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Highly Diastereoselective Reduction of Enantiomerically Pure Aziridino Ketones

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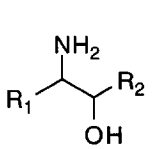
Abstract: Various enantiomerically pure aziridino ketones were prepared from the corresponding secondary alcohols by Swern oxidation. Those configurationally stable α-amino ketones were stereoselectively reduced by L-Selectride® to provide the corresponding alcohol with high diastereoselectivities and chemical yields.

The 1,2-amino alcohols **1** can be found in many important natural products and also biologically active compounds. In this context the preparation of diastereo- and enantiomerically pure 1,2-amino alcohols is becoming increasingly important area.[1-21]



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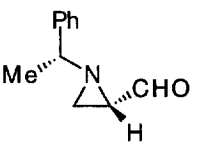

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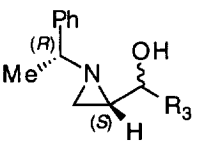
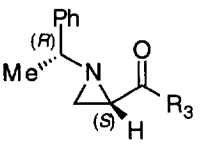


3 (*S,S*)
4 (*S,R*)



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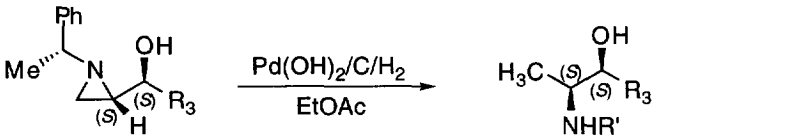
Conceptually, some of 1,2-amino alcohols can be obtained by regioselective reductive ring opening of 2-aziridine methanols **3** or **4**. We recently reported regiospecific reductive ring cleavages of enantiomerically pure *N*-(*R*)-(+)-α-methylbenzyl-2-aziridine methanols by catalytic hydrogenation.[22] We also found that *N*-(*R*)-(+)-methylbenzylaziridine-2(*S*)-carboxaldehyde **2** that was prepared from the corresponding alcohol is configurationally stable due to high inversion barrier of the strained ring system. The configurational stability of the similar system was reported by Seebach.[23] Organometallic additions to the α-amino aldehyde **2** provided diastereomeric mixtures of aziridine alcohols, **3** and **4**, which were readily separable by flash column chromatography. The C(3)-*N* bond of the aziridine ring of **3** and **4** was also regioselectively reduced by

catalytic hydrogenation in the presence of 10wt% of the Pearlman's catalyst to yield various enantiomerically pure 1,2-amino alcohols **6** (Scheme 1).



3 **6**

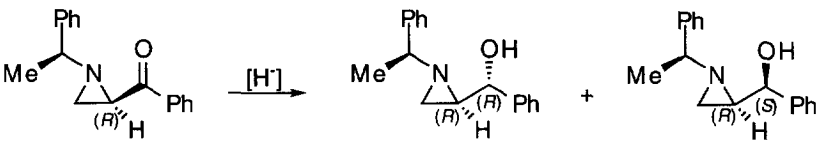
R' = (*R*)-(+)-α-methylbenzyl

R_3 = alkyl or aryl

Scheme 1

The diastereoselectivities in the addition reaction of organometallic reagents to the enantiomerically pure aziridine-2(*S*)-carboxaldehyde **2** varies from (1:1) to (32:1) depending on the reaction conditions. The diastereoselectivities are influenced by the source of the organometallic reagent, reaction solvent, and the presence of extra lithium salt in the reaction media.[24]

As a continuing effort to increase the diastereoselectivity in the organometallic addition reaction to the aldehyde **2** we varied the reaction conditions to obtain high stereoselectivity for the bulky nucleophiles.



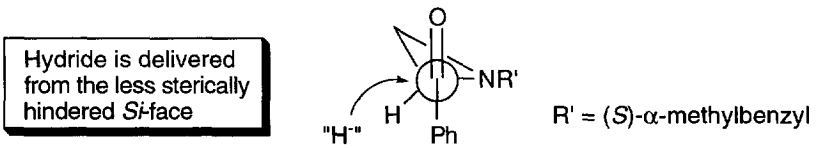
7e **8e** **9e**

Hydride Source	Solvent	Diastereomer Ratio (**8e** : **9e**)
$NaBH_4$	Ethanol	2 : 1
L-Selectride®	THF	>99 : <1
DIBAL	Toluene	2 : 1
DIBAL	Dichloromethane	1 : 1
$LiAlH_4$	THF	2 : 1
$LiAlH_4$	Ether	1 : 4
$Na[Et_2AlH_2]$	THF/Toluene	1 : 1

Scheme 2

However, we found a better route to increase the diastereomeric ratio of the addition products by oxidation of the diastereomeric mixture **3** and **4** to the corresponding ketone **5** and reduction of the ketone with a suitable hydride reducing agent. We prepared the ketone **7** that is the enantiomeric pair of the ketone **5** by the same procedure we reported[24] and studied the reduction characteristics of the compound.

