Asymmetric Synthesis of 2-Acetyl-4(5)-(1,2,3,4-tetrahydroxybutyl)imidazoles

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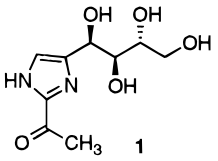
A method for preparing the eight stereoisomers of the biologically active compound (1*R*,2*S*,3*R*)-2-acetyl-4(5)-(1,2,3,4-tetrahydroxybutyl)imidazole (THI, **1**) is reported. This method employs a palladium(0)-catalyzed coupling of 1-(ethoxymethyl)-4-iodoimidazole (**7**) to functionalized vinylstannanes (*R*)- or (*S*)-**12a,b** or **13a,b** or 1-alkynylstannanes (*R*)- or (*S*)-**6a,b** to introduce the C-4 imidazole four-carbon side chain. The 1,2-dihydroxy functionality of the butyl side chain was introduced by Sharpless catalytic asymmetric dihydroxylation reactions.

Introduction

(1*R*,2*S*,3*R*)-2-Acetyl-4(5)-(1,2,3,4-tetrahydroxybutyl)-imidazole (THI, **1**), a constituent of Caramel Color III, has been found to depress blood lymphocyte counts in both mice and rats.[1] THI produces lymphopenia, apparently without toxic effects, in rats and mice and is able to affect the immune competence in the rat in quite small quantities (e.g., 1−50 ppm in drinking water).[2] THI has also been reported to prevent spontaneous and cyclophosphamide-induced diabetes in non-obese diabetic mice.[3] To investigate the structure−activity relationships of this structurally simple but biologically intriguing molecule, we desired a general and flexible synthesis of THI analogues. Three earlier syntheses of THI have been reported, and these all rely on the use of glucose derivatives to prepare the 1,2,3,4-tetrahydroxybutyl side chain.[4−6] These syntheses are not sufficiently flexible for the synthesis of the stereoisomers of THI. In a recent communication,[7] we reported a new synthetic protocol for the synthesis of THI. We now report the full details of this synthesis and the synthesis of the other seven tetrahydroxybutyl side-chain stereoisomers of THI. The general synthetic strategy involved the conversion of 1-protected-4-iodoimidazole **3** to the (*E*)- or (*Z*)-alkenes **2**, followed by a Sharpless catalytic asymmetric dihydroxylation (AD) to introduce the 1,2-dihydroxy functionality into the butyl side chain (Scheme 1).



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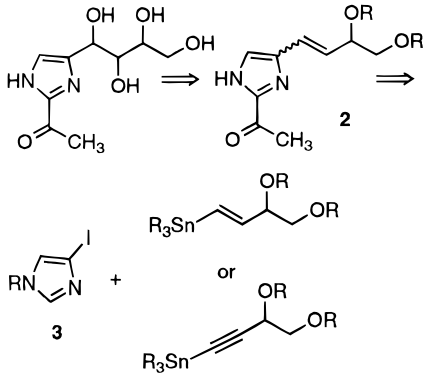
Results and Discussion

Synthesis of 4-[(1*Z*)-Butenyl]imidazole Derivatives. The protected (2*R*)- and (2*S*)-glyceraldehydes **4a** ([α]$^{28}_{D}$ +76.3° (*c* 1.06, toluene), lit.[8] [α]$^{28}_{D}$ +80.1° (*c* 0.166, toluene) and **4b** ([α]$^{23}_{D}$ −74.8° (*c* 1.18, toluene), lit.[8] [α]$^{28}_{D}$ −79.4° (*c* 1.18, toluene)) were converted to their respective alkynes **5a** and **5b** in good overall yields, using the procedure of Corey and Fuchs (Scheme 2).[9] Treatment of these individual alkynes with *n*-BuLi, followed by quenching of the resulting 1-lithioalkyne derivative with chlorotrimethylstannane gave the 1-(trimethylstannyl)-alkynes **6a** and **6b**, respectively. Attempted palladium-(0) catalyzed couplings of **5b** with 1-(ethoxymethyl)-4-iodoimidazole (**7**)[10] using $PdCl_2(PPh_3)_2$ in the presence of copper(I) iodide and triethylamine in acetonitrile at reflux[10] for 4 h gave poor yields (23%) of the desired alkyne **8b**. The major product (69%) was the undesired dialkyne **9** that was difficult to separate from the desired imidazole product. However, treatment of **7** with either **6a** or **6b** under Stille-type coupling conditions,[10−12] using $Pd(PPh_3)_4$ as catalyst in DMF at 80 °C for 24 h gave enhanced yields (53−59%) of the desired alkynes **8a** and **8b**, respectively. Deprotonation of **8a** and **8b** with *n*-BuLi in THF at −78 °C followed by quenching of the resulting 2-lithioimidazole derivative with *N*-methoxy-*N*-methylacetamide[10,13] gave the 2-acetyl derivatives **10a** and **10b**, respectively, in 67−69% yields. Catalytic hydrogenation of **10a** and **10b** over Lindlar's catalyst,[14]

Scheme 1



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[⊗] Abstract published in *Advance ACS Abstracts,* January 1, 1997.

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(2) Golin, S. J. P.; Phillips, J. A. *Clin. Exp. Immunol.* **1991**, *85*, 335.
(3) Mandel, T. E.; Koulmanda, M.; Mackay, I. R. *Clin. Exp. Immumol.* **1992**, *88*, 414.
(4) Kroplien, U.; Rosdorfer, J.; Vander Geef, J.; Long, R. C., Jr.; Goldstein, J. H. *J. Org. Chem.* **1985**, *50*, 1131.
(5) Sweeny, J. G.; Ricks, E.; Estrada-Valdes, M. C.; Iacobucci, G. A.; Long, R. C., Jr. *J. Org. Chem.* **1985**, *50*, 1133.
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(8) Schmid, C. R.; Bradley, D. A. *Synthesis* **1992**, 587.
(9) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, *13*, 3769.
(10) Cliff, M. D.; Pyne, S. G. *J. Org. Chem.* **1995**, *60*, 2378.
(11) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508.
(12) For a recent review on the palladium-catalyzed coupling reactions of heterocyclic compounds, see: Kalinin, V. N. *Synthesis* **1992**, 413.
(13) Prepared according to the general method described in the following: Nahm, S.; Weinreb, S. M. *Tetrahedron Lett.* **1981**, *22*, 3815.
(14) Marvell, E. N.; Thomas, L. *Synthesis* **1973**, 457.

