD, and OD-H columns (0.46×

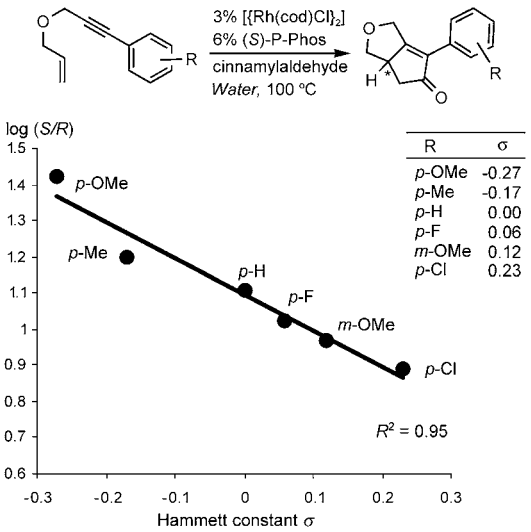


Figure 1. Hammett plot of rhodium-catalyzed asymmetric aqueous Pauson–Khand-type cyclization.

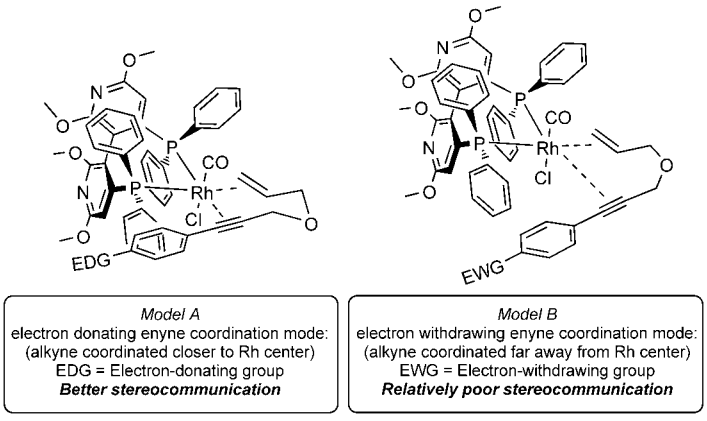
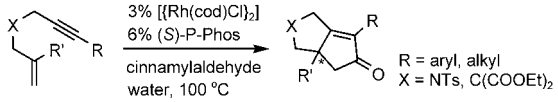
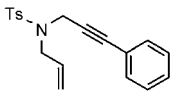
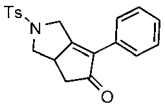
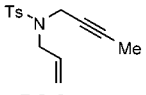
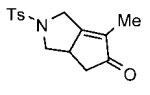
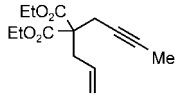
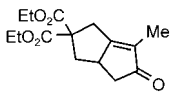


Figure 2. Suggested transition-state models for electronically controlled asymmetric aqueous Pauson–Khand-type reactions.

Table 3. Rhodium-catalyzed asymmetric aqueous Pauson–Khand-type reaction of nitrogen- and carbon-tethered enynes.[a]



Entry	Substrate	Product	Yield[b] [%]	*ee* [%]
1			96	80
2			98	88
3			91	77

[a] Reaction conditions: see Table 2 footnotes. Ts = toluene-4-sulfonyl. [b] Yield of isolated product.

25 cm). Racemic bicyclic cyclopentenone products (for calibration of chiral HPLC analysis) were obtained from the same PKR representative procedure except that racemic ligand was used. GC-MS analysis was conducted on a Hewlett-Packard G1800C GCD system by using a HP5MS column (30 m × 0.25 mm).

Preparation of enyne substrates:

3-(Allyloxy)-1-phenyl-1-propyne:[25] General procedure for condensation of an arylpropargyl alcohol with allyl bromide: NaH (1.44 g, 60 mmol, freshly prewashed with dry hexane) was added portionwise to a solution of 3-phenyl-2-propyn-1-ol (5.28 g, 40 mmol) in freshly distilled THF (80 mL) under a nitrogen atmosphere at 0 °C. The white suspension was slowly warmed to room temperature and stirred for 2 h. The reaction mixture was then cooled to 0 °C and allyl bromide (6.8 mL, 80 mmol) was added dropwise. After complete addition, the reaction was warmed to room temperature and further stirred for 2 h. Water (≈30 mL) was slowly added and the aqueous layer was extracted with diethyl ether (3 × ≈100 mL). The combined organic layers were washed with water (≈50 mL) and brine (≈50 mL) and dried over sodium sulfate. Solvent was removed by rotary evaporation and the light-yellow crude product was purified by distillation under reduced pressure (b.p. = 101–102 °C, 5 mmHg) to give the title compound as a colorless liquid (6.53 g, 95 % yield): R_f = 0.2 (hexane); ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.30–7.43 (m, 5H), 6.02 (tdd, J = 17.0, 10.0, 5.5 Hz, 1H), 5.38 (dd, J = 17.0, 2.0 Hz, 1H), 5.27 (dd, J = 10.0, 2.0 Hz, 1H), 4.39 (s, 2H), 4.17 ppm (dd, J = 5.5, 1.5 Hz, 2H); IR (neat): $\tilde{\nu}$ = 3080, 3019, 2982, 2938, 2849, 2237, 1954, 1881, 1647, 1598, 1571, 1489, 1442, 1424, 1354, 1256, 1124, 1081, 1027, 991, 964, 925, 757, 691, 626, 549, 585, 538, 525 cm^{-1}; MS (EI): m/z (relative intensity): 172 $[M]^+$ (20), 131 (100).

4-(Allyloxy)-2-butyne:[26] The general procedure for condensation of an arylpropargyl alcohol with allyl bromide was followed: 2-Butyn-1-ol (4.0 g, 57.1 mmol), NaH (2.1 g, 87.5 mmol, prewashed with dry hexane), allyl bromide (9.7 mL, 115 mmol), and freshly distilled THF (200 mL) were used to obtain the title compound as a colorless liquid (5.5 g, 88 % yield). Purification was conducted by distillation under reduced pressure (40–42 °C, 10 mmHg =: R_f = 0.2 (hexane); ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 5.90 (tdd, J = 17.0, 10.0, 5.5 Hz, 1H), 5.28 (dd, J = 17.0, 2.0 Hz, 1H), 5.19 (dd, J = 10.0, 2.0 Hz, 1H), 4.10 (q, J = 2.5 Hz, 2H), 4.04 (d, J = 5.5 Hz, 2H), 1.85 ppm (t, J = 2.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 134.1, 117.5, 82.3, 75.0, 70.4, 57.6, 3.5 ppm; MS (EI): m/z (relative intensity): 110 $[M]^+$ (10), 69 (100).

5-(Allyloxy)-3-pentyne:[26] The general procedure for condensation of an arylpropargyl alcohol with allyl bromide was followed: 3-Pentyn-1-ol (4.2 g, 50 mmol), NaH (1.8 g, 75 mmol, prewashed with dry hexane), allyl bromide (8.5 mL, 100 mmol), and freshly distilled THF (150 mL) were used to obtain the title compound as a colorless liquid (5.3 g, 85 % yield). Purification was conducted by distillation under reduced pressure (b.p. = 30–33 °C, 5 mmHg): R_f = 0.2 (hexane); ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 5.91 (tdd, J = 17.0, 10.0, 5.5 Hz, 1H), 5.31 (dd, J = 17.0, 2.0 Hz, 1H), 5.20 (dd, J = 10.0, 2.0 Hz, 1H), 4.12 (t, J = 2.5 Hz, 2H), 4.04 (d, J = 5.5 Hz, 2H), 2.21–2.25 (m, 2H), 1.14 ppm (t, J = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 133.1, 117.6, 82.5, 75.1, 70.5, 57.7, 11.8, 9.5 ppm; IR (neat): $\tilde{\nu}$ = 3078, 2978, 2938, 2851, 2289, 2223, 1649, 1454, 1424, 1357, 1316, 1137, 1084, 999, 926, 748, 650, 563 cm^{-1}; MS (EI): m/z (relative intensity): 125 $[M]^+$ (15), 84 (100).

3-[(2-Methyl-2-propenyl)oxy]-1-phenyl-1-propyne:[27] The general procedure for condensation of an arylpropargyl alcohol with allyl bromide was followed: 3-Phenyl-2-propyn-1-ol (5.28 g, 40 mmol), NaH (1.44 g, 60 mmol, freshly prewashed with dry hexane), 3-bromo-2-methyl-1-propene (10.8 g, 80 mmol), and freshly distilled THF (100 mL) were used to obtain the title compound as a colorless liquid (6.8 g, 92 % yield). Purification was carried out by distillation under reduced pressure (b.p. = 125–128 °C, 4 mmHg): R_f = 0.2 (hexane); ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.30–7.43 (m, 5H), 5.38 (d, J = 2.0 Hz, 1H), 5.27 (d, J = 2.0 Hz, 1H), 4.39 (s, 2H), 4.17 (s, 2H), 1.88 ppm (s, 3H); IR (neat): $\tilde{\nu}$ = 3452, 3078, 2980, 2914, 2842, 2233, 1946, 1885, 1798, 1654, 1593, 1489, 1443, 1356, 1250, 1086, 1034, 903, 757, 691, 594, 523 cm^{-1}; MS (EI): m/z (relative intensity): 186 $[M]^+$ (20), 131 (100).