The phenyl ketone **7e** was prepared from the mixture of the corresponding secondary alcohols by Swern oxidation[25] in 83% yield and the ketone was reduced by various hydride reducing agents. The reduction of the ketone showed that L-Selectride® provided the best selectivity (>99:<1) and 97% chemical yield. Most other reducing agents gave no selectivity or low stereoselectivity. The excellent stereochemical control of L-Selectride® can be explained by hydride delivery through the "Felkin-Anh" transition state (Scheme 2).[26-29]



On the basis of the above results we prepared various aziridino ketones **7(a-j)** from the corresponding secondary alcohols and reduced them with L-Selectride® in THF to obtain excellent diastereoselectivities and high chemical yields (Table 1).

Table 1. The Results of L-Selectride® Reduction of Various Ketones.

Entry	Ketone **7** R_3	Diastereomer Ratio **8** : **9**	yield (% isolated)
a	Methyl	>99 : <1	95
b	*tert*-Butyl	>99 : <1	99
c	*n*-Butyl	>99 : <1	98
d	1-Hexynyl	4 : 1	95
e	Phenyl	>99 : <1	97
f	3-Methylphenyl	>99 : <1	96
g	2-Methoxyphenyl	5 : 1	99
h	4-Chlorophenyl	26 : 1	93
i	4-Fluorophenyl	>99 : <1	97
j*	2-Thiazolyl	>99 : <1	93

***8j** and **9j** are inseparable by chromatography but the reduction of **7j** provides only **8j**.

Most of the substrates provide high stereoselectivity except for 1-hexynyl ketone **7d** that does not have enough steric requirement due to the geometry of the triple bond at the α-position of the ketone. However, we do not have a clear explanation on the low selectivity from **7g** at this moment.

We recently reported the efficient preparation of ephedra alkaloid analogs using regioselective reductive ring opening of aziridines. With this highly selective reduction of the aziridino ketones, we can prepare a variety of optically active 1,2-amino alcohols diastereoselectively. We are currently investigating the synthetic utility of this methodology for the preparation of biologically active compounds.

Experimental

General: ^{1}H-NMR and ^{13}C-NMR spectra were recorded on Varian Gemini-200 or 300 instruments using $CDCl_3$ as solvent and chemical shifts (d) are related to tetramethylsilane. Elemental analyses were determined by Carlo Erba EA 1180 elemental analyzer. Optical rotations were obtained on a Rudolph Autopol III digital polarimeter. The reactions involving organometallic reagents were carried out under inert atmosphere in dry THF. Tetrahydrofuran and diethyl ether were distilled from sodium-benzophenone ketyl at atmospheric pressure immediately before use. Methylene chloride and DMSO were distilled from calcium hydride prior to use.

The preparations of aziridino secondary alcohols **8(b, e, h, i)** and **9(b, e, h, i)** were previously reported.[24]

