JOC*Note*

Asymmetric Synthesis of Highly Substituted β-Nitro Alcohols and Enantiomerically Enriched 4,4,5-Trisubstituted Oxazolidinones

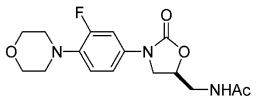
David Crich,* Krishnakumar Ranganathan, Sochanchingwung Rumthao, and Michio Shirai
Department of Chemistry, University of Illinois at Chicago, 845 West Taylor Street, Chicago, Illinois 60607-7061

dcrich@uic.edu

Received November 13, 2002

Abstract: It is demonstrated that α,α-disubstituted-α-nitroketones are reduced to the corresponding trisubstituted nitro alcohols in good to excellent yield and enantiomeric excess by borane−dimethyl sulfide in the presence of a chiral oxazaborolidine catalyst. Reduction of the nitro alcohols to the corresponding amino alcohols and their subsequent conversion to enantiomerically enriched 4,4,5-trisubstituted oxazoldinones is also reported.

The asymmetric synthesis of oxazolidinones is of wide interest to a broad spectrum of chemists, ranging from those interested in the development of improved chiral auxiliaries[1−3] to those pursuing the exploitation of the new oxazolidinone class of antibiotics active against multi-drug-resistant gram-positive bacteria exemplified by Linezolid (**1**).[4−6]



1: Linezolid

One entry into such compounds involves the reduction of diastereomerically enriched vicinal nitro alcohols to the corresponding amino alcohols followed by cyclization with phosgene or a surrogate. Accordingly, in the past few years there has been considerable interest and progress in asymmetric variants of the Henry reaction.[7−15] We report here on an alternative approach to the asymmetric synthesis of 1,1,2-trisubstituted-1-nitro-2-alkanols and their conversion, via the amino alcohols, to enantiomerically enriched 4,4,5-trisubstituted oxazolidinones.

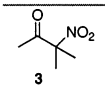
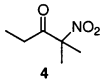
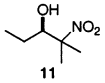
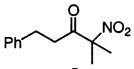
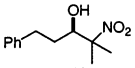
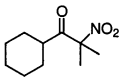
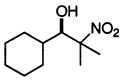
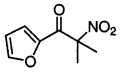
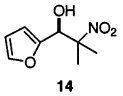
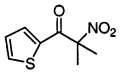
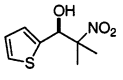
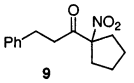
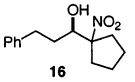
In connection with an ongoing project we required a method for the enantioselective synthesis of 1,1,2-trisubstituted-1-nitro-2-alkanols. In principle these might be obtained directly by stereocontrolled Henry reactions; however, we noted that all examples to date of the Lewis acid-catalyzed asymmetric nitroaldol reaction make use of primary nitroalkanes. Faced with the need to screen for catalysts capable of promoting the more sterically hindered, highly reversible condensation of secondary nitroalkanes with aldehydes, we opted instead to explore the stereocontrolled reduction of α,α-dialkyl-α-nitroketones. We elected to follow this route as we considered that tertiary nitroalkyl groups would perform as ideal large groups in the stereocontrolled oxazaborolidine-catalyzed reduction[16] of ketones. The recent report[17] of the *anti*-selective reduction of α-nitroketones by borane−dimethyl sulfide in the presence of $TiCl_4$ provided a measure of confidence that the tertiary nitro groups themselves would be inert to the reaction conditions and would not interfere actively in the reduction.

A series of substrates were readily prepared by classical condensation of secondary nitroalkanes with aldehydes,[18] providing the racemic nitroaldols, followed by Swern oxidation to the nitroketones. These were then subjected to reduction with the (*S*)-oxazaborolidine catalyst **2** in the presence of borane−dimethyl sulfide, using the optimized conditions of Prasad and Joshi,[19] resulting in the formation of highly enantioenriched nitroaldols as set out in Table 1. With the exception of alcohol **10**, wherein GC analysis over a cyclodextrin column was employed, the enantiomeric excesses of the products were determined by formation of the Mosher ester (**18**−**23**). The absolute configurations displayed in Table 1 are consistent with the use of the (*S*)-enantiomer of the catalyst and the operation of the standard Corey model, assuming no interference by the nitro group and the tertiary nitro group as the large substituent. That this is the case is borne out by the first example with the absolute configuration of the product being confirmed by comparison of the specific rotation with the literature value.[20] The absolute configuration of a further example

