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## Ni-CATALYZED ASYMMETRIC ADDITION of GRIGNARD REAGENTS TO UNSATURATED CYCLIC ACETALS. THE INFLUENCE OF ADDED PHOSPHINE ON ENANTIOSELECTIVITY

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### Supporting Information

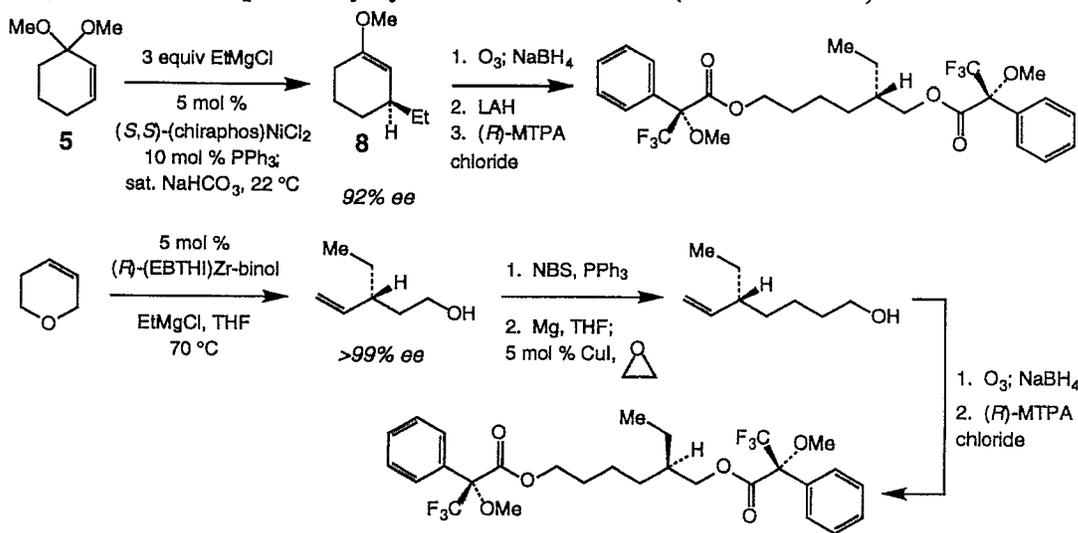
**General.** Infrared (IR) spectra were recorded on a Perkin Elmer 781 spectrophotometer,  $\nu_{\max}$  in  $\text{cm}^{-1}$ . Bands are characterized as broad (br), strong (s), medium (m), and weak (w).  $^1\text{H}$  NMR spectra were recorded on a Varian Unity 300 (300 MHz) or Varian GN-400 (400 MHz). Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ( $\text{CHCl}_3$ :  $\delta$  7.26). Data are reported as follows: chemical shift, integration, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, br=broad, m=multiplet), coupling constants (Hz), and assignment.  $^{13}\text{C}$  NMR spectra were recorded on a Varian Unity 300 (75 MHz) or Varian GN-400 (100 MHz) with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent as the internal reference ( $\text{CDCl}_3$ :  $\delta$  77.7 ppm). An Alltech Associates DB-1 capillary column (30mx0.32mm) was used to determine conversions. Microanalyses were performed by Robertson Microlit Laboratories (Madison, New Jersey). High resolution mass spectrometry was performed by University of Illinois Mass Spectrometry Laboratories.

All reactions were conducted in oven (135 °C) and flame-dried glassware under an inert atmosphere of dry argon. Tetrahydrofuran was distilled from sodium metal/benzophenone ketyl; dichloromethane was distilled from calcium hydride. All Grignard reagents were purchased from Strem or Aldrich and used without further purification. Triphenylphosphine was purchased from Aldrich and recrystallized from ethanol. All other achiral and chiral phosphines and achiral nickel complexes were purchased from Strem and used without further purification. (*S,S*) chiraphosNiCl<sub>2</sub> and 1,2-bis(diphenylphosphino)ethaneNiCl<sub>2</sub> were prepared according to existing procedures.<sup>1</sup> Cyclopentenone-dimethylacetal and cyclohexenone-dimethylacetal were prepared according to methods reported by Garbish.<sup>2</sup> Cyclopentenone ethylene ketal was purchased from Aldrich and distilled before use. Cyclohexenone ethylene ketal was prepared according to the procedure published by Noyori.<sup>3</sup>

**Representative experimental procedure for the Ni-catalyzed alkylation of unsaturated acetals to afford chiral non-racemic ketones.** A 5.0 mL flame dried round-bottomed flask was charged with 6.8 mg (1.05  $\mu\text{mol}$ ) of bis(triphenylphosphino)NiCl<sub>2</sub>, 4.5 mg (1.05  $\mu\text{mol}$ ) of (*S,S*)-chiraphos and 1.3 mL THF. To this was added 30  $\mu\text{L}$  (0.21 mmol) of unsaturated acetal **5**. The reaction mixture was allowed to cool to 0 °C and 0.25 mL (0.63 mmol) of ethylmagnesium bromide was added to the mixture in a dropwise fashion. The resulting mixture was allowed to stir at 22 °C for 15 h. The reaction was quenched by the dropwise addition of a 1.0 mL solution of 10% HCl. After 30 min, the resulting mixture was washed with 3x25 mL Et<sub>2</sub>O. Combined organic layers were dried over anhydrous MgSO<sub>4</sub>, filtered, and concentrated *in vacuo* to afford a pale yellow oil. Silica gel chromatography with 4:1 pentane:ether afforded 24 mg (0.19 mmol) of the desired alkylation product **6b** (91% yield).

