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Highly stereoselective epoxidation of *O*-protected 3-hydroxy-1-nitroalkenes

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ABSTRACT

The diastereoselectivity of the nucleophilic epoxidation of *O*-protected 3-hydroxy-1-nitroalkenes was investigated. Epoxidation of the *O*-protected 3-hydroxy-1-nitroalkenes was highly stereoselective, giving rise to the *anti* isomer. The resulting nitroepoxides have been transformed into nitroaldols through hydrogenation. The nucleophilic epoxidation of nitroalkenes was found to be irreversible. Models to explain the observed stereoselectivities are proposed.

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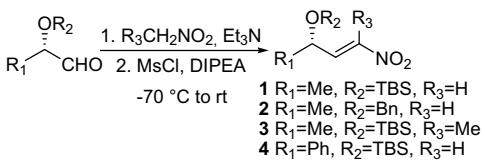
1. Introduction

Nitroalkenes are extremely versatile reagents, which have found extensive applications in organic synthesis.[1] Asymmetric epoxidation of chiral nitroalkenes provides chiral nitroepoxides that can be converted into useful chiral building blocks.[2] We previously communicated the epoxidation of γ-hydroxy enoates[3] and now wish to report that the epoxidation of *O*-protected 3-hydroxy-1-nitroalkenes is highly stereoselective (dr up to 19/1). We believe this finding will find synthetic applications.

2. Results

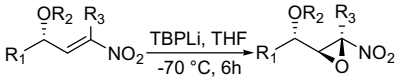
3-Hydroxy-1-nitroalkenes **1**–**4** were prepared from *O*-protected (*S*)-lactaldehyde or (*S*)-mandelaldehyde by a nitroaldol reaction followed by activation of the resulting alcohols to the mesylate and then elimination[4] (Scheme 1).



Scheme 1. Preparation of 1-nitroalkenes.

Nitroalkenes **1**–**4**[5] were epoxidized using lithium *tert*-butylperoxide[6] as the oxidizing reagent in THF as solvent at −70 °C. Nitroalkenes **1**, **2**, and **4** gave rise to the *anti* isomer in a high stereoselective fashion (entries 2, 3, and 6, Table 1). The epoxidation of nitroalkene **3** having a methyl group in the double bond resulted to be less selective (entries 4 and 5, Table 1).

Table 1
Epoxidation of *O*-protected 3-hydroxy-1-nitroalkenes



Entry	Substrate	EtLi soln[a]	*anti*/*syn*[b]	Product	Yield (%)
1	1	Benzene/cyclohexane	3/1	**5**	72
2	1	Dibutylether	19/1	**5**	75
3	2	Dibutylether	9/1	**6**	70
4	3	Dibutylether	3.5/1	**7**	75
5	3	Benzene/cyclohexane	2/1	**7**	70
6	4	Dibutylether	10/1	**8**	88[c]

[a] Two commercial ethyl lithium solutions were used: 0.5 M in benzene/cyclohexane (9/1) solution from Aldrich and 1.7 M in dibutylether solution from Acros.
[b] Ratio measured by ^{13}C NMR of the crude reaction mixtures.
[c] 16 mol % of peroxide intermediate **14** was also obtained.

The diastereoselectivity of the epoxidation of nitroalkenes proved to be dependent on the commercial organolithium solution. If the organolithium solution is in dibutylether then the selectivity is better than in benzene/cyclohexane (9/1). This solvent effect can be rationalized in terms of the solvation or aggregation[7] of the lithium species by the solvent: the better the solvent coordinates to lithium, the better selectivity is observed.

From the epoxidation reaction of nitroalkene **4** some peroxide intermediate **14** was isolated.

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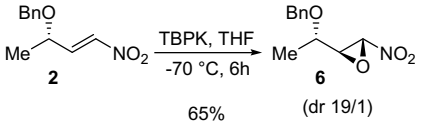
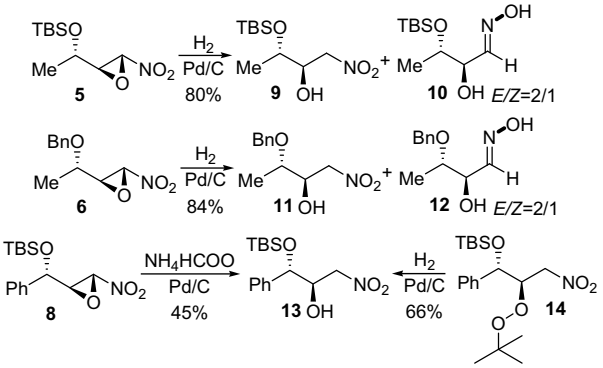
If the epoxidation reaction of compound **2** was carried out using potassium *tert*-butylperoxide, then a better selectivity was observed (Scheme 2).