(1) Bull, S. D.; Davies, S. G.; Key, M.-S.; Nicholson, R. L.; Savory, E. D. *Chem. Commun.* **2000**, 1721.
(2) Guz, N. R.; Phillips, A. J. *Org. Lett.* **2002**, *4*, 2253.
(3) Sibi, M. P.; Ji, J.; Sausker, J. B.; Jasperse, C. P. *J. Am. Chem. Soc.* **1999**, *121*, 7517.
(4) Brickner, S. J.; Hutchinson, D. K.; Barbachyn, M. R.; Manninen, P. R.; Ulanowicz, D. A.; Garmon, S. A.; Grega, K. C.; Hendges, S. K.; Toops, D. S.; Ford, C. W.; Zurenko, G. E. *J. Med. Chem.* **1996**, *39*, 673.
(5) Zurenko, G. E.; Gibson, J. K.; Shinabarger, D. L.; Aristoff, P. A.; Ford, C. W.; Tarpley, W. G. *Curr. Opin. Pharamcol.* **2001**, *1*, 470.
(6) Very recently an *N*-acryloyl-4-benzyloxazolidinone has also been described as a nonantibacterial oxazolidinone that, however, possesses the very interesting property of inhibiting epithelial cell growth. McHenry, K. T.; Ankala, S. V.; Ghosh, A. K.; Fenteany, G. *ChemBioChem* **2002**, *3*, 101.
(7) For a review see: Shibasaki, M.; Groger, H. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer-Verlag: Berlin, Germany, 1999; Vol. 3; p 1075.
(8) Christensen, C.; Juhl, K.; Jorgensen, K. A. *Chem. Commun.* **2001**, 2222. Christensen, C.; Juhl, K.; Hazell, R, G.; Jorgensen, K, A. *J. Org. Chem* **2002**, *67*, 4875.
(9) Trost, B. M.; Yeh, V. S. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 861.
(10) Trost, B. M.; Yeh, V. S. C.; Ito, H.; Bremeyer, N. *Org. Lett.* **2002**, *4*, 2621.
(11) Corey, E. J.; Zhang, F.-Y. *Angew. Chem., Int. Ed.* **1999**, *38*, 1931.
(12) Misumi, Y.; Matsumoto, K. *Angew. Chem., Int. Ed.* **2002**, *41*, 1031.
(13) Sasai, H.; Watanabe, S.; Shibasaki, M. *Enantiomer* **1997**, *2*, 267.
(14) Sasai, H.; Tohunaga, T.; Watanabe, S.; Suzuki, T.; Itoh, N.; Shibasaki, M. *J. Org. Chem.* **1995**, *60*, 7388.
(15) Chinchilla, R.; Najera, C.; Sanchez-Agullo, P. *Tetrahedron: Asymmetry* **1994**, *5*, 1393.
(16) Corey, E. J.; Helal, C. J. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 1987.
(17) Ballini, R.; Bosica, G.; Marcantoni, E.; Vita, P. *J. Org. Chem.* **2000**, *65*, 5854.
(18) Ono, N. *The Nitro Group in Organic Synthesis*; Wiley-VCH: New York, 2001.
(19) Prasad, K. R. K.; Joshi, N. N. *Tetrahedron: Asymmetry* **1996**, *7*, 3147.
(20) Moriarty, R. M.; Zhuang, H.; Penmasta, R.; Liu, K.; Awasthi, A. K.; Tuladhar, S. M.; Rao, M. S. C.; Singh, V. K. *Tetrahedron Lett.* **1993**, *34*, 8029.

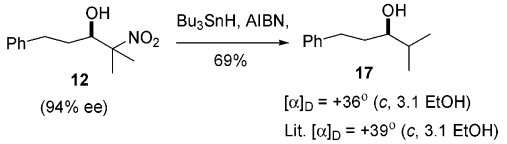
10.1021/jo026707g CCC: $25.00
Published on Web 02/11/2003

TABLE 1. Oxazaborolidine Reduction of Nitroketones

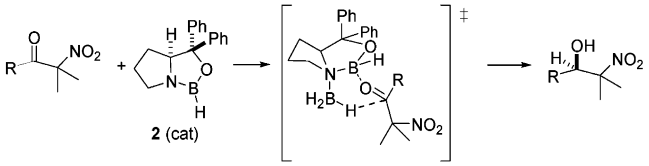
substrate	product	% yield	% ee (method)[a]
 3	 10	71	93 (A)
 4	 11	74	86 (B)
 5	 12	83	94 (B)
 6	 13	92	60 (B)
 7	 14	81	74 (B)
 8	 15	51	49 (B)
 9	 16	76	94 (B)

[a] A: GC analysis over a cyclodextrin column. B: ^{19}F NMR analysis of Mosher esters.

