An Unusual Approach Towards the Synthesis of Enantiomerically *Cis*-Linear Homoallylic Alcohol Based on the Steric Interaction Mechanism of Camphor Scaffold

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Supporting Information

General

Experiments involving moisture and/or air sensitive components were performed in oven-dried glassware. Commercial solvents and reagents were used without further purification with the following exceptions: Hexane, dichloromethane, ethyl acetate were fractionally distilled. Aldehydes were distilled before used.

Analytical thin layer chromatography (TLC) was performed using Merck 60 F254 precoated silica gel plate (0.2 mm thickness). Subsequent to elution, plates were visualized using UV radiation (254 nm) on Spectroline Model ENF-24061/F 254 nm. Further visualization was possible by staining with basic solution of potassium permanganate or acidic solution of ceric molybdate, followed by heating on a hot plate.

Flash chromatography was performed using Merck silica gel 60 with freshly distilled solvents. Columns were typically packed as slurry and equilibrated with the appropriate solvent system prior to use.

Infrared spectra were recorded on a Bio-Rad FTS 165 FTIR spectrometer. Liquid samples were examined as film between NaCl salt plates.

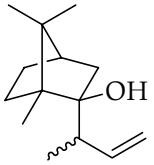
Proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded on a Bruker Avance DPX 300 and Bruker AMX 500 spectrophotometer ($CDCl_3$ as solvent). Chemical shifts for ^{1}H NMR spectra are reported as δ in units of parts per million (ppm) downfield from SiMe4 (δ 0.0) and relative to the signal of chloroform-d (δ 7.2600, singlet). Multiplicities were given as: s (singlet); bs (broad singlet); d (doublet); t (triplet); q (quartet); dd (doublets of doublet); dt (doublets of triplet); dtq (doublets of triplets of quartet); or m (multiplets). The number of protons (n) for a given resonance is indicated by nH. Coupling constants are reported as a J value in Hz. Carbon nuclear magnetic resonance spectra (^{13}C NMR) are reported as δ in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0) and relative to the signal of chloroform-d (δ 77.04, triplet). The proportion of diastereomers was determined from the integration of ^{1}H NMR and ^{13}C NMR spectra.

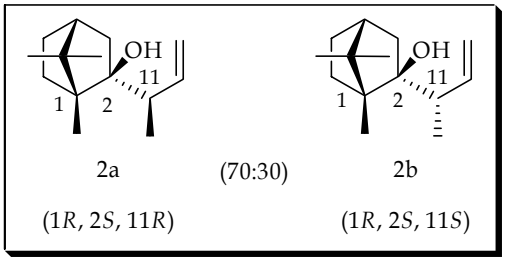
Mass spectral analyses were carried out on a VG 7035 micromass mass spectrophotometer at a source temperature of 200 ^{o}C and at an ion current of 70 eV. Mass spectral data were reported in units of mass to charge (m/z) and % intensity.

Experimental Section

Preparation of camphor-derived homoallylic alcohol[1]

To a cooled (0 °C) solution of (1*R*)-(+)-camphor (7.612 g, 50 mmol, 1 equiv.) in diethyl ether (100 mL) under nitrogen was added freshly prepared crotylmagnesium bromide (150 mmol, 3 equiv.) dropwise. The reaction mixture was allowed to warm up to room temperature slowly and stir for another 3 hours. The reaction mixture was quenched using 40 mL saturated NH_4Cl solution and was extracted with diethyl ether (3 x 30 mL). The combined organic phases were washed with water, and then with brine, before drying over $MgSO_4$. The crude mixture was then filtered and concentrated in vacuo. The crude product was purified via column chromatography (hexane/Et_2O = 60:1). The product was obtained (9.06 g, 87 %) as colorless oil (1*R*, 2*S*, 11*R* – **2a**/1*R*, 2*S*, 11*S* – **2b** = 70:30 by ^1H NMR)





2-(but-3-en-2-yl)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol

R_f = 0.70 (2:1 hexane/ethyl acetate);

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[1]Dimitrov, V.; Simova, S.; Kostova, K. *Tetrahedron*. **1996**, *52*, 1699.

