Hydrovinylation of Norbornene. Ligand Dependent Selectivity and Asymmetric Variations

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Supporting Information

General. Reactions requiring air-sensitive manipulations were conducted under an inert atmosphere of nitrogen by using either Schlenk techniques or a Vacuum Atmospheres drybox. Methylene chloride and toluene were distilled from calcium hydride under nitrogen and stored over molecular sieves. Tetrahydrofuran, diethyl ether, and hexane were distilled under nitrogen from sodium/benzophenone ketyl. Ethylene (99.5%) was purchased from Matheson Inc. and passed through Drierite before use. For ozonolysis, ozone gas was delivered using a Welsbach ozone generator. Analytical TLC was performed on E. Merck precoated (0.25 mm) silica gel 60 F_{254} plates. Flash column chromatography was carried out on silica gel 40 (Scientific Adsorbents). Gas chromatographic analyses were performed on a Hewlett-Packard 5890 equipped with an HP-ultra-1 crosslinked methyl silicone capillary column (25 m length x 0.2 mm i.d.) and a FID detector connected to a HP 3396 integrator. Helium was used as the carrier gas. Compounds for which an exact mass is reported exhibited no significant peaks at *m/z* greater than that of the parent.

Hydrovinylation of Norbornene Using Tricyclohexylphosphine as a Ligand. Synthesis of (1*R,2*S**,4*S**)-2-Vinylnorbornane (± 2).** To a red solution of $[Ni(allyl)Br]_2$ (3.7 mg, 0.010 mmol) in dichloromethane (1.5 mL) was added a solution of tricyclohexylphosphine (5.8 mg, 0.021 mmol) in dichloromethane (1.5 mL). The mixture was then added to a suspension of silver triflate (7.5 mg, 0.029 mmol) in dichloromethane in (2.0 mL). The resulting brown suspension was stirred for 1.5 h at rt, filtered through a short pad of Celite into a Schlenk flask, and then taken out of the drybox. It was cooled to -70 ˚C, oxygen-free ethylene (1 atm) was introduced, and norbornene (188 mg, 2.00 mmol) was added dropwise through a rubber septum with a syringe. The resulting reaction mixture was stirred for 2 h at -70 ˚C under an ethylene atmosphere (1 atm), quenched with half-saturated aqueous ammonium chloride (5 mL), and then extracted with diethyl ether (50 mL). The organic phase was dried over magnesium sulfate, analyzed by GC (> 99% yield), and concentrated under reduced

pressure to get varying amounts of **2** (94-55%, as a function of how long the evaporation of the solvent took) as a colorless oil. From the crude NMR and GC traces of the product it was obvious that the low recovery was due to high volatility of the product. GC (HP-ultra-1 cross-linked methyl silicone capillary column (25 m length x 0.2 mm i.d) R_T = 9.13 min.; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.74 (ddd, J_{trans} = 17.3 Hz, J_{cis} = 10.0 Hz, J = 7.3 Hz, 1 H), 4.90 (dt, J_{trans} = 17.3 Hz, J = 1.5 Hz, 1 H), 4.84 (dt, J_{cis} = 10.0 Hz, J = 1.5 Hz, 1 H), 2.23 (m, 1 H), 2.10-2.06 (m, 2 H), 1.52-1.08 (m, 8 H); ^{13}C NMR 29.4, 30.1, 36.0, 37.0, 37.6, 42.7, 46.3, 111.8, 144.7.; MS: *m/z* 122 (M^+), calcd for C_9H_{14} 122.21.

