Stereoselective Pauson−Khand Reactions via the Chiral [(alkyne)$Co_2(CO)_5${P(OMe)$_3$}]

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Received December 28, 1994[⊗]

Summary: Dicobalt hexacarbonyl complexes of menthyl-substituted propargyl alcohol react with PR_3 (R = OMe, Ph) to form diastereomeric mixtures of complexes **3**. *The isomeric complexes can be separated chromatographically. The isolated diastereomers can be used in the intra- and intermolecular Pauson−Khand reaction to give high yields of cyclopentenones with high diastereoselectivities or high enantioselectivities.*

Introduction

Among the transition-metal-mediated syntheses of cyclopentenones,[1] the Pauson−Khand reaction is the most powerful and popular. Thus there have been extensive studies of the Pauson−Khand reaction.[2] However, most of the reactions studied are not asymmetric. Recently asymmetric Pauson−Khand reactions were reported by several researchers.[3,4] One of them is based on the use of conventional chiral auxiliaries.[3] The other involves chirality transfer from another ligand, e.g., the optically active phosphorus donor.[4] Pauson et al.[4] reported the use of glyphos as an optically active phosphine. When the glyphos reacted with $Co_2(CO)_6$(HC≡CPh), two diastereomers were obtained in the ratio of 60:40 at 60 °C. Both diastereomers can be separated by preparative liquid chromatography. Thus the optically pure diastereomer gave the enantiomerically pure cyclopentenone derivative. However, the replacement of carbonyl by phosphine or phosphite ligands reduced the final yield or reduced the rate of reaction.[5] The yield was 22%−31%. In addition, the diastereomer was epimerized at high temperatures. Nicholas also reported[6] a partial isomerization of one diastereomer of (alkyne)$Co_2(CO)_5(PPh_3)$. Thus the epimerization is rather common. Recently, we reported[7] the promotion of the Pauson−Khand reaction in the mild reaction condition. Thus the use of promoters will solve the problems of low yield and epimerization. We investigated the asymmetric Pauson−Khand reaction by using the chiral (alkyne)$Co_2(CO)_5$L and amine *N*-oxide in THF/CH_2Cl_2. We herein report the stereoselective intra- and intermolecular Pauson−Khand reactions.

Experimental Section

All reactions were conducted under nitrogen using standard Schlenk type flasks. Workup procedures were done in air. THF was freshly distilled from sodium benzophenone ketyl prior to use, and CH_2Cl_2 was distilled over anhydrous P_2O_5. Hexane and ethyl acetate were used after simple distillation. Most organic compounds were purchased from Aldrich Chemical Co., and $Co_2(CO)_8$ was purchased from Strem Chemical Co. Most chemicals were used as received. Anhydrous Me_3NO was obtained from Me_3NO dihydrates by azeotropic removal of water with benzene and subsequent sublimation. Thiol compound **13** used in this study was prepared from (−)-menthol according to the modified method.[8]

^1H or ^{13}C NMR spectra were obtained with a Varian XL-200, an ARX 300, or a Bruker AMX-500 instrument. IR spectra were recorded on a Shimadzu IR-470 spectrophotometer (spectra measured as films on NaCl by evaporation of solvent). Mass spectra were recorded on a VG ZAB-E double-focusing mass spectrometer.

The procedure reported by Pauson[9] was employed for the preparation of **2** from **1**. The preparation of **3** was reported by McGlinchey et al.[10] However, they did not succeed in separating diastereomers. Thus we report the separation and physical properties of both diastereomers.

[⊗] Abstract published in *Advance ACS Abstracts,* May 15, 1995.

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0276-7333/95/2314-3104$09.00/0

Separation of Diastereomers of 3. A column (diameter, 2 cm) was packed with flash silica gel to a height of 15 cm. The column was washed with 100 mL of diethyl ether and then washed with 200 mL of hexane. Compound **3**, dissolved in 2–3 mL of hexane, was loaded and column chromatographed eluting with hexane. After column chromatography, we obtained the two diastereomers in the ratio of 1:1.