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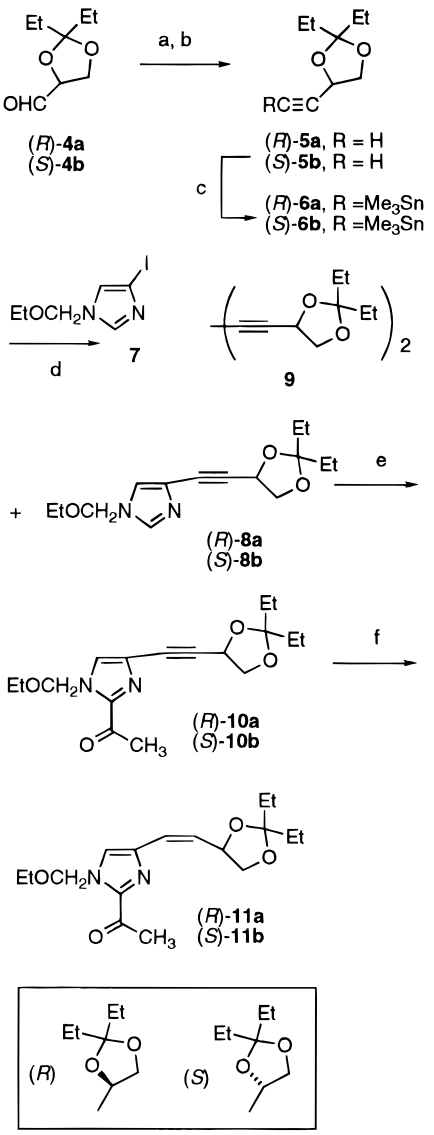
Scheme 2[a]



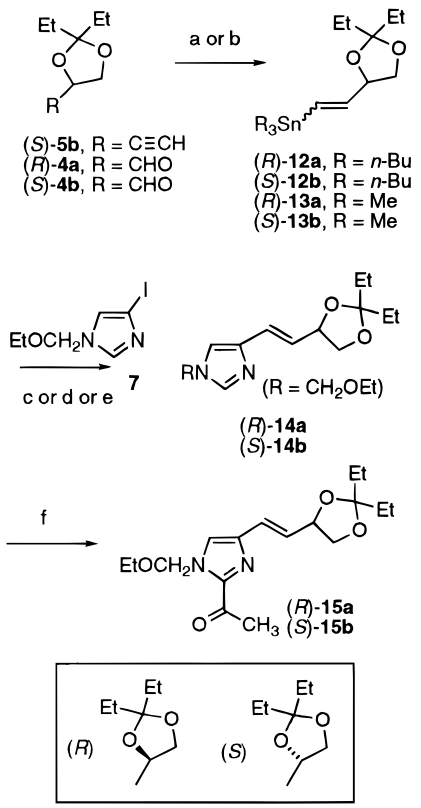
[a] Key: (a) Ph_3P, CBr_4, Zn, 77−87%. (b) *n*-BuLi/THF, −78 °C to rt, 69−76%. (c) *n*-BuLi/THF, −78 to 0 °C; Me_3SnCl, 0 °C to rt, 59−60%. (d) From **5b**:5% $PdCl_2(Ph_3P)_2$, Et_3N, CuI, MeCN, reflux, 4 h, 23% of **8b**, 69% of **9**. From **6a,b**: 5% $Pd(PPh_3)_4$, DMF, 80 °C, 24 h, 53−58% of **8a,b**. (e) *n*-BuLi, THF, −78 °C, 1 h; MeCON-Me(OMe), −78 °C to rt, 67−69%. (f) 10% Pd on $CaCO_3$, quinoline, H_2, 2 h, rt, 79−80%.

in the presence of quinoline, gave the pure (*Z*)-alkenes **11a** and **11b**, respectively, in yields of 79−80% after purification by column chromatography to remove small quantities of the corresponding (*E*)-alkene (5−6%) and over-reduced material (4−7%).

Synthesis of 4-[(1*E*)-Butenyl]imidazole Derivatives. Hydrostannylation[15] of **5b** at 130 °C gave an inseparable 81:19 mixture of the (*E*)- and (*Z*)-vinyltri-*n*-butylstannanes **12b** in 85% yield (Scheme 3). The related trimethylstannanes **13a** and **13b** were directly prepared from their respective aldehydes, **4a** and **4b**, in good yields (80−85%) and high stereoselectivity ((*E*):(*Z*) *ca.* 90:10) using trimethyl(dibromomethyl)stannane ($Me_3SnCHBr_2$), lithium iodide, and chromium(II) chloride.[16]

Treatment of iodoimidazole **7** with **12b** ((*E*):(*Z*) = 81:19)) at 80 °C in the presence of $Pd(PPh_3)_4$ (5 mol %) in

Scheme 3[a]



[a] Key: (a) From (S)-**5b**: Bu_3SnH, AlBN (cat.), 130 °C, 2.5 h, 85% of **12b**. (b) From **4a,b**: $CrCl_2$, $Br_2CHSnMe_3$, LiI, THF, DMF, 16 h, rt, 80−85% of **13a,b**. (c) **12**, 5% $Pd(PPh_3)_4$, DMF, 80 °C, 24 h, 26−31% (see Experimental Section for details). (d) **12**, $Pd_2(dba)_3$, $AsPh_3$, CuI, DMF, 80 °C, 24 h, 45%. (e) **13a** or **13b**, 5% $Pd(PPh_3)_4$, DMF, 80 °C, 24 h, 46−83%. (f) *n*-BuLi, THF, −78 °C; MeCON-Me(OMe), −78 °C to rt, 65−72%.

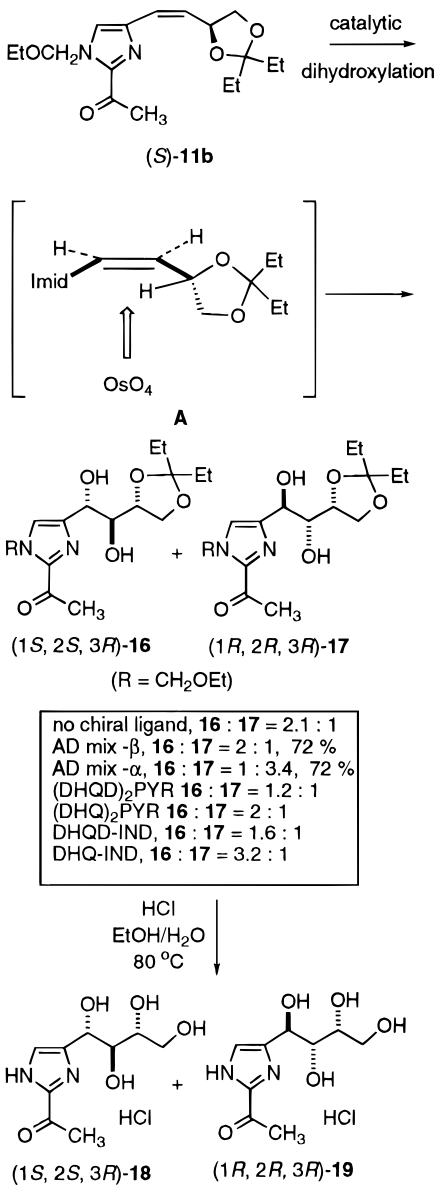
DMF, THF, or MeCN as solvent gave the desired (*E*)-alkene **14b** in yields of 26−31% (Scheme 3). A better yield (45%) of **14b** was achieved using 5 mol % of $Pd_2(dba)_3$, 10 mol % of $AsPh_3$, and 10 mol % of CuI in DMF and at 80 °C for 24 h.[17]

Alternatively compounds **14a** and **14b** could more readily and reliably be obtained via Stille-type coupling reactions of **7** and the vinyl-trimethylstannanes **13a,b** using 5 mol % of $Pd(PPh_3)_4$ in DMF at 80 °C for 24 h. These conditions gave the pure (*E*)-alkenes **14a,b** in yields ranging from 45 to 83%. The (*Z*)-geometric isomers of vinylstannes **13a** and **13b** underwent coupling at a much slower rate than their (*E*) counterparts, and none of the (*Z*)-isomer of **14a** or **14b** could be isolated from these reactions after purification by column chromatography on silica gel. The alkenes **14a** or **14b** were converted to their corresponding 2-acetylimidazole derivatives **15a** and **15b** in yields of 65−72% using the previously described acylation method (Scheme 3).

