Efficient Enantioselective Reduction of Ketones with *Daucus carota* Root

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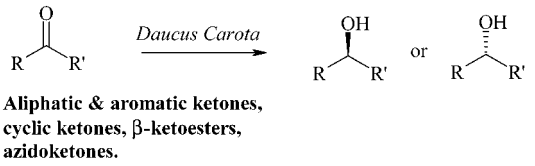
Abstract: A novel and efficient reduction of various prochiral ketones such as acetopehones, α-azido aryl ketones, *β*-ketoesters, and aliphatic acyclic and cyclic ketones to the corresponding optically acive secondary alcohols with moderate to excellent chemical yield was achieved by using *Daucus carota*, root plant cells under extremely mild and environmentally benign conditions in aqueous medium, has been described. Many of these optically active alcohols are the potential chiral building blocks for the synthesis of pharmaceutically important molecules and asymmetric chiral ligands. Hence, this biocatalytic approach is found to be the most suitable for the preparation of a wide range of chiral alcohols and gave inspiration for the development of a new biotechnological process.

In recent years, a great amount of attention has been paid to asymmetric synthesis of chiral synthons, the demand for which is increasing as precursors in the development of modern drugs and agrochemicals. Chiral alcohols are one of the many well-known synthons and can be obtained from the corresponding prochiral ketones by asymmetric reduction. Though numerous chemical[1] and biocatalytic[2] reductions are reported in the literature, difficulties still remain in attaining high chemical and optical yield. Asymmetric reduction by means of chemical methods involves the use of expensive chiral reagents, and environmentally hazardous heavy metals are often employed.[3] On the contrary, baker's yeast is by far the most widely used microorganism for the reduction of prochiral ketones yielding the corresponding optically active alcohols with fair to excellent enantioselectivity; unfortunately,[4] recovery of the desired product might not be straightforward. In baker's yeast, sometimes reduction of carbonyl compounds is carried out by enzymes requiring costly cofactors (NADH, NADPH); thus, one condition of their activity is the regeneration of oxidized cofactors. The use of plant cells in biotechnology has been steadily increasing over the past decade.[5] Biotransformations of organic xenobiotics, e.g., ethyl-3-oxobutanoate and acetophenone by immobilized plant cell cultures of carrot[6] have been investigated. Recently, Baldassarre et al.,[7] first reported the use of whole plant cell, e.g., carrot root for the asymmetric reduction of prochiral ketones.

Scheme 1



Herein, we describe for the first time our systematic and well-defined investigation of the reduction of some prochiral ketones with *Daucus carota* root.

We have performed the chiral reduction of various compounds containing the keto functionality, e.g., acetophenones, cyclic ketones, *β*-ketoesters, azidoketones, and aliphatic ketones (Scheme 1). The reduction products in all the cases lead to valuable chiral intermediates, which can be further employed in the total synthesis of various chiral drugs and agrochemicals. The general feature of these reductions is, for most cases, well documented by Prelog's rule, which predicts that hydrogen transfer to the prochiral ketone always occurs from the *Re*-face,[8a] where L represents a large substituent and S a small substituent adjacent to the carbonyl group (Scheme 2) to yield chiral alcohols. But as Sih[8b] pointed out one should exercise considerable caution when Prelog's rule is applied to intact cell systems.

(a) Reduction of Acetophenones. Acetophenone and substituted acetophenones underwent the reduction in a well-defined fashion. Several substituted acetophenones were subjected to the reduction protocol (Table 1). In almost all the cases, the reduction was completed within 40−50 h. Excellent chemical (70−80%) and optical purity (>90%) was observed. The product alcohol had *S* configuration, which is in perfect agreement with Prelog's rule.