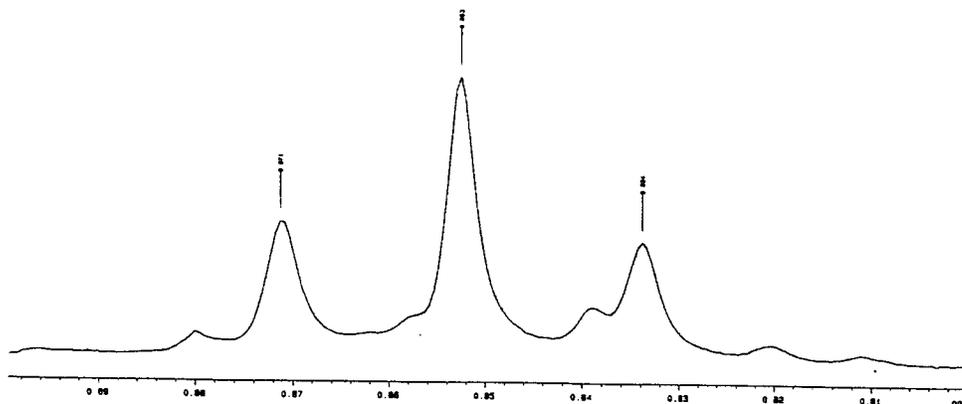
**Representative experimental procedure for the Ni-catalyzed alkylation of unsaturated acetals to afford chiral non-racemic enol ethers.** A 10.0 mL flame dried round-bottomed flask was charged with 13.3 mg (3.45  $\mu\text{mol}$ ) of (*S,S*)-chiraphosNiCl<sub>2</sub>, 13 mg (3.45  $\mu\text{mol}$ ) of PPh<sub>3</sub> and 2.8 mL THF. To this mixture was added 100  $\mu\text{L}$  (0.69 mmol) of unsaturated acetal **5**. The resulting mixture was allowed to chill to 0 °C, after which 0.54 mL (2.1 mmol) of ethylmagnesium bromide was added slowly. The reaction was allowed to stir at 22 °C for 15 h. The reaction was quenched by the dropwise addition of a 1.0 mL of a saturated solution of NaHCO<sub>3</sub>. The mixture was subsequently washed with 25 mL portions of Et<sub>2</sub>O three times and the combined organic layers were dried over anhydrous MgSO<sub>4</sub>, filtered, and concentrated *in vacuo* to afford a pale yellow oil. Chromatography on neutral alumina (ICN Grade I) with pentane afforded 80 mg (5.7 mmol) of trisubstituted enol ether **8** (82% yield).

**Determination of product stereochemical identity:** The identity of the major enantiomer obtained from the Ni-catalyzed reaction was determined by comparison with authentic material synthesized independently by established methods (Scheme below).<sup>4</sup>

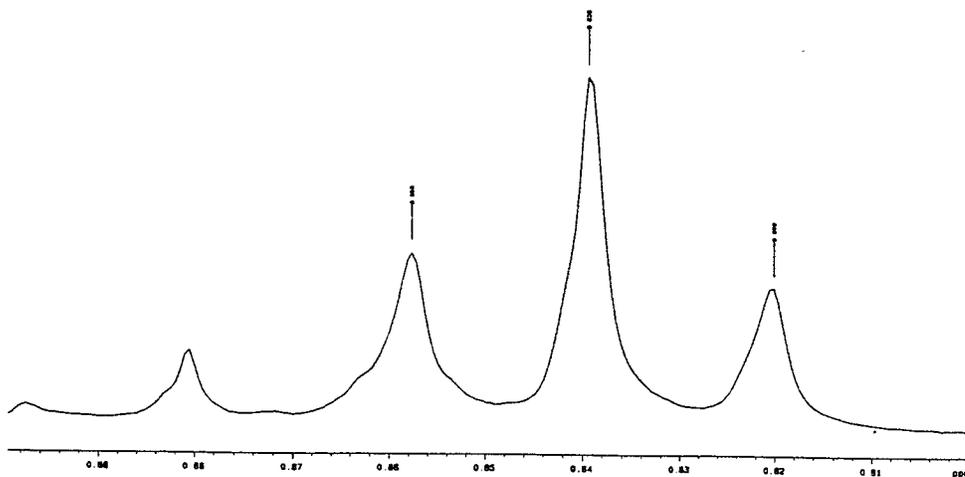


■ 400 MHz  $^1\text{H}$  NMR spectra (partial) of the (bis)-Mosher ester obtained from the Ni-catalyzed reaction, compared with that obtained from the authentic and racemic samples.