Scheme 2. Epoxidation using potassium *tert*-butylperoxide.

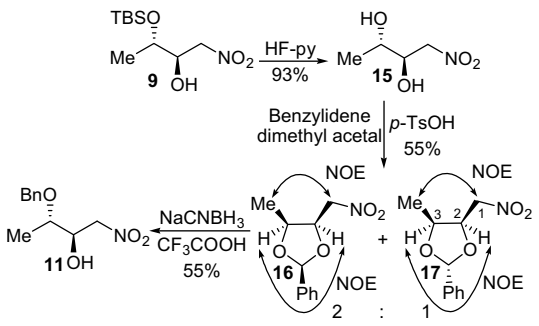
The resulting nitroepoxides were submitted to hydrogenation giving rise to the corresponding *anti* nitroaldols (Scheme 3). Oximes **10** and **12** were also obtained as secondary products in the hydrogenation reaction of compounds **5** and **6**, respectively.[8] Compound **8** was hydrogenated using ammonium formate[9] instead of hydrogen furnishing *anti* aldol **13**. Hydrogenation of peroxyether **14** furnished also compound **13**.



Scheme 3. Hydrogenation of nitroepoxides.

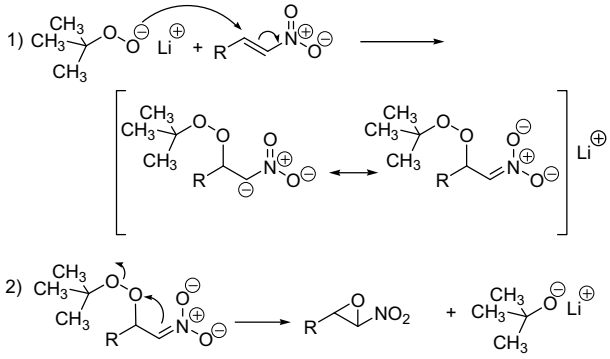
The stereochemistry of the resulting nitroaldols **9** and **13** and therefore of the preceding nitroepoxides **5** and **8** was assigned by comparison with reported data in the literature.[10] The spectroscopic data for **9** and **13** were identical to those previously described, denoting relative *anti* stereochemistry for nitroepoxides **5** and **8**, respectively.[11]

The stereochemistry of nitroaldol **11** and therefore of the preceding nitroepoxide **6** was assigned through chemical correlation with nitroaldol **9** as follows: compound **9** was deprotected and the resulting diol was cyclized using benzylidene diethyl acetal and *p*-toluene sulfonic acid[12] furnishing a 2/1 mixture of acetals **16** and **17**, which were separated by column chromatography. Both acetals **7** and **8** exhibited NOE effects between H-2 and H-3, and between H-1 and methyl. Then compound **16** was submitted to reductive opening using sodium cyanoborohydride in the presence of trifluoroacetic acid[13] giving rise to nitroaldol 11 (Scheme 4).



Scheme 4. Chemical correlation of nitroepoxides.

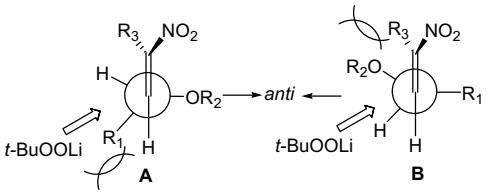
A nucleophilic epoxidation reaction is thought to proceed by the addition of a *tert*-butyl-peroxy anion to the activated double bond, giving rise to an enolate (Scheme 5). Upon elimination of *tert*-butoxide from the enolate, the epoxide is furnished.



Scheme 5. Mechanism of nucleophilic epoxidation of nitroalkenes.

To conduct a meaningful analysis of transition states, it was necessary to determine whether the epoxidation reaction is kinetic (irreversible) or reversible, it is whether the initial Michael addition of the peroxy anion to the nitroalkene is irreversible or reversible. Then *tert*-butyl-peroxyether **14** was treated with LHMDS in the presence of chalcone, nitroepoxide **8** was obtained,[14] and chalcone was recovered.[3b] The epoxidation of the chalcone was never observed, demonstrating the irreversibility of the reaction.