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Scheme 2

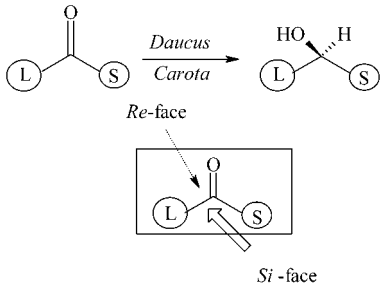

Table 1. Reduction of Acetophenones with *Daucas carota* Root

entry	compd	time of conversion (h)	yield (%)	ee (%)	config
1	acetophenone	40	73	92	*S*
2	*p*-chloroacetophenone	42	76	95	*S*
3	*p*-bromoacetophenone	48	61	95	*S*
4	*p*-fluoroacetophenone	41	80	90	*S*
5	*p*-nitroacetophenone	40	82	96	*S*
6	*p*-methylacetophenone	50	75	92	*S*
7	*p*-methoxyacetophenone	45	72	94	*S*
8	*p*-hydroxyacetophenone	47	73	91	*S*
9	1-(2-naphthyl)-1-ethanone	49	70	97	*S*
10	1-(6-methoxy-2-naphthyl)-1-ethanone	42	78	98	*S*
11	1-(2-furyl)-1-ethanone	50	65	92	*S*

Table 2. Reduction of Cyclic Ketones with *D. carota* Root

entry	compd	time of conversion (h)	yield (%)	ee (%)	config
12	1-tetralone	70	52	96	*S*
13	2-tetralone	72	58	95	*S*
14	6-methoxy-1-tetralone	69	60	93	*S*
15	1-indanone	78	57	98	*S*

It was observed that the presence of electron-donating substituents in the aromatic ring (−Me, −OMe) slows down the reaction rate. No influence on the steric course of the reduction was observed. When compared to our observation with fermentative reduction (yeast) of substituted acetophenones, (*S*)-1-arylethanols were obtained in low to moderate yields and ee values between 82% and 96%.[9]

(b) Reduction of Cyclic Alkanones. Different substituted tetralones and indanone were reduced efficiently with *D. carota* root. The reduction was completed within 70−80 h (Table 2) as determined by GC. The absolute configuration of the product alcohol was (*S*), as predicted by Prelog's rule. The enantioselectivity was >95% in all the cases as determined by chiral HPLC.

(c) Reduction of *β*-Ketoesters. Reduction of *β*-ketoesters is probably the most extensively studied small-molecule microbial transformation leading to chiral intermediates in asymmetric synthesis. Recently, some discrepancies regarding the ee and chemical yield[10] have been reported for the yeast-mediated reduction of *β*-ketoesters. When we employed *D. carota* root as the biocatalyst, completed reduction was effected within 55−70 h, yielding the products in high chemical and optical yield (Table 3). Furthermore, the need for costly cofactor recycling was avoided since the whole cell automatically does it. The enantioselectivity of the reduction products for the cyclic *β*-ketoesters are higher than that of open chain *β*-ketoesters.

Table 3. Reduction of *β*-Ketoesters with *D. carota* Root

entry	compd	time of conversion (h)	yield (%)	ee (%)	config
16	ethyl acetoacetate	58	58	95	*S*
17	ethyl 4-chloro-3-oxobutanoate	60	50	90	*S*
18	ethyl 4-bromo-3-oxobutanoate	62	53	95	*S*
19	ethyl 4-azido-3-oxobutanoate	65	68	90	*R*
20	ethyl 3-oxo-3-phenyl-propanoate	56	62	98	*S*
21	ethyl 4,4,4-trichloro-3-oxo-butanoate	70	51	88	*S*
22	ethyl 4,4,4-trifluoro-3-oxo-butanoate	56	72	78	*R*
23	ethyl 3-oxo-4-phenylsulfonyl-butanoate	66	70	98	*R*
24	ethyl 2-oxo-1-cyclopentane-carboxylate	60	60	97	1*R*,2*S*
25	ethyl 2-oxo-1-cyclohexane-carboxylate	62	63	98	1*R*,2*S*

When two racemic *β*-ketoesters (**24** and **25**) were treated with carrot root, the (*R*)-isomer was reduced faster than the (*S*)-enantiomer (the two esters are in equilibrium under the reaction conditions), and the hydrogen transfer took place preferentially from the diastereotopic *Re*-face yielding (1*R*,2*S*) product with high enantioselection. For compounds **24** and **25**, the erythro isomer was obtained as the major one due to equilibrium by enolization (with concomitant racemization) of the educt followed by kinetic resolution.[2a] A possible coordination through hydrogen bonded interaction between the hydroxyl group and the carbonyl oxygen of the carboethoxy group also cannot be ruled out.