SCHEME 1. Confirmation of the Absolute Configuration of Nitro Alcohol 12

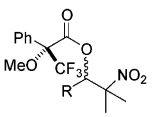


SCHEME 2. Transition State Model for the Reduction of Nitroketones by Oxazaborolidine 2

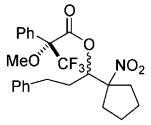


was confirmed by conversion to a substance of established absolute configuration[21] (Scheme 1) and comparison of specific rotations. These two positive correlations provide strong support for conformity with the standard Corey model (Scheme 2).

Inspection of Table 1 reveals that high enantioselectivities are obtained provided that the smaller substituent on the ketone is a primary alkyl group, i.e., when the size difference between the two substituents is maximized. A moderate enantioselectivity was observed in the case of the 2-furanyl ketone whereas a significant decrease was observed in the case of the thiophene- and cyclohexane-substituted systems. The final example of Table 1 reveals that the system is not limited to α-nitroketones derived from 2-nitropropane. In this feasibility study we have only explored the use of the first generation oxazaborolidine catalyst (**2**). It is likely, however, that higher enantioselectivities may be possible with some of the later additions to the class which incorporate substituents other than hydrogen on the ring boron.[16]



18: R = Et
19: R = $(CH_2)_2Ph$
20: R = c-C_6H_{11}
21: R = 2-furanyl
22: R = 2-thienyl



23

Finally, in view of the importance of oxazolidinones in both asymmetric synthesis and medicinal chemistry we briefly investigated reduction of the nitro alcohols to the corresponding amino alcohols followed by phosgenation to give the heterocycle. Nitro alcohols have been reduced to amino alcohols under a variety of conditions although the yields are often very modest.[22−28] In our hands similarly disappointing yields were obtained by most methods. Eventually, it was found that hydrogenation with Raney nickel afforded amino alcohols in modest yield accompanied by considerable retro-Henry product which, it was reasoned, arose from the basic nature of the Raney nickel. Accordingly, this problem was circumvented by the use of acetic acid as cosolvent with ethanol for Raney nickel reductions when significantly improved yields were obtained as reported in Table 2.

In summary, the oxazaborolidine-catalyzed reduction of α-nitroketones by borane−dimethyl sulfide provides the corresponding nitro alcohols in good yield and good to excellent enantiomeric excess. Reduction of the nitro alcohols by Raney nickel in the presence of acetic acid, followed by phosgenation affords enantiomerically enriched 4,4,5-trisubstituted oxazolidinones, a class of compound previously restricted to the racemic modification.

Experimental Section

General Procedures. All solvents were dried and distilled by standard methods. All reactions were carried out under an argon atmosphere unless otherwise stated. All NMR spectra were recorded in $CDCl_3$ as solvent unless otherwise stated. Mass

(21) Soai, K.; Hayase, T.; Takai, K.; Sugiyama, T. *J. Org. Chem.* **1994**, *59*, 7908.

(22) Zn/HOAc: La Forge, R. G.; Whitehead, C. R.; Keller, B. R.; Hummel, C. E. *J. Org. Chem.* **1952**, *17*, 457.

(23) Pt/H_2: Jones, G. D. *J. Org. Chem.* **1944**, *9*, 491.

(24) Raney Ni/H_2: Hass, H. B.; Hudgin, D. E. *J. Am. Chem. Soc.* **1954**, *76*, 2692. Skiles, J. W.; Fuchs, V.; Miao, C.; Sorcek, R.; Grozinger, K. G.; Mauldin, S. C.; Vitous, J.; Mui, P. W.; Jacober, S.; Chow, G.; Matteo, M.; Skoog, M.; Weldon, S. M.; Possanza, G.; Keirns, J.; Letts, G.; Rosenthal, A. S. *J. Med. Chem.* **1992**, *35*, 641. Al-Hassan, S. S.; Cameron, R. J.; Curran, A. W. C.; Lyall, W. J. S.; Nicholson, S. H.; Robinson, D. R.; Stewart, A. S. C.; Stirling, I.; Wood, H. C. S. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1645.

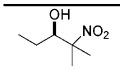
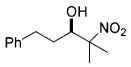
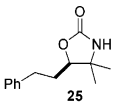
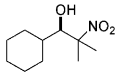
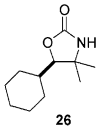
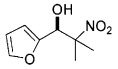
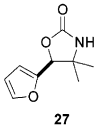
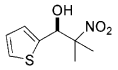
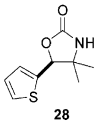
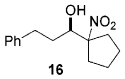
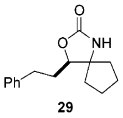
(25) PtO_2/H_2/HOAc: Lichtenthaler, F. W.; Leinert, H.; Scheidegger, U. *Chem. Ber.* **1968**, *101*, 1819.