Asymmetric Dihydroxylations of 4-[(1*Z*)-Butenyl]-imidazole Derivatives. Catalytic dihydroxylation of **11b**, in the absence of chiral ligand ($K_2OsO_4 \cdot H_2O$ (3 mol %)/$K_3Fe(CN)_6$ (3 equiv)/K_2CO_3 (3 equiv)/$MeSO_2NH_2$ (3 equiv)/*t*-BuOH, H_2O at 0 °C, 16 h), gave a mixture of **16** and its diastereomeric *anti*-(1*S*,2*R*)-diol **17** in a ratio of 2.1:1, respectively. The major diastereoisomer (**16**) was that expected on the basis of Kishi's[18] (**A** in Scheme 4) or

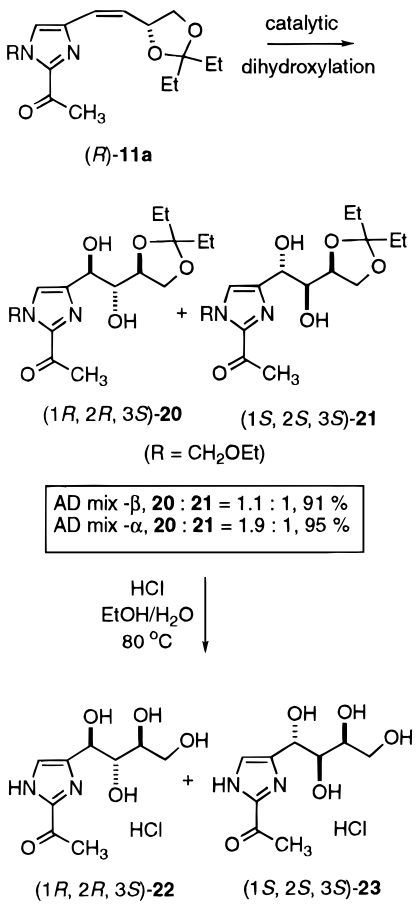
(15) Tolstikov, G. A.; Miftakhov, M. S.; Danilova, N. A.; Vel'der, Ya. L. *Synthesis* **1986**, 496.
(16) Cliff, M. D.; Pyne, S. G. *Tetrahedron Lett.* **1995**, *36*, 763.
(17) Farina, V.; Krishnan, B. *J. Am. Chem. Soc.* **1991**, *113*, 9585.
(18) Cha, J. K.; Christ, W. J.; Kishi, Y. *Tetrahedron* **1984**, *40*, 2247.

Scheme 4



Vedejs's[19] transition state models for the osmylation reaction. Catalytic asymmetric dihydroxylation (AD) of **11b** at 0 °C for 2 days using commercially available AD mix-β or AD mix-α[20,21] gave mixtures of the same diastereomeric *anti*-diols **16** and **17** with poor diastereofacial selection. Using AD mix-β, the ratio of **16** to **17** (2:1, Scheme 4) was essentially the same as that obtained from the catalytic dihydroxylation of **11b** in the absence of a chiral ligand, while AD mix-α resulted in a reversal in the diastereoselectivity (**16**:**17** = 1:3.4). Little improvement in the diastereoselectivity of these reactions was observed using Sharpless's indoline (IND)[22] or pyrimidine (PYR)[23] based DHQ or DHQD chiral ligands, the former have been successfully employed in the AD of *cis*-alkenes (Scheme 4). In the case of **11a**, the enantiomer of **11b**, the diastereoselectivities of the catalytic asymmetric dihydroxylations were similarly poor. Both AD mix-α and AD mix-β gave **20** as the major diastereoisomer, albeit in low diastereomeric excess (Scheme 5). The failure of the pseudoenantiomeric DHQ and DHQD ligands to provide opposite diastereoisomers from the AD of chiral alkenes has been noted previously.[24] Unfortunately these diastereomeric diols could not be separated by column chromatography on silica gel, but they could be separated as their tetraacetate esters (see later). While the AD of (*Z*)-alkenes is known to give 1,2-diols in lower enantiomeric purities than their isomeric (*E*)-alkenes,[22] it has been reported that higher enantiomeric purities can be realized from (*Z*)-allylic alcohols and (*Z*)-homoallylic alcohols.[25] It has been suggested that hydrogen bonding between the hydroxy group and an oxo group on the osmium is responsible for the higher enantiotopic π-face selectivity in these substrates. However, the AD of the diol formed from hydrolysis of **11b** with $PdCl_2(MeCN)_2$ in aqueous MeCN[26] gave a mixture of diastereomeric 1,2,3,4-tetrols in a similar diastereomeric ratio to that obtained from the AD of **11b** with the various chiral ligands. Acid-catalyzed hydrolysis of the diastereomeric mixtures of **16** and **17** or **20** and **21** with aqueous 10% hydrochloric acid/ethanol (2:1) at 80 °C for 90 min gave mixtures of the diastereomeric imidazole hydrochloride salts **18** and **19** or **22** and **23**, respectively, in yields of 85−90%.

Scheme 5



(19) Vedejs, E.; McClure, C. K. *J. Am. Chem. Soc.* **1986**, *108*, 1094.
(20) AD mix-α and AD mix-β were purchased from the Aldrich Chemical Co.
(21) Sharpless, K. B.; Amberg, W.; Bennani, Y. L.; Crispino, G. A.; Harting, J.; Jeong, K. S.; Kwong, H. L.; Morikawa, K.; Wang, Z. M.; Xu, D.; Zhang, X. L. *J. Org. Chem.* **1992**, *57*, 2768.
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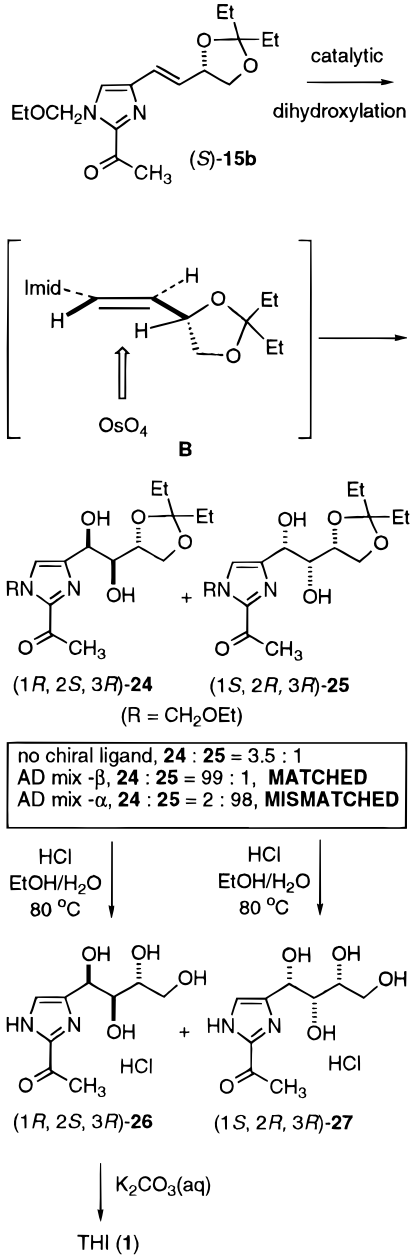
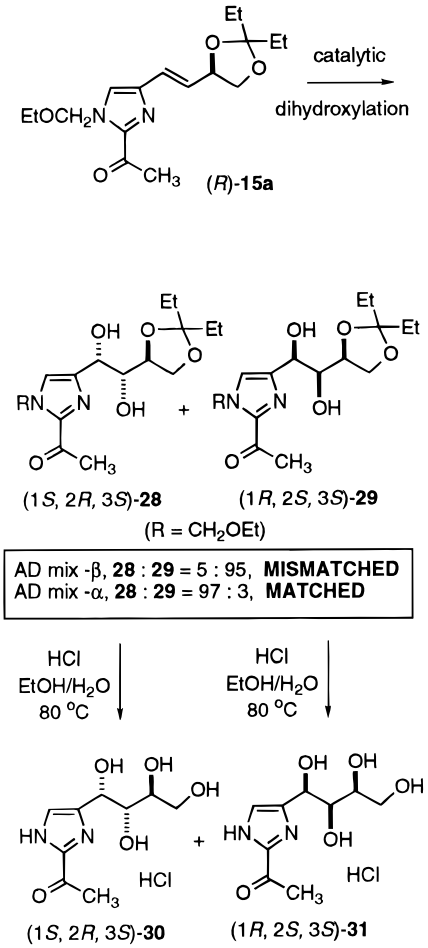
(25) Sharpless, K. B.; Van Nieuwenhze, M. S; *Tetrahedron Lett.* **1994**, *35*, 843.
(26) Lipshutz, B. H.; Pollart, D.; Monforte, J.; Kotsuki, H. *Tetrahedron Lett.* **1985**, *26*, 705.