The general stereochemical feature of the reaction is, for most cases, well explained by Prelog's rule. However, it was established that the absolute configuration and the optical purity of the products depend strongly upon both the nature and the size of the substituents adjacent to the carbonyl group and that of the ester moiety. For compounds **19**, **22**, and **23**, the opposite stereochemistry was observed as predicted by Prelog's rule. The absolute configuration of the reduced product (CF_3-ester, **22**) was (*R*); thus, the hydride transfer to the keto group has taken place from the *Si*-face. This is the opposite steric course as compared with CCl_3-ester (**21**), which is reduced from the *Re*-face. It was assumed that CCl_3 group is sterically more demanding than the CF_3 group. For compounds **19** and **23**, the configuration of final reduced product alcohols were (*R*), which suggests that hydride transfer occurs from the *Si*-face. It was concluded that, like yeast, *D. carota* produces several enzymes, which are able to distinguish between, in an enantiomeric way, small and large groups; thus, hydrogen is delivered from both the *Re*- and *Si*-faces.

(d) Reduction of Azidoketones. In our continuing interest for the synthesis of chiral azido alcohols[11] that

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Table 4. Reduction of Azidoketones with *D. carota* Root

entry	compd	time of conversion (h)	yield (%)	ee (%)	config
26	2-azido-1-phenyl-1-ethanone	42	70	100	*R*
27	2-azido-1-(4-chlorophenyl)-1-ethanone	40	72	98	*R*
28	2-azido-1-(4-methylphenyl)-1-ethanone	58	71	98	*R*
29	2-azido-1-(4-methoxyphenyl-1-ethanone	78	58	99	*R*
30	2-azido-1-(4-fluorophenyl)-1-ethanone	60	65	95	*R*
31	2-azido-1-(4-bromophenyl)-1-ethanone	66	77	97	*R*
32	2-azido-(4-*tert*-butyldimethyl-silyloxyphenyl)-1-ethanone	78	62	99	*R*
33	2-azido-1-(2-furyl)-1-ethanone	52	69	92	*S*
34	2-azido-1-(2-thienyl)-1-ethanone	69	58	94	*S*
35	2-azido-1-(2-naphthyl)-1-ethanone	70	49	93	*R*

Table 5. Reduction of Open-Chain Ketones with *D. carota* Root

entry	compd	time of conversion (h)	yield (%)	ee (%)	config
36	2-butanone	80	38	87	*S*
37	2-pentanone	88	49	82	*S*
38	2-hexanone	85	50	90	*S*
39	4-methyl-2-pentanone	90	32	71	*S*
40	3,3-dimethyl-2-butanone	102	49	75	*S*
41	2-heptanone	86	30	92	*S*

can be effectively employed in the total synthesis of various drugs, we have investigated the reduction of different substituted azidoketones with *D. carota* root. All the azido ketones investigated were efficiently reduced with carrot root. The reaction was completed within 40−78 h (Table 4). Both the chemical yield and the optical purity of the product azido alcohols were excellent. No influence on the steric course of the reduction was observed when the substituents were changed, but the velocity of the reaction was decreased by electron-donating substituents. Though high chemical yield and low conversion time was reported for the reduction of azidoketones with baker's yeast in our earlier communication, [11b] it is noteworthy to mention that sometimes isolation of the desired product is intrinsically messy, as the aqueous media contains the cellular mass, nutrients, usual metabolites, and the azidoketones.