(26) Zn/HCl: Bobowski, G.; Gottlieb, J. M. *J. Heterocycl. Chem.* **1982**, *19*, 21.

(27) Pd/C/H_2: Benson, O.; Gaudiano, G.; Haltiwagner, C. R.; Koch, T. H. *J. Org. Chem.* **1988**, *53*, 3036.

(28) $LiAlH_4$: Colvin, E. W.; Beck, A. K.; Seebach, D. *Helv. Chim. Acta* **1981**, *64*, 2264.

TABLE 2. Formation of Oxazolidinone from Nitro Alcohols

substrate	product	% yield
 11	 24	50[a]
 12	 25	53[a]
 13	 26	67
 14	 27	45[a]
 15	 28	64[a]
 16	 29	87[a]

[a] Reduction conducted in the presence of acetic acid.

spectra were recorded by the Research Resources Center at the University of Illinois at Chicago. Melting points were recorded on a hotstage microscope and are uncorrected. Microanalyses were carried out by Midwest Microlabs, Indianapolis, IN.

General Procedure for the Swern Oxidation of Nitroaldols. A 0.4 M solution of oxalyl chloride in CH_2Cl_2 (2 equiv wrt substrate) was treated at −78 °C with a 0.6 M solution of DMSO in CH_2Cl_2 (4.0 equiv wrt substrate). After the mixture was stirred for 15 min a 0.2 M solution of nitroaldol in CH_2Cl_2 was added dropwise, followed by stirring at −78 °C for 1 h. Triethylamine (5.0 equiv) was then added over 5 min, during which time the reaction mixture became a colorless solution. After being stirred for 20 min, the reaction mixture was allowed to warm to room temperature over 1.5 h. Water was then added, the resulting mixture washed with 10% sodium acetate and brine and dried (Na_2SO_4), and the solvent removed under reduced pressure. Purification by silica gel chromatography (eluent: ethyl acetate/hexanes, 7:1) afforded the respective nitroketones.

2-Methyl-2-nitro-3-butanone (3). Following the general procedure, except for purification which was achieved by careful distillation of the solvent under atmospheric pressure followed by the bulb-to-bulb distillation of the residue, (±)-**10** (2.52 g, 18.92 mmol) afforded **3**[29] (1.57 g, 63%) as a colorless oil. IR (film, cm^{-1}) ν 1730, 1548, 1350; ^1H NMR δ 2.18 (s, 3H), 1.70 (s, 6H); ^{13}C NMR δ 199.6, 94.2, 24.0, 23.1.

2-Methyl-2-nitro-3-pentanone (4). Following the general procedure, except for purification which was achieved by careful distillation of the solvent under atmospheric pressure followed by the bulb-to-bulb distillation of the residue under reduced pressure, (±)-**11** (4.51 g, 30.6 mmol) afforded **4**[29] (3.2 g, 72%) as a colorless oil. IR (film, cm^{-1}) ν 1731, 1553, 1346; ^1H NMR δ 2.44 (q, J = 7.2 Hz, 2H), 1.64 (s, 6H), 0.98 (t, J = 7.2 Hz, 3H); ^{13}C NMR δ 202.8, 94.1, 29.6, 23.1, 7.8.

4-Methyl-4-nitro-1-phenyl-3-pentanone (5). Following the general procedure, (±)-**12** (1.90 g, 8.5 mmol) afforded **5**[30] (1.56 g, 83%) as a colorless oil. IR (film, cm^{-1}) ν 1728, 1543; ^1H NMR δ 7.28−7.14 (m, 5H), 2.93 (t, J = 7.2 Hz, 2H), 2.80 (t, J = 6.5 Hz, 2H), 1.66 (s, 6H); ^{13}C NMR δ 201.2, 128.7, 128.7, 128.4, 128.4, 128.3, 126.5, 38.5, 29.9, 23.1.