Scheme 6



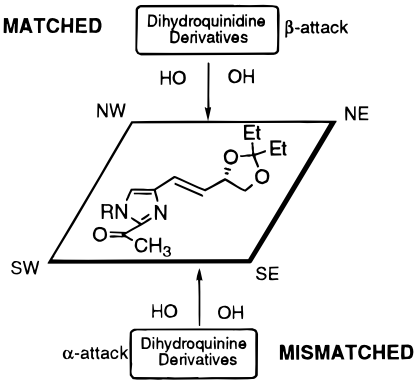
Scheme 7



Asymmetric Dihydroxylations of 4-[(1*E*)-Butenyl]-imidazole Derivatives. In contrast to the (*Z*)-alkenes **11a,b**, catalytic asymmetric dihydroxylation of **15b** at 0 °C for 3 days using AD mix-β and additional chiral ligand ((DHQD)$_2$-PHAL (4 mol %) and methanesulfonamide (2 equiv)) in *t*-BuOH/H_2O gave the *syn* (1*R*,2*S*)-diol **24**, in good yield (80%) and high diastereoselectivity (de 98%) as determined by ^{1}H NMR analysis (Scheme 6).[27] Catalytic dihydroxylation of **15b** in the absence of chiral ligand ($K_2OsO_4 \cdot H_2O$ (5 mol %)/$K_3Fe(CN)_6$ (3 equiv)/ K_2CO_3 (3 equiv)/ $MeSO_2NH_2$ (2 equiv)/*t*-BuOH, H_2O at 0 °C, 3 days) gave a mixture of **24** and its diastereomeric *syn*-(1*S*,2*R*)-diol **25** in a ratio of 3.5:1 respectively. The major diastereoisomer (**24**) was that expected on the basis of Kishi's[18] (**B** in Scheme 5) or Vedejs's[19] transition state models for the osmylation reaction. The AD of **15b** using AD mix-α was also highly diastereoselective and gave the *syn*-(1*S*,2*R*)-diol **25** in 96% de and in 67% yield after purification by column chromatography (Scheme 6). The AD reactions of **15a** with AD mix-β or AD mix-α were also highly diastereoselective and gave the diols **28** (de 90%) and **29** (de 94%), respectively, in good to excellent yields (Scheme 7). Hydrolysis of **24** with aqueous 10% hydrochloric acid/ethanol (2:1) at 80 °C for 90 min gave the imidazole hydrochloride salt **26**, which was identical in all respects to authentic THI·HCl. Neutralization of this mixture with aqueous potassium carbonate solution and then cooling to 5 °C and collection of the precipitate gave THI (**1**) in 24% yield from **24**. The physical properties of our synthetic **1** (mp 240−244 °C (lit.[6] mp 234−236 °C), $[\alpha]^{23}_D$ −14.9° (*c* 1.4, HCl/H_2O) (lit.[5] $[\alpha]^{25}_D$ −12° (*c* 1.17, 1 N HCl), ^{1}H NMR (DCl/D_2O)) were in agreement with those of **1** that was prepared according to the method of Buchi.[6] In a similar fashion the diols **25**, **28**, and **29** were converted to their corresponding imidazole hydrochloride salts **27**, **30**, and **31**, respectively, in high yields (Schemes 6 and 7). Attempts to isolate the free imidazole derivatives of **27**, **30**, or **31**, as was successfully achieved above with THI, by neutralization of an aqueous solution of these hydrochloride salts with aqueous potassium carbonate solution and then cooling to 5 °C failed to provide a precipitated product. Consequently, these tetrols were characterized as their hydrochloride salts. The hydrochloride salt **30** had identical ^{1}H and ^{13}C NMR spectral data to those of THI·HCl (**26**) and an equal and opposite specific rotation ($[\alpha]^{23}_D$ +14.9 (*c* 0.7, H_2O)). While the salts **27** and **31** had identical NMR spectra. The stereochemical outcomes of the AD

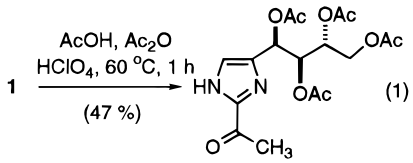
(27) (a) For the AD of chiral (*E*)-alkenes, see: Morikawa, K.; Sharpless, K. B. *Tetrahedron Lett.* **1993**, *34*, 5575. Wade, P. A.; Cole, D. T.; D'Ambrosio, S. G. *Tetrahedron Lett.* **1994**, *35*, 53. (b) For the AD of chiral (*E*)-alkenes, see: Honda, T.; Horiuchi, S.; Mizutani, H.; Kanai, K. *J. Org. Chem.* **1996**, *61*, 4944.

Scheme 8

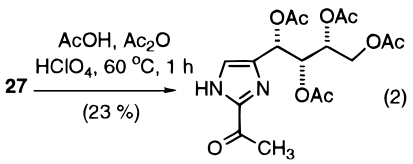


reactions of **15a,b** were consistent with Sharpless's mnemonic[21,28,29] (Scheme 8) in which the imidazole group occupies the southwest corner, which is believed to be attractive to flat aromatic groups, and the dioxolane ring occupies the NE corner. Both the matched and mismatched cases were highly diastereoselective (Schemes 6 and 7).

Proof of Stereochemistry. While the stereochemistry of the *syn*-1,2-diols **26**, **27**, **30**, and **31** was clear, from the chemical correlations of **26** and **30** with THI (**1**) and the known *cis* dihydroxylations of alkenes, the stereochemistry of the *anti*-1,2-diols **18**, **19**, **22**, and **23** was not. To assist in these stereochemical assignments, and in the separation of diastereoisomers, the tetrols were converted to their corresponding tetraacetates by acetylation with acetic anhydride/acetic acid/perchloric acid (cat.) at 60 °C. Acetylation of THI (**1**) or **27** at 60 °C for 1 h gave the tetraacetates **32** and **33**, respectively, as single diastereoisomeric compounds in moderate to poor yields (47 and 23%, respectively, eqs 1 and 2). The poor yield of acetylated product **33** was thought to be due to the poor solubility of the hydrochloride salt **27** in the reaction medium. Acetylation of **30** or **31** under similar