3-(Allyloxy)-1-(4-methoxyphenyl)-1-propyne:[10] General procedure for Sonogashira coupling of propargyl alcohol with ArI: 4-Iodoanisole (11.7 g, 50 mmol), $[Pd(PPh_3)_2Cl_2]$ (3 mol%), and CuI (6 mol%) were dissolved in freshly distilled toluene (50 mL) under nitrogen at room temperature. Piperidine (8.4 g, 100 mmol) was added and this was followed by slow addition of the propargyl alcohol (3.07 mL, 52 mmol) by syringe. (Caution: exothermic reaction when propagyl alcohol is added). The resulting dark brown reaction mixture was stirred at 30–35 °C for 3 h under nitrogen. (ArI was completely consumed as judged by GC analysis.) The reaction was allowed to reach room temperature and the dark-brown crude product was filtered over a silica pad (5×5 cm) and rinsed with dichloromethane (≈200 mL). Solvent was removed by rotary evaporation to give a viscous brown liquid, which was purified by flash column chromatography on silica gel with dichloromethane as the eluent to afford 3-(4-methoxyphenyl)-2-propyn-1-ol[28] as a yellow solid (6.07 g, 75% yield): R_f=0.4 (dichloromethane); ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.37 (d, J=8.5 Hz, 2H), 6.83 (d, J=8.5 Hz, 2H), 4.47 (d, J=6.0 Hz), 3.81 (s, 2H), 1.75 ppm (t, J=5.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=138.8, 131.3, 128.8, 119.3, 86.5, 85.4, 51.2, 43.6 ppm; MS (EI): m/z (relative intensity): 162 $[M]^+$ (100).

The general procedure for condensation of an arylpropargyl alcohol with allyl bromide was followed: 3-(4-Methoxyphenyl)-2-propyn-1-ol[28] (1.0 g, 6.2 mmol), NaH (223 mg, 9.3 mmol, prewashed with dry hexane), allyl bromide (1.05 mL, 12.4 mmol), and freshly distilled THF (10 mL) were used to obtain the title compound as a pale yellow liquid (1.18 g, 95% yield). Purification of the crude product was conducted by filtration over a short silica pad followed by flash column chromatography on silica gel with hexane/ethyl acetate (10:1) as the eluent: R_f=0.5 (hexane/ethyl acetate (10:1)); ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.39 (d, J=8.5 Hz, 2H), 6.84 (d, J=8.5 Hz, 2H), 5.92–5.98 (m, 1H), 5.33 (dd, J=17.0, 1.0 Hz, 1H), 5.23 (dd, J=17.5, 1.0 Hz, 1H), 4.37 (s, 2H), 4.13 (d, J=5.0 Hz, 2H), 3.81 ppm (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=159.7, 134.1, 133.2, 117.8, 114.7, 113.9, 86.2, 83.6, 70.6, 57.9, 55.2 ppm; IR (neat): $\tilde{\nu}$=3077, 3039, 3006, 2935, 2901, 2839, 2541, 2235, 2049, 1967, 1885, 1648, 1606, 1568, 1509, 1462, 1442, 1354, 1291, 1251, 1175, 1085, 1032, 927, 833, 800, 675, 567, 536, 417 cm^{-1}; MS (EI): m/z (relative intensity): 202 $[M]^+$ (10), 161 (100).

3-(Allyloxy)-1-(4-methylphenyl)-1-propyne: The general procedure for Sonogashira coupling of propagyl alcohol with ArI was used: 4-Iodotoluene (10.9 g, 50 mmol), $[Pd(PPh_3)_2Cl_2]$ (3 mol%), CuI (6 mol%), piperidine (8.4 g, 100 mmol), propagyl alcohol (3.07 mL, 52 mmol), and freshly distilled toluene (50 mL) were used to obtain 3-(4-methylphenyl)-2-propyn-1-ol[29] (5.26 g, 72% yield) as a light-brown solid. Purification was conducted by filtration of the reaction mixture over a silica pad (5×5 cm) followed by flash column chromatography on silica gel with dichloromethane as the eluent: R_f=0.5 (dichloromethane); ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.33 (d, J=8.0 Hz, 2H), 7.12 (d, J=8.0 Hz, 2H), 4.49 (s, 2H), 3.23 (brs, 1H), 2.35 ppm (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=138.2, 131.3, 128.6, 119.3, 86.5, 85.3, 51.2, 21.0 ppm; MS (EI): m/z (relative intensity): 146 $[M]^+$ (100); HRMS: calcd for $C_{10}H_{10}O$: 146.07316; found: 146.07311.

The general procedure for condensation of an arylpropargyl alcohol with allyl bromide was followed: 3-(4-Methylphenyl)-2-propyn-1-ol[29] (1.46 g, 10 mmol), NaH (360 mg, 15 mmol, prewashed with dry hexane), allyl bromide (1.7 mL, 20 mmol), and freshly distilled THF (20 mL) were used to obtain the title compound as a light yellow liquid (1.78 g, 96% yield). Purification was conducted by distillation under reduced pressure (b.p.= 130–133 °C, 3 mmHg): R_f=0.2 (hexane); ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.35 (d, J=8.5 Hz, 2H), 7.12 (d, J=8.0 Hz, 2H), 5.92–6.00 (m, 1H), 5.33 (dd, J=17.0, 1.0 Hz, 1H), 5.23 (dd, J=17.5, 1.0 Hz, 1H), 4.38 (s, 2H), 4.13 (d, J=5.0 Hz, 2H), 2.35 ppm (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=137.5, 137.4, 132.0, 128.8, 119.3, 115.1, 89.4, 85.5, 72.2, 57.4, 20.1 ppm; IR (neat): $\tilde{\nu}$=3080, 3028, 2982, 2921, 2851, 2243, 1910, 1649, 1509, 1442, 1424, 1354, 1260, 1123, 1080, 991, 926, 817, 666, 558, 526 cm^{-1}; MS (EI): m/z (relative intensity): 186 $[M]^+$ (15), 145 (100); HRMS: calcd for $C_{13}H_{14}O$: 186.10447; found: 186.10451.

3-(Allyloxy)-1-(4-fluorophenyl)-1-propyne: The general procedure for Sonogashira coupling of propagyl alcohol with ArI was used: 4-Iodoflurobenzene (11.1 g, 50 mmol), $Pd(PPh_3)_2Cl_2$ (3 mol%), CuI (6 mol%), piperidine (8.4 g, 100 mmol), propagyl alcohol (3.07 mL, 52 mmol), and freshly distilled toluene (50 mL) were used to obtain 3-(4-fluorophenyl)-2-propyn-1-ol[30] (5.85 g, 78% yield) as a light yellow viscous liquid. Purification was conducted by filtration of the reaction mixture over a silica pad (5×5 cm) followed by flash column chromatography on silica gel with dichloromethane as the eluent: R_f=0.5 (dichloromethane); ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.39 (d, J=8.5 Hz, 2H), 6.97 (d, J=8.5 Hz, 2H), 4.78 (s, 2H), 2.69 ppm (brs, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=163.5, 161.5, 133.5 (d, $J_{C,F}$=8.3 Hz), 118.5 (d, $J_{C,F}$=3.0 Hz), 115.5 (d, $J_{C,F}$=22.1 Hz), 86.9, 84.5, 51.3 ppm; MS (EI): m/z (relative intensity): 150 $[M]^+$ (100); HRMS: calcd for C_9H_7FO: 150.04809; found: 150.04820.