1-Cyclohexyl-2-methyl-2-nitro-1-propanone (6). Following the general procedure, (±)-**13** (1.20 g, 5.97 mmol) afforded **6** (0.97 g, 82%) as a colorless oil. IR (film, cm^{-1}) ν 1726, 1546; ^1H NMR δ 2.58−2.50 (m, 1H), 1.80−1.65 (m, 10H), 1.50−1.43 (m, 3H), 1.25−1.21 (m, 3H); ^{13}C NMR δ 205.3, 94.4, 46.2, 30.6, 29.0, 25.5, 25.5, 25.4, 23.2. ESIHRMS: calcd for $C_{10}H_{17}NO_3$ [M + Na] 222.1114, found 222.1106.

1-(2-Furanyl)-2-methyl-2-nitro-1-propanone (7). Following the general procedure, (±)-**14** (2.50 g, 13.5 mmol) afforded **7** (2.08 g, 84%) as a pale yellow oil. IR (film, cm^{-1}) ν 1681, 1548; ^1H NMR δ 7.51 (dd, J = 0.6, 0.6 Hz, 1H), 7.28 (dd, J = 0.6, 0.6 Hz, 1H), 6.51 (dd, J = 3.6, 3.6 Hz, 1H), 1.82 (s, 6H); ^{13}C NMR δ 180.6, 147.2, 120.1, 112.9, 91.7, 24.0. ESIHRMS: calcd for $C_8H_9NO_4$ [M + Na] 206.0433, found 206.0429.

2-Methyl-2-nitro-1-(2-thienyl)-1-propanone (8) Following the general procedure, (±)-**15** (0.124 g, 0.616 mmol) afforded **8** (0.112 g, 91%) in the form of white crystals. Mp 43−44 °C; IR (film, cm^{-1}) ν 1675, 1558; ^1H NMR δ 7.69 (dd, J = 4.5, 0.9 Hz, 1H), 7.49 (dd, J = 3.9, 0.9 Hz, 1H), 7.09 (dd, J = 4.5, 3.9 Hz, 1H), 1.92 (s, 6H); ^{13}C NMR δ 184.9, 139.2, 135.5, 132.1, 128.8, 92.7, 25.3. Anal. Calcd for $C_8H_9NO_3S$: C, 48.23; H, 4.55. Found: C, 48.56; H, 4.56.

1-(1-Nitrocyclopentyl)-3-phenyl-1-propanone (9). Following the general procedure, (±)-**16** (1.75 g, 6.99 mmol) afforded **9** (1.1 g, 64%) as a colorless oil. IR (film, cm^{-1}) ν 2962, 1726, 1540, 1452; ^1H NMR δ 7.31−7.14 (m, 5H), 2.94 (t, J = 7.0 Hz, 2H), 2.81 (t, J = 7.5 Hz, 2H), 2.54−2.46 (m, 2H), 2.24−2.15 (m, 2H), 1.80−1.69 (m, 4H); ^{13}C NMR δ 200.1, 140.3, 128.7, 128.5, 126.6, 105.1, 39.2, 35.4, 30.0, 25.0. ESIHRMS: calcd for $C_{14}H_{17}NO_3Na$ [M + Na] 270.1106, found 270.1095.

General Procedure for the Oxazaborolidine-Catalyzed Reduction of Nitroketones. To a solution of (*S*)-(−)-α,α-diphenyl-2-pyrrolidinemethanol (5−10 mol %) in THF/toluene (1/1, 0.3 M in substrate) was added borane−dimethyl sulfide (1.0 M in CH_2Cl_2, 1.2 equiv). The mixture was warmed to 45 °C with stirring for 17 h after which a solution of substrate in THF (0.5 M in substrate) was added over a period of 2 h with the use of a motor-driven syringe pump. The reaction mixture was maintained at 45 °C until the starting material was consumed, then cooled to room temperature and quenched by addition of methanol (1.5 mL) dropwise until the vigor of the reaction subsided. The reaction mixture was then diluted with ethyl acetate and the organic layer washed with 1 M HCl, water, saturated sodium bicarbonate solution, and brine, dried (Na_2SO_4), and concentrated under reduced pressure to afford the crude product. Purification by silica gel chromatography (eluent: ethyl acetate/hexanes, 1:5) afforded the corresponding enantiomerically enriched nitro alcohols.

(*R*)-3-Methyl-3-nitro-2-butanol (10). Following the general procedure with 10 mol % catalyst, **3** (0.30 g, 2.30 mmol) afforded **10**[20] (0.217 g, 71%, ee 92.1% based on chiral GC analysis over a α-cyclodextrin column) as a colorless oil, $[\alpha]_D^{26}$ −25.3 (*c* 1.0, $CHCl_3$) [lit.[20] $[\alpha]_D^{23}$ −25.6 (*c* 0.5−1.0, $CHCl_3$)], whose spectral characteristics matched those of the racemate (±)-**10**.