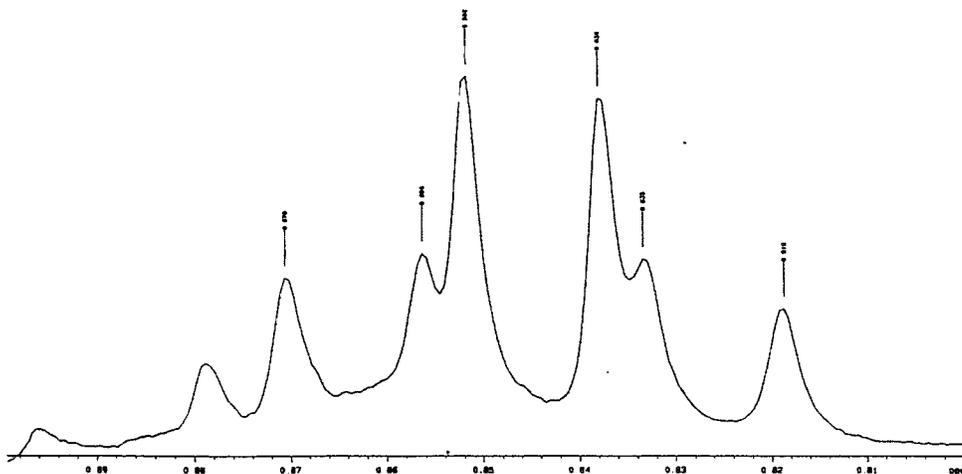
*Derived from Ni-Catalyzed Reaction*



*Derived from Authentic Sample*



*Derived from Racemic Mixture*

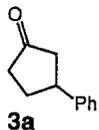


**Determination of product optical purity:** The optical purity of each of the 3-substituted cyclic ketones was determined by conversion to a mixture of the derived diastereomeric acetals upon treatment with (*R*)-(-)-2,3-butanediol and subsequent analysis of  $^{13}\text{C}$  NMR spectra<sup>5</sup> (for **3b** and **6c**) or chiral GLC (BETA-DEX 120 chiral column by Supelco for **6a** and **6e** and ALPHADEX for **6b**). The optical purity of 3-*i*-butylcyclohexanone (**6d**) has been determined by chiral GLC analysis (ALPHADEX 120 chiral column by Supelco).

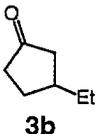
**Representative procedure for preparation of (*R,R*)-(-)-2,3-ethylene ketals:** Ketone **6c** (0.33 mmol), *p*-toluenesulfonic acid (2 mg), and (*R,R*)-(-)-2,3-butanediol (0.66 mmol) were heated to reflux in toluene (3 mL) for one h. The reaction was quenched by the addition of water (2 mL); after aqueous extraction with ether as the organic solvent, organic layers were dried over anhydrous  $\text{MgSO}_4$ . Removal of volatile solvents *in vacuo* was followed by silica gel chromatography (pentane, then 5:1 pentane:ether).

The  $^{13}\text{C}$  NMR signals due to C(3) of the 3-alkylcyclic ketals (ppm upfield from  $\text{CDCl}_3$  (77.7 ppm)): For 3-ethylcyclopentanone (**3b**)= $\delta$  45.22 and 44.90 (major); for 3-*n*-butylcyclohexanone (**6c**)= $\delta$  44.68 (major), 43.72. In support of the stereochemical identity determination detailed above, the (*S*)-absolute configuration was determined by the negative sign of optical rotation obtained for 3-*n*-butylcyclohexanone (**6c**);<sup>6</sup> the aforementioned data along with the observed  $^{13}\text{C}$  NMR data are in accordance with literature reports.<sup>7</sup>

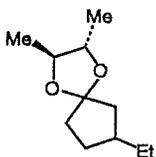
**3-Phenylcyclopentanone (3a).** IR (KBr): 2990 (w), 2990 (m), 2860 (s), 1720 (s), 1580 (w), 1470 (m), 1100 (m), 680 (w)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR:  $\delta$  7.41-7.20 (5H, m,  $\text{C}_6\text{H}_5$ ), 3.40 (1H, m,  $\text{C}_6\text{H}_5\text{CH}$ ), 2.66 (1H, dd,  $J=6.6, 17.1$  Hz,  $\text{COCHHCH}$ ), 2.51 (4H, m,  $\text{COCH}_2\text{CHHCH}$ ,  $\text{COCHH}$ ), 2.02 (1H, m,  $\text{C}_6\text{H}_5\text{CHCH}$ );  $^{13}\text{C}$  NMR:  $\delta$  212.0, 142.0, 129.0, 127.7, 125.6, 45.8, 41.3, 38.8, 31.2. HRMS calcd. for  $\text{C}_{11}\text{H}_{12}\text{O}$  requires 160.0888, found 160.0888.



**3-Ethylcyclopentanone (3b).** IR (KBr): 2931 (s), 2865 (m), 1712 (s), 1496 (w), 1451 (w), 699 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR:  $\delta$  2.45-2.40 (4H, m,  $\text{CH}_2\text{COCH}_2$ ), 2.10-2.01 (2H, m,  $\text{COCH}_2\text{CH}_2$ ), 1.80 (1H, m,  $\text{COCH}_2\text{CH}$ ), 1.45 (2H, m,  $\text{CH}_2\text{CH}_3$ ), 0.95 (3H, t,  $J=6.6$  Hz,  $\text{CH}_2\text{CH}_3$ );  $^{13}\text{C}$  NMR:  $\delta$  219.0, 44.9, 40.1, 38.4, 36.6, 29.0, 12.9. HRMS calcd. for  $\text{C}_7\text{H}_{12}\text{O}$  requires 112.0888, found 112.0891.