The stereoselectivity in the epoxidation of compounds **1**–**4** can be accounted for by the models depicted in Scheme 6.[15]



Scheme 6. Kinetic models to explain *anti* stereoselectivity.

To explain the anti-selectivity observed for compounds **1**, **2**, and **4**, transition state geometry A (Scheme 6) would be electronically favored because the alkoxy group is *anti*. However, there is steric repulsion between the incoming reagent and the R_1 group. Transition state geometry B also furnishes *anti* isomer and would explain the poor selectivity observed for compound **3** due to 1,3-allylic strain between the alkoxy group and vinylic methyl group.

3. Conclusions

In summary, the nucleophilic epoxidation of *O*-protected 3-hydroxy-1-nitroalkenes is a highly diastereoselective reaction that favors the *anti* isomer. The nucleophilic epoxidation of nitroalkenes is an irreversible process because the enolization of a 2-peroxy nitrocompound gives only the nitroepoxide. The observed selectivities for epoxides **5**–**8** can be explained by modified Felkin–Anh models.

4. Experimental section

4.1. General experimental methods

All solvents used in reactions were freshly distilled from appropriate drying agents before use. ^{1}H NMR spectra and ^{13}C NMR

spectra were measured in $CDCl_3$ (^1H, 7.24 ppm; ^{13}C 77.0 ppm) solution at 30 °C on a 300 MHz Mercury Varian or a 500 MHz Innova Varian NMR spectrometer at the Serveis Centrals d'Instrumentació Científica de la Universitat Jaume I. Mass spectra were measured in a QTOF I (quadrupole–hexapole-TOF) mass spectrometer with an orthogonal Z-spray-electrospray interface (Micromass, Manchester, UK). IR spectra were recorded as oily films on NaCl plates on a Perkin–Elmer 2000 FT-IR spectrometer. EM Science Silica Gel 60 was used for column chromatography while TLC was performed with E. Merck precoated plates (Kieselgel 60, F_{254}, 0.25 mm). Unless otherwise specified, all reactions were carried out under argon atmosphere with magnetic stirring. About the X-ray crystallographic study, the crystals are air stable and were mounted on the tip of a glass fiber with the use of epoxi cement. X-ray diffraction experiment was carried out on a Bruker SMART CCD diffractometer using Mo Kα radiation (λ=0.71073 Å) at room temperature. The data were collected with a frame width of 0.3° in ω and a counting time of 30 and 60 s per frame for compounds **2** and **3** at a crystal to detector distance of 4 cm. The diffraction frames were integrated using the SAINT package and corrected for absorption with SADABS.[10] The structures were solved by direct methods and refined by the full-matrix method based on F^2 using the SHELXTL software package.[11] All non hydrogen atoms were refined anisotropically. Hydrogen atoms were generated geometrically, assigned isotropic thermal parameters, and allowed to ride on their respective parent carbon atoms.

4.2. General experimental procedure for the preparation of nitroalkenes 1–4

To a solution of *O*-protected (*S*)-lactaldehyde (or (*S*)-mandelaldehyde) (23.92 mmol) in nitromethane (or nitroethane) (119.60 mmol) was added triethyl amine (0.50 mL, 3.56 mmol). The resulting mixture was stirred at room temperature for 3 h. Then the excess of nitromethane (or nitroethane) was removed under reduced pressure. The resulting mixture of diastereomeric nitroaldols (*anti*/*syn*=ca. 6/4) in the form of yellow oil was submitted to the next step without any further purification.

To a −70 °C cold solution of nitroaldols (*anti*/*syn*=ca. 6/4) in dichloromethane (50 mL) was added dropwise methanesulfonylchloride (2.24 mL, 28.89 mmol) and then a solution of *N*,*N*-diisopropylethylamine (10.48 mL, 60.19 mmol) in dichloromethane (10 mL). The mixture was stirred at −70 °C for 2 h and then was allowed to warm to room temperature. Then was quenched with water (10 mL) and extracted with CH_2Cl_2 (4×30 mL), the organic layers were washed with HCl 1 N and brine, dried (Na_2SO_4), and concentrated. The crude oil was purified through chromatography (silica gel, hexanes/EtOAc (9/1) and (8/2)) to afford the corresponding nitroalkene as a yellow oil.