The general procedure for condensation of an arylpropargyl alcohol with allyl bromide was followed: 3-(4-Fluorophenyl)-2-propyn-1-ol[30] (1.5 g, 10 mmol), NaH (360 mg, 15 mmol, prewashed with dry hexane), allyl bromide (1.7 mL, 20 mmol), and freshly distilled THF (30 mL) were used to obtain the title compound as a colorless liquid (1.42 g, 75% yield). Purification was conducted by distillation under reduced pressure (b.p.=89–90 °C, 2 mmHg): R_f=0.2 (hexane); ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.41 (d, J=8.5 Hz, 2H), 7.00 (t, J=8.5 Hz), 5.95 (tdd, J=17.0, 10.0, 5.5 Hz, 1H), 5.34 (dd, J=17.0, 1.0 Hz, 1H), 5.24 (dd, J=17.5, 1.0 Hz, 1H), 4.36 (s, 2H), 4.13 ppm (d, J=6.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=163.5, 161.6, 134.0, 133.6 (d, $J_{C,F}$=8.4 Hz), 118.7, (d, $J_{C,F}$=3.0 Hz), 117.9, 115.5 (d, $J_{C,F}$=22.0 Hz), 85.1, 84.7, 70.7, 57.8 ppm; IR (neat): $\tilde{\nu}$=3073, 3016, 2986, 2934, 2851, 2248, 1885, 1649, 1601, 1506, 1354, 1229, 1156, 1088, 992, 928, 837, 815, 563, 529 cm^{-1}; MS (EI): m/z (relative intensity): 190 $[M]^+$ (10), 149 (100); HRMS: calcd for $C_{12}H_{11}FO$: 190.07939; found: 190.07923.

3-(Allyloxy)-1-(3-methoxyphenyl)-1-propyne: The general procedure for Sonogashira coupling of propagyl alcohol with ArI weas used: 3-Iodoanisole (11.7 g, 50 mmol), $[Pd(PPh_3)_2Cl_2]$ (3 mol%), CuI (6 mol%), piperidine (8.4 g, 100 mmol), propagyl alcohol (3.07 mL, 52 mmol), and freshly distilled toluene (50 mL) were used to afford 3-(3-methoxyphenyl)-2-propyn-1-ol[31] (5.91 g, 73% yield) as a light-yellow viscous liquid. Purification was conducted by filtration of the reaction mixture over a silica pad (5×5 cm) followed by flash column chromatography on silica gel with dichloromethane as the eluent: R_f=0.4 (dichloromethane); ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.22 (t, J=8.0 Hz, 1H), 7.03 (d, J=7.5 Hz, 1H), 6.97 (m, 1H), 6.89 (m, 1H), 4.50 (d, J=6.5 Hz, 2H), 3.80 (s, 3H), 1.72 ppm (t, J=6.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ= 138.9, 131.1, 128.6, 119.6, 86.5, 85.3, 51.2, 44.8 ppm; MS (EI): m/z (relative intensity): 162 $[M]^+$ (100); HRMS: calcd for $C_{10}H_{10}O_2$: 162.06808; found: 162.06829.

The general procedure for condensation of an arylpropargyl alcohol with allyl bromide was followed: 3-(3-Methoxyphenyl)-2-propyn-1-ol[31] (1.0 g, 6.2 mmol), NaH (223 mg, 9.3 mmol, prewashed with dry hexane), allyl bromide (1.05 mL, 12.4 mmol), and freshly distilled THF (10 mL) were used to afford the title compound as a light yellow liquid (1.16 g, 94% yield). Purification of the crude product was conducted by filtration over a short silica pad followed by flash column chromatography on silica gel with hexane/ethyl acetate (10:1) as the eluent: R_f=0.5 (hexane/ethyl acetate (10:1)); ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.21 (t, J=8.0 Hz, 1H), 7.02 (d, J=7.5 Hz, 1H), 6.96 (m, 1H), 6.89 (m, 1H), 5.94 (m, 1H), 5.32 (dd, J=17.0, 1.0 Hz, 1H), 5.23 (dd, J=17.5, 1.0 Hz, 1H), 4.37 (s, 2H), 4.13 (d, J=5.0 Hz, 2H), 3.81 ppm (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=159.7, 134.1, 133.2, 117.8, 114.7, 113.9, 86.2, 83.6, 70.6, 57.9, 55.2 ppm; IR (neat): $\tilde{\nu}$=3077, 3004, 2939, 2911, 2840, 2228, 1644, 1600, 1572, 1483, 1419, 1353, 1318, 1289, 1204, 1165, 1124, 1046, 992, 927, 855, 784, 687, 584, 512 cm^{-1}; MS (EI): m/z (relative intensity): 202 $[M]^+$ (10), 161 (100); HRMS: calcd for $C_{13}H_{14}O_2$: 202.09938; found: 202.09923.

3-(Allyloxy)-1-(4-chlorophenyl)-1-propyne: The general procedure for Sonogashira coupling of propagyl alcohol with ArI was used: 3-Iodoanisole (11.9 g, 50 mmol), $[Pd(PPh_3)_2Cl_2]$ (3 mol%), CuI (6 mol%), piperidine (8.4 g, 100 mmol), propagyl alcohol (3.07 mL, 52 mmol), and freshly distilled toluene (50 mL) were used to obtain 3-(4-chlorophenyl)-2-propyn-1-ol[32] (5.91 g, 73% yield) as a light-yellow viscous liquid. Purification was conducted by filtration of the reaction mixture over a silica

pad (5×5 cm) followed by flash column chromatography on silica gel with dichloromethane as the eluent: R_f=0.5 (dichloromethane); ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.36 (d, J=8.0 Hz, 2H), 7.27 (d, J=8.0 Hz, 2H), 4.45 (s, 2H), 1.98 ppm (br s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=133.2, 131.3, 128.2, 119.3, 86.5, 85.1, 51.2 ppm; MS (EI): m/z (relative intensity): 168 $[M]^+$ (30), 166 $[M]^+$ (100); HRMS: calcd for C_9H_7ClO: 166.01854; found: 166.01850.

The general procedure for condensation of an arylpropargyl alcohol with allyl bromide was followed: 3-(4-Chlorophenyl)-2-propyn-1-ol[32] (1.67 g, 10 mmol), NaH (360 mg, 15 mmol, prewashed with dry hexane), allyl bromide (1.7 mL, 20 mmol), and freshly distilled THF (30 mL) were used to obtain the title compound as a light yellow liquid (1.84 g, 89% yield). Purification of the crude product was conducted by filtration over a short silica pad followed by flash column chromatography on silica gel with hexane/ethyl acetate (30:1) as the eluent: R_f=0.4 (hexane/ethyl acetate (30:1)); ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.38 (d, J=8.5 Hz, 2H), 7.27 (d, J=8.5 Hz, 2H), 5.94 (tdd, J=17.0, 10.0, 5.5 Hz, 1H), 5.34 (dd, J=17.0, 1.0 Hz, 1H), 5.24 (dd, J=17.5, 1.0 Hz, 1H), 4.36 (s, 2H), 4.12 ppm (d, J=6.0 Hz); IR (neat): $\tilde{\nu}$=3078, 3011, 2980, 2939, 2850, 2243, 1895, 1644, 1583, 1488, 1353, 1260, 1124, 1089, 1015, 991, 927, 828, 753, 526 cm^{-1}; MS (EI): m/z (relative intensity): 208 $[M]^+$ (10), 206 $[M]^+$ (40), 167 (30), 165 (100); HRMS: calcd for $C_{12}H_{11}ClO$: 206.04984; found: 206.04989.

3-(Allyloxy)-1-(2-methylphenyl)-1-propyne: The general procedure for Sonogashira coupling of propagyl alcohol with ArI was used: 2-Iodotoluene (10.9 g, 50 mmol), $[Pd(PPh_3)_2Cl_2]$ (3 mol%), CuI (6 mol%), piperidine (8.4 g, 100 mmol), propagyl alcohol (3.07 mL, 52 mmol), and freshly distilled toluene (50 mL) were used to obtain 3-(2-methylphenyl)-2-propyn-1-ol[31] (5.26 g, 72% yield) as a light-brown solid. Purification was conducted by filtration of the reaction mixture over a silica pad (5×5 cm) followed by flash column chromatography on silica gel with dichloromethane as the eluent: R_f=0.5 (dichloromethane); ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.41 (d, J=7.5 Hz, 1H), 7.11–7.24 (m, 3H), 4.54 (d, J=6.0 Hz), 2.43 ppm (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=138.2, 131.3, 128.6, 128.1, 119.3, 115.3, 86.5, 85.3, 51.2, 21.2 ppm; MS (EI): m/z (relative intensity): 146 $[M]^+$ (100); HRMS: calcd for $C_{10}H_{10}O$: 146.07316; found: 146.07310.

The general procedure for condensation of an arylpropargyl alcohol with allyl bromide was followed: 3-(2-Methylphenyl)-2-propyn-1-ol (1.46 g, 10 mmol), NaH (360 mg, 15 mmol, prewashed with dry hexane), allyl bromide (1.7 mL, 20 mmol), and freshly distilled THF (20 mL) were used to obtain the title compound as a light yellow liquid (1.73 g, 94% yield): ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.43 (d, J=8.0 Hz, 1H), 7.12–7.25 (m, 3H), 5.95–6.01 (m, 1H), 5.36 (dd, J=17.0, 1.0 Hz, 1H), 5.27 (dd, J=17.5, 1.0 Hz, 1H), 4.44 (s, 2H), 4.16 (d, J=6.0 Hz), 2.46 ppm (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=137.6, 137.4, 132.0, 128.8, 128.6, 119.6, 119.3, 115.1, 89.4, 85.5, 72.3, 57.4, 20.2 ppm; IR (neat): $\tilde{\nu}$=3069, 3020, 2981, 2920, 2850, 2223, 1644, 1603, 1485, 1455, 1425, 1353, 1249, 1117, 1085, 926, 758, 716, 599, 452 cm^{-1}; HRMS: calcd for $C_{13}H_{14}O$: 186.10447; found: 186.10453.