$[\alpha]_D^{25}$ = -2.7 ° (1.0, CH_2Cl_2);

^{1}H NMR (300 MHz, $CDCl_3$): δ 6.04 – 5.87 (m, 1H), 5.06 (dd, *J* = 15.2, 2.8 Hz, 1H), 4.95 (dd, *J* = 10.6, 1.2 Hz, 1H), 2.31 (dq, *J* = 7.6, 7.2 Hz, 1H), 1.90 – 1.73 (m, 1H), 1.67 – 1.30 (m, 6H), 0.99 (d, *J* = 4.0 Hz, 3H), 0.95 (s, 3H), 0.79 (s, 3H), 0.76 (s, 3H);

^{13}C NMR (75.4 MHz, $CDCl_3$): (2 isomers) δ 141.4, 115.9, 114.2, 82.1, 80.9, 52.8, 52.4, 50.4, 50.1, 47.3, 47.0, 46.3, 46.0, 44.7, 44.5, 29.7, 29.3, 27.6, 27.5, 21.4, 21.0, 15.5, 14.7, 12.2, 12.0;

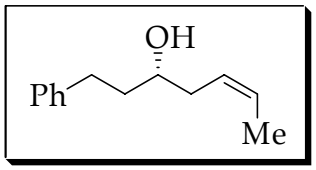
FTIR (neat): 3479, 3075, 2963, 2881, 1634, 1459, 1381, 1268, 1081, 1001, 913 cm^{-1};

HRMS (EI) Calcd for $C_{14}H_{24}O$ [M^+]: 208.1827, found 208.1803.

General procedures for allyl transfer reaction

To a solution of (1*R*)-(-)-10-camphorsulfonic acid (7 mg, 0.03 mmol, 0.1 equiv.) and aldehyde (0.3 mmol, 1 equiv.) in dichloromethane (0.05 mL, 6 M) under nitrogen at room temperature was added 2-(but-3-en-2-yl)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol (as a mixture of isomers 70:30; 187 mg, 0.9 mmol, 3 equiv.). The reaction mixture was allowed to stir for 5-6 days. The reaction mixture was diluted with 20 mL diethyl ether, washed with saturated $NaHCO_3$ solution and followed by brine, before drying over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified via column chromatography (hexane/ethyl acetate = 30:1).

Characterization of homoallylic alcohols in Table 2



(*S*,*Z*)-1-phenylhept-5-en-3-ol

(94 %*ee*, 99% *Z*)

Colorless oil (50 mg, 88 %);

R_f = 0.35 (4:1 hexane/ethyl acetate);

$[\alpha]_D^{25}$ = - 21.2 ^{o} (1.0, CH_2Cl_2);

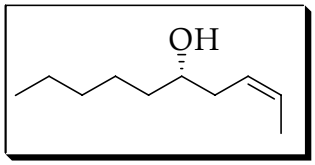
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.28 – 7.09 (m, 5H), 5.59 (ddq, *J* = 10.8, 7.2, 0.8 Hz, 1H), 5.36 (dtq, *J* = 10.8, 7.6, 1.6 Hz, 1H), 3.65 – 3.55 (m, 1H), 2.75 – 2.62 (m, 2H), 2.20 (t, *J* = 7.2 Hz, 2H), 1.73 (dq, *J* = 13.5, 7.2 Hz, 2H), 1.58 (dd, *J* = 7.2, 0.8 Hz, 3H);

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 142.1, 128.4, 128.3, 127.5, 125.9, 125.8, 70.8, 38.4, 35.1, 32.1, 13.0;

FTIR (neat): 3376, 3062, 3022, 2929, 2862, 1661, 1602, 1494, 1447, 1407, 1373, 1361, 1049, 395, 861, 744, 701, 580, 506 cm^{-1};

HRMS (EI) Calcd for $C_{13}H_{18}0$ [M^+]: 190.1358, found: 190.1357.