Hydrovinylation of Norbornene Using Triphenylphosphine as a Ligand.
(1*S,1'*S**,2*S**,2'*S**,3*S**,3'*S**,4*R**,4'*R**)-3-vinyl-2,2'-binorbornane (±6).** To a solution of [(allyl)NiBr]$_2$ (10.8 mg, 0.0300 mmol) in 1 mL of CH_2Cl_2 under nitrogen at room temperature was added a solution of triphenylphosphine (15.7 mg, 0.060 mmol) in 1 mL of CH_2Cl_2. The resulting brown solution was added to a mixture of AgOTf (21.8 mg, 0.084 mmol) in 1 mL of CH_2Cl_2. After stirring for 1.5 h at rt, the mixture was filtered through a small plug of Celite, and the precipitate was rinsed with 2 mL of CH_2Cl_2. The filtrate was collected in a Schlenk flask, and was taken out of the drybox. The catalyst solution was cooled to -55 ˚C. Under one atmosphere of ethylene, 188.3 mg (2.00 mmol) of norbornene in 1 mL of CH_2Cl_2 was added dropwise to the catalyst solution. After stirring at -55 ˚C for 30 min, the mixture was quenched with saturated aqueous NH_4Cl solution and extracted three times with 10 mL portions of CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo* to give alkene **6** as a clear oil (203 mg, 94%) contaminated with < 0.7% of **2.** GC (HP-ultra-1 cross-linked methyl silicone capillary column (25 m length x 0.2 mm i.d) R_T = 35.82 min.; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.82 (dt, J_{trans} = 17.0 Hz, J = 10.1 Hz, 1 H), 4.90 (ddd, J_{trans} = 17.0 Hz, J = 2.4, 0.8 Hz, 1 H), 4.85 (dd, J = 10.1, 2.4 Hz, 1 H), 2.23-2.09 (m, 4 H), 1.94 (m, 1 H), 1.58-0.98 (m, 16 H);); ^{13}C NMR (75 MHz, $CDCl_3$) d 28.9, 29.0, 30.3, 30.6, 33.5, 35.4, 37.2, 39.6, 40.9, 43.7, 44.7, 46.2, 51.2, 53.9, 113.3, 142.1.; MS: *m/z* 216 (M^+), calcd for $C_{16}H_{23}$ 215.36. The structure of **6** was further confirmed by the transformation into a primary alcohol via hydroboration followed by oxidative workup and further derivatization with Mosher acid chloride (see below).

The yield of the hydrovinylation reaction increased to >97% upon carrying out the reaction at –55 ^{o}C, for 2 h using 0.7 mol% catalyst. About 1.9% of an unidentified C-16 isomer (R_t = 35.13 min.) was also formed under these conditions. .

Typical Experimental Procedure for Asymmetric Hydrovinylation of Norbornene. To a red solution of [Ni(allyl)Br]$_2$ (3.6 mg, 0.01 mmol) in 1.5 mL of CH_2Cl_2 was added 0.021 mmol of the appropriate phosphine ligand dissolved in CH_2Cl_2. The resulting mixture was added dropwise to a suspension of 0.029 mmol of the additive (AgOTf, NaBARF, $NaNTf_2$, $AgSbF_6$) in 2 mL of CH_2Cl_2 at room temperature. The brownish mixture was stirred for 1.5 h and then filtered through Celite® into a Schlenk flask. The reaction flask was removed from the drybox and cooled to the appropriate temperature. Oxygen free ethylene was introduced followed by a CH_2Cl_2 (1.5 mL) solution of norbornene (188 mg, 2 mmol) dropwise. After the reaction was over, aqueous ammonium chloride (1 mL) was added and the product was extracted with pentane (2 x 15 mL). The combined organic layers was washed with brine and dried over $MgSO_4$. Concentration to a volume of 3 mL afforded the product in pentane which was analyzed by GC. A sample for NMR was prepared for by careful removal of pentane and adding the appropriate deuterated solvent.

Preparation of Alcohol 7. To 2 mL (1.0 M in THF, 2.0 mmol) of BH_3•THF solution at 0 °C under nitrogen was added 2 mL (2.0 M in THF, 4.0 mmol) of 2-methyl-2-butene solution. After the mixture was stirred at 0 °C for 1 h, 100 mg (0.463 mmmol) of alkene **6a** in 2 mL of THF was added. The resulting mixture was stirred at rt for 24 h and quenched with 3.0 mL of 2 N aqueous NaOH solution and 0.6 mL of 30% aqueous H_2O_2 solution. After stirring for 30 min, the aqueous layer was extracted three times with 10 mL portions of ether. The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel, eluting with hexanes/ethyl acetate (9:1), to produce alcohol **7** as a clear oil (95 mg, 88%). ^{1}H NMR (200 MHz, $CDCl_3$) d 0.89-2.22 (m, 23 H), 3.41-3.75 (m, 2 H); ^{13}C NMR (50 MHz, $CDCl_3$) d 28.8, 29.2, 30.1, 31.0, 33.1, 33.5, 35.2, 37.1, 40.4, 40.6, 40.7, 41.0, 42.3, 43.2, 53.0, 63.1; EIMS m/z (relative intensity) 234 (M^+, 3); HRMS calcd for $C_{16}H_{26}O$ 234.1984, found 234.1998.