4.2.1. ((S,E)-4-Nitrobut-3-en-2-yloxy)(tert-butyl)dimethylsilane ***1***. Yield=70%. $[\alpha]_D^{25}$=+3.3 (*c*=0.5, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 7.16 (1H, dd, *J*=13.0, 4.0 Hz), 7.02 (1H, dd, *J*=13.0, 2.0 Hz), 4.52 (1H, ddq, *J*=6.5, 3.0, 1.5 Hz), 1.25 (3H, d, *J*=7.0 Hz), 0.83 (9H, s), 0.01 (3H, s), 0.00 (3H, s). ^{13}C NMR ($CDCl_3$) δ 146.1, 139.3, 65.9, 26.1, 23.7, 18.5, −4.5, −4.7 ppm. IR (NaCl) ν 3122, 2959, 2923, 2856, 1653, 1529, 1351, 1255, 1156, 1093, 1053, 835, 776, 665 cm^{-1}. HRMS (EI) *m*/*z* calcd for $C_{10}H_{21}NO_3Si$ [M]: 231.1291, found: 231.1298.

4.2.2. ((S,E)-4-Nitropent-3-en-2-yloxy)(tert-butyl)dimethylsilane ***3***. Yield=68%. $[\alpha]_D^{25}$=+11.9 (*c*=0.5, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 6.99 (1H, d, *J*=8.0 Hz), 4.55 (1H, dq, *J*=7.5 and 6.5 Hz), 2.16 (3H, s), 1.28 (3H, d, *J*=6.5 Hz), 0.86 (9H, s), 0.05 (s, 3H), 0.02 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 145.8, 138.9, 65.4, 26.0, 23.6, 18.0, 12.8, −4.8, −4.9 ppm. IR (NaCl) ν 2957, 2930, 2858, 1529, 1473, 1389, 1336, 1254, 1133, 1090, 1005, 973, 903, 832, 778, 724 cm^{-1}. HRMS (FAB) *m*/*z* calcd for $C_{11}H_{23}NO_3Si$ [M]: 245.1447, found: 245.1458.

4.2.3. ((R,E)-3-Nitro-1-phenylallyloxy)(tert-butyl)dimethylsilane ***4***. Yield=15%. $[\alpha]_D^{25}$=+39.4 (*c*=0.4, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ 7.41–7.23 (7H, m), 5.45 (1H, d, *J*=2.7 Hz), 0.92 (9H, s), 0.09 (3H, s), −0.06 (3H, s). ^{13}C NMR ($CDCl_3$) δ 144.6, 140.1, 138.6, 129.2, 128.8, 126.6, 72.4, 26.0, 18.5, −4.6, −4.8 ppm. IR (NaCl) ν 2928, 1526, 1351, 1255, 1125, 838, 779 cm^{-1}. HRMS (EI) *m*/*z* calcd for $C_{15}H_{23}NO_3Si$ [M]: 225.1287, found: 225.1295.

4.3. Experimental procedure for the preparation of 11 from 16/17

To a solution of compounds **16** and **17** (3/1) (30 mg, 0.13 mmol) in dimethylformamide (1 mL) and 3 Å molecular sieves was added sodium cyanoborohydride (45 mg, 0.67 mmol) and then a solution of trifluoroacetic acid (105 μL, 1.35 mmol) in dimethylformamide (0.8 mL). The resulting mixture was stirred at room temperature for 24 h. Then was diluted with dichloromethane and neutralized using a saturated sodium hydrogen carbonate aqueous solution, then extracted with dichloromethane, washed with brine, dried (Na_2SO_4), filtered, and concentrated. Then the solvent was removed under reduced pressure. The resulting mixture was purified through chromatography (silica gel, CH_2Cl_2/MeOH (9/1)) to afford 3 mg of compound **11** (yield over recovered starting material=55%).

4.4. General experimental procedure for the epoxidation

To a −70 °C cold THF (3.5 mL) was added TBHP (3.3 M in toluene)[16] (2.2 mmol) and then ethyl lithium (1.61 mmol). The resulting mixture was stirred at −70 °C for 15 min and then a solution of the nitroalkene (1.46 mmol) in THF (2 mL) was added dropwise and then the mixture was stirred at −70 °C for 6 h. Then solid Na_2SO_3 (120 mg) was added in one portion and stirring for 15 min, then diluted with satd aq NH_4Cl soln and extracted with Et_2O (3×30 mL), the organic layers were washed (brine), dried (Na_2SO_4), and concentrated. The crude oil was purified through chromatography (silica gel, hexanes/EtOAc (9/1) and (8/2)).