(e) Reduction of Aliphatic Ketones. It is difficult to obtain pure simple aliphatic secondary alcohols by the reduction of corresponding ketones by chemical methods despite their utility as chiral building blocks. Our investigation demonstrated that the open-chain aliphatic ketones can be reduced with *D. carota* root used as a biocatalyst. The reduction time was usually longer for these classes of compounds (Table 5). The chemical yield of the products are often lower (30−50%) when compared to the other ketones, as the product alcohols easily evaporated during the purification process due to their low boiling point. The absolute configuration of the product alcohol was (*S*), which indicates the addition of hydrogen follows the Prelog's rule. Simple aliphatic ketones were reduced by bakers' yeast predominantly to the (*S*)-configured alcohols, often with high ee, but poorer yield (15−35%) was observed when compared with our findings.

Table 6. Reduction of Ketones on a Preparative Scale

substrate	isolated yield (%)	substrate/carrot (w/w)	ee (%)	config
acetophenone	75	1/100	90	*S*
tetralone	68	1/100	95	*S*
ethyl acetoacetate	65	1/100	92	*S*
2-azido-1-phenyl-1-ethanone	40	1/100	94	*R*
2-hexanone	25	1/100	90	*S*

Preparative Scale Reduction. Since several ketones afforded high enantioselectivities for the reduction on a small scale, it was decided to conduct the transformations on a large scale to demonstrate the viability of this protocol as industrially feasible. The isolated yields and ee's of the products are summarized in Table 6.

We have also performed the reduction of some ketones with *D. carota* root in an aqueous−organic biphasic reaction system. Common organic solvents, which are immiscible with water, were investigated, e.g., ethyl acetate, hexane, and cyclohexane. It was observed that a significant amount of substrate was unconverted, leading to a decrease in the yield of reduced product. The propensity of organic solvents to cause serious damages to microbial cells probably contributed to this decreased reaction rate.[12] They may destroy the lipid layer and other structures of microbial cells and diminish their activities of reduction.

In summation, we have described an ecofriendly and environmental benign asymmetric reduction system employing *D. carota* root as a biocatalyst. The main advantages of this reduction over the traditional yeast-mediated reductions are easy isolation of the product, elimination of the need of costly cofactor, and its recycling, easy availability, and cheapness of the carrot root. Further studies are in progress in order to obtain chiral alcohols on an industrial scale by increasing the substrate−catalyst contact surface area and by changing other parameters such as pH, temperature and different carrot cultivar.

Experimental Section

Experimental Details. All the ketones were obtained from commercial suppliers. Carrots were obtained from a local market. To increase the contact of the substrate with the biocatalyst, the external layer was removed and the rest was carefully cut into small thin pieces (approximately 1 cm long slice). Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm silica gel plates with UV light and 2.5% ethanolic anisaldehyde (with 1% AcOH and 3% concentrated H_2SO_4)−heat as developing agents. Silica gel 100−200 mesh was used for column chromatography. Yields refer to chromatographically and spectroscopically homogeneous materials unless otherwise stated. NMR spectra were recorded on 200 MHz spectrometers at room temperature in $CDCl_3$ using tetramethylsilane as internal standard, and the chemical shifts are reported in δ. ^{13}C NMR spectra were recorded with a complete proton-decoupling instrument. Optical purity of all the compounds (ee) was determined from chiral HPLC analysis as well as measuring the optical rotations and comparing with literature values. Solvents for HPLC use were spectrometric grade. The column was 4.6 × 250 nm, Chiralcel OD column (Daicel). The eluents were hexane-2-propanol (HPLC grade, 85:15) at 0.5 mL per min flow rate and monitored at 254 nm wavelength.