The spectral properties of the first-eluting diastereomer (**3a**): ^{1}H NMR ($CDCl_3$) δ 5.50 (1 H, d, 3.4 Hz), 4.76 (1 H, dd, 12.8, 2.4 Hz), 4.40 (1 H, d, 12.8 Hz), 3.61 (9 H, d, 12.0 Hz), 3.18 (1 H, td, 10.4, 4.2 Hz), 2.39–2.31 (1 H, m), 2.11 (1 H, dm, 13.0 Hz), 1.68–1.18 (4 H, m), 1.03–0.81 (9 H, m), 0.77 (3 H, d, 6.8 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 201.6, 90.06, 89.92, 78.79, 68.73, 68.57, 68.54, 51.69, 48.45, 40.42, 34.57, 31.56, 25.17, 23.19, 22.35, 20.93, 16.08 ppm.

The spectral properties of the second-eluting diastereomer (**3a′**): ^{1}H NMR ($CDCl_3$) δ 5.53 (1 H, d, 3.4 Hz), 4.67 (1 H, d, 12.7 Hz), 4.47 (1 H, dd, 12.6, 1.7 Hz), 3.60 (9 H, d, 12.0 Hz), 3.18 (1 H, td, 10.5, 4.2 Hz), 2.34 (1 H, md, 7.2, 2.0 Hz), 2.12 (1 H, dm, 13.2 Hz), 1.68–1.18 (4 H, m), 1.07–0.81 (9 H, m), 0.75 (3 H, d, 6.8 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 201.6, 90.10, 78.81, 68.61, 51.69, 51.62, 48.37, 40.42, 34.56, 31.60, 25.04, 23.09, 22.32, 21.01, 15.99 ppm.

Reaction between 3a and Norbornene. To a solution of **3a** (0.20 g, 0.35 mmol) and norbornene (0.16 g, 1.8 mmol) in CH_2Cl_2/THF (v/v, 1:1, 10 mL) was added Me_3NO (0.21 g, 2.8 mmol). The resulting solution was stirred at room temperature under O_2 overnight. To remove excess Me_3NO, the reaction mixture was filtered on silica gel and then the filtrate was concentrated. The filtrate was column chromatographed on silica gel eluting with a mixture solvent of hexane/ethyl acetate (v/v, 10:1). The yield was 98%. IR (NaCl, neat) 1696, 1632 cm^{-1}; HRMS, m/z, M^+, calcd 316.2394, obsd 316.2384; ^{1}H NMR ($CDCl_3$) δ 7.38 (1 H, s), 4.35 (1 H, d, 14.2 Hz), 4.00 (1 H, d, 14.1 Hz), 3.12 (1 H, td, 10.4, 3.6 Hz), 2.63 (1 H, s), 2.39 (1 H, s), 2.20–2.11 (4 H, m), 1.67–1.54 (4 H, m), 1.35–1.22 (4 H, m), 1.05–0.82 (11 H, m), 0.77 (3 H, d, 6.8 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 209.75, 159.74, 147.17, 79.96, 62.41, 54.36, 48.59, 48.15, 40.24, 38.88, 37.96, 34.49, 31.43, 31.11, 29.05, 28.34, 25.76, 23.44, 22.25, 20.83, 16.33 ppm.

Reaction between 3a′ and Norbornene. A typical procedure was almost the same as the reaction between **3a** and norbornene. Compound **3a′** (0.21g, 0.36 mmol), norbornene (0.17 g, 1.8 mmol), and Me_3NO (0.22 g, 2.9 mmol) were used. The yield was 80%. ^{1}H NMR ($CDCl_3$) δ 7.38 (1 H, s), 4.31 (1 H, d, 14.1 Hz), 4.04 (1 H, d, 14.1 Hz), 3.12 (1 H, td, 10.4, 3.8 Hz), 2.63 (1 H, s), 2.40 (1 H, s), 2.21–2.10 (4 H, m), 1.68–1.54 (4 H, m), 1.35–1.22 (4 H, m), 1.05–0.80 (11 H, m), 0.76 (3 H, d, 6.8 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 209.75, 160.09, 147.12, 79.73, 62.03, 54.33, 48.54, 48.13, 40.28, 38.88, 37.96, 34.50, 31.46, 31.12, 29.03, 28.34, 25.74, 23.44, 22.26, 20.86, 16.33 ppm.