4.4.1. ((S)-1-((2S,3R)-3-Nitrooxiran-2-yl)ethoxy)(tert-butyl)dimethylsilane ***5***. Yield=75%. $[\alpha]_D^{25}$=−27.6 (*c*=2.5, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 5.33 (1H, s), 4.06 (1H, qd, *J*=6.5 and 2.5 Hz), 3.42 (1H, dd, *J*=2.5 and 1.0 Hz), 1.27 (3H, d, *J*=6.5 Hz), 0.86 (9H, s), 0.05 (s, 3H), 0.04 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 77.8, 63.8, 61.9, 25.7, 20.3, 18.0, −5.0, −5.1 ppm. IR (NaCl) ν 2957, 2932, 2837, 2856, 1736, 1571, 1473, 1377, 1362, 1255, 1166, 1130, 1104, 1053, 1005, 983, 936, 836, 779, 720, 667 cm^{-1}. HRMS (EI) *m*/*z* calcd for $C_{10}H_{21}NO_4Si$ [M]: 247.1238, found: 247.1238.

4.4.2. (2S,3R)-2-((S)-1-(Benzyloxy)ethyl)-3-nitrooxirane ***6***. Yield=70%. $[\alpha]_D^{25}$=−92.8 (*c*=0.5, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 7.39–7.31 (5H, m), 5.40 (1H, s), 4.57 (2H, d), 3.75 (1H, qd, *J*=6.5 and 3.0 Hz), 3.50 (1H, d, *J*=3.5 Hz), 1.32 (3H, d, *J*=6.5 Hz). ^{13}C NMR ($CDCl_3$) δ 137.7, 128.8, 128.2, 127.9, 78.5, 72.4, 70.4, 61.2, 17.4 ppm. IR (NaCl) ν 3065, 3032, 2981, 2934, 2872, 1741, 1567, 1497, 1454, 1365, 1101, 1058, 956, 924, 806, 737, 699 cm^{-1}. HRMS (EI) *m*/*z* calcd for $C_{11}H_{13}NO_4$ [M]: 223.0845, found: 223.0860.

4.4.3. ((S)-1-((2S,3R)-3-Methyl-3-nitrooxiran-2-yl)ethoxy)(tert-butyl)dimethylsilane ***7***. Yield=75%. $[\alpha]_D^{25}$=−20.2 (*c*=0.5, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 3.74 (1H, qd, *J*=6.5 Hz) (major isomer), 3.51 (1H, qd, *J*=6.5 Hz) (minor isomer), 3.35 (1H, d, *J*=8.0 Hz) (minor isomer), 3.26 (1H, d, *J*=6.5 Hz) (major isomer), 1.95 (1H, s) (major isomer), 1.86 (1H, s) (minor isomer), 1.25 (3H, d, *J*=6.5 Hz) (major isomer), 1.18 (3H, d, *J*=6.5 Hz) (minor isomer), 0.83 (9H, s) (minor isomer), 0.81 (9H, s)

(major isomer), 0.04 (3H, s) (minor isomer), 0.01 (3H, s) (major isomer), 0.00 (3H, s) (minor isomer), 0.00 (3H, s) (major isomer). ^{13}C NMR ($CDCl_3$) δ 194.0 (major isomer), 185.3 (minor isomer), 72.6 (minor isomer), 68.0 (major isomer), 61.5 (major isomer), 59.0 (minor isomer), 25.6 (major isomer), 25.6 (minor isomer), 21.6 (major and minor isomer), 20.4 (major and minor isomer), 18.0 (major isomer), 17.9 (minor isomer), −4.0 (minor isomer), −4.3 (major isomer), −4.9 (minor isomer), −5.0 (major isomer) ppm. IR (NaCl) ν 2957, 2932, 2897, 2859, 1563, 1473, 1388, 1362, 1258, 1198, 1152, 1107, 1061, 986, 959, 920, 885, 836, 778, 666 cm^{-1}. HRMS (EI) m/z calcd for $C_{11}H_{23}NO_4Si$ [M]: 261.1396, found: 261.1392.