***N*-Allyl-*N*-(3-phenyl-2-propynyl)-4-tolylsulfonamide**:[11,33] Triphenylphosphane (14.4 g, 55 mmol) was dissolved in dichloromethane (250 mL). Bromine (8.8 g, 2.82 mL, 55 mmol) was then added dropwise at 0°C and the mixture was stirred for 30 min. 3-Phenyl-2-propyn-1-ol was added at 0°C and the reaction mixture was left to stir for 1 h. Hexane (≈800 mL) was added and the white suspension was passed through a short silica pad (5×10 cm) and washed with hexane. The crude product was concentrated and distilled under reduced pressure (b.p.=88–90°C, 1 mmHg) to afford 3-bromo-1-phenyl-1-propyne[34] (9.01 g, 92% yield) as a light-yellow liquid: R_f=0.4 (hexane); ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.44–7.46 (m, 2H), 7.32–7.36 (m, 3H), 4.17 ppm (s, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=132.1, 129.1, 128.6, 122.4, 87.0, 84.5, 15.6 ppm; MS (EI): m/z (relative intensity): 196 $[M]^+$ (100), 194 $[M]^+$ (100).

Allylamine (4.0 mL, 53 mmol) was charged into a three-necked round-bottomed flask and freshly distilled diethyl ether (10 mL) was added at room temperature under nitrogen. 3-Bromo-1-phenyl-1-propyne (1.0 g, 5.13 mmol) was added dropwise at 0°C and the reaction mixture was stirred at room temperature for 2 h. The reaction was quenched with water and extracted with ethyl acetate (3×≈50 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. The crude mixture was passed through a short silica pad (3×10 cm). Solvent was removed in vacuo and the *N*-allyl-*N*-(3-phenyl-2-propynyl)amine product was used in the next step without further purification.

A dichloromethane solution of *p*-toluenesulfonyl chloride (967 mg, 5.07 mmol) was added to a mixture of *N*-allyl-*N*-(3-phenyl-2-propynyl)amine (crude), triethylamine (0.9 mL), and dichloromethane (5 mL) at 0°C. The reaction mixture was slowly warmed to room temperature and stirred for 2 h. Water (≈50 mL) was added to quench the reaction and the aqueous phase was extracted with chloroform (2×≈50 mL). The combined organic layers were washed with brine and dried over sodium sulfate. Solvent was removed by rotary evaporation and the crude product was purified by column chromatography on silica gel with hexane/dichloromethane (2:1→1:1) as the eluent to afford the title compound as a white solid (1.39 g, 83% yield over two steps): R_f=0.3 (hexane/dichloromethane (2:1)); ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.78 (d, J=8.0 Hz, 2H), 7.22–7.28 (m, 5H), 7.06 (d, J=7.0 Hz, 2H), 5.77–5.83 (m, 1H), 5.33 (d, J=17.5 Hz, 1H), 5.26 (d, J=10.0 Hz, 1H), 4.31 (s, 2H), 3.89 (d, J=6.0 Hz, 2H), 2.33 ppm (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=143.5, 135.9, 132.0, 131.4, 129.5, 128.3, 128.1, 127.7, 122.2, 119.9, 85.6, 81.6, 49.2, 36.7, 21.4 ppm; IR (neat): $\tilde{\nu}$=2904, 1460, 1376, 723 cm^{-1}; MS (EI): m/z (relative intensity): 325 $[M]^+$ (5), 222 (20), 170 (80), 142 (70), 115 (100).

***N*-Allyl-*N*-(2-butynyl)-4-tolylsulfonamide**: Allylamine (15.0 mL, 200 mmol) was charged into a three-necked round-bottomed flask and freshly distilled diethyl ether (50 mL) was added at room temperature under nitrogen. 1-Bromo-2-butyne (1.86 mL, 20 mmol) was added dropwise at 0°C and the reaction mixture was stirred at room temperature for 2 h. The reaction was quenched with water and extracted with ethyl acetate (3×≈100 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. The crude mixture was passed through a short silica pad (5×10 cm). Solvent was removed in vacuo and the *N*-allyl-*N*-(2-butynyl)amine product was used in the next step without further purification.

A dichloromethane solution of *p*-toluenesulfonyl chloride (4 g, 22 mmol) was added to a mixture of *N*-allyl-*N*-(2-butynyl)amine (crude), triethylamine (4 mL), and dichloromethane (50 mL) at 0°C. The reaction mixture was slowly warmed to room temperature and stirred for 2 h. Water (≈100 mL) was added to quench the reaction and the aqueous phase was extracted with chloroform (2×≈100 mL). The combined organic layers were washed with brine and dried over sodium sulfate. Solvent was removed by rotary evaporation and the crude product was purified by column chromatography on silica gel with hexane/dichloromethane (4:1) as the eleuent to afford the title compound as a colorless liquid (2.30 g, 44% yield over two steps): R_f=0.2 (hexane/dichloromethane (4:1)); ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.70 (d, J=7.5 Hz, 2H), 7.27 (d, J=7.5 Hz, 2H), 5.67–5.73 (m, 1H), 5.25 (d, J=17.0 Hz, 1H), 5.18 (d, J=10.5 Hz, 1H), 3.98 (d, J=2.0 Hz, 2H), 3.77 (d, J=5.0 Hz, 2H), 2.39 (s, 3H), 1.51 ppm (t, J=6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=143.5, 136.4, 132.4, 129.5, 128.1, 119.7, 81.8, 71.9, 49.2, 36.5, 21.7, 3.4 ppm; IR (neat): $\tilde{\nu}$=3073, 3062, 2980, 2914, 2847, 2294, 2223, 1644, 1593, 1491, 1439, 1349, 1255, 1162, 1092, 1055, 899, 814, 735, 663, 572, 545 cm^{-1}; MS (EI): m/z (relative intensity): 263 $[M]^+$ (5), 248 (10), 184 (40), 155 (60), 108 (100); HRMS: calcd for $C_{14}H_{17}NO_2S$: 263.09800; found: 263.09809.

Diethyl 7-octen-2-yne-5,5-dicarboxylate:[35] Diethyl 1-butene-4,4-dicarboxylate (2.0 g, 10 mmol) was charged to a three-necked round-bottomed flask and dry THF (30 mL) was added under nitrogen at room temperature. NaH (360 mg, 15 mmol, prewashed with dry hexane) was added portionwise to the reaction mixture at 0°C and stirred for 2 h. A white suspension was observed. 1-Bromo-2-butyne (1.86 mL, 20 mmol) was then added dropwise at 0°C and the reaction mixture was slowly warmed to room temperature with stirring for 3 h. The reaction was quenched by water (≈50 mL) and the aqueous phase was extracted with diethyl ether (3×≈100 mL). The combined organic phase was washed with water and brine and dried over sodium sulfate. Solvent was removed by rotary evaporation and the crude mixture was purified by distillation under reduced pressure to afford the title compound as a colorless oil (2.31 g, 92% yield): ^{1}H NMR ($CDCl_3$, 500 MHz): δ=5.63 (m, 1H), 5.15 (d, J=17.0 Hz, 1H), 5.09 (d, J=10.0 Hz, 1H), 4.19 (q, J=7.0 Hz, 4H), 2.78 (d,

J=7.5 Hz, 2H), 2.72 (q, J=2.5 Hz, 2H), 1.75 (t, J=2.5 Hz, 3H), 1.24 ppm (t, J=7.5 Hz, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=169.9, 131.8, 119.3, 78.6, 73.2, 61.3, 56.8, 36.3, 22.7, 13.9, 3.3 ppm; IR (neat): $\tilde{\nu}$= 3646, 3472, 3083, 2982, 2929, 2233, 1739, 1639, 1465, 1441, 1325, 1292, 1218, 1136, 1096, 1036, 912, 855, 661, 574 cm^{-1}; MS (EI): m/z (relative intensity): 252 $[M]^+$ (20), 194 (100).