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Reduction of Ketones with *D. carota* Root. Ketones (100 mg) were added to a suspension of freshly cut carrot root (10 g) in 70 mL of water, and the reaction mixtures were incubated in an orbital shaker (150 rpm) at room temperature for the time necessary to obtain the appropriate conversion. Finally, the suspension was then filtered off, and carrot root was washed three times with water. Filtrates were extracted with EtOAc (3 × 125 mL). The organic phase was dried (Na_2SO_4) and then evaporated in a vacuum. The final products were purified by flash chromatography. If the ketone was solid, ethanolic solution was added to the carrot root. For the preparative-scale reduction ketones (1 g) were taken in a 2 L conical flask. Water (700 mL) was added to it followed by addition of freshly cut carrot (100 g). The reaction mixture was stirred in an incubator shaker for the required time. After that the product alcohol was isolated as described before. It is important to note that the reaction container should be large enough for efficient agitation.

Recycling of the *D. carota* Root. After completion of the reduction, the reaction mixture was filtered and the carrot roots were washed successively with water and then kept in distilled water at 0 °C for 3 days. After that, water was decanted and the carrot roots were wiped with soft tissue paper to remove the remaining water. These roots were again used for another reduction reaction. It was observed that the activity of the roots was decreased significantly. Only 20% conversion was achieved for acetophenone after 10 days incubation. So it was concluded that the whole cell loses its activity significantly after one reduction reaction.

Spectral Data for the Compounds. 1-Phenyl-(1*S*)-ethan-1-ol (1): $[\alpha]^{25}_D = -39.1$ ($c = 3.5$, MeOH) (lit.[13] ($[\alpha]_D$, NMR identical)).

1-(4-Chlorophenyl)-(1*S*)-ethan-1-ol (2): $[\alpha]^{25}_D = -41.2$ ($c = 2.5$, $CHCl_3$) (lit.[14] ($[\alpha]_D$, NMR identical)).

1-(4-Bromophenyl)-(1*S*)-ethan-1-ol (3): $[\alpha]^{25}_D = -25.6$ ($c = 3.4$, $CHCl_3$) (lit.[14] ($[\alpha]_D$, NMR identical)).

1-(4-Fluorophenyl)-(1*S*)-ethan-1-ol (4): $[\alpha]^{25}_D = -35.0$ ($c = 9.2$, $CHCl_3$) (lit.[14] ($[\alpha]_D$, NMR identical)).

1-(4-Nitrophenyl)-(1*S*)-ethan-1-ol (5): $[\alpha]^{25}_D = -30.5$ ($c = 4.0$, $CHCl_3$) (lit.[14] ($[\alpha]_D$, NMR identical)).

1-(4-Methylphenyl)-(1*S*)-ethan-1-ol (6): $[\alpha]^{25}_D = -21.0$ ($c = 1.5$, $CHCl_3$) (lit.[13] ($[\alpha]_D$, NMR identical)).

1-(4-Methoxylphenyl)-(1*S*)-ethan-1-ol (7): $[\alpha]^{25}_D = -30.0$ ($c = 1.75$, $CHCl_3$) (lit.[13] ($[\alpha]_D$, NMR identical)).

1-(4-Hydroxyphenyl)-(1*S*)-ethan-1-ol (8): $[\alpha]^{25}_D = -47.5$ ($c = 4.2$, EtOH) (lit.[16] ($[\alpha]_D$, NMR identical)).

1-(2-Naphthyl)-(1*S*)-ethan-1-ol (9): $[\alpha]^{25}_D = -31.0$ ($c = 3.5$, MeOH) (lit.[15] ($[\alpha]_D$, NMR identical)).

1-(6-Methoxy-2-naphthyl)-(1*S*)-ethan-1-ol (10): $[\alpha]^{25}_D = -41.8$ ($c = 1.5$, $CHCl_3$) (lit.[17] ($[\alpha]_D$, NMR identical)).

1-(2-Furyl)-(1*S*)-ethan-1-ol (11): $[\alpha]^{25}_D = -19.2$ ($c = 3.0$, MeOH) (lit.[15] ($[\alpha]_D$, NMR identical)).