Reaction between 3a and Norbornadiene. Norbornadiene (0.61 mL, 5.8 mmol) and Me_3NO (0.69 g, 9.2 mmol) were added to the solution of **3a** (1.15 mmol) in CH_2Cl_2/THF (v/v, 1:1, 10 mL). After being stirred for 12 h at room temperature, the reaction mixture was filtered on silica gel to remove excess Me_3NO and then the filtrate was evaporated *in vacuo*. The filtrate was column chromatographed on silica gel eluting with a mixture solvent of hexane and ethyl acetate (v/v, 10:1). The yield was 90%. IR (NaCl) 1692, 1628 cm^{-1}; HRMS, m/z, M^+, calcd 314.2238, obsd 314.2264. ^{1}H NMR ($CDCl_3$) δ 7.36 (1 H, s), 6.21 (1 H, s), 6.12 (1 H, s), 4.25 (1 H, d, 14.1 Hz), 3.93 (1 H, d, 14.1 Hz), 3.05 (1 H, td, 10.5, 4.1 Hz), 2.84 (1 H, s), 2.70 (1 H, s), 2.63 (1 H, s), 2.25 (1 H, d, 4.0 Hz), 2.14 (1 H, m), 2.05 (1 H, d, 12.1 Hz), 1.56 (2 H, m), 1.31 (2 H, d, 9.3 Hz), 1.18 (2 H, d, 9.5 Hz), 0.93–0.76 (3 H, m), 0.84 (3 H, d, 8.1 Hz), 0.82 (3 H, d, 7.5 Hz), 0.70 (3 H, d, 7.2 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 208.46, 159.66, 148.33, 138.38, 136.92, 79.91, 62.29, 52.99, 48.06, 43.44, 42.83, 41.19, 40.14, 34.41, 31.35, 25.67, 23.33, 22.21, 20.78, 16.26 ppm.

Reaction between 3a′ and Norbornadiene. A typical procedure was almost the same as the reaction between **3a** and norbornene. When CH_2Cl_2 was used as a solvent to compare the medium effect, the yield was 40%. ^{1}H NMR ($CDCl_3$) δ 7.37 (1 H, d, 2.2 Hz), 6.22 (1 H, m), 6.13 (1 H, m), 4.23 (1 H, d, 14.1 Hz), 3.94 (1 H, d, 14.2 Hz), 3.05 (1 H, td, 10.6, 4.1 Hz), 2.80 (1 H, s), 2.70 (1 H, s), 2.60 (1 H, s), 2.25 (1 H, d, 4.9 Hz), 2.10 (1 H, m, 7.0, 2.7 Hz), 2.05 (1 H, d, 12.2 Hz), 1.60–1.50 (2 H, m), 1.32 (2 H, d, 9.4 Hz), 1.22–1.16 (2 H, m), 0.94–0.76 (3 H, m), 0.84 (3 H, d, 6.6 Hz), 0.83 (3 H, d, 7.1 Hz), 0.69 (3 H, d, 7.0 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 208.50, 160.10, 148.37, 138.42, 137.01, 79.75, 61.94, 53.02, 48.09, 43.50, 42.89, 41.24, 40.25, 34.48, 31.45, 26.84, 25.72, 23.40, 22.25, 20.85, 16.29 ppm.

Syntheses of Compounds 7, 8, and 9. Typical reaction: compound **3a** or **3a′** (0.286 g, 0.50 mmol) was dissolved in 10 mL of diethyl ether. To the ether solution was added $HBF_4 \cdot OEt_2$ (0.37 mL, 2.5 mmol) at 0 °C. While stirring for 1 h, red solids were precipitated. The red precipitates were filtered by using a cannula, washed three times with diethyl ether (10 mL × 3), and then redissolved in 5 mL of THF. Allyl alcohol (0.17 mL, 2.5 mmol) in 10 mL of THF was added to the reddish THF solution. After stirring for 1 h, water (50 mL) and ethyl acetate (50 mL) were poured into the reaction mixture. The ethyl acetate layer was separated and column chromatographed on silica gel eluting with a mixture of hexane and ethyl acetate (v/v, 10:1). The product (**4**, 90%) was reacted further. To a solution of **4** in a solvent mixture of CH_2Cl_2 and THF (v/v, 1:1, 10 mL) was added Me_3NO (0.37 g, 4 mmol). The resulting solution was stirred for 1 h under oxygen. After column chromatography on silica gel eluting with a mixture of hexane and ethyl acetate (v/v, 2:1), **7** was isolated in 80% yield. Compound **7** is a known compound. Thus we only confirmed the formation of **7** by checking its ^{1}H NMR spectrum.