The enantiomeric excess and the *E*/*Z* selectivity were determined by HPLC analysis employing a Daicel Chiracel OD column (Hexane: i-propanol 99:1, 1.0 mL/min): t_1 = 11.13, t_2 = 13.21 and t_3 = 21.80 min.



(*S*,*Z*)-dec-2-en-5-ol

(97 %*ee*, >99% *Z*)

Colorless oil (32 mg, 68 %);

R_f = 0.43 (4:1 hexane/ethyl acetate);

$[\alpha]_D^{25}$ = + 1.3 ^{o} (1.0, CH_2Cl_2);

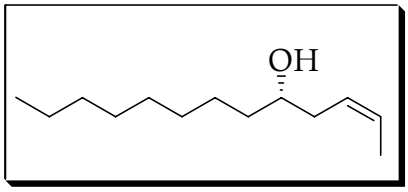
^{1}H NMR (300 MHz, $CDCl_3$): δ 5.70 – 5.59 (m, 1H), 5.48 - 5.39 (m, 1H), 3.62 (q, *J* = 5.9 Hz, 1H); 2.22 (t, *J* = 6.97 Hz, 2H), 1.64 (dd, *J* = 7.0, 0.7 Hz, 3H); 1.46 (bs, 2H), 1.30 (m, 4H), 0.89 (t, *J* = 6.0 Hz, 3H);

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 127.2, 126.3, 71.6, 36.9, 35.0, 31.9, 25.5, 22.7, 14.1, 13.0;

FTIR (neat): 3400, 3019, 2957, 2957, 2930, 2858, 2370, 2345, 1656, 1639, 1459, 1378, 1124, 1030, 968 cm^{-1};

HRMS (EI) Calcd for $C_{10}H_{10}0$ [M^+]: 156.1514, found: 156.1521.

Product was derivatized with *R*-(+)-α-trifluoromethyl-α-methoxy-phenylacetic acid (Mosher acid) before the enantiomeric excess and the *E*/*Z* selectivity were determined by HPLC analysis employing a Daicel Chiracel AD column (Hexane: i-propanol 99.5:0.5, 0.5 mL/min): t_1 = 7.77 and t_2 = 9.95 min.



(*S*,*Z*)-tridec-2-en-5-ol

(90 %*ee*, 94% *Z*)

Light yellow oil (24 mg, 95 %);

R_f = 0.50 (4:1 hexane/ethyl acetate);

$[\alpha]_D^{25}$ = - 4.5 ^{o} (1.0, CH_2Cl_2);

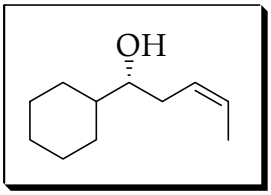
^{1}H NMR (300 MHz, $CDCl_3$): δ 5.58 (ddq, *J* = 10.9, 6.8, 1.6 Hz, 1H), 5.37 (dtq, *J* = 10.9, 7.2, 0.8 Hz, 1H), 3.58 – 3.54 (m, 1H), 2.15 (dt, *J* = 6.8 Hz, 2H), 1.57 (dd, *J* = 6.8, 0.8 Hz, 3H), 1.40 (m, 2H), 1.26 (m, 12H) 0.81 (t, *J* = 6.4 Hz, 3H);

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 127.2, 127.1, 71.5, 36.9, 35.0, 31.9, 29.7, 29.6, 29.3, 25.8, 22.6, 14.1, 13.0;

FTIR (neat): 3361, 3018, 2925, 2858, 1658, 1457, 1373, 1124, 1029, 859, 706 cm^{-1};

HRMS (EI) Calcd for $C_{13}H_{26}0$ [M^+]: 198.1984, found: 198.1984.