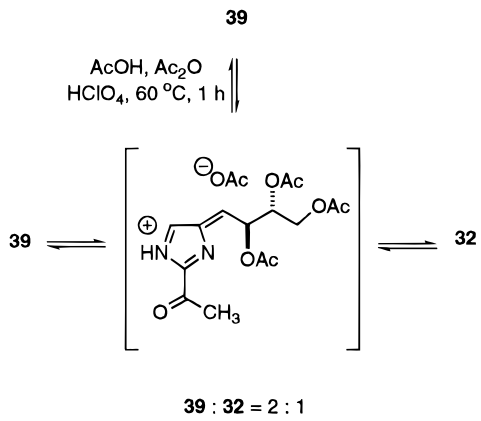
(1*R*, 2*S*, 3*R*)-**32**



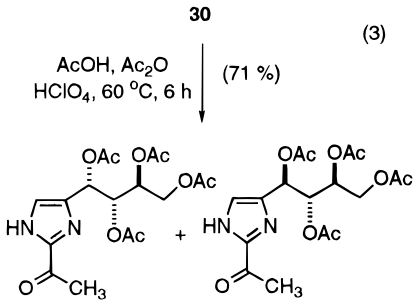
(1*S*, 2*R*, 3*R*)-**33**

reaction conditions also gave poor yields of acetylated products. Extended reaction times (6 h) gave good to excellent yields of acetylated products; however mixtures of two diastereomeric acetates resulted in each case (eqs 3 and 4). The major tetraacetate **34** ($[\alpha]^{24}_D$ + 19.4° (*c* 0.06, MeCN)) from the acetylation of **30** was identical spectroscopically to **32** ($[\alpha]^{24}_D$ −22.6° (*c* 0.58, MeCN)) which was obtained from **1**, while the major tetraacetate **36** from the acetylation of **31** was identical spectroscopically to **33**. The minor diastereomeric tetraacetates (**35** and **37**) were clearly *anti*-1,2-acetates that were the result of epimerization at C-1. Likewise, acetylation of mixtures of the diastereomeric imidazole hydrochloride salts **18** and **19** or **22** and **23** at 60 °C for 6 h gave mixtures of four (two *syn*-1,2-diacetates and two *anti*-1,2-diacetates) diastereomeric acetates. For example, acetylation of a 3.4:1 mixture of **19** and **18**, respectively, gave, in 65% yield, a 4:2.7:1.1:1 mixture of the tetraacetates **38**, **33**, **39**, and **32**, respectively (eq 5). The diastereoisomeric tetraacetates could be separated by preparative HPLC. Exposure of diastereomerically pure **39** to the acetylation conditions also gave a mixture (*ca.* 2:1) of **39** and **32**. A proposed stabilized cationic intermediate for this latter epimerization reaction is shown in Scheme 9. Thus the formation of the C-1 epimeric acetates in these acetylation reactions allowed us to

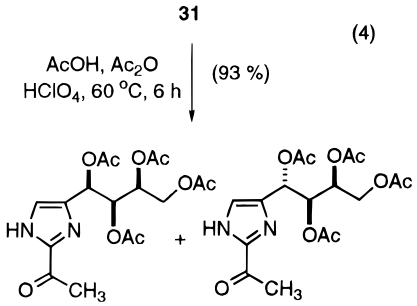
Scheme 9



39 : **32** = 2 : 1



(**34** : **35** = 5.3 : 1)

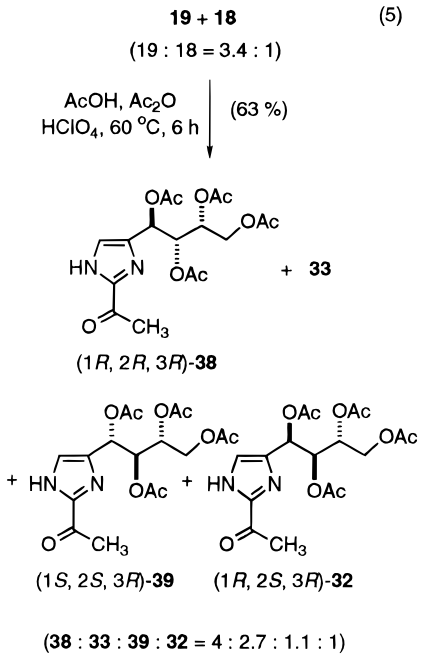


(**36** : **37** = 1.3 : 1)

(28) Johnson, R. A.; Sharpless, K. B. in *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 1993; Chapter 4.4, pp 243−245.

(29) For examples of anomalous face selectivity in the AD reaction, see: Hale, K. J.; Manaviazar, S.; Peak, S. A. *Tetrahedron Lett.* **1994**, *35*, 425. Boger, D. L.; McKie, J. A.; Nishi, T.; Ogiku, T. *J. Am. Chem. Soc.* **1996**, *118*, 2301. Salvadori, P.; Superchi, S.; Minutolo, F. *J. Org. Chem.* **1996**, *61*, 4190.

unequivocally assign the stereochemistry to the 1,2-*anti*-tetraacetates **35**, **37**, **38**, and **39**.



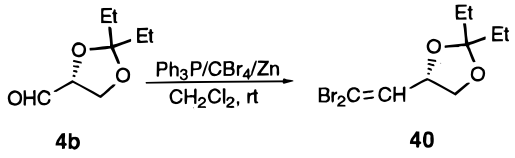
Conclusion

In summary, we have developed a new method for the synthesis of THI and its *syn* 1,2-dihydroxy analogues in high diastereomeric and enantiomeric purities. The synthesis of the *anti* 1,2-dihydroxy analogues of THI have proven more difficult due to the poor diastereofacial control in the AD reaction of the (*Z*)-alkenes **11a,b.** The biological activities of these tetrols are currently under investigation and will be reported elsewhere.

Experimental Section

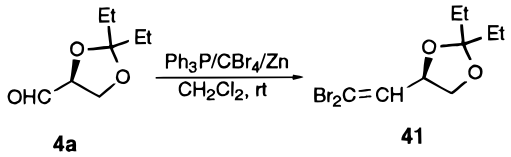
General procedures were as previously described.[10] Preparative HPLC was carried out using a Waters pump Model 510 and a Waters μ-Porasil column (particle size 10 mm, pore size 125, dimensions 25 mm × 100 mm). The UV detector was a Waters Series 450 variable wavelength detector operating at 254 nm.

(4*S*)-2,2-Diethyl-4-(2′,2′-dibromoethenyl)-1,3-dioxolane (40). A mixture of triphenylphosphine (26.56 g, 101.3 mmol), carbon tetrabromide (33.58 g, 101.3 mmol), and zinc dust (6.62 g, 101.3 mmol) were suspended in anhydrous CH_2Cl_2 (200 mL), and the mixure was stirred for 24 h under N_2.



The aldehyde **4b**[8] (5.16 g, 32.7 mmol) was then added, and the mixture was stirred for a further 24 h. The mixture was diluted with hexane (800 mL) and filtered, and the insoluble residue was taken into CH_2Cl_2 (100 mL). The CH_2Cl_2 solution was then diluted with hexane (400 mL) and filtered. The combined filtrates were washed with saturated aqueous NH_4Cl (400 mL) and H_2O (300 mL) and dried ($MgSO_4$). The solvent was removed to give a light yellow oil of essentially pure olefin (8.90g, 87%), $[\alpha]^{28}_D$ +6.8° (*c* 1.18, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.52 (1H, d, J = 7.2 Hz); 4.72 (1H, dd, J = 6.4, 7.6 Hz); 4.21 (1H, dd, J = 6.4, 8.4 Hz); 3.63 (1H, t, J = 7.6 Hz); 1.65 (2 × 2H, p, J = 7.6 Hz); 0.93; 0.89 (2 × 3H, 2 × t, J = 7.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.9; 113.4; 92.4; 76.3; 68.2; 29.59; 29.35; 8.07; 7.96. MS (CI positive): *m*/*z* 315 (M + H$^+$, 6); 285 (70); 229 (20); 215 (31); 160 (100); 119 (100); 107 (100). IR (neat): 2971; 2938; 2880; 1718; 1616; 1458; 1172; 1078; 915; 808; 665 cm^{-1}. HRMS: calcd for $C_9H_{15}{}^{79}Br_2O_2$ 312.9440, found 312.9446.