4.4.4. ((S)-((2S,3R)-3-Nitrooxiran-2-yl)(phenyl)methoxy)(tert-butyl)dimethylsilane ***8***. Yield=75%. $[\alpha]_D^{25}$=+20.6 (c=0.52, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ 7.49–7.40 (5H, m), 5.60 (1H, s) (major isomer), 5.39 (1H, s) (minor isomer), 5.05 (1H, s) (major isomer), 4.85 (1H, d, J=4.0 Hz) (minor isomer), 3.73 (1H, d, J=4.0 Hz) (minor isomer), 3.65 (1H, s) (major isomer), 0.98 (9H, s) (minor isomer), 0.95 (9H, s) (major isomer), 0.17 (3H, s) (minor isomer), 0.15 (3H, s) (major isomer), 0.03 (3H, s) (minor isomer), 0.00 (3H, s) (major isomer). ^{13}C NMR ($CDCl_3$) δ 138.5 (major isomer), 138.5 (minor isomer), 128.9, 128.8, 128.7, 128.6, 126.4, 126.2 (major and minor isomer), 79.1 (minor isomer), 77.6 (major isomer), 71.9 (minor isomer), 70.2 (major isomer), 62.4 (major isomer), 61.8 (minor isomer), 25.8 (major and minor isomer), 18.2 (major and minor isomer), −4.8 (minor isomer), −4.9 (major isomer), −5.0 (minor isomer), −5.1 (major isomer) ppm. IR (NaCl) ν 2929, 2857, 1707, 1569, 1471, 1362, 1255, 1153, 975, 837, 780, 755, 689 cm^{-1}. HRMS (EI) m/z calcd for $C_{15}H_{23}NO_4Si$ [M]: 309.1396, found: 309.1382.

4.4.5. ((1S,2R)-2-(tert-Butyl-peroxy)-3-nitro-1-phenylpropoxy)(tert-butyl)dimethylsilane ***14***. $[\alpha]_D^{20}$=+57.7 (c=0.84, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ 7.45–7.40 (5H, m), 5.21 (2H, m), 4.80 (1H, m), 4.65 (1H, m), 4.47 (1H, m), 1.24 (9H, s), 0.98 (9H, s), 0.18 (3H, s), 0.01 (3H, s). ^{13}C NMR ($CDCl_3$) δ 140.5, 128.8, 128.3, 126.3, 86.0, 81.7, 73.8, 73.2, 26.7, 26.1, 18.6, −4.6, −4.7 ppm. IR (NaCl) ν 2930, 1560, 1364, 1101, 837, 779 cm^{-1}. HRMS (FAB) m/z calcd for $C_{19}H_{34}NO_5Si$ [M+H$^+$]: 384.2206, found: 384.2195.

4.5. General experimental procedure for the hydrogenation of nitroepoxides

A solution of nitroepoxide (1 mmol) in anhydrous methanol (2 mL) was added to a pre-hydrogenated suspension of Pd/C (10% in Pd) (40 mg) in anhydrous methanol (20 mL). The resulting mixture was stirred under hydrogen atmosphere at room temperature for 15 h. Then was filtered through Celite and concentrated under vacuum. The resulting light yellow oil was purified through chromatography (silica gel, hexanes/EtOAc (7/3) and (6/4)) to afford the corresponding nitroaldol and an (*E*/*Z*) mixture of oximes.

4.5.1. (2R,3S)-3-(tert-Butyldimethylsilyloxy)-1-nitrobutan-2-ol ***9***. Yield=80%. $[\alpha]_D^{25}$=+22.3 (c=2.5, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ 4.55 (1H, dd, J=13.0 and 2.5 Hz), 4.38 (1H, dd, J=13.0 and 9.0 Hz), 4.08 (1H, m), 3.83 (1H, q, J=6.5 Hz), 1.18 (3H, d, J=6.5 Hz), 0.86 (9H, s), 0.06 (3H, s), 0.05 (3H, s). ^{13}C NMR ($CDCl_3$) δ 77.8, 73.2, 69.8, 25.7, 19.8, 17.8, −4.4, −5.0 ppm. IR (NaCl) ν 3447, 2956, 2931, 2888, 2859, 1737, 1558, 1473, 1378, 1257, 1147, 1091, 1006, 978, 837, 778, 668 cm^{-1}. HRMS (EI) m/z calcd for $C_{10}H_{21}NO_3Si$ [M−H_2O]: 231.1291, found: 231.1297.