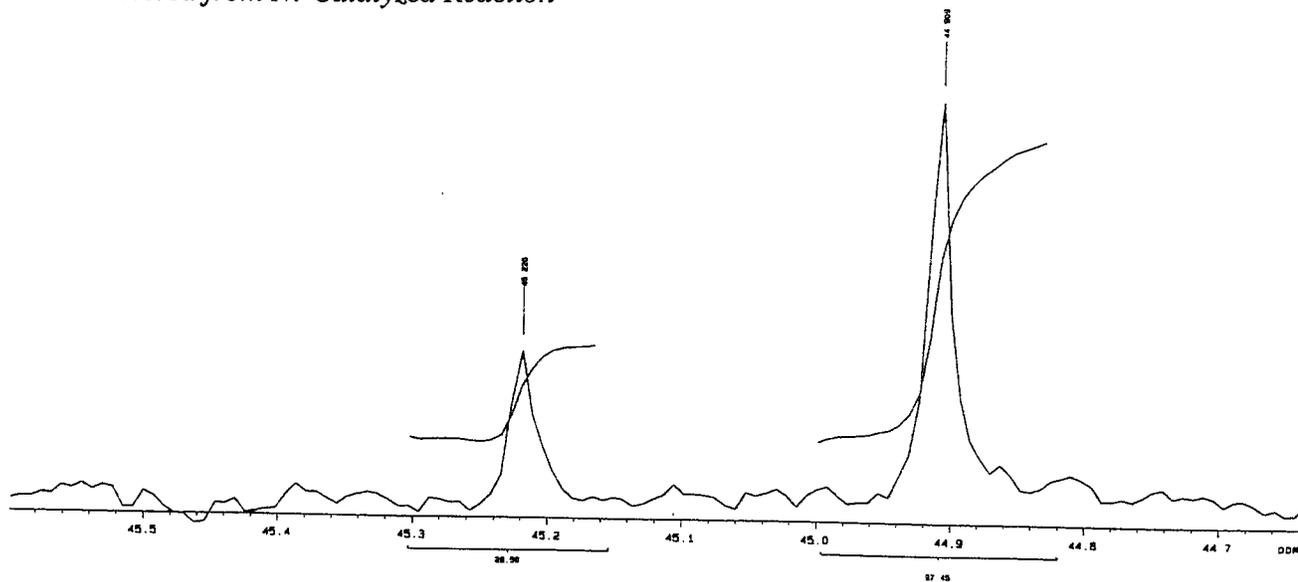
**3-(*S*)-Ethylcyclopentanone (*R,R*)-2,3-dimethylethylene ketal.** IR (KBr): 2967 (m), 2930 (m), 2873 (m), 1451 (w), 1375 (w), 1293 (w), 1142 (w), 1098 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR:  $\delta$  3.65-3.55 (2H, m,  $\text{OCHCH}_3$ ), 1.78-1.63 (4H, m,  $\text{CH}_2\text{C}(\text{OR})_2\text{CH}_2$ ), 1.55-1.35 (4H, m,  $\text{CH}_2\text{CH}_2\text{CH}(\text{CH}_2)_2$ ), 1.23 (3H, d,  $J=6.4$  Hz,  $\text{CHCH}_3$ ), 1.22 (3H, d,  $J=6.4$  Hz,  $\text{CHCH}_3$ ), 1.22-1.10 (3H, m,  $\text{CHCH}_2\text{CH}_3$ ), 0.84-0.87 (3H, t,  $J=7.6$  Hz,  $\text{CH}_2\text{CH}_3$ );  $^{13}\text{C}$  NMR:  $\delta$  109.3, 78.7, 78.3, 44.3, 37.3, 36.8, 31.9,



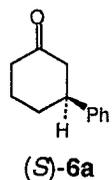
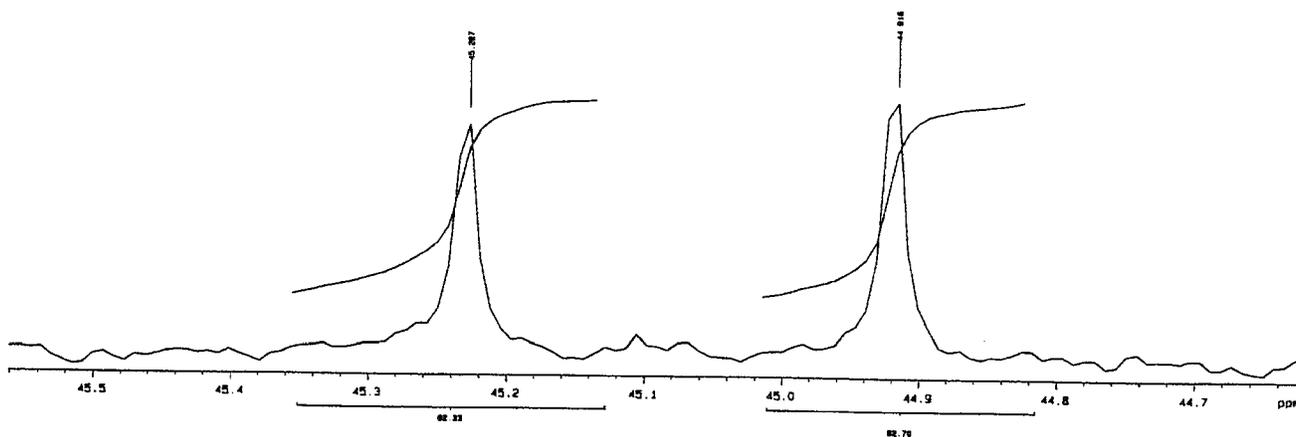
30.3, 23.9, 17.8, 17.6, 11.9. HRMS calcd. for  $C_{11}H_{20}O_2$  requires 184.1463, found 184.1465.

■  $^{13}C$  NMR analysis, in comparison with authentic racemic mixture:

*Derived from Ni-Catalyzed Reaction*



*Derived from Authentic Sample*

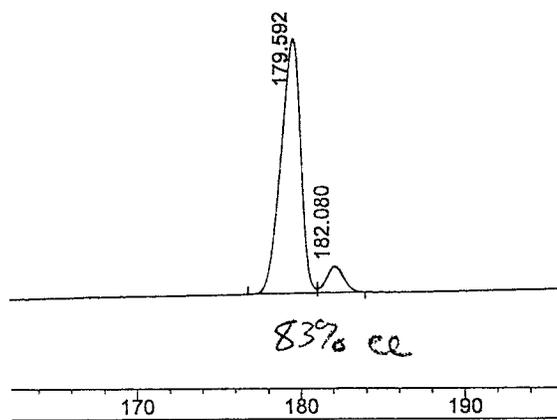


**3-(S)-Phenylcyclohexanone (6a).** IR (KBr): 2950 (s), 2890 (s), 1720 (s), 1580 (w), 1470 (m), 1100 (m), 680 (w)  $cm^{-1}$ ;  $^1H$  NMR:  $\delta$  7.41-7.20 (5H, m,  $C_6H_5$ ), 3.01 (1H, br m,  $CHC_6H_5$ ), 2.62-2.40 (4H, m,  $CH_2COCH_2$ ), 2.11 (2H, m,  $COCH_2CHCH_2$ ), 1.92 (2H, m,  $C_6H_5CHCH_2$ );  $^{13}C$  NMR:  $\delta$  212.0, 142.0, 129.7, 127.6, 125.3, 48.8, 43.8, 41.0, 32.7, 25.4. Anal. calcd. for  $C_{12}H_{14}O$ : C, 82.46; H, 8.10. Found: C, 82.50; H, 8.30. HRMS calcd. for  $C_{12}H_{14}O$  requires 174.1045, found

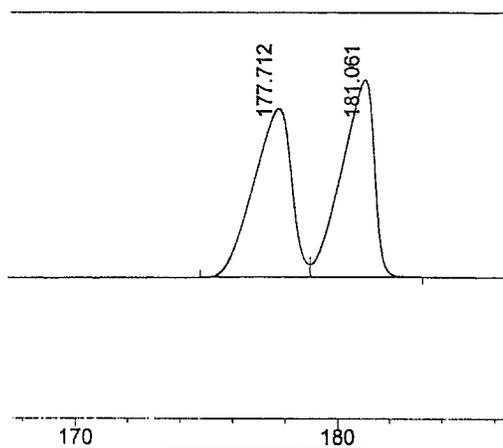
174.1038.

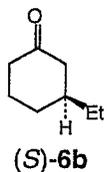
- GLC analysis of the ethylene ketal derived from reaction of **6a** with (*R,R*)-(-)-2,3-butanediol (BETADEX 120 chiral column by Supelco), in comparison with authentic racemic mixture:

*Derived from Ni-Catalyzed Reaction*

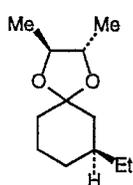


*Derived from Racemic Sample*





**(S)-3-Ethylcyclohexanone (6b).** IR (KBr): 2961 (s), 2935 (m), 1715 (s), 1460 (m), 1451 (w), 699 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR:  $\delta$  2.45 (2H, m,  $\text{COCH}_2$ ), 2.41 (2H, m,  $\text{CH}_2\text{CO}$ ), 2.12-1.85 (3H, m,  $\text{COCH}_2\text{CH}$  and  $\text{COCH}_2\text{CH}_2$ ), 1.75-1.55 (3H, m,  $\text{CHCH}_3$ ,  $\text{CO}(\text{CH}_2)_2\text{CH}_2$ ), 0.9 (3H, t,  $J=6.2$  Hz,  $\text{CH}_2\text{CH}_3$ );  $^{13}\text{C}$  NMR:  $\delta$  212.0, 47.7, 43.1, 41.7, 30.8, 26.8, 25.1, 10.27; Anal. Calcd for  $\text{C}_8\text{H}_{14}\text{O}$ : C, 76.19; H, 11.10. Found: C, 76.0; H, 11.09.



**(S)-3-Ethylcyclohexanone (R,R)-2,3-dimethylethylene ketal.** IR (KBr): 2967 (m), 2930 (m), 2873 (m), 1451 (w), 1375 (w), 1293 (w), 1142 (w), 1098 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR:  $\delta$  3.65-3.55 (2H, m,  $\text{OCHCH}_3$ ), 1.78-1.63 (4H, m,  $\text{CH}_2\text{C}(\text{OR})_2\text{CH}_2$ ), 1.55-1.35 (4H, m,  $\text{CH}_2\text{CH}_2\text{CH}(\text{CH}_2)_2$ ), 1.23 (3H, d,  $J=6.4$  Hz,  $\text{CHCH}_3$ ), 1.22 (3H, d,  $J=6.4$  Hz,  $\text{CHCH}_3$ ), 1.22-1.10 (3H, m,  $\text{CHCH}_2\text{CH}_3$ ), 0.84-0.87 (3H, t,  $J=7.6$  Hz,  $\text{CH}_2\text{CH}_3$ );  $^{13}\text{C}$  NMR:  $\delta$  109.3, 78.7, 78.3, 44.3, 37.3, 36.8, 31.9, 30.3, 23.9, 17.8, 17.6, 11.9. Anal. calcd. for  $\text{C}_{12}\text{H}_{22}\text{O}_2$ : C, 72.68; H, 11.18. Found: C, 72.78; H, 10.96.

■ GLC analysis, in comparison with authentic racemic mixture:

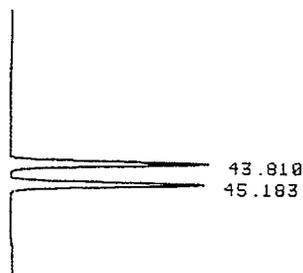
*Derived from Ni-Catalyzed Reaction*



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PEAK FILE : Y?SIGNAL.PRA

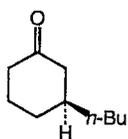
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	8.055	810	BB	.094	.00202
	17.689	1464	BB	.168	.00366
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	45.000	21943	BB	.377	.05482

*Derived from Racemic Sample*

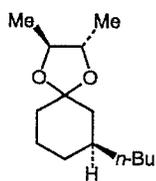


SIGNAL FILE: M:SIGNAL.BNA  
PEAK FILE : Y?SIGNAL.PRA

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	21.946	1032	PB	.233	.00354
	43.810	88408	PB	.370	.17076
	45.183	88336	BB	.379	.17062