Catalytic asymmetric Pauson–Khand-type reaction:

General procedure for asymmetric Pauson–Khand-type cyclization of various enynes: [{Rh(cod)Cl}$_2$] (4.4 mg, 9.0 μmol), (*S*)-P-Phos (11.6 mg, 18.0 μmol), and cinnamylaldehyde (59 mg, 0.45 mmol, 1.5 equiv with respect to the enyne) were charged to a screw-cap vial on the bench top at room temperature with continuous stirring (magnetic stirrer bar, 2× 6 mm). Enynes (0.3 mmol) was then added under air. These vials were evacuated and backfilled with nitrogen (3 cycles) and this was followed by addition of water (0.2 mL, concentration of enyne 1.5 M). The reaction mixtures were heated to 100 °C (±2 °C) for 36 h (reaction times were unoptimized for each substrate). The vials were allowed to cool to room temperature. Ethyl acetate (≈2 mL) was added and the crude product was passed through a short plug of Na_2SO_4. Solvent was removed by rotary evaporation and the crude mixture was purified by flash column chromatography on silica gel with hexane/ethyl acetate as the eluent to afford the chiral bicyclic cyclopentenones. (Alternative workup procedure: dichloromethane (≈2 mL) was added and the reaction mixture was passed through a short plug of Na_2SO_4 for initial screening by GC-MS analysis.) The enantiomeric excess values of the products were determined by chiral HPLC analysis with Daicel AS, AS-H, and AD-H columns.

2-Phenyl-7-oxabicyclo[3.3.0]oct-1-en-3-one (Table 2, entry 1):[9] Purified by column chromatography (1.8× ≈15 cm) on silica gel with hexane/ethyl acetate (3:1) as the eluent to obtain the title compound as a light yellow oil (82% yield; 84% *ee* (*S* configuration)): HPLC conditions: AD column, hexane (Hex):isopropyl alcohol (IPA)=9:1, 1.0 mL min^{-1}, 254 nm, R_t=12.4, 16.9 min; R_f=0.3 (hexane/ethyl acetate (2:1)); ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.52 (d, J=7.5 Hz, 2H), 7.39–7.42 (m, 2H), 7.33–7.37 (m, 1H), 4.93 (d, J=16.5 Hz, 1H), 4.59 (d, J=16.0 Hz, 1H), 4.38 (t, J=8.0 Hz, 1H), 3.30–3.35 (m, 1H), 3.23 (dd, J=8.0 Hz, 11.5 Hz, 1H), 2.85 (dd, J=6.5 Hz, 18.5 Hz, 1H), 2.34 ppm (dd, J=4.0 Hz, 18.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=206.7, 177.3, 134.5, 130.5, 128.6, 128.5, 127.9, 71.2, 66.2, 43.2, 40.2 ppm; MS (EI): m/z (relative intensity): 200 $[M]^+$ (70), 170 (40), 158 (50), 141 (100).

2-Phenyl-5-methyl-7-oxabicyclo[3.3.0]oct-1-en-3-one (Table 2, entry 2):[36] Purified by column chromatography (1.8× ≈15 cm) on silica gel with hexane/ethyl acetate (3:1) as the eluent to obtain the title compound as a light yellow oil (71% yield; 90% *ee*): HPLC conditions: AS-H column, Hex:IPA=9:1, 1.0 mL min^{-1}, 254 nm, R_t=9.7, 10.8 min; R_f=0.3 (hexane/ethyl acetate (2:1)); ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.33–7.51 (m, 5H), 4.98 (d, J=17.0 Hz, 1H), 4.60 (d, J=17.0 Hz, 1H), 4.03 (d, J=8.0 Hz, 1H), 3.43 (d, J=8.0 Hz, 1H), 2.60 (d, J=17.0 Hz, 1H), 2.54 (d, J= 17.0 Hz, 1H), 1.39 ppm (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=206.7, 180.6, 133.2, 130.5, 128.7, 128.6, 128.1, 76.5, 65.3, 48.7, 47.8, 24.7 ppm; MS (EI): m/z (relative intensity): 214 $[M]^+$ (80), 184 (20), 169 (40), 141 (100), 115 (70).

2-Methyl-7-oxabicyclo[3.3.0]oct-1-en-3-one (Table 2, entry 3):[9] Purified by column chromatography (1.8× ≈15 cm) on silica gel with hexane/ethyl acetate (3:1) as the eluent to obtain the title compound as a colorless oil (82% yield; 95% *ee*): HPLC conditions: AS-H column, Hex:IPA=9:1, 1.0 mL min^{-1}, 210 nm, R_t=12.2, 13.7 min; R_f=0.3 (hexane/ethyl acetate (2:1)); ^{1}H NMR ($CDCl_3$, 500 MHz): δ=4.54 (q, J= 15.0 Hz, 2H), 4.30–4.32 (m, 1H), 3.19–3.23 (m, 2H), 2.64–2.71 (dd, J= 5.5, 18.0 Hz, 1H), 2.09–2.17 (dd, J=2.0, 18.0 Hz, 1H), 1.77 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ=209.0, 176.1, 132.6, 71.8, 64.7, 43.2, 38.6, 8.9 ppm; MS (EI): m/z (relative intensity): 138 $[M]^+$ (100), 123 (60), 105 (30).

2-Ethyl-7-oxabicyclo[3.3.0]oct-1-en-3-one (Table 2, entry 4):[26] Purified by column chromatography (1.8× ≈15 cm) on silica gel with hexane/ethyl acetate (3:1) as the eluent to obtain the title compound as a colorless oil (60% yield; 95% *ee*): HPLC conditions: AS-H column, Hex:IPA=9:1, 1.0 mL min^{-1}, 210 nm, R_t=9.6, 11.7 min; R_f=0.3 (hexane/ethyl acetate (2:1)); ^{1}H NMR ($CDCl_3$, 500 MHz): δ=4.61 (q, J=15.5 Hz, 2H), 4.30–4.34 (m, 1H), 3.19–3.23 (m, 2H), 2.64–2.71 (dd, J=5.5, 18.0 Hz, 1H), 2.19–2.33 (m, 2H), 2.10–2.17 (dd, J=2.5, 18.0 Hz, 1H), 1.12 ppm (t, J=7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=208.0, 175.1, 138.6, 71.8, 64.8, 43.2, 38.6, 17.6, 16.3 ppm; MS (EI): m/z (relative intensity): 152 $[M]^+$, 100), 123 (40), 105 (50).

2-(4-Methoxyphenyl)-7-oxabicyclo[3.3.0]oct-1-en-3-one (Table 2, entry 7):[12a] Purified by column chromatography (1.8× ≈15 cm) on silica gel with hexane/ethyl acetate (2:1) as the eluent to obtain the title compound as a light-yellow solid (93% yield; 93% *ee*): HPLC conditions: AS column, Hex:IPA=9:1, 1.0 mL min^{-1}, 254 nm, R_t=15.9, 25.7 min; R_f=0.2 (hexane/ethyl acetate (2:1)); ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.48 (d, J= 9.0 Hz, 2H), 6.93 (d, J=9.0 Hz, 1H), 4.89 (d, J=16.0 Hz, 1H), 4.57 (d, J=16.0 Hz, 1H), 4.35 (t, J=8.0 Hz, 1H), 3.82 (s, 3H), 3.26–3.30 (m, 1H), 3.20 (dd, J=7.5, 11.0 Hz, 1H), 2.81 (dd, J=6.0, 17.5 Hz, 1H), 2.31 ppm (dd, J=3.0, 17.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=202.3, 175.2, 159.8, 134.1, 129.3, 123.2, 114.0, 71.3, 66.3, 55.2, 43.1, 40.2 ppm; MS (EI): m/z (relative intensity): 230 $[M]^+$ (100), 201 (10), 189 (30), 172 (60).

2-(4-Methylphenyl)-7-oxabicyclo[3.3.0]oct-1-en-3-one (Table 2, entry 6): Purified by column chromatography (1.8× ≈15 cm) on silica gel with hexane/ethyl acetate (3:1) as the eluent to obtain the title compound as a white solid (92% yield; 87% *ee*): HPLC conditions: AS-H column, Hex:IPA=9:1, 1.0 mL min^{-1}, 254 nm, R_t=13.0, 18.5 min; R_f=0.4 (hexane/ethyl acetate (2:1)); $[\alpha]_D^{25}$=+53.7° (c=0.010 in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.42 (d, J=8.0 Hz, 2H), 7.22 (d, J= 8.0 Hz, 1H), 4.93 (d, J=16.0 Hz, 1H), 4.59 (d, J=16.0 Hz, 1H), 4.37 (t, J=7.5 Hz, 1H), 3.28–3.32 (m, 1H), 3.23 (dd, J=8.0, 11.5 Hz, 1H), 2.84 (dd, J=6.5, 17.5 Hz, 1H), 2.37 (s, 3H), 2.32 ppm (dd, J=3.5, 18.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=202.3, 175.2, 159.8, 134.1, 129.3, 123.2, 114.0, 71.3, 66.3, 43.1, 40.2, 23.8 ppm; IR (neat): $\tilde{\nu}$=3020, 2397, 1747, 1511, 1419, 1215, 1040, 922, 756, 669 cm^{-1}; MS (EI): m/z (relative intensity): 214 $[M]^+$ (100), 184 (30), 169 (40), 156 (45), 141 (70); HRMS: calcd for $C_{14}H_{14}O_2$: 214.09938; found: 214.09943.