Representative procedure of oxidation of a secondary alcohol to the corresponding ketone. Preparation of (2*R*)-2-N-[(*S*)-α-methylbenzyl]aziridinyl methyl ketone 7a. To a solution of oxalyl chloride (0.17 mL, 1.96 mmol) in 2.6 mL of CH_2Cl_2 under a nitrogen at -78 °C was added DMSO (0.19 mL, 2.61 mmol). The solution was stirred for 5 min at -78 °C and was treated with a solution of a mixture of **8a** and **9a** (247 mg, 1.31 mmol) in 2 mL of CH_2Cl_2. The mixture was stirred for 30 min at -78 °C and was treated with Et_3N (0.73 mL, 5.22 mmol) at -78 °C. The mixture was stirred for 15 min and warmed to room temperature. To the mixture was added 4.0 mL of water and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (4 mL x 5) and the combined organic extracts were dried, filtered, and concentrated *in vacuo*. Purification by silica gel flash chromatography (EtOAc / hexane, 30:70) provided 222 mg of **7a** (91%) as a colorless oil. **7a**: $[\alpha]^{27}_D$ = +53.1° (*c* 1.40, $CHCl_3$), ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.32-7.23 (m, 5H), 2.55 (q, *J*=6.2 Hz, 1H), 2.28 (d, *J*=2.9 Hz, 1H), 2.11 (dd, *J*=6.6, 2.7 Hz, 1H), 2.02 (s, 3H), 1.81 (d, *J*=6.8 Hz, 1H), 1.43 (d, *J*=6.6 Hz, 3H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 207.4, 144.1, 128.6, 127.4, 126.6, 69.7, 44.5, 35.0, 25.3, 23.3. Anal. Calcd for $C_{12}H_{15}NO$: C, 76.16; H, 7.99; N, 7.40. Found: C, 76.07; H, 8.04; N, 7.34.

7b: $[\alpha]^{24}_D$ = +34.5° (*c* 1.00, $CHCl_3$); mp 60-62 °C ; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.38-7.18 (m, 5H), 2.55 (q, *J*=6.6 Hz, 1H), 2.43 (dd, *J*=6.3, 3.2 Hz, 1H), 2.34 (dd, *J*=3.1, 1.7 Hz, 1H), 1.78 (dd, *J*=6.3, 1.7 Hz, 1H),1.47 (d, *J*=6.6 Hz, 3H), 0.95 (s, 9H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 211.3, 144.2, 128.5, 127.4, 126.9, 70.7, 43.7, 37.9, 37.3, 25.4, 23.0. Anal. Calcd for $C_{15}H_{21}NO$: C, 77.88; H, 9.15; N, 6.05. Found: C, 77.73; H, 9.01; N, 6.07.

7c: $[\alpha]^{24}_D$ = +62.6° (*c* 1.00, $CHCl_3$) ; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.41-7.18 (m, 5H), 2.53 (q, *J*=6.5 Hz, 1H), 2.31 (m, 2H), 2.25 (d, *J*=2.6 Hz, 1H), 2.12 (dd, *J*=6.9, 3.2 Hz, 1H), 1.78 (d, *J*=6.6 Hz, 1H), 1.44 (d, *J*=6.6 Hz, 3H), 1.38 (m, 2H), 1.21 (sextet, *J*=7.0 Hz, 2H), 0.83 (t, *J*=7.0 Hz, 3H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 209.0, 144.1, 128.6, 127.4, 126.7, 69.9, 43.8, 38.1, 35.2, 25.3, 23.1, 22.0, 13.5. Anal. Calcd for $C_{15}H_{21}NO$: C, 77.88; H, 9.15; N, 6.05. Found: C, 77.58; H, 9.37; N, 6.21.

7d: $[\alpha]^{21}_D$ = +59.2° (*c* 0.50, $CHCl_3$); mp 113-115 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.42-7.15 (m, 5H), 2.61 (q, *J*=6.6 Hz, 1H), 2.42 (m, 1H), 2.36 (t, *J*=6.6 Hz, 2H), 2.26 (dd, *J*=6.3, 3.1 Hz, 1H), 1.86 (d, *J*=6.5 Hz, 1H), 1.67-1.30 (m, 4H), 1.44 (d, *J*=6.5 Hz, 3H), 0.92 (t, *J*=6.7 Hz, 3H). ^{13}C NMR (75.4 MHz,

$CDCl_3$) δ 185.7, 144.0, 128.5, 127.2, 126.6, 96.5, 79.3, 69.4, 45.2, 36.0, 29.4, 23.5, 21.6, 18.5, 13.2. Anal. Calcd for $C_{17}H_{21}NO$: C, 79.96; H, 8.29; N, 5.49. Found: C, 80.01; H, 8.22; N, 5.56.