(1*S*)-1,2,3,4-Tetrahydro-1-naphthalenol (12): $[\alpha]^{25}_D = 24.5$ ($c = 1.2$, $CHCl_3$) (lit.[13] ($[\alpha]_D$, NMR identical)).

(2*S*)-1,2,3,4-Tetrahydro-2-naphthalenol (13): $[\alpha]^{25}_D = -58.2$ ($c = 1.5$, EtOH) (lit.[18] ($[\alpha]_D$, NMR identical)).

6-Methoxy-(1*S*)-1,2,3,4-tetrahydro-1-naphthalenol (14): ^{1}H NMR 7.15 (m, 1H), 7.0 (m, 1H), 6.8 (m, 1H), 4.7 (m, 1H), 3.8 (s, 3H), 2.7 (m, 1H), 2.5 (m, 1H), 2.0 (m, 4H); $[\alpha]^{25}_D = +10.1$ ($c = 1.75$, $CHCl_3$).

(1*S*)-2,3-Dihydro-1*H*-1-indenol (15): $[\alpha]^{25}_D = 29.8$ ($c = 2.0$, $CHCl_3$) (lit.[13] ($[\alpha]_D$, NMR identical)).

Ethyl 3-hydroxy- (3*S*)-butanoate (16): $[\alpha]^{25}_D = 32.8$ ($c = 3.0$, $CHCl_3$) (lit.[19] ($[\alpha]_D$, NMR identical)).

Ethyl 4-chloro-3-hydroxy-(3*S*)-butanoate (17): $[\alpha]^{25}_D = -19.9$ ($c = 3.8$, $CHCl_3$) (lit.[20] ($[\alpha]_D$, NMR identical)).

Ethyl 4-bromo-3-hydroxy-(3*S*)-butanoate (18): $[\alpha]^{25}_D = -10.1$ ($c = 2.0$, EtOH) (lit.[20] ($[\alpha]_D$, NMR identical)).

Ethyl 4-azido-3-hydroxy-(3*R*)-butanoate (19): $[\alpha]^{25}_D = -16.8$ ($c = 1.8$, H_2O) (lit.[20] ($[\alpha]_D$, NMR identical)).

Ethyl 3-hydroxy-(3*S*)-3-phenylpropanoate (20): $[\alpha]^{25}_D = -7.2$ ($c = 3.0$, $CHCl_3$) (lit.[21] ($[\alpha]_D$, NMR identical)).

Ethyl 4,4,4-trichloro-3-hydroxy-(3*S*)-butanoate (21): $[\alpha]^{25}_D = -18.3$ ($c = 1.1$, $CHCl_3$) (lit.[22] ($[\alpha]$, NMR identical)).

Ethyl 4,4,4-trifluoro-3-hydroxy-(3*R*)-butanoate (22): $[\alpha]^{25}_D = 21.1$ ($c = 0.9$, MeOH) (lit.[22] ($[\alpha]_D$, NMR identical)).

Ethyl 3-hydroxy-4-phenylsulfonyl-(3*R*)-butanoate (23): $[\alpha]^{25}_D = -21.0$ ($c = 1.5$, $CHCl_3$) (lit.[23] ($[\alpha]_D$, NMR identical)).

Ethyl 2-hydroxy-(1*R*,2*S*)-cyclopentane-1-carboxylate (24): $[\alpha]^{25}_D = 15.0$ ($c = 2.8$, $CHCl_3$) (lit.[24] ($[\alpha]_D$, NMR identical)).

Ethyl 2-hydroxy-(1*R*,2*S*)-cyclohexane-1-carboxylate (25): $[\alpha]^{25}_D = 28.9$ ($c = 10.5$, $CHCl_3$) (lit.[24] ($[\alpha]_D$, NMR identical)).

2-Azido-1-phenyl-(1*R*)-ethan-1-ol (26): $[\alpha]^{25}_D = -80.0$ ($c = 1.0$, $CHCl_3$) (lit.[11b] ($[\alpha]_D$, NMR identical)).