Product was derivatized with *R*-(+)-α-trifluoromethyl-α-methoxy-phenylacetic acid (Mosher acid) before the enantiomeric excess and the *E*/*Z* selectivity were determined by HPLC analysis employing a Daicel Chiracel AD column (Hexane: i-propanol 99.5:0.5, 1 mL/min): t_1 = 5.86, t_2 = 5.89 and t_3 = 6.94 min.



(*R*,*Z*)-1-cyclohexylpent-3-en-1-ol

(92 %*ee*, 96% *Z*)

Colorless oil (20 mg, 40 %);

R_f = 0.51 (4:1 hexane/ethyl acetate);

$[\alpha]_D^{25}$ = -2.5 ^{o} (1.0, CH_2Cl_2);

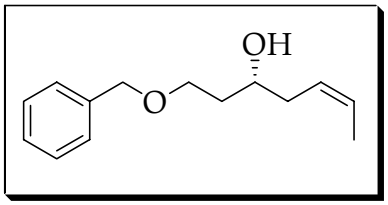
^{1}H NMR (300 MHz, $CDCl_3$): δ 5.69 – 5.61 (m, 1H), 5.49 – 5.41 (m, 1H), 3.38 (dt, *J* = 6.6, 5.6 Hz, 1H), 2.28 – 2.23 (m, 2H), 1.64 (d, *J* = 6.3 Hz, 3H), 1.32 – 1.27 (m, 1H), 1.13 – 1.09 (m, 5H), 1.05 – 0.91 (m, 5H);

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 127.3, 126.7, 75.6, 43.2, 31.8, 29.3, 28.2, 26.6, 26.4, 26.2, 13.0;

FTIR (neat): 3591, 3020, 2925, 2854, 1625, 1448, 1261, 1086, 1065, 1030, 968, 892 cm^{-1};

HRMS (EI) Calcd for $C_{11}H_{20}0$ [M^+]: 168.1514 , found: 168.1520.

Product was derivatized with 3,5-dinitrobenzolic chloride before the enantiomeric excess and the *E*/*Z* selectivity were determined by HPLC analysis employing a Daicel Chiracel OD followed by a Daicel Chiracel ODH column (Hexane: i-propanol 99:1, 0.3 mL/min): t_1 = 68.86, t_2 = 70.16 and t_3 = 78.78 min.



(*R*,*Z*)-1-(benzyloxy)hept-5-en-3-ol

(97 %*ee*, >99% *Z*)

Light yellow oil (27 mg, 40 %);

R_f = 0.44 (2:1 hexane/ethyl acetate);

$[\alpha]_D^{25}$ = + 72.8 ^{o} (1.00, MeOH);

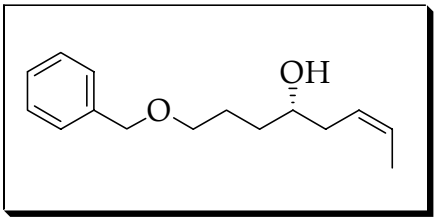
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35 - 7.26 (m, 5H), 5.66 - 5.55 (m, 2H), 5.55 - 5.29 (m, 2H), 4.52 (s, 2H), 3.89 - 3.81 (m, 1H), 3.73 (t, *J* = 6.42 Hz, 2H), 2.34-2.15 (m, 2H), 1.79 - 1.74 (m, 2H), 1.63 (d, *J* = 6.6 Hz, 3H);

^{13}C NMR (75.4 MHz, $CDCl_3$) δ 138.0, 128.5, 127.7, 126.7, 126.2, 73.4, 71.1, 69.1, 35.9, 34.9, 13.0;

FTIR (neat): 3429, 3031, 2939, 2858, 1638, 1453, 1095, 969, 697 cm^{-1};

HRMS (EI) Calcd for $C_{14}H_{20}O_2$ [M^+]: 220.1463, found 220.1459.

The enantiomeric excess and the *E*/*Z* selectivity were determined by HPLC analysis employing a Daicel Chiracel OB x 2 (Hexane 100%; 3.0 mL/min): t_1 = 33.01, t_2 = 46.03 and t_3 = 52.52 min.