(*R*)-4-Methyl-4-nitro-3-pentanol (11). Following the general procedure with 10 mol % catalyst, **4** (0.4 g, 2.76 mmol) afforded **11** (0.30 g, 74%, 86% ee) as a colorless oil, $[\alpha]_D^{26}$ +5.24 (*c* 2.1, $CHCl_3$), whose spectral characteristics matched those of the racemate (±)-**11**.

(*R*)-4-Methyl-4-nitro-1-phenyl-3-pentanol (12). Following the general procedure with 5 mol % catalyst, **5** (0.10 g, 0.45 mmol) afforded **12** (0.083 g, 83%, 94% ee) as a colorless oil, $[\alpha]_D^{25}$ +32 (*c* 1.67 CH_2Cl_2), whose spectral characteristics matched those of the racemate (±)-**12**.

(29) Al-Hassan, S. S.; Cameron, R. J.; Curran, A. W. C.; Lyall, W. J. S.; Nicholson, S. H.; Robinson, D. R.; Stewart, A. S. C.; Stirling, I.; Wood, H. C. S. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1645.

(30) Ballini, R.; Petrini, M.; Rosini, G. *J. Org. Chem.* **1990**, *55*, 5159.

(*R*)-4-Methyl-1-phenyl-3-pentanol (17). A mixture of **12** (0.091 g, 0.40 mmol), AIBN (33 mg, 0.20 mmol), and Bu_3SnH (0.174 g, 0.60 mmol) in degassed benzene (5 mL) was heated to reflux at 90 °C for 10 h under an inert atmosphere. The reaction mixture was then cooled to room temperature and concentrated under reduced pressure to afford the crude reaction mixture. Purification by silica gel chromatography (eluent: ethyl acetate/hexane 1:10) afforded **17** (0.049 g, 69%) as a colorless oil. $[\alpha]_D^{25}$ +36 (*c* 3.08, EtOH) [lit.[21] $[\alpha]_D^{26}$ +39 (*c* 3.08, EtOH)]; IR (film, cm^{-1}) ν 3417; ^1H NMR δ 7.25−7.12 (m, 5H), 3.35−3.32 (m, 1H), 2.78−2.73 (m, 1H), 2.61−2.58 (m, 1H), 1.74−1.58 (m, 4H), 0.86 (s, 3H), 0.84 (s, 3H); ^{13}C NMR δ 142.5, 128.6, 128.5, 125.9, 76.2, 36.1, 33.8, 32.6, 18.9, 17.3.

(*R*)-Cyclohexyl-2-methyl-2-nitro-1-propanol (13). Following the general procedure with 5 mol % catalyst, **6** (1.1 g, 5.5 mmol) afforded **13** (0.998 g, 92%, 60% ee) as a colorless oil, $[\alpha]_D^{25}$ +30 (*c* 0.15, CH_2Cl_2), whose spectral characteristics matched those of the racemate (±)-**13**.

(*S*)-(2-Furanyl)-2-methyl-2-nitro-1-propanol (14). Following the general procedure, with 5 mol % catalyst, **7** (0.50 g, 2.73 mmol) afforded **14** (0.409 g, 81%, 68% ee) as a colorless oil, $[\alpha]_D^{25}$ −26 (*c* 3.85, CH_2Cl_2), whose spectral characteristics matched those of the racemate (±)-**14**.

(*S*)-2-Methyl-2-nitro-1-(2-thioenyl)-1-propanol (15). Following the general procedure with 10 mol % catalyst in THF as the only solvent **8** (0.092 g, 0.46 mmol) afforded (±)-**15** (47 mg, 51%, 49% ee) as a white solid, $[\alpha]_D^{26}$ +3.68 (*c* 2.2, $CHCl_3$), whose spectral characteristics matched those of the racemate (±)-**15**.

(*R*)-(1-Nitrocyclopentyl)-3-phenyl-1-propanol (16). Following the general procedure with 10 mol % catalyst, **9** (0.44 g, 1.78 mmol) afforded **16** (0.34 g, 76%, 94% ee) as a colorless oil, $[\alpha]_D^{23}$ +34.3 (*c* 3.1, $CHCl_3$), whose spectral characteristics matched those of the racemate (±)-**16**.