Characterization of **4**: IR (NaCl) 2060, 2003, 1992 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.86 (m, 1 H), 5.48 (d, 3.2 Hz, 1 H), 5.25 (dd, 17.3, 1.7 Hz, 1 H), 5.15 (dd, 11.4, 1.7 Hz), 4.58 (d, 13.5 Hz, 1 H), 4.49 (d, 13.5 Hz, 1 H), 4.06 (td, 5.31, 1.22 Hz, 2 H), 3.54 (d, 12 Hz, 9 H) ppm; HRMS, m/z, $M^+ - 2CO$, calcd 421.9376, obsd 421.9379.

^{1}H NMR ($CDCl_3$) spectrum of **7**: δ 6.06 (1 H, s), 4.65 (1 H, d, 16.0 Hz), 4.50 (1 H, d, 16.0 Hz), 4.31 (1 H, t, 6.1 Hz), 3.27–3.23 (2 H, m), 2.63 (1 H, dd, 17.7, 6.1 Hz), 2.14 (1 H, d, 17.4 Hz) ppm.

In the same way as the synthesis of compounds **4** and **7**, compounds **5** and **8** were obtained in 80% and 65% yields, respectively.

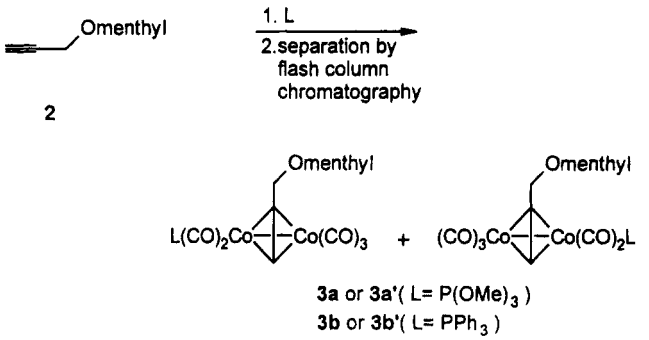
Characterization of **5**: IR (NaCl) 2064, 2006, 1991 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.36–7.29 (m, 5 H), 5.75 (m, 2 H), 5.51 (d, 3.17 Hz, 2 H), 4.51 (s, 2 H), 4.17 (m, 2 H), 4.11 (d, 4.1 Hz, 2 H), 3.59 (d, 12 Hz, 9 H) ppm; HRMS, m/z, $M^+ - Co_2(CO)_5P(OMe)_3$, calcd 216.1150, obsd 216.1170.

Characterization of **8**: IR (NaCl) 1699 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.39–7.25 (5 H, m), 6.04 (1 H, d, 1.7 Hz), 4.72–4.37 (4 H, m), 4.28 (1 H, t, 7.3 Hz), 3.66 (1 H, dd, 9.5, 4.4 Hz), 3.50 (1 H, d, 7.3 Hz), 3.43 (1 H, d,9.5 Hz), 3.68–3.35 (1 H, m), 3.09–2.99 (1 H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 208.58, 184.76, 137.40, 128.32, 127.72, 127.65, 123.11, 73.13, 68.20, 68.02, 65.62, 49.47, 48.77 ppm; HRMS, m/z, M^+, calcd 244.1095, obsd 244.1128.

In the same way as the synthesis of compounds **4** and **7**, compounds **6** and **9** were obtained in 95% and 86% yields, respectively.

Characterization of **6**: IR (NaCl) 2063, 2005, 1991 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.39–7.19 (m, 5 H), 5.97–5.79 (m, 1 H), 5.58 (d, 3. 4 Hz, 1 H), 5.20 (dd, 18, 1.46 Hz, 1 H), 5.13 (dd, 8, 1.46 Hz, 1 H), 3.89 (d, 13.8 Hz, 1 H), 3.85 (s, 2 H), 3.82 (d, 13.8 Hz, 1 H), 3.54 (d, 12 Hz, 9 H), 3.35 (dd, 14, 5.61 Hz, 1 H), 3.08 (dd, 14, 7.1 Hz, 1 H) ppm; HRMS, m/z, $M^+ - CO$, calcd 538.9954, obsd 539.0096.