2-(4-Fluorophenyl)-7-oxabicyclo[3.3.0]oct-1-en-3-one (Table 2, entry 7): Purified by column chromatography (1.8× ≈15 cm) on silica gel with hexane/ethyl acetate (3:1) as the eluent to obtain the title compound as a light-yellow oil (90% yield; 82% *ee*): HPLC conditions: AS-H column, Hex:IPA=98:2, 1.0 mL min^{-1}, 254 nm, R_t=29.8, 35.7 min; R_f=0.3 (hexane/ethyl acetate (2:1)); $[\alpha]_D^{25}$=+0.7° (c=0.0083 in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.52 (dd, J=5.5, 8.0 Hz, 2H), 7.09 (t, J=8.0 Hz, 2H), 4.91 (d, J=16.5 Hz, 1H), 4.56 (d, J=16.5 Hz, 1H), 4.37 (t, J=7.5 Hz, 1H), 3.29–3.33 (m, 1H), 3.24 (dd, J=7.5, 11.0 Hz, 1H), 2.84 (dd, J=6.5, 18.0 Hz, 1H), 2.33 ppm (dd, J=3.5, 17.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=204.1, 177.0, 161.7, 133.6, 129.8 (d, $J_{C,F}$=8.4 Hz), 126.7, 115.6 (d, $J_{C,F}$=22.0 Hz), 71.3, 66.2, 43.2, 40.1 ppm; IR (neat): $\tilde{\nu}$=3021, 2392, 1701, 1506, 1215, 1029, 758, 669 cm^{-1}; MS (EI): m/z (relative intensity): 218 $[M]^+$ (70), 188 (50), 176 (50), 159 (100), 146 (60); HRMS: calcd for $C_{13}H_{11}FO_2$: 218.07431; found: 218.07439.

2-(3-Methoxyphenyl)-7-oxabicyclo[3.3.0]oct-1-en-3-one (Table 2, entry 8): Purified by column chromatography (1.8× ≈15 cm) on silica gel with hexane/ethyl acetate (3:1) as the eluent to obtain the title compound as a light-yellow viscous oil (88% yield; 81% *ee*): HPLC conditions: AS-H column, Hex:IPA=9:1, 1.0 mL min^{-1}, 254 nm, R_t=20.9, 47.0 min; R_f=0.3 (hexane/ethyl acetate (2:1)); $[\alpha]_D^{25}$=+21.4° (c=0.011 in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.31 (t, J=7.5 Hz, 1H), 7.16 (s, 1H), 7.04 (d, J=8.0 Hz, 1H), 6.90 (dd, J=2.5, 8.0 Hz, 1H), 4.92 (d, J= 16.0 Hz, 1H), 4.59 (d, J=16.0 Hz, 1H), 4.37 (t, J=7.5 Hz, 1H), 3.82 (s, 3H), 3.29–3.33 (m, 1H), 3.23 (dd, J=7.5, 11.5 Hz, 1H), 2.84 (dd, J=6.5, 17.5 Hz, 1H), 2.33 ppm (dd, J=4.0, 17.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=206.7, 177.7, 159.6, 134.5, 131.8, 129.6, 120.5, 114.3, 113.4, 71.3, 66.3, 55.2, 43.3, 40.3 ppm; IR (neat): $\tilde{\nu}$=3019, 2386, 1705, 1511, 1413, 1215, 1045, 1024, 922, 758, 669 cm^{-1}; MS (EI): m/z (relative intensity): 230 $[M]^+$ (100), 213 (5), 199 (10), 185 (20), 171 (20), 159 (30); HRMS: calcd for $C_{14}H_{14}O_3$: 230.09430; found: 230.09422.

2-(4-Chlorophenyl)-7-oxabicyclo[3.3.0]oct-1-en-3-one (Table 2, entry 9):[12a] Purified by column chromatography (1.8× ≈15 cm) on silica gel with hexane/ethyl acetate (3:1) as the eluent to obtain the title compound as a light-yellow oil (91% yield; 77% *ee*): HPLC conditions: AS-

H column, Hex:IPA = 98:2, 1.0 mL min^{-1}, 254 nm, R_t = 26.3, 32.0 min; R_f = 0.3 (hexane/ethyl acetate (2:1)); ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.48 (d, J = 9.0 Hz, 2H), 7.38 (d, J = 9.0 Hz, 1H), 4.92 (d, J = 16.0 Hz, 1H), 4.57 (d, J = 16.0 Hz, 1H), 4.38 (t, J = 8.0 Hz, 1H), 3.30–3.37 (m, 1H), 3.25 (dd, J = 7.5, 11.0 Hz, 1H), 2.85 (dd, J = 6.0, 18.0 Hz, 1H), 2.33 ppm (dd, J = 3.5, 18.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 205.3, 175.1, 159.7, 134.0, 129.3, 123.3, 114.1, 71.1, 66.3, 43.2, 40.2 ppm; MS (EI): m/z (relative intensity): 236 $[M]^+$ (20), 234 $[M]^+$ (60), 204 (15), 192 (25), 169 (95), 141 (100).

2-(2-Methylphenyl)-7-oxabicyclo[3.3.0]oct-1-en-3-one (Table 2, entry 10): Purified by column chromatography (1.8 × ≈15 cm) on silica gel with hexane/ethyl acetate (3:1) as the eluent to obtain the title compound as a colorless oil (49% yield; 74% *ee*): HPLC conditions: AD-H column, Hex:IPA = 9:1, 1.0 mL min^{-1}, 254 nm, R_t = 11.8, 12.6 min; R_f = 0.4 (hexane/ethyl acetate (2:1)); $[\alpha]_D^{25} = +31.4°$ (c = 0.012 in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.19–7.29 (m, 3H), 7.10 (d, J = 7.5 Hz, 1H), 4.63 (d, J = 16.0 Hz, 1H), 4.42 (t, J = 7.5 Hz, 1H), 4.36 (d, J = 15.5 Hz, 1H), 3.38–3.42 (m, 1H), 3.34 (dd, J = 7.0, 11.0 Hz, 1H), 2.85 (dd, J = 5.5, 17.5 Hz, 1H), 2.35 (dd, J = 3.5, 17.5 Hz, 1H); 2.18 ppm (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 202.3, 175.2, 159.8, 134.1, 129.3, 128.9, 123.2, 114.0, 111.3, 71.3, 66.3, 43.1, 40.2, 23.8 ppm; IR (neat): $\tilde{\nu}$ = 3021, 2397, 1737, 1510, 1419, 1215, 1043, 922, 758, 669 cm^{-1}; MS (EI): m/z (relative intensity): 214 $[M]^+$ (100), 199 (5), 183 (40), 169 (50), 154 (30), 141 (70); HRMS: calcd for $C_{14}H_{14}O_2$: 214.09938; found: 214.09946.

2-Phenyl-7-[(4-methylphenyl)sulfonyl]-7-azabicyclo[3.3.0]oct-1-en-3-one (Table 3, entry 1):[37] Purified by column chromatography (2.0 × ≈15 cm) on silica gel with hexane/ethyl acetate (2:1) as the eluent to obtain the title compound as a light-yellow solid (96% yield; 80% *ee*): HPLC conditions: AD-H column, Hex:IPA = 9:1, 1.0 mL min^{-1}, 254 nm, R_t = 43.8, 52.8 min; R_f = 0.3 (hexane/ethyl acetate (2:1)); m.p. = 159–160 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.71 (d, J = 8.0 Hz, 2H), 7.36–7.46 (m, 5H), 7.30 (d, J = 8.0 Hz, 2H), 4.63 (dd, J = 2.0, 17.0 Hz, 1H), 4.04–4.09 (m, 2H), 3.18–3.23 (m, 1H), 2.78 (dd, J = 6.5, 17.5 Hz, 1H), 2.61 (dd, J = 9.0, 10.5 Hz, 1H), 2.40 (s, 3H), 2.25 ppm (dd, J = 4.0, 18.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 206.4, 171.9, 144.0, 136.0, 133.6, 130.0, 129.8, 128.9, 128.7, 128.2, 127.4, 52.0, 48.3, 41.8, 40.7, 21.5 ppm; MS (EI): m/z (relative intensity): 353 $[M]^+$ (20), 198 (100), 171 (50), 141 (60), 128 (45).