7e: $[\alpha]^{28}_D$ = +22.7° (*c* 0.55, $CHCl_3$); mp 56-57 °C; ^1H NMR (200 MHz, $CDCl_3$) δ 7.69 (d, *J*=8.3 Hz, 2H), 7.52-7.21 (m, 8H), 2.88 (dd, *J*=6.4, 3.1 Hz, 1H), 2.71 (q, *J*=6.6 Hz, 1H), 2.55 (d, *J*=3.1 Hz, 1H), 1.94 (d, *J*=6.4 Hz, 1H), 1.52 (d, *J*=6.6 Hz, 3H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 196.6, 144.2, 137.0, 133.2, 128.7, 128.6, 128.4, 127.4, 126.8, 70.6, 40.2, 36.8, 23.3. Anal. Calcd for $C_{17}H_{17}NO$: C, 81.24; H, 6.82; N, 5.57. Found: C, 81.26; H, 6.85; N, 5.53.

7f: $[\alpha]^{24}_D$ = +14.0° (*c* 1.00, $CHCl_3$); mp 62-64 °C; ^1H NMR (200 MHz, $CDCl_3$) δ 7.52-7.14 (m, 9H), 2.88 (dd, *J*=6.4, 3.2 Hz, 1H), 2.68 (q, *J*=6.5 Hz, 1H), 2.56 (dd, *J*=3.2 Hz, *J*=1.4 Hz, 1H), 2.28 (s, 3H),1.93 (dd, *J*=6.4, 1.4 Hz, 1H), 1.52 (d, *J*=6.6 Hz, 3H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 196.8, 144.3, 138.4, 137.1, 134.0, 128.9, 128.7, 128.4, 127.4, 126.9, 125.5, 70.8, 40.1, 36.8, 23.4, 21.0 Anal. Calcd for $C_{18}H_{19}NO$: C, 81.48; H, 7.22; N, 5.28. Found: C, 81.44; H, 7.47; N, 5.33.

7g: $[\alpha]^{24}_D$ = -9.2° (*c* 1.00, $CHCl_3$); mp 77-79 °C; ^1H NMR (200 MHz, $CDCl_3$) δ 7.52-7.18 (m, 7H), 6.96-6.80 (m, 2H), 3.45 (s, 3H), 3.05 (dd, *J*=6.4, 3.2 Hz, 1H), 2.71 (q, *J*=6.6 Hz, 1H), 2.48 (m, 1H), 1.86 (dd, *J*=6.1, 1.3 Hz, 1H), 1.48 (d, *J*=6.7 Hz, 3H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 199.7, 158.8, 144.8, 133.6, 130.4, 128.4, 127.0, 126.7, 120.7, 111.4, 70.0, 54.9, 43.6, 37.6, 23.8. Anal. Calcd for $C_{18}H_{19}NO_2$: C, 76.84; H, 6.81; N, 4.98. Found: C, 76.63; H, 6.83; N, 5.01.

7h: $[\alpha]^{24}_D$ = +21.8° (*c* 1.00, $CHCl_3$); mp 74-76 °C; ^1H NMR (200 MHz, $CDCl_3$) δ 7.68-7.18 (m, 9H), 2.82 (dd, *J*=6.4, 3.2 Hz, 1H), 2.70 (q, *J*=6.6 Hz, 1H), 2.57 (dd, *J*=3.2, 1.4 Hz, 1H), 1.97 (dd, *J*=6.4, 1.4 Hz, 1H), 1.51 (d, *J*=6.6 Hz, 3H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 195.5, 144.1, 138.5, 134.9, 133.1, 129.9, 128.8, 128.4, 127.6, 126.8, 126.5, 70.8, 40.2, 37.0, 23.3. Anal. Calcd for $C_{17}H_{16}ClNO$: C, 71.45; H, 5.64; N, 4.90. Found: C, 71.48; H, 5.53; N, 4.80.

7i: $[\alpha]^{22}_D$ = +26.8° (*c* 0.50, $CHCl_3$); mp 65-67 °C; ^1H NMR (200 MHz, $CDCl_3$) δ 7.70 (m, 2H), 7.48-7.18 (m, 5H), 6.98 (m, 2H), 2.81 (dd, *J*=6.3, 3.1 Hz, 1H), 2.70 (q, *J*=6.6 Hz, 1H), 2.57 (d, *J*=2.0 Hz, 1H), 1.94 (d, *J*=6.3 Hz, 1H), 1.52 (d, *J*=6.6 Hz, 3H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 195.0, 167.6, 164.2, 144.2, 131.2, 131.1, 128.7, 127.5, 126.9, 115.7, 115.5, 70.8, 40.1, 36.6, 23.2. Anal. Calcd for $C_{17}H_{16}FNO$: C, 75.82; H, 5.99; N, 5.20. Found: C, 75.67; H, 6.27 ; N, 5.21.