Reaction of 7 with (*R*)-Mosher Acid Chloride. Oxalyl chloride (0.042 mL) was added to a solution of (*R*)-(+)-Mosher acid (0.025 g, 0.1 mmol) and DMF (0.075 g) in hexane (3.6 mL) at room temperature. The solution containing the white precipitate was stirred for an hour, then it was transferred into another flask via syringe and the solvents were removed under vacuum. A solution of the alcohol **7** (0.017 g, 0.072 mmol) and 4-DMAP (0.031 g, 0.25 mmol) in CH_2Cl_2 (0.5 mL) was added to the residue. The reaction mixture was stirred overnight at room temperature. The mixture was

diluted with CH_2Cl_2, washed with 5 % HCl, saturated $NaHCO_3$ and brine and then dried over Na_2SO_4. Purification by column chromatography (10 % ethylacetate / hexane) gave 0.022 g, (68 %) of product esters (**8**) which were characterized by NMR spectroscopy. Fluorine-19 (C_6D_6) NMR showed only two peaks at d 70.43 and 70.45 in a ratio of 1:1 in the characteristic range for the CF_3-groups, thereby confirming the homogeneity of the 2:1 adduct. The two diastereomeric esters result from the two enantiomers of **7**.

Enantioselectivity for the reactions listed in Table 1 (entries 2c and 6) were calculated based on the ratio of the two ^{19}F resonances listed above.

Mandelate Ester Formation of the Carboxylic Acid Derived from 2-Vinylbicyclo-[2.2.1]-heptene and Assignment of the Configuration of the Major Product. The mixture of 2-vinylbicyclo-[2.2.1]-heptane (0.122 g, 1 mmol), CH_2Cl_2 (2 mL) and CH_3OH (2 mL) was cooled to -78^oC and was flushed with O_2 for 10 min. Ozone was passed through the solution for 5 min till the blue color persited. At that time, ozone flow was stopped and N_2 was passed for 15 min to remove any dissolved O_3. A pinch of sodium bicarbonate was added followed by excess (0.14 mL, 0.2 mmol) of dimethylsulfide. The solution was warmed to room temperature and stirred for 30 min. Excess water was added and the product aldehyde (**16**) was extracted with ether. The ether was removed and the residue was dissolved in 5 mL of acetone. To the acetone solution, was added a suspension of $MgSO_4$ (0.175 g, 1.45 mmol) and $KMnO_4$ (0.165 g, 1.04 mmol) in acetone (25 mL) over the period of 2 h at room temperature. The mixture was stirred overnight at room temperature. Then solvent was removed, and the solid residue was extracted by hot water and filtered. The aqueous layer was acidified with concentrated HCl (pH 2), and extracted with $CHCl_3$. The $CHCl_3$ extracts were dried over $MgSO_4$ and concentrated to get the desired acid **17** (crude wt 0.058 g) which was used for subsequent step without purification.

Norborane-2-carboxylic acid (**17**, 0.058 g, 41 mmol) and DMAP (0.002 g, 0.016 mmol) were dissolved in CH_2Cl_2 (1 mL). *S*-methyl mandelate (0.093 g, 0.60 mmol) and DCC (0.126 g, 0.61 mmol) in CH_2Cl_2 (1 mL) was added to the acid solution dropwise. The mixture was stirred at -10^oC for 3 h. The residue was concentrated and was passed through a silica gel pad and subsequently the compound was purified by column chromatography using 20 % ethylacetate / hexane. The mandelate ester was isolated in 87 % (0.104 g) yield. ^1H NMR ($CDCl_3$) 7.45-7.55 (m, 2 H), 7.35-7.45 (m, 3 H), 5.91 (s, 1 H), 3.72 (s, 3 H), 2.70-2.80 (s, br, 0.2 H), 2.40-2.65 (m, 1.8 H), 2.25-2.35 (1 H), 1.80-2.00 (m, 1 H),