2-Azido-1-(4-chlorophenyl-(1*R*)-ethan-1-ol (27): $[\alpha]^{25}_D = -79.0$ ($c = 1.25$, $CHCl_3$) (lit.[11b] ($[\alpha]_D$, NMR identical)).

2-Azido-1-(4-methylphenyl-(1*R*)-ethan-1-ol (28): $[\alpha]^{25}_D = -28.9$ ($c = 1.5$, $CHCl_3$) (lit.[11b] ($[\alpha]_D$, NMR identical)).

2-Azido-1-(4-methoxyphenyl-(1*R*)-ethan-1-ol (29): $[\alpha]^{25}_D = -39.0$ ($c = 1.2$, $CHCl_3$) (lit.[11b] ($[\alpha]_D$, NMR identical)).

2-Azido-1-(4-fluorophenyl-(1*R*)-ethan-1-ol (30): $[\alpha]^{25}_D = -14.5$ ($c = 2.0$, $CHCl_3$) (lit.[11b] ($[\alpha]_D$, NMR identical)).

2-Azido-1-(4-bromophenyl-(1*R*)-ethan-1-ol (31): $[\alpha]^{25}_D = -35.9$ ($c = 1.0$, $CHCl_3$) (lit.[11b] ($[\alpha]_D$, NMR identical)).

2-Azido-(4-*tert*-butyldimethylsilyloxyphenyl)-(1*R*)-ethan-1-ol (32): ^{1}H NMR 7.25 (d, $J = 7.2$ Hz, 2H), 6.85 (d, $J = 7.2$ Hz, 2H), 4.80 (m, 1H), 3.40 (m, 2H), 2.35 (brs, 1H), 1.0 (s, 9H), 0.2 (s, 6H); ^{13}C NMR −4.46, 25.62, 58.1, 73.09, 120.24, 127.0, 127.1, 133.1; $[\alpha]^{25}_D = -59.2$ ($c = 1.0$, $CHCl_3$).

2-Azido-1-(2-furyl)-(1*S*)-ethan-1-ol (33): $[\alpha]^{25}_D = -28.9$ ($c = 2.0$, $CHCl_3$) (lit.[11b] ($[\alpha]_D$, NMR identical)).

2-Azido-1-(2-thienyl)-(1*S*)-ethan-1-ol (34): $[\alpha]^{25}_D = -34.6$ ($c = 1.5$, $CHCl_3$) (lit.[11b] ($[\alpha]_D$, NMR identical)).

2-Azido-1-(2-naphthyl)-(1*R*)-ethan-1-ol (35): $[\alpha]^{25}_D = -79.5$ ($c = 0.5$, $CHCl_3$) (lit.[11b] ($[\alpha]_D$, NMR identical)).

(2*S*)-Butan-2-ol (36): $[\alpha]^{25}_D = 13.1$ ($c = 6.0$, MeOH) (lit.[25] ($[\alpha]_D$, NMR identical)).

(2*S*)-Pentan-2-ol (37): $[\alpha]^{25}_D = 14.0$ (neat) (lit.[26] ($[\alpha]_D$, NMR identical)).

(2*S*)-Hexan-2-ol (38): $[\alpha]^{25}_D = 10.4$ (neat) (lit.[27] ($[\alpha]_D$, NMR identical)).

1,3-Dimethyl-(1*S*)-butyl alcohol (39): $[\alpha]^{25}_D = 19.5$ ($c = 3.5$, MeOH) (lit.[28] ($[\alpha]_D$, NMR identical)).

1,2,2-Trimethyl-(1*S*)-propyl alcohol (40): $[\alpha]^{25}_D = 18.5$ (neat) (lit.[17] ($[\alpha]_D$, NMR identical)).

(2*S*)-Heptan-2-ol (41): $[\alpha]^{25}_D = 10.1$ (neat) (lit.[15] ($[\alpha]_D$, NMR identical)).

Supporting Information Available: NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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