7j: $[\alpha]^{24}_D$ = +61.0° (*c* 1.20, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 7.93 (d, *J*=2.9 Hz, 1H), 7.64 (d, *J*=2.8 Hz, 1H), 7.51-7.08 (m, 5H), 3.58 (dd, *J*=6.3, 2.9 Hz, 1H), 2.78 (q, *J*=6.5 Hz, 1H), 2.51 (s, 1H), 2.06 (d, *J*=6.4 Hz, 1H), 1.51 (d, *J*=6.4 Hz, 3H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 189.3, 166.5, 145.0, 143.9, 128.5, 127.2, 126.6, 69.7, 39.7, 38.1, 23.3. Anal. Calcd for $C_{14}H_{14}N_2OS$: C, 65.09; H,5.46; N, 10.84; S, 12.41. Found: C, 65.38; H, 5.29; N, 10.61; S, 12.09.

Representative procedure of L-Selectride® reduction of aziridino ketones. L-Selectride® reduction of 7a. To a solution of (2*R*)-2-N-[(*S*)-α-methylbenzyl]aziridinyl methyl ketone **7a** (100 mg, 0.53 mmol) in 1.0 mL of THF under a nitrogen at -78 °C was added L-Selectride® (1.0 M, 1.01 mL, 1.01 mmol) in THF. The mixture was stirred for 30 min. at -78 °C and warmed to room temperature. The reaction mixture was treated with 10% NaOH solution and the organic layer was separated. The aqueous layer was extracted with EtOAc (3.0 mL x 5) and the combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by silica gel flash chromatography (EtOAc /hexane, 30:70) provided 97 mg (95%) of **8a** and **9a** (>99:1<). The minor diastereomer was not detected in ^1H NMR spectrum but the physical data for **9a** could be obtained from MeMgBr addition to N-[(*S*)-α-methylbenzyl]aziridine-2(*R*)-carboxaldehyde to produce both diastereomers. **8a**: $[\alpha]^{24}_D$ = -70.0° (*c* 1.00, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$) δ 7.36-7.22 (m, 5H), 3.36 (m, 1H), 2.48 (q, *J*=6.6 Hz, 1H), 1.86 (d, *J*=2.2 Hz 1H), 1.75 (m, 1H), 1.48 (d, *J*=1.6 Hz, 1H), 1.45 (d, *J*=6.6 Hz, 3H), 0.93 (d, *J*=6.5 Hz, 3H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 144.8, 128.8, 127.6, 127.0, 69.6, 67.6, 43.9, 31.3, 22.3, 20.5. Anal. Calcd for $C_{12}H_{17}NO$: C, 75.35; H, 8.96; N, 7.32. Found: C,75.50; H, 8.70; N, 7.06. **9a:** $[\alpha]^{24}_D$ = -38.1° (*c* 0.81, $CHCl_3$).; mp 64-66 °C ; ^1H NMR (200 MHz, $CDCl_3$) δ 7.33-7.22 (m, 5H), 3.69 (m, 1H), 2.59 (q, *J*=6.6 Hz, 1H), 1.95 (d, *J*=3.4 Hz 1H), 1.55 (m, 1H), 1.42 (d, *J*=6.6 Hz, 3H), 1.39(d, *J*=6.9 Hz, 1H), 1.00 (d, *J*=6.2 Hz, 3H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 144.7, 128.5, 127.3, 126.7, 69.2, 64.5, 42.7, 29.1, 22.9, 19.6. Anal. Calcd for $C_{12}H_{17}NO$: C, 75.35; H, 8.96; N, 7.32. Found: C, 75.17; H, 8.67; N, 7.03.