2-Methyl-7-[(4-methylphenyl)sulfonyl]-7-azabicyclo[3.3.0]oct-1-en-3-one (Table 3, entry 2):[38] Purified by column chromatography (2.0 × ≈15 cm) on silica gel with hexane/ethyl acetate (2:1) as the eluent to obtain the title compound as a white solid (98% yield; 88% *ee*): HPLC conditions: AD-H column, Hex:IPA = 9:1, 1.0 mL min^{-1}, 254 nm, R_t = 34.1, 37.1 min; R_f = 0.2 (hexane/ethyl acetate (2:1)); m.p. = 103–104 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.73 (d, J = 8.5 Hz, 2H), 7.34 (d, J = 8.5 Hz, 2H), 4.23 (d, J = 16.0 Hz, 1H), 3.96–4.00 (m, 2H), 2.96–3.06 (m, 1H), 2.54–2.62 (m, 2H), 2.44 (s, 3H), 2.03 (dd, J = 3.0, 17.5 Hz, 1H), 1.68 ppm (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 205.3, 171.0, 144.0, 134.1, 133.9, 129.9, 127.4, 52.6, 46.7, 41.6, 39.2, 21.5, 8.8 ppm; MS (EI): m/z (relative intensity): 291 $[M]^+$ (30), 263 (5), 155 (10), 136 (100).

Diethyl 2-methyl-3-oxobicyclo[3.3.0]oct-1-ene-7,7-dicarboxylate (Table 3, entry 3):[39] Purified by column chromatography (1.8 × ≈15 cm) on silica gel with hexane/ethyl acetate (4:1) as the eluent to obtain the title compound as a light-yellow viscous oil (91% yield; 77% *ee* (*S* configuration)): HPLC conditions: AS-H column, Hex:IPA = 9:1, 1.0 mL min^{-1}, 254 nm, R_t = 12.5, 15.9 min; R_f = 0.3 (hexane/ethyl acetate (4:1)); ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 4.21 (q, J = 6.5 Hz, 2H), 4.17 (q, J = 6.5 Hz, 2H), 3.16 (q, J = 14.5 Hz, 2H), 2.94 (m, 1H), 2.74 (dd, J = 7.0, 12.5 Hz, 1H), 2.60 (dd, J = 6.0, 18.0 Hz, 1H), 2.04 (dd, J = 3.0, 18.5 Hz, 1H), 1.68 (s, 3H), 1.61 (t, J = 13.0 Hz, 3H), 1.24 (t, J = 7.0 Hz, 3H), 1.22 ppm (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 203.9, 177.7, 171.5, 170.9, 132.8, 61.9, 61.8, 60.8, 42.6, 41.3, 39.0, 33.9, 13.9 (overlapped), 8.4 ppm; MS (EI): m/z (relative intensity): 280 $[M]^+$ (40), 235 (20), 206 (80), 178 (30), 133 (100).

Acknowledgements

We thank the University Grants Committee Areas of Excellence Scheme in Hong Kong (project no. AoE/P-10/01) and The Hong Kong Polytechnic University Area of Strategic Development Fund for financial support of this study. We are grateful to Prof. Chun Wai Tsang and Mr. Yiu Kwok Au in The Hong Kong Polytechnic University for performing high-resolution mass spectrometry analyses.

[1] For initial development of the PKR, see: a) I. U. Khand, G. R. Knox, P. L. Pauson, W. E. Watts, *J. Chem. Soc. Chem. Commun.* **1971**, 36. For recent reviews on the PKR, see: b) N. Jeong in *Transition Metals In Organic Synthesis, Vol. 1* (Eds.: M. Beller, C. Bolm), Wiley-VCH, Weinheim, **1998**, p. 560; c) Y. K. Chung, *Coord. Chem. Rev.* **1999**, *188*, 297; d) S. L. Buchwald, F. A. Hicks in *Comprehensive Asymmetric Catalysis II* (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer, Heidelberg, **1999**, p. 491; e) K. M. Brummond, J. L. Kent, *Tetrahedron* **2000**, *56*, 3263; f) A. J. Fletcher, S. D. R. Christie, *J. Chem. Soc. Perkin Trans. 1* **2000**, 1657; g) M. R. Rivero, J. Adrio, J. C. Carretero, *Eur. J. Org. Chem.* **2002**, 2881; h) S. T. Ingate, J. Marco-Contelle, *Org. Prep. Proced. Int.* **1998**, *30*, 121; i) L. V. R. Boñaga, M. E. Krafft, *Tetrahedron* **2004**, *60*, 9795.

[2] For recent selected examples, see: a) T. F. Jamison, S. Shambayati, W. E. Crowe, S. L. Schreiber, *J. Am. Chem. Soc.* **1994**, *116*, 5505; b) K. M. Brummond, D. Gao, *Org. Lett.* **2003**, *5*, 3491; c) B. Jiang, M. Xu, *Angew. Chem.* **2004**, *116*, 2597; *Angew. Chem. Int. Ed.* **2004**, *43*, 2543; d) J. Velcicky, A. Lanver, J. Lex, A. Prokop, T. Wieder, H.-G. Schmalz, *Chem. Eur. J.* **2004**, *10*, 5087. For a recent review, see: e) J. Blanco-Urgoiti, L. Añorbe, L. Pérez-Serrano, G. Domínguez, J. Pérez-Castells, *Chem. Soc. Rev.* **2004**, *33*, 32.

[3] For recent reviews on the catalytic PKR, see: a) S. E. Gibson, A. Stevenazzi, *Angew. Chem.* **2003**, *115*, 1844; *Angew. Chem. Int. Ed.* **2003**, *42*, 1800; b) B. E. Hanson, *Comments Inorg. Chem.* **2002**, *23*, 289.

[4] I. U. Khand, G. R. Knox, P. L. Pauson, W. E. Watts, M. I. Foreman, *J. Chem. Soc. Perkin Trans. 1* **1973**, 977.

[5] a) D. C. Billington, *Tetrahedron Lett.* **1983**, *24*, 2905; b) P. Magnus, L. M. Principe, M. J. Slater, *J. Org. Chem.* **1987**, *52*, 1483; c) V. Rautenstrauch, P. Mégard, J. Conesa, W. Küster, *Angew. Chem.* **1990**, *102*, 1441; *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 1413.

[6] N. Jeong, S. H. Hwang, Y. Lee, Y. K. Chung, *J. Am. Chem. Soc.* **1994**, *116*, 3159.

[7] For the enantioselective cobalt-catalyzed PKR with CO gas, see: a) S. J. Sturla, S. L. Buchwald, *J. Org. Chem.* **1999**, *64*, 5547; b) S. J. Sturla, S. L. Buchwald, *J. Org. Chem.* **2002**, *67*, 3398; c) K. Hiroi, T. Watanabe, R. Kawagishi, I. Abe, *Tetrahedron Lett.* **2000**, *41*, 891; d) K. Hiroi, T. Watanabe, R. Kawagishi, I. Abe, *Tetrahedron: Asymmetry* **2000**, *11*, 797; e) X. Verdaguer, M. A. Pericàs, A. Riera, M. A. Maestro, J. Mahía, *Organometallics* **2003**, *22*, 1868; f) D. Konya, F. Robert, Y. Gimbert, A. E. Greene, *Tetrahedron Lett.* **2004**, *45*, 6975.

[8] For the enantioselective titanium-catalyzed PKR with CO gas, see: a) F. A. Hicks, S. L. Buchwald, *J. Am. Chem. Soc.* **1996**, *118*, 11688; b) F. A. Hicks, S. L. Buchwald, *J. Am. Chem. Soc.* **1999**, *121*, 7026; c) S. K. Mandal, S. R. Amin, W. E. Crowe, *J. Am. Chem. Soc.* **2001**, *123*, 6457.

[9] For the enantioselective rhodium-catalyzed PKR with CO gas, see: a) N. Jeong, B. K. Sung, Y. K. Choi, *J. Am. Chem. Soc.* **2000**, *122*, 6771; b) N. Jeong, D. H. Kim, J. H. Choi, *Chem. Commun.* **2004**, 1134; c) ref. [14c]. For the most recent reference with molecular sieves as a CO gas reservoir, see: d) T. M. Schmid, G. Consiglio, *Chem. Commun.* **2004**, 2318.

[10] For the enantioselective iridium-catalyzed PKR with CO gas, see: T. Shibata, K. Takagi, *J. Am. Chem. Soc.* **2000**, *122*, 9852.

[11] a) T. Morimoto, K. Fuji, K. Tsutsumi, K. Kakiuchi, *J. Am. Chem. Soc.* **2002**, *124*, 3806; b) T. Morimoto, M. Fujioka, K. Fuji, K. Tsutsumi, K. Kakiuchi, *Chem. Lett.* **2003**, *32*, 154; c) K. Fuji, T. Morimoto, K. Tsutsumi, K. Kakiuchi, *Angew. Chem.* **2003**, *115*, 2511; *Angew. Chem. Int. Ed.* **2003**, *42*, 2409. For the most recent minireview, see:

d) T. Morimoto, K. Kakiuchi, *Angew. Chem.* **2004**, *116*, 5698; *Angew. Chem. Int. Ed.* **2004**, *43*, 5580.