(4*R*)-Diethyl-4-(2′,2′-dibromoethenyl)-1,3-dioxolane (41). Using the procedure described above for the synthesis of **40**, the title compound was obtained as a light yellow oil (77%), $[\alpha]^{25}_D$ −6.4° (*c* 1.05, $CHCl_3$). Spectral data are identical to those of **40**.



(4*S*)-2,2-Diethyl-4-ethynyl-1,3-dioxolane (5b). To a solution of alkene **40** (6.88 g, 22.1 mmol) in anhydrous THF (50 mL) at −78 °C under N_2 was added *n*-BuLi in hexanes (48.7 mmol). The solution was stirred for 1 h at −78 °C and then for 1 h at ambient temperature. Water (15 mL) and hexane (60 mL) were added, and the phases were separated. The aqueous phase was extracted with hexane (15 mL), and the combined extracts were washed with H_2O (10 mL) and dried ($MgSO_4$). The solvent was removed to leave an orange oil which was purified by bulb-to-bulb distillation (61 °C/6 mmHg) to give the title dioxolane as a clear oil (2.36 g, 69%), $[\alpha]^{27}_D$ +44.1° (*c* 0.75, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.70 (1H, ddd, J = 2.0, 6.4, 8.0 Hz); 4.18 (1H, dd, J = 6.4, 8.0 Hz); 3.89 (1H, dd, J = 6.8, 8.0 Hz); 2.49 (1H, d, J = 2.0 Hz); 1.74; 1.63 (2 × 2H, 2 × q, J = 7.6 Hz); 0.94; 0.89 (2 × 3H, 2 × t, J = 7.6 Hz). ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 114.5; 81.3; 73.8; 70.3; 65.5; 29.6; 29.3; 8.1; 7.8. MS (CI positive): *m*/*z* 155 (M + H$^+$, 26); 125 (100); 87 (96). IR (neat): 3300 (HC≡C); 2972; 2940; 2883; 1464; 1355; 1172; 1079; 912; 665 cm^{-1}. HRMS: calcd for $C_9H_{15}O_2$ 155.1072, found 155.1070.

(4*R*)-2,2-Diethyl-4-ethynyl-1,3-dioxolane (5a). Using the procedure described above for **5b**, the title compound was obtained as a clear oil (76%) after bulb-to-bulb distillation (85 °C/10 mmHg), $[\alpha]^{26}_D$ −38.3° (*c* 1.75, $CHCl_3$). Spectral data are identical to those of **5b**.

(4*S*)-2,2-Diethyl-4-((trimethylstannyl)ethynyl)-1,3-dioxolane (6b). To a solution of alkyne **5b** (1.0 g, 6.5 mmol) in anhydrous THF (5 mL) at −78 °C under N_2 was added *n*-BuLi in hexanes (7.15 mmol). The reaction was stirred for 10 min at −78 °C and 20 min at 0 °C. A solution of trimethyltin chloride (1.60 g, 7.80 mmol) in THF (5 mL) was then added dropwise. The solution was stirred for 35 min at 0 °C and then warmed to rt and left to stir for 16 h. The mixture was diluted with CH_2Cl_2 (20 mL), washed consecutively with H_2O (10 mL) and saturated aqueous NaCl (10 mL), and then dried ($MgSO_4$). The solvent was removed to leave a thick black oil. Bulb-to-bulb distillation (104 °C/0.5 mmHg) gave the title stannane as a fluorescent green oil (1.23 g, 60%), $[\alpha]^{27}_D$ +24.4° (*c* 1.3, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.70 (1H, dd, J = 6.4, 7.6 Hz); 4.16 (1H, dd, J = 6.4, 8.0 Hz); 3.83 (1H, t, J = 8.0 Hz); 1.74; 1.62 (2 × 2H, 2 × q, J = 7.6 Hz); 0.94; 0.89 (2 × 3H, 2 × t, J = 7.6 Hz); 0.289 (9H, s, $^2J(^{117}Sn,H)$ = 58.0 Hz, $^2J(^{119}Sn,H)$ = 60.4 Hz). MS (EI positive): *m*/*z* 289* (M − Et$^+$, 51); 217* (31); 165* ($SnMe_3^+$, 100). HRMS: calcd for $C_{10}H_{17}O_2{}^{120}Sn$ 289.0250, found 289.0241. *identifies ^{120}Sn isotope peak.

(4*R*)-2,2-Diethyl-4-((trimethylstannyl)ethynyl)-1,3-dioxolane (6a). Using the procedure described above for the synthesis of **6b**, the title compound was obtained as a bright green oil (59%) after bulb-to-bulb distillation, $[\alpha]^{26}_D$ −23.4° (*c* 0.97, $CHCl_3$). Spectral data are identical to those of **6b**.

(3′*S*)-4-[3′,4′-*O*-(3′-Pentylidene)-3′,4′-dihydroxybut-1′-ynyl]-1-(ethoxymethyl)imidazole (8b). A solution of trimethylstannane **6b** (0.80 g, 2.53 mmol), iodoimidazole **7** (0.76 g, 3.03 mmol), and $Pd(Ph_3P)_4$ (290 mg, 0.25 mmol) in anhydrous DMF (10 mL) in a thick-walled reaction vessel was degassed with a stream of argon. The vessel was sealed, and the solution was stirred at 80 °C for 24 h in the dark. The

resulting dark solution was then cooled to rt, diluted with ethyl acetate (50 mL), and filtered. The filtrate was washed with a half-saturated aqueous solution of NaCl (2 × 20 mL), dried ($MgSO_4$), and concentrated to give a dark oil. Purification by column chromatography (50% ethyl acetate/hexane) gave the title compound as a tan oil (405 mg, 58%), $[\alpha]^{29}_D$ +18.0° (*c* 5.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (1H, d, J = 1.2 Hz); 7.24 (1H, d, J = 1.6 Hz); 5.26 (2H, s); 4.92 (1H, t, J = 6.8 Hz); 4.22 (1H, dd, J = 6.4, 8.0 Hz); 3.97 (1H, t, J = 7.6 Hz); 3.44 (2H, q, J = 6.8 Hz); 1.76; 1.65 (2 × 2H, 2 × q, J = 7.6 Hz); 1.18 (3H, t, J = 6.8 Hz); 0.95; 0.91 (2 × 3H, 2 × t, J = 7.6 Hz). ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 137.1; 124.2; 122.9; 114.1; 86.2; 77.2; 76.3; 70.1; 66.1; 64.4; 29.5; 29.2; 14.5; 8.0; 7.7. MS (ES positive): m/z 279 (M + H^+, 100); 193 (14); 59 (8); 42 (63). IR (neat): 2973; 2937; 2881; 2238; 1493; 1355; 1107; 1078; 913; 752 cm^{-1}. HRMS: calcd for $C_{15}H_{22}N_2O_3$ 278.1630, found 278.1626.