L-Selectride® reduction of 7c: **8c**: $[\alpha]^{25}_D$ = -56.0° (*c* 0.50, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$) δ 7.41-7.20 (m, 5H), 3.17 (m, 1H), 2.48 (q, *J*=6.6 Hz, 1H), 1.91(d, *J*=3.2 Hz 1H), 1.63 (d, *J*=5.0 Hz 1H), 1.51 (t, *J*=1.9 Hz, 2H), 1.45 (d, *J*=6.5 Hz, 3H), 1.18 (m, 5H) 0.79(t, 6.6 Hz, 3H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 144.7, 128.8, 127.7, 127.0, 71.4, 69.7, 42.7, 34.9, 31.5, 27.3, 22.3, 22.3, 13.6. Anal. Calcd for $C_{15}H_{23}NO$: C, 77.21; H, 9.93; N, 6.00. Found: C,76.97; H, 10.23; N, 6.34. **9c:** $[\alpha]^{27}_D$ = -25.0° (*c* 0.50, $CHCl_3$).; ^1H NMR (200 MHz, $CDCl_3$) δ 7.41-7.20 (m, 5H), 3.55 (m, 1H), 2.58 (q, *J*=6.5 Hz, 1H), 2.45 (s, 1H), 1.95 (d, *J*=3.5 Hz, 1H), 1.57 (quint, *J*=3.5 Hz, 1H), 1.42 (d, *J*=6.6 Hz, 3H), 1.40 (m, 2H) , 1.30 (m, 5H), 0.85 (m, 3H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 144.8, 128.4, 127.1, 126.9, 69.4, 68.5, 42.0, 34.4, 29.4, 27.4, 23.1, 22.8, 13.9. Anal. Calcd for $C_{15}H_{23}NO$: C, 77.21; H, 9.93; N, 6.00. Found: C,77.28; H, 10.16; N, 6.21.

L-Selectride® reduction of 7d: **8d**: $[\alpha]^{24}_D$ = -92.6° (*c* 1.00, $CHCl_3$), mp 86-87 °C. ^1H NMR (200 MHz, $CDCl_3$) δ 7.33-7.22 (m, 5H), 3.98 (d, *J*=4.9 Hz, 1H), 2.59 (q, *J*=6.4 Hz, 1H), 2.14 (d, *J*=6.2 Hz 1H), 1.95 (m, 3H), 1.82 (m, 1H), 1.51 (d, *J*=6.3 Hz, 1H), 1.44 (d, *J*=6.5 Hz, 3H), 1.31 (m, 4H), 0.86 (t, *J*=7.0 Hz, 3H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 144.3, 128.5, 127.4, 127.1, 85.4, 79.0, 69.1, 61.9, 42.9, 30.7, 30.3, 22.6, 21.7, 18.0, 13.3. Anal. Calcd for $C_{17}H_{23}NO$: C, 79.33; H, 9.01; N, 5.44. Found: C,79.28; H, 9.48; N, 5.61. **9d:** $[\alpha]^{24}_D$ = -49.6° (*c* 1.00, $CHCl_3$).; mp 52-54 °C. ^1H NMR (200 MHz, $CDCl_3$) δ 7.33-7.22 (m, 5H), 4.30 (s, 1H), 2.62 (q, *J*=6.6 Hz, 1H), 2.55 (s, 1H), 2.10 (m, 3H), 1.82 (m, 1H), 1.50 (d, *J*=6.4 Hz, 1H), 1.42 (d, *J*=6.6 Hz, 3H), 1.41 (s. 4H), 0.88 (t, *J*=6.7 Hz, 3H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 144.4, 128.6, 127.3, 126.8, 85.9, 78.4, 69.0, 60.2, 41.8, 30.4, 30.1, 22.8, 21.6, 18.1, 13.3. Anal. Calcd for $C_{17}H_{23}NO$: C, 79.33; H, 9.01; N, 5.44. Found: C,79.37; H, 9.02; N, 5.58.