4.5.2. (2R,3S)-3-(tert-Butyldimethylsilyloxy)-2-hydroxybutanal oxime ***10***. ^{1}H NMR ($CDCl_3$) δ 9.26 (1H, br s), 7.44 (1H, d, J=6.5 Hz) (major isomer), 6.76 (1H, d, J=6.5 Hz) (minor isomer), 4.75 (1H, t, J=4.5 Hz) (minor isomer), 4.17 (1H, dq, J=6.5 and 4.5 Hz) (minor isomer), 4.05 (1H, t, J=5.5 Hz) (major isomer), 3.90 (1H, dq, J=6.5 Hz) (major isomer), 3.30 (1H, br s), 1.15 (1H, d, J=6.0 Hz) (major isomer), 1.11 (1H, d, J=6.5 Hz) (minor isomer), 0.88 (9H, s) (minor isomer), 0.87 (9H, s) (major isomer), 0.08 (3H, s) (minor isomer), 0.06 (3H, s) (major isomer). ^{13}C NMR ($CDCl_3$) δ 151.7 (minor isomer), 150.8 (major isomer), 73.5 (major isomer), 70.8 (major isomer), 69.8 (minor isomer), 68.8 (minor isomer), 25.8 (major and minor isomer), 19.3 (major isomer), 18.2 (minor isomer), 18.0 (minor isomer), 17.9 (major isomer), −4.4 (major isomer), −4.6 (minor isomer), −4.8 (major and minor isomer) ppm. IR (NaCl) ν 3346, 2956, 2931, 2887, 2859, 1660, 1473, 1377, 1257, 1100, 1006, 972, 938, 886, 837, 777, 676 cm^{-1}. HRMS (EI) m/z calcd for $C_{10}H_{24}NO_3Si$ [M+H$^+$]: 234.1517, found: 234.1525.

4.5.3. (2R,3S)-3-(Benzyloxy)-1-nitrobutan-2-ol ***11***. Yield=84%. $[\alpha]_D^{25}$=+71.9 (c=0.6, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ 7.30–7.38 (m, 5H), 4.65 (1H, d, J=11.5 Hz), 4.60 (1H, dd, J=13.5 and 3.0 Hz), 4.48–4.43 (2H, m), 4.25 (1H, ddd, J=8.0, 5.5 and 3.0 Hz), 3.63 (1H, dq, J=6.0 and 5.5 Hz), 2.81 (1H, br s), 1.28 (3H, d, J=6.0 Hz). ^{13}C NMR ($CDCl_3$) δ 137.6, 128.6, 128.0. 127.8, 77.7, 75.3, 71.9, 15.6 ppm. IR (NaCl) ν 3433, 3032, 2919, 1727, 1554, 1496, 1454, 1379, 1260, 1089, 800, 738, 698 cm^{-1}. HRMS (FAB) m/z calcd for $C_{11}H_{16}NO_4$ [M+H$^+$]: 226.1079, found: 226.1080.

4.5.4. (2R,3S)-3-(Benzyloxy)-2-hydroxybutanal oxime ***12***. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.51 (1H, d, J=5.4 Hz) (major isomer), 7.26–7.37 (5H, m), 6.83 (1H, d, J=5.1 Hz) (minor isomer), 4.99 (1H, dd, J=5.1 and 3.9 Hz) (minor isomer), 4.64 (1H, d, J=12.0 Hz) (minor isomer), 4.65 (1H, d, J=11.7 Hz) (major isomer), 4.56 (1H, d, J=12.0 Hz) (minor isomer), 4.51 (1H, d, J=11.7 Hz) (major isomer), 4.27 (1H, t, J=4.8 Hz) (major isomer), 3.93 (1H, dq, J=6.6 and 3.9 Hz) (minor isomer), 3.70 (1H, dq, J=6.3 and 4.5 Hz) (major isomer), 1.22 (1H, d, J=6.3 Hz) (major isomer), 1.20 (1H, d, J=6.9 Hz) (minor isomer). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 151.9 (minor isomer), 150.6 (major isomer), 138.0, 128.7, 128.0, 127.9, 127.7, 76.8 (major isomer), 75.1 (minor isomer), 72.0 (major isomer), 71.1 (major isomer), 71.0 (minor isomer), 67.6 (minor isomer), 15.1 (major isomer), 14.9 (minor isomer) ppm. HRMS (FAB) m/z calcd for $C_{11}H_{16}NO_3$ [M+H$^+$]: 210.1130, found: 210.1123.

4.5.5. (1S,2R)-1-(tert-Butyldimethylsilyloxy)-3-nitro-1-phenylpropan-2-ol ***13***. Yield=45% from **8**; 66% from **14**. $[\alpha]_D^{20}$=+48.2 (c=0.5, $CHCl_3$) (lit.[8] $[\alpha_D^{20}]$=+51.8 (c=1.3, $CHCl_3$)). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.25–7.40 (5H, m), 4.77 (1H, d, J=5.1 Hz), 4.46 (2H, m), 4.38 (1H, m), 2.48 (1H, br s), 0.91 (9H, s), 0.07 (3H, s), −0.14 (3H, s). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 139.8, 128.8, 128.7, 126.5, 77.1, 76.3, 73.6, 25.7, 18.1, −4.6, −5.1 ppm. IR (NaCl) ν 3630, 2939, 2860, 1553, 1258, 1082, 847, 450 cm^{-1}. HRMS (FAB) m/z calcd for $C_{15}H_{26}NO_4Si$ [M+H$^+$]: 312.1639, found: 312.1631.