(3′*R*)-4-[3′,4′-*O*-(3′-Pentylidene)-3′,4′-dihydroxybut-1′-ynyl]-1-(ethoxymethyl)imidazole (8a). Using the procedure described above for the synthesis of imidazole **8b**, the title compound was obtained as a tan oil (53%) after purification by column chromatography (40% ethyl acetate/hexane), $[\alpha]^{23}_D$ −25.9° (*c* 1.03, $CHCl_3$). Spectral data are identical to those of **8b**.

Synthesis of Imidazole 8b and (2*S*,7*S*)-1,2:7,8-*O*-di(3-pentylidene)-1,2,7,8-tetrahydroxy-3,5-octadiyne (9) *via* Palladium(0)/Alkyne Coupling. A solution of alkyne **5b** (1.83 g, 11.88 mmol), iodoimidazole **7** (3.59 g, 14.26 mmol), CuI (230 mg, 1.21 mmol), $PdCl_2(Ph_3P)_2$ (420 mg, 0.60 mmol), and triethylamine (12.0 g, 0.119 mmol) in anhydrous CH_3CN (20 mL) was degassed using a stream of argon, and the solution was heated to reflux for 4 h under N_2. The mixture was then cooled to rt, poured into H_2O (100 mL), and extracted with CH_2Cl_2 (4 × 80 mL). The combined extracts were dried ($MgSO_4$), and the solvent was removed to leave a thick black oil. Purification by column chromatography (50% ethyl acetate/hexane) gave the target imidazole **8b** (0.76 g, 23%) plus the dialkyne **9** (1.26 g, 69%). **Data for 9.** ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.77 (2H, t, J = 6.0 Hz); 4.17 (2H, dd, J = 6.4, 8.0 Hz); 3.92 (2H, dd, J = 6.4, 8.0 Hz); 1.73; 1.63 (2 × 4H, 2 × q, J = 7.6 Hz); 0.94; 0.88 (2 × 6H, 2 × t, J = 7.6 Hz). ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 114.8; 77.2; 69.9; 69.5; 65.9; 29.5; 29.2; 8.1; 7.8. MS (EI positive): m/z 277 (M − Et^+, 44); 217 (10); 191 (15); 135 (23); 87 (31); 57 (100). IR (neat): 2972; 2938; 2881; 2150; 1463; 1336; 1171; 1082; 910; 762 cm^{-1}. HRMS: calcd for $C_{16}H_{21}O_4$ 277.1440, found 277.1446.

(3′*S*)-2-Acetyl-4-[3′,4′-*O*-(3′-pentylidene)-3′,4′-dihydroxybut-1′-ynyl]-1-(ethoxymethyl)imidazole (10b). To a solution of alkyne **8b** (550 mg, 1.98 mmol) in anhydrous THF (5 mL) at −78 °C under N_2 was added *n*-BuLi in hexanes (2.37 mmol), and the solution was stirred for 90 min at −78 °C. Freshly distilled *N*-methoxy-*N*-methylacetamide (0.29 g, 2.77 mmol) in THF (5 mL) was then added dropwise, and the reaction mixture was stirred for 1 h at −78 °C and then was slowly warmed to rt and stirred for a further 1 h. The mixture was diluted with CH_2Cl_2 (15 mL), washed with a 5% aqueous solution of $NaHCO_3$ (5 mL), and dried ($MgSO_4$), and the solvent was removed to leave a black oil. Purification by column chromatography (40% ethyl acetate/hexane) gave the title compound as a tan oil (**10b**, 67% corrected for recovered starting alkyne), $[\alpha]^{29}_D$ +23.3° (*c* 2.40, $CHCl_3$) plus the starting alkyne **8b** (150 mg). **Data for 10b.** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (1H, s); 5.75 (2H, s); 4.93 (1H, t, J = 7.2 Hz); 4.24 (1H, t, J = 7.2 Hz); 4.00 (1H, t, J = 7.2 Hz); 3.54 (2H, q, J = 7.2 Hz); 2.67 (3H, s); 1.77; 1.66 (2 × 2H, 2 × q, J = 7.2 Hz); 1.20 (3H, t, J = 7.2 Hz); 0.96; 0.92 (2 × 3H, 2 × t, J = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.6; 142.3; 128.1; 123.8; 114.4; 86.9; 78.4; 77.6; 70.1; 66.2; 65.3; 29.6; 29.3; 27.5; 14.8; 8.2; 7.9. MS (ES positive): m/z 321 (M + H^+, 100). IR (neat): 2973; 2937; 2881; 2201; 1685; 1457; 1352; 1170; 1108; 1079; 913; 764 cm^{-1}. HRMS: calcd for $C_{17}H_{24}N_2O_4$ 320.1736, found 320.1749.

(3′*R*)-2-Acetyl-4-[3′,4′-*O*-(3′-pentylidene)-3′,4′-dihydroxybut-1′-ynyl]-1-(ethoxymethyl)imidazole (10a). Using the procedure described above for the synthesis of the methyl ketone **10b**, the title compound was obtained pure as a tan oil (69%), with the starting alkyne (11%) also isolated after column chromatography (20% ethyl acetate/hexane), $[\alpha]^{23}_D$ −32.4° (*c* 1.0, $CHCl_3$). Spectral data are identical to those of **10b**.

(3′*S*)-(*Z*)-2-Acetyl-4-[3′,4′-*O*-(3′-pentylidene)-3′,4′-dihydroxybut-1′-enyl]-1-(ethoxymethyl)imidazole (11b). To a solution of alkyne **10b** (740 mg, 2.31 mmol) and quinoline (300 mg, 2.31 mmol) in hexane (10 mL) was added 10% Pd on $CaCO_3$ (70 mg). The mixture was stirred for 2 h under a H_2 atmosphere until the hydrogenation was complete by ^{1}H NMR analysis. The mixture was vacuum filtered through a bed of Celite and the plug washed thoroughly with ethyl acetate. The filtrate was then concentrated *in vacuo* to give a tan oil which was purified by column chromatography (15% ethyl acetate/hexane) to give the title (*Z*)-alkene as a tan oil (595 mg, 80%), $[\alpha]^{21}_D$ +18.7° (*c* 0.87, $CHCl_3$). A small amount of the (*E*)-alkene (35 mg, 5%) and over-reduced alkane (30 mg, 4%) were also separately isolated from the column, both as tan oils. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 (1H, s); 6.39 (1H, dd, J = 1.2, 7.6 Hz); 5.79−5.73 (3H, m,); 5.69−5.64 (1H, m); 4.43 (1H, dd, J = 6.4, 8.0 Hz); 3.63 (1H, t, J = 8.0 Hz); 3.54 (2H, q, J = 7.2 Hz); 2.66 (3H, s); 1.72; 1.71 (2 × 2H, 2 × q, J = 7.2 Hz); 1.20 (3H, t, J = 7.2 Hz); 0.97; 0.96 (2 × 3H, 2 × t, J = 7.2 Hz). ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 190.8; 142.4; 130.4; 139.0; 124.0; 122.1; 113.1; 77.1; 73.9; 70.2; 65.0; 30.04; 29.85; 27.2; 14.8; 8.11; 7.92. MS (ES positive): m/z 323 (M + H^+, 100); 237 (56). HRMS: calcd for $C_{17}H_{26}N_2O_4$ 322.1892, found 322.1901.