(*S*,*Z*)-1-(benzyloxy)oct-6-en-4-ol

(>99 %*ee*, >99% *Z*)

Light yellow oil (66 mg, 94 %);

R_f = 0.33 (4:1 hexane/ethyl acetate);

$[\alpha]_D^{25}$ = - 1.7 ^{o} (1.00, CH2Cl2);

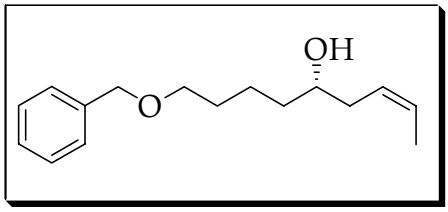
1H NMR (300 MHz, CDCl3): δ 7.36 – 7.27 (m, 5H), 5.69 – 5.59 (m, 1H), 5.51 – 5.42 (m, 1H), 4.53 (s, 2H), 3.72 – 3.62 (m, 1H), 3.53 (t, *J* = 5.9 Hz, 2H), 2.33 – 2.24 (m, 2H), 1.65 (d, *J* = 6.6 Hz, 3H), 1.53 (q, *J* = 7.3 Hz, 2H), 1.31 – 1.25 (m, 2H);

^{13}C NMR (75.4 MHz, $CDCl_3$) δ 138.3, 128.4, 127.7, 127.6, 126.8, 126.4, 73.0, 71.3, 70.5, 35.0, 34.0, 26.4, 13.0;

FTIR (neat): 3393, 3067, 2926, 1717, 1602, 1584, 1452, 1278, 1114, 1071, 1027, 859, 801, 715 cm^{-1};

HRMS (EI) Calcd for $C_{15}H_{22}O_2$ [M^+]: 234.1620, found 234.1617.

The enantiomeric excess and the *E*/*Z* selectivity were determined by HPLC analysis employing a Daicel Chiracel OD followed by a Daicel Chiracel ODH column (Hexane: i-propanol 99:1, 1.0 mL/min): t_1 = 23.592 min.



(*S*,*Z*)-9-(benzyloxy)non-2-en-5-ol

(98 %*ee*, 98% *Z*)

Light yellow oil (74 mg, 80 %);

R_f = 0.35 (4:1 hexane/ethyl acetate);

[(]D25 = - 2.0 º (1.0, CH2Cl2);

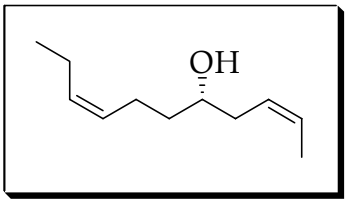
1H NMR (300 MHz, CDCl3): δ 7.36 – 7.27 (m, 5H), 5.71 – 5.61 (m, 1H), 5.49 – 5.41 (m, 1H), 4.52 (s, 2H), 3.66 – 3.63 (m, 1H), 3.50 (d, *J* = 6.3 Hz, 2H), 2.26 – 2.21 (m, 2H), 1.65 (d, *J* = 6.6 Hz, 3H), 1.57 – 1.44 (m, 4H), 1.31 – 1.25 (m, 2H);

^{13}C NMR (75.4 MHz, $CDCl_3$) δ 138.6, 128.4, 127.6, 127.5, 127.2, 126.2, 72.9, 71.4, 70.3, 36.6, 35.0, 29.7, 22.4, 13.0;

FTIR (neat): 3414, 3026, 2932, 2858, 1720, 1452, 1364, 1101, 1028, 939, 735, 698 cm^{-1};

HRMS (EI) Calcd for $C_{16}H_{24}O_2$ [M^+]: 248.1776, found 248.1770.

The enantiomeric excess and the *E*/*Z* selectivity were determined by HPLC analysis employing a Daicel Chiracel OD followed by a Daicel Chiracel ODH column (Hexane: i-propanol 99:1, 1.0 mL/min): t_1 = 20.80, t_2 = 21.68 and t_3 = 22.31 min.