4.5.6. (2R,3S)-1-Nitrobutane-2,3-diol ***15***. To a solution of compound **9** (100 mg, 0.40 mmol) in THF (5 mL) and pyridine (480 μL) was added a previously prepared solution of hydrogen fluoride–pyridine complex (65–70% in hydrogen fluoride) (1.05 mL) in THF (9.7 mL) and pyridine (817 μL). The resulting mixture was stirred at room temperature for 26 h. Then sodium hydrogen carbonate was added. Then the resulting suspension was filtered and washed with dichloromethane and the solvent was removed under reduced pressure. The resulting mixture was purified through chromatography (silica gel, CH_2Cl_2, CH_2Cl_2/MeOH (9/1) and (8/2)) to afford 50 mg (93%) of compound **15**. $[\alpha]_D^{25}$=+39.5 (c=2.4, $CHCl_3$). ^{1}H NMR (CD_3OD) δ 4.76 (1H, dd, J=13.0 and 3.0 Hz), 4.39 (1H, dd, J=13.0 and 10.0 Hz), 4.01 (1H, m), 3.63 (1H, dq, J=6.5 Hz), 3.35 (1H, s), 1.23 (1H, d, J=6.5 Hz). ^{13}C NMR (CD_3OD) δ 80.8, 75.5, 70.6, 20.7 ppm. IR (NaCl) ν 3300, 2922, 1652, 1544, 1378, 1098 cm^{-1}.

4.5.7. (2S,4S,5R)-4-Methyl-5-(nitromethyl)-2-phenyl-1,3-dioxolane ***16***. To a solution of diol **15** (50 mg, 0.37 mmol) in benzene (0.5 mL) were added benzylidene dimethyl acetal (60 μL, 0.4 mmol) and *p*-toluene sulfonic acid (8.5 mg, 0.45 mmol). The resulting mixture

was heated connected to a distillation system until benzene–methanol azeotropic mixture distilled (bp 57 °C) and then refluxed for 6 h. Then the reaction mixture was cooled down to room temperature. Then was diluted with dichloromethane and neutralized using a saturated sodium hydrogen carbonate aqueous solution, then extracted with dichloromethane, washed with brine, dried (Na_2SO_4), filtered, and concentrated. Then the solvent was removed under reduced pressure. The resulting mixture was purified through chromatography (silica gel, hexanes/EtOAc (9/1)) to afford 34 mg of compound **16** and 11 mg of compound **17** (yield=55%). ^{1}H NMR ($CDCl_3$) δ 7.54–7.50 (2H, m), 7.46–7.42 (3H, m), 5.99 (1H, s), 4.88 (1H, ddd, J=10.0, 6.5, and 3.0 Hz), 4.69 (1H, dd, J=13.0 and 3.0 Hz), 4.58 (1H, dd, J=13.0 and 10.0 Hz), 4.52 (1H, dq, J=6.5 and 3.5 Hz), 1.32 (3H, d, J=6.5 Hz). ^{13}C NMR ($CDCl_3$) δ 136.30, 129.65, 128.47, 126.47, 103.84, 75.75, 74.60, 14.03 ppm. IR (NaCl) ν 2935, 2854, 1557,1376, 1093, 710 cm^{-1}. HRMS (EI) m/z calcd for $C_{11}H_{13}NO_4$ [M]: 223.0845, found: 223.0848.

4.5.8. (2R,4S,5R)-4-Methyl-5-(nitromethyl)-2-phenyl-1,3-dioxolane ***17***. ^{1}H NMR (CD_3CN) δ 7.26–7.21 (5H, m), 5.99 (1H, s), 4.79 (1H, q, J=6.5 Hz), 4.50 (2H, d, J=6.5 Hz), 4.36 (1H, dq, J=6.5 Hz), 1.08 (3H, d, J=6.5 Hz). ^{13}C NMR (CD_3CN) δ 138.92, 130.20, 129.88, 127.75, 102.18, 75.59, 75.22, 73.16, 13.20 ppm. IR (NaCl) ν 2924, 2854, 1556, 1452, 1376, 1093, 700 cm^{-1}.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.08.010.

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