General Procedure for the Reduction of Nitro Alcohols with Raney Nickel in Acetic Acid/Ethanol with Subsequent Oxazolidinone Formation. To a solution of nitro alcohol in a 1/1 mixture of ethanol and acetic acid (0.1 M in substrate) was added Raney nickel (50% slurry in water, 1 g). The reaction mixture was then shaken in a Parr hydrogenator under a positive pressure of hydrogen (40−45 psi) overnight. The reaction mixture was then filtered, the filter cake rinsed with water, and the filtrate removed under reduced pressure. The residue was redissolved in water and adjusted to pH 14 with a saturated solution of NaOH. The aqueous solution was then extracted with $CHCl_3$ (thrice), the combined organic layers washed with water and brine and dried (Na_2SO_4), and the solvent removed under reduced pressure to afford the crude amino alcohol, which was used as such for the subsequent reaction. The crude amino alcohol was dissolved in toluene (0.1 M in substrate) and cooled to 0 °C, and triethylamine (2.2 equiv) was added followed by phosgene (20% solution in toluene, 1.1 equiv) over a period of 10 min. The reaction mixture was then stirred for 1.5 h at the same temperature. The contents were then diluted with ethyl acetate, the organic layer washed thoroughly with a saturated solution of sodium bicarbonate, water, and brine and dried (Na_2SO_4), and the solvent removed under reduced pressure. Purification by silica gel column (eluent: ethyl acetate/hexanes, 1:3) afforded the corresponding oxazolidinones.

General Procedure for the Reduction of Nitro Alcohols with Raney Nickel in Ethanol with Subsequent Oxazolidinone Formation. To a solution of nitro alcohol in absolute ethanol was added Raney nickel (50% slurry in water, 1 g) followed by shaking in a Parr hydrogenator under a positive pressure of hydrogen (40−45 psi) overnight. The reaction mixture was filtered, the filter cake rinsed with ethanol, and the filtrate removed under reduced pressure. The crude amino alcohol was then dissolved in water (0.1 M) and K_2CO_3 (1.2 equiv) was added. After the mixture was cooled to 0 °C, phosgene (20% solution in toluene, 1.1 equiv) was added over a period of 10 min. The reaction mixture was stirred for an additional 2-h period at the same temperature, then diluted with CH_2Cl_2. The organic layer was separated and the aqueous layer extracted with CH_2Cl_2 (twice). The combined organic layers were then washed with water and brine and dried (Na_2SO_4) and the solvent removed under reduced pressure to afford crude oxazolidinone. Purification of by silica gel chromatography (eluent: ethyl acetate/hexanes, 1:3) afforded the pure oxazolidinones.

(*R*)-5-Ethyl-4,4-dimethyloxazolidin-2-one (24). Following the general procedure for reduction in the presence of acetic acid, (*R*)-**11** (0.42 g, 2.82 mmol) afforded (*R*)-**24** (0.2 g, 50%) as a pale yellow oil. $[\alpha]_D^{26}$ +36.4 (*c* 1.0, $CHCl_3$); IR (film, cm^{-1}) ν 3296, 2975, 1745; ^1H NMR δ 6.04 (br s, 1H), 4.04 (dd, J = 9.9 Hz, 3.6 Hz, 1H), 1.73−1.63 (m, 1H), 1.62−1.46 (m, 1H), 1.29 (s, 3H), 1.17 (s, 3H), 1.05 (t, J = 7.3 Hz, 3H); ^{13}C NMR δ 159.4, 87.9, 57.9, 27.5, 22.8, 22.5, 10.9. ESIHRMS: calcd for $C_7H_{13}NO_2Na$ [M + Na] 166.0844, found 166.0841.

(*R*)-4,4-Dimethyl-5-(2-phenylethyl)oxazolidin-2-one (25). Following the general procedure for reduction in the presence of acetic acid, (*R*)-**12** (77 mg, 0.347 mmol) provided (*R*)-**25** (33 mg, 53%) as white solid. $[\alpha]_D^{25}$ +67 (*c* 0.15, CH_2Cl_2); mp 113−116 °C; IR (film, cm^{-1}) ν 3287, 1751; ^1H NMR δ 7.32−7.18 (m, 5H), 6.17 (br s, 1H), 4.14 (dd, J = 2.27, 2.70 Hz, 1H), 2.95−2.89 (m, 1H), 2.73−2.63 (m, 1H), 2.00−1.91 (m, 1H), 1.81−1.73 (m, 1H), 1.28 (s, 3H), 1.19 (s, 3H); ^{13}C NMR δ 159.0, 141.0, 128.7, 128.6, 126.3, 85.2, 57.9, 32.4, 31.4, 27.3, 23.0. Anal. Calcd for $C_{13}H_{16}NO_2$: C, 71.21; H, 7.81. Found: C, 71.17; H, 7.83.