Scheme 1



Characterization of **9**: IR (NaCl) 1705, 1638 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.33–7.25 (5 H, m), 5.90 (1 H, s), 3.96 (1 H, d, 17.9 Hz), 3.85 (1 H, d, 13.0 Hz), 3.69 (1 H, d, 13.0 Hz), 3.34 (1 H, t, 7.6 Hz), 3.26 (1 H, m), 3.15 (1 H, d, 17.8 Hz), 2.57 (1 H, dd, 17.6, 6.3 Hz), 2.11 (1 H, dd, 17.6, 3.6 Hz), 2.04 (1 H, dd, 10.7, 8.3 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 209.46, 186.24, 138.11, 128.60, 128.37, 127.23, 124.29, 59.93, 58.07, 53.15, 45.70, 40.21 ppm; HRMS, *m/z*, M^+, calcd 213.1150, obsd 213.1111.

Reaction between 7 and Chiral Thiol 13. Compound **7** was reacted with chiral thiol **13** (3 equiv) and Bu_4NF (0.1 equiv) in THF. The reaction mixture was stirred for 3 h. After removal of the solvent, the residue was column chromatographed on silica gel eluting with a mixture of hexane and ethyl acetate (v/v, 5:1). The unreacted thiol was recovered, and the product was isolated in 70% yield. When we took ^1H NMR spectra (500 MHz) for the chiral compounds, we could confirm the stereoselective formation of one diastereomer with 90% *ee* (the diastereomer ratio was 95:5). We took the *de* as the *ee* value of the chiral bicyclic enone compounds. HRMS, *m/z*, M^+, calcd 296.1810, obsd 296.1801.

^1H NMR spectrum of **10** (major isomer) ($CDCl_3$): δ 4.14 (1 H, t, 8.8 Hz), 4.02 (1 H, d, 8.9 Hz), 3.86 (1 H, d, 8.9 Hz), 3.60 (1 H, dd, 9.2, 5.6 Hz), 3.21 (1 H, d, 2.9 Hz), 2.82–2.77 (1 H, m), 2.72 (1 H, dd, 18.5, 1.7 Hz), 2.71 (1 H, d, 18.7 Hz), 2.59 (1 H, d, 18.7 Hz), 2.26 (1 H, dd, 18.5, 2.4 Hz), 2.18–1.98 (1 H, m), 1.78–1.65 (2 H, m), 1.65–1.57 (1 H,m), 1.34–1.24 (2 H, m), 1.17–1.08 (2 H, m), 0.92–0.83 (10 H, m) ppm.

Reaction between 8 and Chiral Thiol 13. In the same way as the synthesis of **10**, compound **11** was obtained in 70% yield with 80% *ee* (the diastereomer ratio was 90:10). HRMS, *m/z*, M^+, calcd 416.2385, obsd 416.2376.

^1H NMR spectrum of **11** (major isomer) ($CDCl_3$): δ 7.35–7.26 (5 H, m), 4.51 (1 H, d, 15.1 Hz), 4.49 (1 H, d, 15.1 Hz), 4.20 (1 H, dd, 9.0, 6.1 Hz), 3.92 (1 H, d, 9.6 Hz), 3.84 (1 H, dd, 9.0, 2.1 Hz), 3.83 (1 H, d, 9.6 Hz), 3.71 (1 H, d, 1.4 Hz), 3.70 (1 H, s), 3.26 (1 H, s), 2.89–2.84 (1 H, m), 2.76 (1 H, d, 3.2 Hz), 2.43 (1 H, q, 6.9 Hz), 2.03–1.92 (1 H, m), 1.82 (1 H, dq, 14.4, 2.9 Hz), 1.76–1.66 (3 H, m), 1.32–1.03 (4 H, m), 0.93–0.82 (10 H, m) ppm.

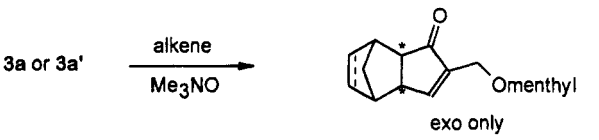
Reaction between 9 and Chiral Thiol 13. In the same way as the synthesis of **10**, compound **12** was obtained quantitatively with 92% *ee* (the diastereomer ratio was 96:4). HRMS, *m/z*, M^+ – menthyl, calcd 246.0952, obsd 246.0911.