1.35-1.61 (m, 4 H), 1.05-1.3 (m, 4 H); (C_6D_6) inter alia, δ 2.88 (s, 1 H, ring CH, from the 2(*R*)-diastereomer), 2.55 (s, 1 H, ring CH, from the 2(*S)*- diastereomer).[12]. In C_6D_6, the benzylic hydrogens of the 2(*S)*- and 2(*R*)- diastereomers appear at d 6.093 and 6. 082 respectively. The ee's (Table 1, entries 1a-c, 2a) were determined from the relative intensities of the proton resonances at δ 2.55 and 2.88.

Chromatographic and spectroscopic data

1. GC of crude product, 1:1 adduct **2** (Scheme 1)
2. ^{1}H NMR of **2**
3. ^{13}C NMR of **2**
4. ^{1}H NMR of aldehyde **17**
5. ^{1}H NMR of mandelate ester [entry 2(a) Table 1] 80% ee
6. ^{1}H NMR (expansion, δ 2.50-2.90) of mandelate ester [entry 2(a) Table 1] 80% ee
7. ^{1}H NMR (expansion, δ 6.05-6.15) of mandelate ester [entry 2(a) Table 1] 80% ee
8. ^{13}C NMR of mandelate ester [entry 2(a) Table 1] 80% ee
9. GC of crude product 2:1 adduct **6a** (Scheme 1)
10. ^{1}H NMR of crude product **6a**
11. ^{13}C NMR of crude product **6a**
12. ^{1}H NMR alcohol **7**
13. ^{1}H NMR Mosher ester of racemic **7**
14. ^{13}C NMR Mosher ester of racemic **7**
15. ^{19}F NMR of Mosher ester of racemic **7**
16. ^{19}F NMR of Mosher ester enriched **7** [33% ee, entry 2(c), Table 1]

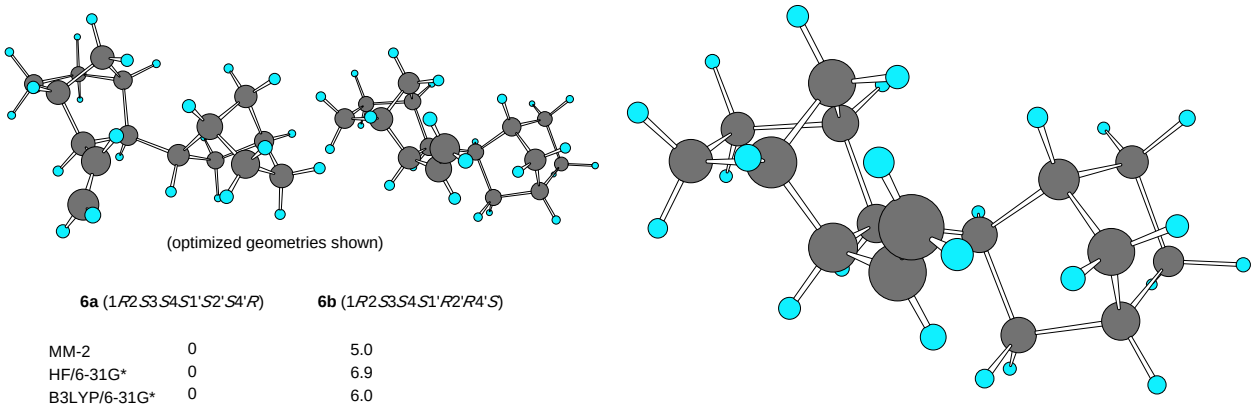

Figure 1. Calculated Relative Energies of the 2:1 Adducts **6a** and **6b**

(optimized geometries shown)

6a (1*R*2*S*3*S*4*S*1'*S*2'*S*4'*R*) **6b** (1*R*2*S*3*S*4*S*1'*R*2'*R*4'*S*)

MM-2	0	5.0
HF/6-31G*	0	6.9
B3LYP/6-31G*	0	6.0

Figure 1. Calculated Relative Energies of the 2:1 Adducts **6a** and **6b**