**(S)-6c**

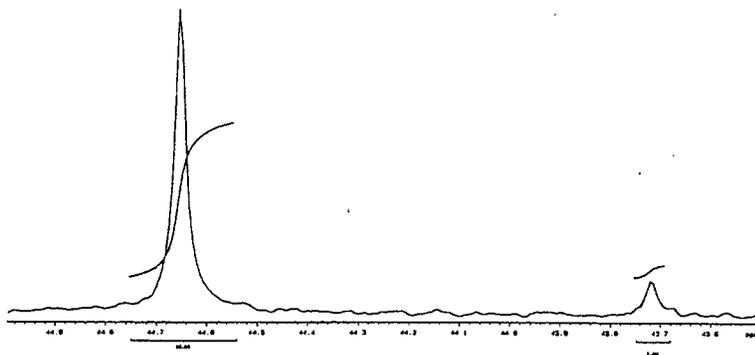
**3-(S)-n-Butylcyclohexanone (6c).** IR (KBr): 1714  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR:  $\delta$  2.36 (1H, m,  $\text{CH}_2\text{CH}_2\text{CO}$ ), 2.25 (1H, m,  $\text{CH}_2\text{CH}_2\text{CO}$ ), 1.95 (1H, m,  $\text{CHCH}_2\text{CO}$ ), 1.82 (1H, m,  $\text{CHCH}_2\text{CO}$ ), 1.65-1.57 (2H, m,  $\text{CH}_2\text{CH}_2\text{CO}$ ), 1.20 (7H, m, aliphatic CH), 0.90 (3H, t,  $J=6.8$  Hz,  $\text{CH}_2\text{CH}_3$ );  $^{13}\text{C}$  NMR:  $\delta$  211.7, 48.1, 41.4, 38.9, 36.1, 31.2, 28.7, 25.18, 22.6, 13.9. HRMS calcd. for  $\text{C}_{10}\text{H}_{18}\text{O}$  ( $M+1$ ) requires 155.1437, found 155.1436. Anal. calcd. for  $\text{C}_{10}\text{H}_{18}\text{O}$ : C, 77.85; H, 11.77. Found: C, 77.66; H, 11.61.  $[\alpha]_{\text{D}}=-47.9^\circ$  ( $\text{CDCl}_3$ ,  $c=0.015$ ).



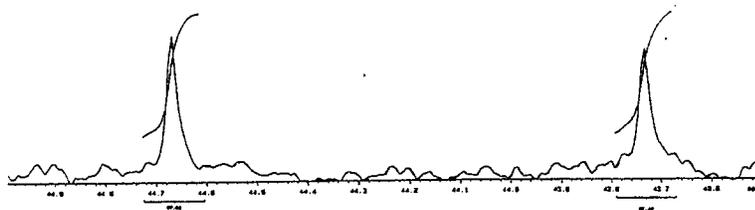
**(S)-3-n-Butylcyclohexanone (R,R)-2,3-dimethylethylene ketal.** IR (KBr): 1142 (m), 1098 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR:  $\delta$  3.55 (2H, m,  $\text{OCHCH}_3$ ), 1.65 (4H, m,  $\text{CH}_2\text{C}(\text{OR})_2\text{CH}_2$ ), 1.50-1.40 (4H, m,  $\text{CH}_2\text{CH}_2\text{CH}(\text{CH}_2)_2$ ), 1.20 (14H, m, aliphatic), 0.90 (3H, t,  $J=7.6$  Hz,  $\text{CH}_2\text{CH}_3$ );  $^{13}\text{C}$  NMR:  $\delta$  108.4, 77.9, 77.5, 43.9, 36.7, 36.0, 34.9, 31.7, 28.9, 23.2, 22.8, 16.9, 16.8, 13.9.

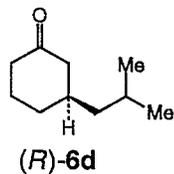
■  $^{13}\text{C}$  NMR analysis (100 MHz), in comparison with authentic racemic mixture:

*Derived from Ni-Catalyzed Reaction*



*Derived from Racemic Sample*

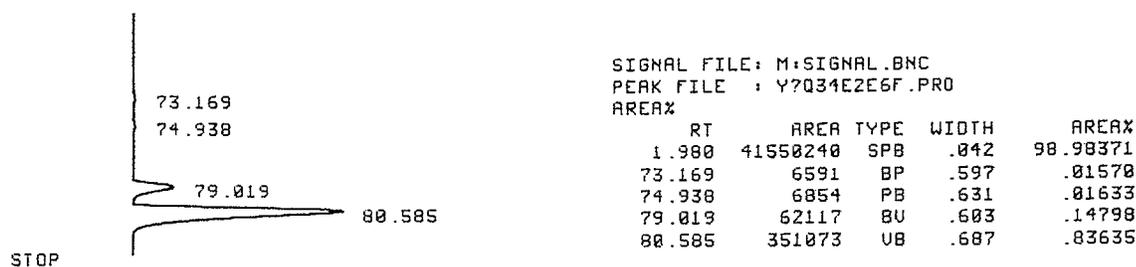




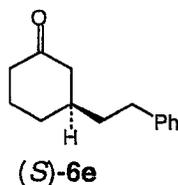
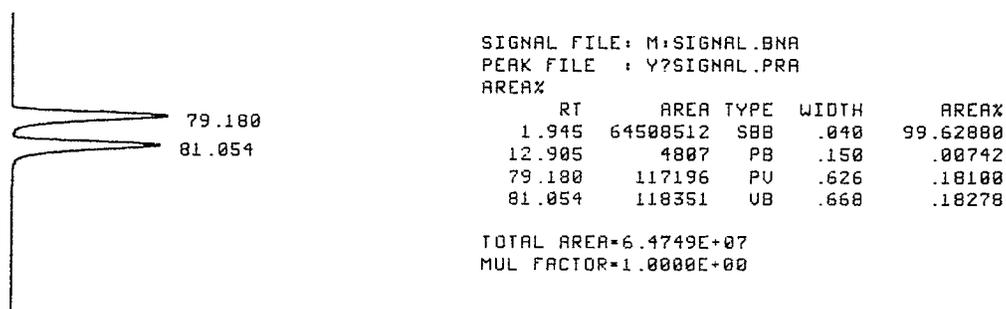
**(R)-3-iso-Butylcyclohexanone (6d).** IR (KBr): 2961 (m), 2936 (m), 2867 (m), 1715 (s), 1469 (w), 1451 (w), 1369 (w), 1224 (w)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR:  $\delta$  0.84-0.86 (6H, d,  $J=6.4$  Hz,  $\text{CH}(\text{CH}_3)_2$ ), 1.58-2.41 (11H, m, aliphatics);  $^{13}\text{C}$  NMR:  $\delta$  212.8, 49.0, 46.7, 42.2, 37.4, 32.2, 26.0, 25.4, 23.4, 23.3. HRMS calcd. for  $\text{C}_{10}\text{H}_{18}\text{O}$  ( $\text{M}+\text{H}$ ) requires 155.1437, found 155.1438.

■ GLC analysis (ALPHADEX 120 chiral column by Supelco), in comparison with authentic racemic mixture:

*Derived from Ni-Catalyzed Reaction*

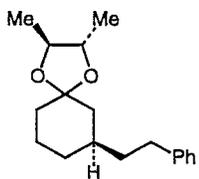


*Derived from Racemic Sample*



**(R)-3-Phenethylcyclohexanone (6e).** IR (KBr): 3056 (w), 3018 (m), 2930 (s), 2860 (s), 1709 (s), 1602 (w), 1495 (m), 1451 (m), 1224 (m), 752 (m), 702 (s)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR:  $\delta$  7.30-26 (2H, m, aromatics), 7.20-7.16 (3H, m, aromatics), 2.65-2.61 (2H, t,  $J=8$  Hz,  $\text{CH}_2\text{CH}_2\text{Ph}$ ), 2.51-2.46 (1H, m,  $\text{CH}_2\text{CH}_2\text{CO}$ ), 2.38-2.22 (2H, m,  $\text{CH}_2\text{COCH}_2$ ), 2.09-2.01 (2H, m,  $\text{COCH}_2\text{CH}$ ), 2.0-1.93 (1H, m, aliphatic), 1.86-1.76 (1H, m, aliphatic), 1.73-1.57 (3H, m, aliphatic), 1.43-1.33 (1H, m, aliphatic);  $^{13}\text{C}$  NMR:  $\delta$  212.4,

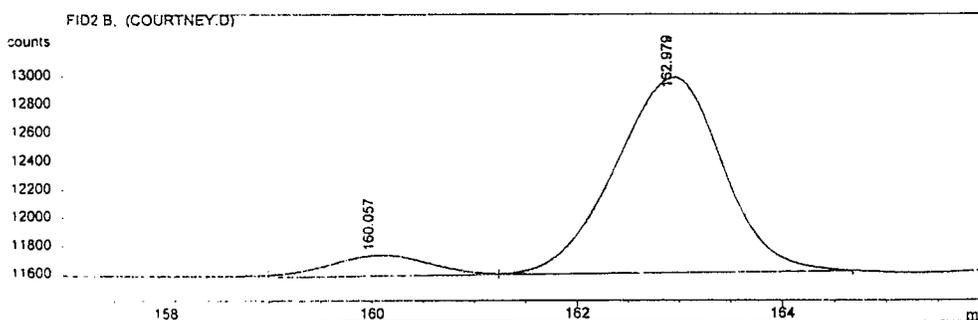
142.7, 129.1, 126.6, 48.7, 42.2, 39.2, 39.1, 33.7, 31.9, 25.9. Anal. calcd. for  $\text{C}_{14}\text{H}_{18}\text{O}$ : C, 83.12; H, 8.97. Found: C, 83.11; H, 8.92.



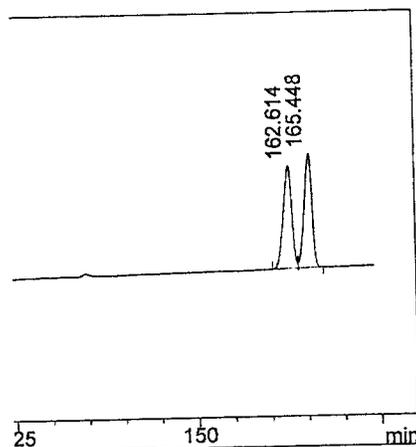
**(R)-3-Phenethylcyclohexanone (R,R)-2,3-dimethylethylene ketal (6e')**. IR (KBr): 3025 (w), 2930 (s), 2856 (m), 1457 (m), 1373 (w), 1148 (m), 1098 (s)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR:  $\delta$  7.28-7.25 (2H, m, aromatics), 7.18-7.16 (3H, m, aromatics), 3.68-3.57 (2H, m,  $\text{CH}_3\text{CHCHCH}_3$ ), 2.61 (2H, dddd,  $J=20.0, 20.0, 12.0, 8.0$  Hz,  $\text{CH}_2\text{Ph}$ ), 1.89-1.38 (9H, m, aliphatics), 1.24 (6H, t,  $J=5.2$  Hz,  $\text{CH}_3\text{CHCHCH}_3$ ), 0.87 (2H, ddd,  $J=24.4, 12.4, 3.6$  Hz,  $\text{CH}_2\text{CH}_2\text{Ph}$ );  $^{13}\text{C}$  NMR:  $\delta$  143.7, 129.0, 128.9, 126.3, 109.1, 78.8, 78.4, 44.5, 39.8, 36.8, 35.7, 34.0, 32.4, 24.0, 17.8, 17.6. Anal. calcd. for  $\text{C}_{18}\text{H}_{26}\text{O}_2$ : C, 78.78; H, 9.56. Found: C, 78.98; H, 9.84.