^1H NMR spectrum of **12** (major isomer) ($CDCl_3$): δ 7.32–7.22 (5 H, m), 3.64 (1 H, d, 13.4 Hz), 3.58 (1 H, d, 13.4Hz), 3.21 (1 H, s), 3.00 (1 H, d, 9.1 Hz), 2.64 (1 H, d, 9.1 Hz), 2.75–2.59 (5 H, m), 2.22 (1 H, d, 15.7 Hz), 2.08–1.97 (1 H, m), 1.78–1.59 (4 H, m), 1.32–1.03 (4 H, m), 0.91–0.84 (10 H, m) ppm.

Results and Discussion

As shown in Scheme 1, treatment of $Co_2(CO)_8$ with (–)-menthyl propargyl ether followed by replacement of carbonyl by phosphine or phosphite generates the alkyne complexes **3** in good yields. Flash column chromatography of **3** enables separation of the two diastereomers, **3a** (the first eluting, L = $P(OMe)_3$) and **3a′** (the second eluting, L = $P(OMe)_3$) (or **3b** and **3b′**; L = PPh_3), in equal amounts. Thus we can obtain diastereomerically pure cobalt complexes. The diastereomers are dark-red crystalline compounds and are configurationally stable for several weeks in a freezer.

Scheme 2



complex	alkene	yield	diastereomeric excess
3a	norbornene	98% [b]	100% by ^1H NMR
3a	norbornadiene	90% [b]	100% by ^{13}C NMR
3a'	norbornene	80% [b]	100% by ^1H NMR
3a'	norbornadiene	40% [a]	100% by ^{13}C NMR

[a] CH_2Cl_2 used as a solvent

[b] 1:1 mixture of THF:CH_2Cl_2 used as a solvent

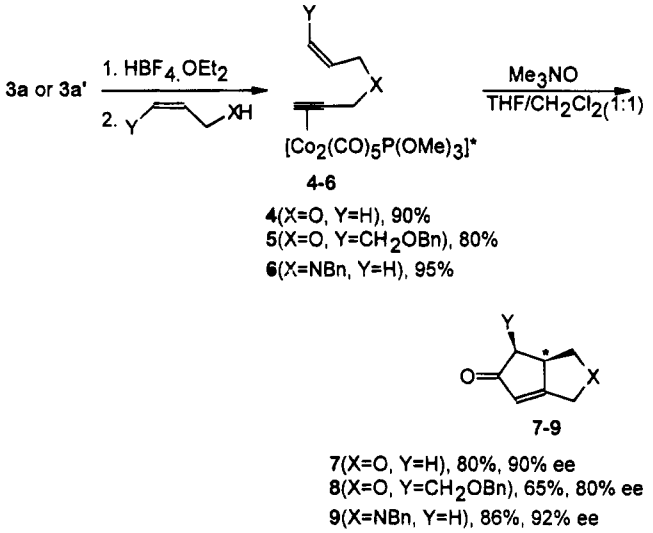
To test the diastereoselectivity in the intermolecular Pauson–Khand reaction, **3b** or **3b′** was reacted with norbornene in the presence of Me_3NO in CH_2Cl_2 (Scheme 2). However, the rate of the reaction was slow. After 2 days, 70% of the expected product was obtained with 100% diastereoselectivity. The use of Me_3NO as a promoter retards the epimerization of the cobalt compound and enables the reaction to take place even in mild reaction conditions. When the reaction was carried with **3a** or **3a′** in the presence of Me_3NO in CH_2Cl_2/THF (v/v, 1:1) (Scheme 2), the reaction time was shortened to 20 h and the yield was improved to 85%–98%. According to the analysis of ^1H and ^{13}C NMR spectra of the products from each diastereomer, the reaction was almost completely diastereoselective. Thus the reaction produced an exo compound with 100% diastereoselectivities. However, when the reaction of ((–)-menthyl propargyl ether)$Co_2(CO)_6$ with norbornadiene in the presence of Me_3NO was carried out, the diastereomeric mixtures of exo and endo product were obtained in 67% and 19% yields, respectively. Thus, we surmise that the diastereoselection mainly arises from the presence of a chiral cluster core. Krafft et al. found[11] that most of the enyne substrates reacted moderately faster in THF/CH_2Cl_2 than in CH_2Cl_2 alone. They explained that the role of the coordinating solvent was similar to the role of the tethered heteroatom. Thus the change of reaction medium and the use of Me_3NO enable the reaction to occur in high yields with high diastereoselectivities. When **3a** or **3a′** was reacted with norbornadiene in the same reaction conditions as above, the expected exo compound was obtained in 85% yield with 100% diastereoselectivity.