(*R*)-5-Cyclohexyl-4,4-dimethyloxazolidin-2-one (26). Following the general procedure for reduction in the absence of acetic acid, (*R*)-**13** (0.112 g, 0.56 mmol) provided (*R*)-**26** (0.072 g, 67%) as a white solid. $[\alpha]_D^{25}$ +10.33 (*c* 0.9, CH_2Cl_2); mp 149−150 °C; IR (film, cm^{-1}) ν 3233, 1721; ^1H NMR δ 6.71 (br s, 1H), 3.84 (d, J = 9.6 Hz, 1H), 2.10−1.06 (m, 1H), 1.78−1.62 (m, 5H), 1.35 (s, 3H), 1.27 (s, 3H), 1.30−1.01 (m, 5H); ^{13}C NMR δ 159.2, 89.9, 58.1, 37.8, 29.7, 29.2, 28.0, 26.1, 25.4, 25.4, 22.4. Anal. Calcd for $C_{11}H_{19}NO_2$: C, 66.97; H, 9.71. Found: C, 66.81; H 9.62.

(*S*)-5-(2-Furanyl)-4,4-dimethyloxazolidin-2-one (27). Following the general procedure for reduction in the presence of acetic acid, (*S*)-**14** (0.89 g, 4.80 mmol) provided (*S*)-**27** (0.180 g, 45%) as a white solid. $[\alpha]_D^{25}$ −24, (*c* 1.25, CH_2Cl_2); mp 89−91 °C; IR (film, cm^{-1}) ν 3294, 1760; ^1H NMR δ 7.42−7.42 (m, 1H), 6.43−6.37 (m, 2H), 6.21 (br s, 1H), 5.19 (s, 1H), 1.46 (s, 3H), 1.05 (s, 3H); ^{13}C NMR δ 158.3, 148.7, 143.2, 110.5, 109.3, 81.5, 59.21, 28.1, 24.0. ESIHRMS: calcd for $C_9H_{11}NO_3$ [M + Na] 204.0635, found 204.0637.

(*S*)-4,4-Dimethyl-5-(2-thioenyl)oxazolidin-2-one (28). Following the general procedure for reduction in the presence of acetic acid, (*S*)-**15** (0.11 g, 0.56 mmol) afforded (*S*)-**28** (0.07 g, 64%) as a white solid. $[\alpha]_D^{26}$ −23.3 (*c* 0.8, $CHCl_3$); mp 91−94 °C; IR (film cm^{-1}) ν 3281, 1754; ^1H NMR δ 7.33 (dd, J = 5.1 Hz, 1.2 Hz 1H), 7.07−7.02 (m, 2H), 5.75 (br s, 1H), 5.47 (s, 1H), 1.47 (s, 3H), 1.01 (s, 3H); ^{13}C NMR δ 158.3, 137.3, 127.3, 126.1, 84.6, 59.9, 27.6, 24.4. Anal. Calcd for $C_9H_{11}NO_2S$; C, 54.80; H, 5.62. Found: C, 54.90; H, 5.56.

(*R*)-1-Aza-3-oxa-4-(2-phenylethyl)spiro[4.4]nonan-2-one (29). Following the general procedure for reduction in the presence of acetic acid, (*R*)-**16** (0.157 g, 0.62 mmol) afforded (*R*)-**29** (0.135 g, 87%) as white solid. $[\alpha]_D^{26}$ +71.6 (*c* 2.7, $CHCl_3$); mp 142−145 °C; IR (film, cm^{-1}) ν 3240, 2960, 1747; ^1H NMR δ 7.32−7.2 (m, 5H), 4.34 (dd, J = 10.8 Hz, 1.8 Hz, 1H), 3.0−2.92 (m, 1H), 2.74−2.64 (m, 1H), 2.08−1.60 (m, 11H); ^{13}C NMR δ 159.6, 141.1, 128.7, 128.6, 126.3, 83.1, 68.8, 38.7, 33.4, 32.7, 32.3, 23.4, 22.3. Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81. Found: C, 73.23; H, 7.82.

Acknowledgment. We thank the NSF, CHE 9986200, for support of this work.

Supporting Information Available: General protocols for the Henry reaction and for the formation of Mosher esters; characterization data for (±)-**10**−(±)-**16**, and **18**−**23**; and copies of the ^1H and ^{13}C NMR spectra of compounds **7**, **9**, **13**, **24**, and **27** and of the ^1H, ^{13}C, and ^{19}F NMR spectra of compounds **18**, **19**, **20**, **21**, **22**, and **23**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO026707G