(*S*,2*Z*,8*Z*)-undeca-2,8-dien-5-ol

(>99 %*ee*, 84% *Z*)

Colorless oil (42 mg, 83 %);

R_f = 0.35 (8:1 hexane/ethyl acetate);

[(]D25 = - 7.4 º (1.00, CH2Cl2);

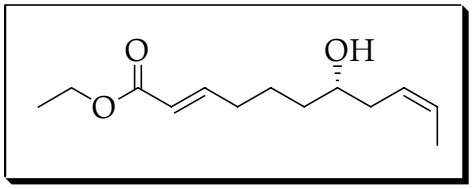
1H NMR (300 MHz, CDCl3): δ 5.67 – 5.59 (m, 1H), 5.47 – 5.33 (m, 3H), 3.67 – 3.61 (m, 1H), 2.24 (dd, *J* = 6.6, 6.2 Hz, 2H), 2.16 (m, 2H), 2.06 (m, 2H), 1.63 (d, *J* = 6.6 Hz, 3H), 1.52 (m, 2H), 0.96 (t, *J* = 7.5 Hz, 3H);

^{13}C NMR (75.4 MHz, $CDCl_3$) δ 132.3, 128.6, 127.2, 126.1, 71.2, 36.7, 35.0, 23.6, 20.5, 14.3, 13.0;

FTIR (neat): 3399, 3007, 2963, 2930, 1653, 1449, 1373, 1305, 1163, 968, 866, 706 cm^{-1};

HRMS (EI) Calcd for $C_{11}H_{20}O$ [M^+]: 168.1517, found 168.1507.

Product was derivatized with *R*-(+)-α-trifluoromethyl-α-methoxy-phenylacetic acid (Mosher acid) before the enantiomeric excess and the *E*/*Z* selectivity were determined by HPLC analysis employing a Daicel Chiracel AD column (Hexane: i-propanol 99.5:0.5, 0.5 mL/min): t_1 = 8.00 and t_2 = 10.99 min.



(*S*,2*E*,9*Z*)-ethyl 7-hydroxyundeca-2,9-dienoate

(98 %*ee*, 99% *Z*)

Light yellow oil (42 mg, 66 %);

R_f = 0.21 (4:1 hexane/ethyl acetate);

[(]D25 = - 1.3 o (1.00, CH2Cl2);

1H NMR (300 MHz, CDCl3): δ 6.95 (dt, J = 15.7, 7.0 Hz, 1H), 5.82 (dt, , J = 15.7, 1.7 Hz, 1H), 5.66 (ddq, J = 10.8, 7.0, 1.4 Hz, 1H), 5.43 (dtq, J = 10.8, 7.3, 1.7 Hz, 1H), 4.18 (q, J = 7.3 Hz, 2H), 3.68 – 3.60 (m, 1H), 2.24 – 2.20 (m, 4H), 1.64 (dd, , J = 6.9, 0.7 Hz, 3H), 1.53 – 1.45 (m, 4H), 1.28 (t, J = 7.3 Hz, 3H);

^{13}C NMR (75.4 MHz, $CDCl_3$) δ 166.8, 149.0, 127.7, 125.9, 121.6, 71.2, 60.2, 36.2, 35.1, 32.2, 24.3, 14.3, 13.1;

FTIR (neat): 3431, 2980, 2934, 2863, 1718, 1653, 1446, 1369, 1270, 1189, 1042, 984, 859, 706 cm^{-1};

HRMS (EI) Calcd for $C_{13}H_{22}O_3$ [M^+]: 226.1569, found 226.1568.

Product was derivatized with Mosher acid before the *ee* and the *E*/*Z* selectivity were determined by HPLC analysis employing a Daicel Chiracel ODH column (Hexane: i-propanol 99:1, 0.5 mL/min): t_1 = 13.58, t_2 = 15.01 and t_3 = 18.55 min.