To test the enantioselectivity in the intramolecular Pauson–Khand reaction, compounds **4**, **5**, and **6** were synthesized from **3a** or **3a′** using Nicholas's reaction[12] (Scheme 3). Compounds **4**, **5**, and **6** were treated with

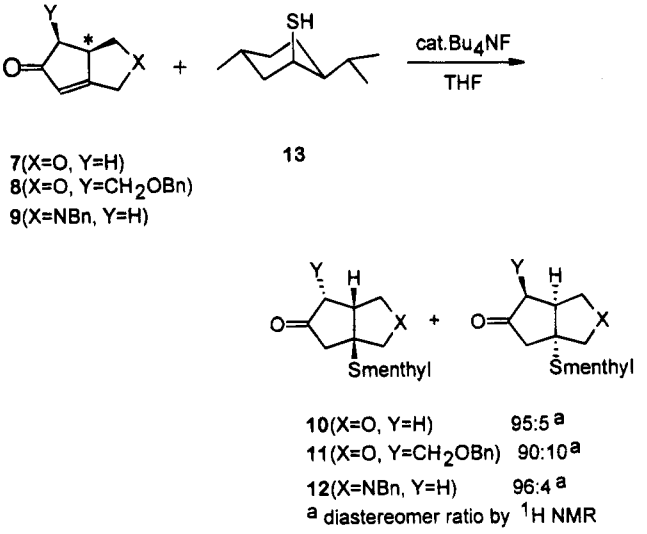
(11) Krafft, M. E.; Scott, I. L.; Romero, R. H.; Feibelmann, S.; Van Pelt, C. E. *J. Am. Chem. Soc.* **1993**, *115*, 7199.

(12) Nicholas, K. M. *Acc. Chem. Res.* **1987**, *20*, 207. Stuart, J. G.; Nicholas, K. M. *Synthesis* **1989**, *6*, 454. Montaña, A. M.; Nicholas, K. M. *J. Org. Chem.* **1990**, 55, 1569.

Scheme 3



Scheme 4



Me_3NO in CH_2Cl_2/THF (v/v, 1:1). After reaction, bicyclized products **7**, **8**, and **9** were obtained in high yields. When CH_2Cl_2 was used as a reaction medium, compounds **7**, **8**, and **9** were obtained in 70%, 34%, and 50% yields, respectively. Thus the choice of the reaction medium (CH_2Cl_2/THF, v/v, 1:1) was critical to the yield of the reaction and shortened the reaction time to less than 1 hr. Compared to **7** and **9**, compound **8** was a less effective substrate. When we used **3b** or **3b'** instead of **3a** or **3a'**, the corresponding **7**, **8**, and **9** were obtained in poor yields (ca. 15%).

To obtain the *ee* values, at first we took ^1H NMR spectra of compounds **7**, **8**, and **9** with a chiral shift reagent $Eu(hfc)_3$. However, the chiral shift reagent did not induce any different chemical shifts for protons in different environments. Thus we used a chiral thiol as a chiral derivatizing reagent to convert an enantiomeric mixture to a pair of diastereomers.

Compounds **7**, **8**, and **9** were treated with chiral thiol **13**, which was derived from (−)-menthol (Scheme 4).[13] In the presence of a catalytic amount of Bu_4NF, the thiol undergoes smooth conjugate addition to α,β-unsaturated carbonyl compounds. Thus, for each bicyclic enone, we obtained the conjugate addition products, **10**, **11**, and **12**. The *ee* values were calculated by the inspection of ^1H NMR spectra of conjugated addition products. The *ee* values for **10**, **11**, and **12** were 90%, 80%, and 92%, respectively.

In conclusion, we have demonstrated that the inter- and intramolecular Pauson–Khand reaction can be carried out with high stereoselectivities using chiral (alkyne)$Co_2(CO)_5P(OMe)_3$ and Me_3NO in CH_2Cl_2/THF (v/v, 1:1). We conjecture that the diastereoselection mainly arises from the presence of a chiral cluster core.

Acknowledgment. We are thankful to the Ministry of Education and Center for Molecular Catalysis.

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