L-Selectride® reduction of 7f: 8f: $[\alpha]^{22}_D$ = -98.6° (*c* 0.50, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$) δ 7.40-7.22 (m, 5H), 7.18-6.88 (m, 4H), 4.20 (m, 1H), 2.53 (q, *J*=6.6 Hz, 1H), 2.34 (d, *J*=3.7 Hz, 1H), 2.24 (s, 3H), 2.02 (d, *J*=3.4 Hz, 1H), 1.80 (quint, *J*=3.3 Hz, 1H), 1.57 (d, *J*=6.5 Hz, 1H), 1.46 (d, *J*=6.6 Hz, 3H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 144.5,142.1,138.0, 128.9, 128.6, 128.3, 128.2, 127.8, 127.0, 123.1, 74.1, 69.3, 44.5, 31.9, 22.3, 21.2. Anal. Calcd for $C_{18}H_{21}NO$: C, 80.86; H, 7.92; N, 5.24. Found: C,80.78; H, 8.18; N, 5.62. **9f:** $[\alpha]^{22}_D$ = -54.0° (*c* 0.20, $CHCl_3$).; mp 64-66 °C. ^1H NMR (200 MHz, $CDCl_3$) δ 7.38-7.25 (m, 5H), 7.24-7.04 (m, 4H), 4.64 (d, *J*=3.0 Hz, 1H), 2.98 (br, 1H), 2.67 (q, *J*=6.6 Hz, 1H), 2.30 (s, 3H), 2.13 (d, *J*=3.4 Hz, 1H), 1.83 (quint, *J*=3.3 Hz, 1H), 1.42 (d, *J*=6.6 Hz, 3H),1.41 (d, *J*=6.4 Hz, 2H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 144.6, 141.7, 138.1, 128.6, 128.5, 128.3, 127.3, 126.9, 126.6, 123.3, 69.8, 68.9, 42.6, 29.1, 23.2, 21.2. Anal. Calcd for $C_{18}H_{21}NO$: C, 80.86; H, 7.92; N, 5.24. Found: C,80.68; H, 8.17; N, 5.62.

L-Selectride® reduction of 7g: 8g: $[\alpha]^{23}_D$ = -118.5° (*c* 3.14, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$) δ 7.30-7.09 (m, 8H), 6.80-6.72 (m, 2H), 4.67 (d, *J*=4.8 Hz, 1H), 3.74 (s. 3H), 2.51 (q, *J*=6.6 Hz, 1H), 2.06 (d, *J*=3.5 Hz, 1H),1.87-1.82 (m, 1H), 1.48 (d, *J*=6.6 Hz, 3H), 1.44 (d, *J*=6.6 Hz, 3H), 1.44 (d, *J*=6.6 Hz, 3H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 156.3, 144.3, 130.6, 128.6, 128.2, 127.4, 127.0, 126.9, 126.7, 120.7, 110.1, 69.1, 68.3, 55.1, 43.3, 31.6, 22.2. Anal. Calcd for $C_{18}H_{21}NO_2$: C, 76.30; H, 7.47; N,4.94. Found: C,76.23; H, 7.12; N, 4.97. **9g:** $[\alpha]^{23}_D$ = -45.7° (*c* 0.94, $CHCl_3$).; mp 56-58 °C. ^1H NMR (200 MHz, $CDCl_3$) δ 7.33-7.15 (m, 7H), 6.89 (t, *J*=7.4 Hz, 1H), 6.75 (d, *J*=8.3 Hz, 1H), 4.86 (d, *J*=3.7 Hz, 1H), 3.70 (s. 3H), 2.63 (q, *J*=6.5 Hz, 1H), 2.06 (m, 1H), 1.99 (d, *J*=3.5 Hz, 1H), 1.41 (d, *J*=6.5 Hz, 3H), 1.37 (d, *J*=5.9 Hz, 3H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 156.6, 144.6, 130.2 128.5, 128.4, 127.0, 126.8, 126.7, 120.7, 110.2, 68.9, 66.4, 55.0, 41.4, 29.7, 23.0. Anal. Calcd for $C_{18}H_{21}NO_2$: C, 76.30; H, 7.47; N,4.94. Found: C, 76.57; H, 7.68; N,5.09.

L-Selectride® reduction of 7j: 8j: $[\alpha]^{24}_D$ = -57.8° (*c* 1.00, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$) δ 7.51 (d, *J*=3.2 Hz, 1H), 7.35-7.10 (m, 5H), 7.06 (d, *J*=3.2 Hz, 1H), 4.73 (m, 1H), 3.42 (d, *J*=6.4 Hz, 1H), 2.61 (q, *J*=6.6 Hz, 1H), 2.20 (m, 1H), 2.12 (d, *J*=3.5 Hz, 1H), 1.64 (d, *J*=6.4 Hz, 1H), 1.42 (d, *J*=6.6 Hz, 3H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 175.0, 143.7, 142.7, 128.5, 127.3, 126.8, 118.5, 69.7, 68.6, 41.8, 30.6, 22.0. Anal. Calcd for $C_{14}H_{16}N_2OS$: C, 64.59; H, 6.19; N, 10.76; S, 12.32. Found: C,64.32; H, 6.35; N, 10.38; S,11.94.

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