[12] a) T. Shibata, N. Toshida, K. Takagi, *J. Org. Chem.* **2002**, *67*, 7446; b) T. Shibata, N. Toshida, K. Takagi, *Org. Lett.* **2002**, *4*, 1619.

[13] a) C. J. Li, T. H. Chan, *Organic Reactions in Aqueous Media*, Wiley, New York, **1997**; b) *Aqueous-Phase Organometallic Catalysis* (Eds.: B. Cornils, W. A. Herrmann), Wiley-VCH, Weinheim, **1998**; c) U. M. Lindström, *Chem. Rev.* **2002**, *102*, 2751; d) P. Tundo, P. T. Anastas, *Green Chemistry: Challenging Perspectives*, Oxford University Press, Oxford, **2000**; e) W. M. Nelson, *Green Solvents for Chemistry, Perspective and Practice*, Oxford University Press, Oxford, **2003**; f) *Clean Solvents, Alternative Media for Chemical Reactions and Processing* (Eds.: M. A. Abraham, L. Moens), American Chemical Society Symposium Series 819, American Chemical Society, Washington, DC, **2002**.

[14] For the nonasymmetric Co_2CO_6-mediated aqueous PKR, which uses water as a cosolvent and/or with the addition of surfactant (sodium dodecylsulfate (SDS)), see: a) M. E. Kraff, J. A. Wright, L. V. R. Boñaga, *Tetrahedron Lett.* **2003**, *44*, 3417; b) S. U. Son, S. I. Lee, Y. K. Chung, S.-W. Kim, T. Hyeon, *Org. Lett.* **2002**, *4*, 277; c) L. V. R. Boñaga, J. A. Wright, M. E. Kraff, *Chem. Commun.* **2004**, 1746. For the Rh-catalyzed asymmetric PKR with a water/dioxane solvent mixture in the presence of surfactant (SDS) with CO gas, see: d) W. H. Suh, M. Choi, S. I. Lee, Y. K. Chung, *Synthesis* **2003**, 2169. **Note added in proof:** During the reviewing process of this manuscript, a close related work on the asymmetric aqueous PKR appeared: e) K. Fuji, T. Morimoto, K. Tsutsumi, K. Kakiuchi, *Tetrahedron Lett.* **2004**, *45*, 9163.

[15] Air-stable ligand, enynes, and aldehyde were weighed on the bench top under air without special precautions.

[16] For micelle reviews, see: a) S. Taşcioğlu, *Tetrahedron* **1996**, *52*, 11113; b) U. M. Lindstrom, *Chem. Rev.* **2002**, *102*, 2751, and references therein.

[17] BINAP = 2,2′-bis(diphenylphosphanyl)-1,1′-binaphthyl, tol-BINAP = 2,2′-bis(di-*p*-tolylphosphanyl)-1,1′-binaphthyl, (*R*,*R*)-Et-DUPHOS = (−)-1,2-bis((2*R*,5*R*)-2,5-diethylphospholano)benzene; (*S*)-PHANEPHOS = (*S*)-(+)-4,12-bis(diphenylphosphano)-[2.2]-paracyclophane; (*S*,*S*)-Et-FerroTANE = (−)-1,1′-bis((2*S*,4*S*)-2,4-diethylphospholano)-ferrocene.

[18] Available from Strem Chemicals 2004 catalogue as CTH-(*S*)-P-Phos; A. S. C. Chan, C. C. Pai, US5886182, **1999**.

[19] 59% yield, 81% *ee* (under the same reaction conditions as in Table 1 except for the aldehyde loading).

[20] For a review of the Hammett study, see: a) C. Hansch, A. Leo, R. W. Taft, *Chem. Rev.* **1991**, *91*, 165; b) A. J. Gordon, R. A. Ford, *The Chemist's Companion*, Wiley, New York, **1972**.

[21] For recent references on electronic effects in asymmetric catalysis, see: a) E. N. Jacobsen, W. Zhang, M. L. Güler, *J. Am. Chem. Soc.* **1991**, *113*, 6703; b) H. C. Zhang, F. Xue, T. C. W. Mak, K. S. Chan, *J. Org. Chem.* **1996**, *61*, 8002; c) M. M. C. Lo, G. C. Fu, *J. Am. Chem. Soc.* **1998**, *120*, 10270; d) H. Doucet, E. Fernandez, T. P. Layzell, J. M. Brown, *Chem. Eur. J.* **1999**, *5*, 1320; e) W. C. Lo, C. M. Che, K. F. Cheng, T. C. W. Mak, *Chem. Commun.* **1997**, 1205; f) F. Y. Kwong, Q. Yang, T. C. W. Mak, A. S. C. Chan, K. S. Chan, *J. Org. Chem.* **2002**, *67*, 2769.

[22] For evidences for the role of dπ–pπ bonding in the rhodium-mediated reaction, see: a) K. Burgess, W. A. van der Donk, M. B. Jarstfer, M. J. Ohlmeyer, *J. Am. Chem. Soc.* **1991**, *113*, 6139. For models that assume that the complexation of the alkene/alkyne (π interaction) to the metal center is the rate stereochemical-determining step of the reaction, see: b) *Homogeneous Transition Metal Catalyzed Reactions* (Eds.: W. R. Moser, D. W. Slocum), Advances in Chemistry Series 230, American Chemical Society, Washington, DC, **1992**, pp. 163. For other mechanistic studies of steric and electronic effects in the insertion of olefins, see: B. J. Burger, B. D. Santarsiero, M. S. Trimmer, J. E. Bercaw, *J. Am. Chem. Soc.* **1988**, *110*, 3134.

[23] We thank a referee during the manuscript-reviewing process for the suggestion of other factors that could be responsible for the observed electronic influence, for example, the interaction of the phenyl π system with the Rh center, which differs in strength and geometry depending on the substitutent (electron-donating group or electron-withdrawing group), or an electronically induced shift from an early to a late transition state.

[24] W. L. F. Armarego, D. D. Perrin, *Purification of Laboratory Chemicals*, 4th ed., Butterworth-Heinemann, Oxford, **1996**.

[25] A. J. Pearson, R. A. Dubbert, *J. Chem. Soc. Chem. Commun.* **1991**, 202.

[26] A. J. Pearson, R. A. Dubbert, *Organometallics* **1994**, *13*, 1656.

[27] A. J. Bartlett, T. Laird, W. D. Ollis, *J. Chem. Soc. Perkin Trans. 1* **1975**, 1315.

[28] E. V. Tretyakov, A. V. Tkachev, T. V. Rybalova, Y. V. Gatilov, D. W. Knight, S. F. Vasilevsky, *Tetrahedron* **2000**, *56*, 10075.

[29] A. Godt, *J. Org. Chem.* **1997**, *62*, 7471.

[30] D. H. Wadsworth, S. M. Geer, M. R. Detty, *J. Org. Chem.* **1987**, *52*, 3662.

[31] F. Liron, P. Le Garrec, M. Alami, *Synlett* **1999**, 246. (No spectral data were given.)

[32] N. A. Bumagin, A. B. Ponomarev, I. P. Beletskaya, *Synthesis* **1984**, 728.

[33] T. Kobayahsi, Y. Koga, K. Narasaka, *J. Organomet. Chem.* **2001**, *624*, 73.

[34] G. B. Jones, J. M. Wright, G. W. Plourde II, G. Hynd, R. S. Huber, J. E. Mathews, *J. Am. Chem. Soc.* **2000**, *122*, 1937.

[35] a) J.-N. Denis, A. E. Greene, A. A. Serra, M.-J. Luche, *J. Org. Chem.* **1986**, *51*, 46; b) R. B. Grossman, S. L. Buchwald, *J. Org. Chem.* **1992**, *57*, 5803.

[36] S. C. Beck, R. B. Grossman, S. L. Buchwald, *J. Am. Chem. Soc.* **1994**, *116*, 8593.

[37] a) B. L. Pagenkopf, T. Livinghouse, *J. Am. Chem. Soc.* **1996**, *118*, 2285; b) T. Sugihara, M. Yamaguchi, *J. Am. Chem. Soc.* **1998**, *120*, 10782.

[38] N. Jeong, S. Lee, B. K. Sung, *Organometallics* **1998**, *17*, 3642.

[39] F. A. Hicks, N. M. Kablaoui, S. L. Buchwald, *J. Am. Chem. Soc.* **1999**, *121*, 5881.

Received: December 3, 2004
Published online: April 13, 2005