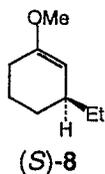
■ GLC analysis (BETADEX 120 chiral column by Supelco), in comparison with authentic racemic mixture:

*Derived from Ni-Catalyzed Reaction*

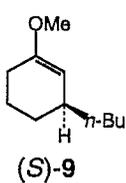


*Derived from Racemic Sample*





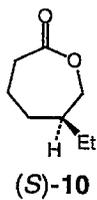
**3-(S)-Ethylcyclohexanone enol ether (8).** IR (KBr): 2967 (m), 2930 (m), 2873 (m), 1451 (w), 1375 (w), 1293 (w), 1142 (w), 1098 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR:  $\delta$  4.43 (1H, s, C(OMe)CH), 3.50 (3H, s, OMe), 2.09-2.01 (3H, m,  $\text{CH}_2\text{C}(\text{OMe})\text{CH}$ ,  $\text{CHCHC}(\text{OMe})$ ), 1.82-1.05 (6H, m, aliphatics), 0.93-0.89 (3H, t,  $J=7.6$  Hz,  $\text{CH}_2\text{CH}_3$ );  $^{13}\text{C}$  NMR:  $\delta$  156.1, 99.1, 54.4, 36.7, 30.8, 29.6, 28.6, 22.3, 12.2. Anal. calcd. for  $\text{C}_{11}\text{H}_{16}\text{O}$ : C, 77.08; H, 11.51. Found: C, 76.79; H, 11.29.



**3-(S)-n-Butylcyclohexanone enol ether (9).** IR (KBr): 1667 (m), 1211 (m), 1168 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR:  $\delta$  4.42 (1H, br s, C(OMe)CH), 3.39 (3H, s, OMe), 2.10 (1H, m,  $\text{CHCHC}(\text{OMe})$ ), 1.95-1.00 (12H, m, aliphatics), 0.80 (3H, t,  $J=6.8$  Hz,  $\text{CH}_2\text{CH}_3$ );  $^{13}\text{C}$  NMR:  $\delta$  155.2, 98.4, 53.6, 37.3, 34.2, 29.4, 29.3, 27.9, 22.9, 21.6, 14.1. HRMS calcd. for  $\text{C}_{11}\text{H}_{20}\text{O}$  requires 168.1514, found 168.1511.

**Procedure for synthesis of lactone 10.** Enol Ether **8** (20 mg, 0.12 mmol) was dissolved in a 5:1 mixture of  $\text{CH}_2\text{Cl}_2$  (5 mL) and MeOH (1 mL). Sodium bicarbonate (5 mg, ) was added and the reaction mixture was cooled to  $-78$  °C and then treated with ozone for approximately four min. At this time, the reaction vessel was charged with  $\text{NaBH}_4$  (19 mg, 0.48 mmol); the mixture was allowed to warm to 22 °C and allowed to stir at this temperature for two h. The reaction was quenched by the addition of 10 mL of water. Aqueous extraction with  $\text{CH}_2\text{Cl}_2$  and drying of the organic layers over anhydrous  $\text{MgSO}_4$  afforded a residue. Subsequent purification by silica gel chromatography (1:1 pentane, ether) gave 17 mg (0.084 mmol) of the derived ester-alcohol (70% yield). The resulting alcohol was dissolved in 8.5 mL of anhydrous toluene containing 3 Å molecular sieves (25% by weight based on the starting material) and 20 mol % *p*-TsOH (3.2 mg, 0.17 mmol) and the mixture was allowed to reflux for 15 h. Silica gel chromatography (pentane, then 1:1 pentane, ether) delivered lactone **10** in 93% yield (0.80 mmol, 11.1 mg).

**(S)-6-Ethoxy-2-cycloheptanone (10).** IR (KBr): 2691 (m), 2955 (m), 2873 (m), 1743 (s), 1457 (w), 1174 (m), 1054 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR:  $\delta$  4.17-4.13 (1H, dt,  $J=12.4$ , 1.6 Hz,  $\text{CHCH}_2\text{O}$ ), 4.06-4.00 (1H, dd,  $J=12.4$ , 8.0 Hz,  $\text{CHCH}_2\text{O}$ ), 2.63-2.59 (2H, m,  $\text{CH}_2\text{CO}$ ), 1.93-1.82 (2H, m, aliphatic CH), 1.70-1.61 (2H, m, aliphatic CH), 1.43-1.23 (3H, m, aliphatic CH), 0.95-0.92 (3H, t,  $J=3.2$  Hz,  $\text{CH}_3$ );  $^{13}\text{C}$  NMR:  $\delta$  176.7, 73.1, 40.9, 35.1, 35.0, 25.2, 2.0, 12.1. HRMS calcd. for  $\text{C}_8\text{H}_{14}\text{O}_2$  requires 142.0993, found 142.0093.



#### References and Footnotes

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