(3′*R*)-(*Z*)-2-Acetyl-4-[3′,4′-*O*-(3′-pentylidene)-3′,4′-dihydroxybut-1′-enyl]-1-(ethoxymethyl)imidazole (11a). Using the procedure described above for the synthesis of **11b**, the title compound was obtained pure as a tan oil (79%), with the (*E*)-alkene (6%) and over-reduced alkane (7%) also isolated after purification by column chromatography (15% ethyl acetate/hexane), $[\alpha]^{27}_D$ −16.5° (*c* 0.62, $CHCl_3$). Spectral data are identical to those of **11b**.

(4*S*)-(*E*)-2,2-Diethyl-4-(2′-(tributylstannyl)ethenyl)-1,3-dioxolane and (4*S*)-(*Z*)-2,2-Diethyl-4-(2′-(tributylstannyl)ethenyl)-1,3-dioxolane (12). A mixture of freshly distilled alkyne **5b** (1.2 g, 7.79 mmol), Bu_3SnH (2.50 g, 8.57 mmol), and a catalytic amount of AIBN under argon was sealed in a thick-walled reaction vessel and set to react at 130 °C for 2.5 h. The solution was then cooled to rt and the solution evaporated *in vacuo*. Purification by bulb-to-bulb distillation (125 °C/0.01 mmHg) gave a mixture of the title stannanes as a clear oil (2.94 g, 85%, *E*:*Z* = 81:19). ***(E)*-Isomer.** ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.31 (1H, dd, J = 0.8, 19.2 Hz); 5.94 (1H, dd, J = 6.4, 18.8 Hz); 4.49−4.43 (1H, m); 4.10 (1H, dd, J = 6.0, 8.0 Hz); 3.56 (1H, t, J = 8.0 Hz); 1.71−1.62 (4H, m); 1.52−1.25 (18H, m); 0.98−0.87 (15H, m). ***(Z)*-Isomer.** ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.44 (1H, dd, J = 8.4, 12.4 Hz); 6.19 (1H, d, J = 12.4 Hz); 4.28−4.23 (1H, m); 4.04 (1H, dd, J = 6.0, 7.6 Hz); 3.58 (1H, t, J = 8.0 Hz); 1.71−1.62 (4H, m); 1.52−1.25 (18H, m); 0.98−0.87 (15H, m).

(4*S*)-(*E*)-2,2-Diethyl-4-(2′-(trimethylstannyl)ethenyl)-1,3-dioxolane (13b). To a stirred slurry of chromium(II) chloride (1.46 g, 11.8 mmol) in anhydrous THF (16 mL) under N_2 was added anhydrous DMF (0.70 g, 11.8 mmol), and the reaction was stirred for 15 min at rt. Aldehyde **4b** (190 mg, 1.18 mmol) and (dibromomethyl)trimethylstannane (700 mg, 2.07 mmol) in anhydrous THF (4 mL) were then added, and the reaction vessel was wrapped in aluminum foil to exclude light. Lithium iodide (0.63 g, 4.72 mmol) in anhydrous THF (4 mL) was added and the reaction left to stir for 16 h. The mixture was then poured into H_2O (30 mL) and extracted with 40−60 °C petroleum ether (3 × 30 mL). The combined extracts were washed with H_2O (20 mL) and saturated aqueous NaCl (20 mL) and then dried ($MgSO_4$) and concentrated to leave a light yellow oil. Purification by bulb-to-bulb distillation (78 °C/0.01 mmHg) gave the vinylstannane as a clear oil (300 mg, 80%, ratio *E*:*Z* = 88:12). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.38 (1H, dd, J = 0.8, 18.8 Hz, $^2J(^{117}Sn,H)$ = 76 Hz, $^2J(^{119}Sn,H)$ = 78 Hz); 5.95 (1H, dd, J = 7.2, 18.8 Hz, $^2J(^{117}Sn,H)$ = 66.4 Hz, $^2J(^{119}Sn,H)$ = 70.4 Hz); 4.49−4.43 (1H, m); 4.10 (1H, dd, J = 6.4, 8.0 Hz); 3.57 (1H, t, J = 8.0 Hz); 1.71−1.59 (4H, m); 1.00−0.88 (6H, m); 0.14 (9H, s, $^2J(^{117}Sn,H)$ = 53.6 Hz, $^2J(^{119}Sn,H)$ = 56.0 Hz). ^{13}C NMR (75.6 MHz, $CDCl_3$) δ 144.5; 134.2; 113.2;

80.2; 67.7; 29.96; 29.76; 8.12; 8.05; −9.8. HRMS: calcd for $C_{12}H_{25}O_2{}^{120}Sn$ 321.0876, found 321.0871.

(4*R*)-(*E*)-2,2-Diethyl-4-(2′-(trimethylstannyl)ethenyl)-1,3-dioxolane (13a). Using the general procedure described above for the synthesis of **13b**, the title compound was obtained as a pale oil (85%, *E:Z* = 94:6) after bulb-to-bulb distillation (51 °C/0.1 mmHg). Spectral data are identical to those of **13a**.

Table 1

run	solvent[a]	catalyst	yield of **14b**, %
1	DMF	$Pd(Ph_3P)_4$	26
2	THF	$Pd(Ph_3P)_4$	28
3	acetonitrile	$Pd(Ph_3P)_4$	31
4	DMF	$Pd_2(dba)_3$, $AsPh_3$, CuI	45

[a] All reactions were carried out in sealed reaction vessels at 80 °C under argon.

(3′*S*)-(*E*)-4-[3′,4′-*O*-(3′-Pentylidene)-3′,4′-dihydroxybut-1′-enyl]-1-(ethoxymethyl)imidazole (14b). See Table 1. Representative Procedure. A solution of iodoimidazole **7** (560 mg, 2.22 mmol), stannane **12** (900 mg, 2.02 mmol, (*E*):(*Z*) = 81:19), and $Pd(PPh_3)_4$ (230 mg, 2.0×10^{-4} mol) in anhydrous DMF (10 mL) in a thick-walled tube was flushed with argon, sealed, and stirred at 80 °C for 24 h. The reaction was then cooled to rt, diluted with CH_2Cl_2 (60 mL), washed with H_2O (30 mL), dried ($MgSO_4$), and concentrated. Purification by column chromatography (45% ethyl acetate/hexane) gave the title compound as a tan oil (120 mg, 26%), $[\alpha]^{25}{}_D$ +18.8° (*c* 3.0, MeOH). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (1H, d, J = 1.2 Hz); 6.95 (1H, d, J = 1.6 Hz); 6.58 (1H, d, J = 15.6 Hz); 6.31 (1H, dd, J = 8.0, 16.0 Hz); 5.24 (2H, s); 4.67−4.61 (1H, m); 4.14 (1H, dd, J = 6.0, 8.0 Hz); 3.65 (1H, t, J = 8.0 Hz); 3.44 (2H, q, J = 7.2 Hz); 1.73−1.65 (4H, m); 1.18 (3H, t, J = 7.2 Hz); 0.944; 0.935 (2 × 3H, 2 × t, J = 7.2 Hz). ^{13}C NMR (75.6 MHz, $CDCl_3$): δ 140.0); 137.3; 125.2; 124.4; 116.6; 112.9; 77.3; 76.0; 69.8; 64.1; 29.8; 29.6; 14.4; 7.9; 7.8. MS (ES positive): m/z 281 (M + H$^+$, 100). HRMS: calcd for $C_{15}H_{24}O_3N_2$ 280.1787, found 280.1793.

Synthesis of 14b *via* the Trimethylvinylstannane 13b. A solution of trimethylvinylstannane **13b** (100 mg, 0.314 mmol), iodoimidazole **7** (87 mg, 3.45×10^{-4} mol), and $Pd(Ph_3P)_4$ (20 mg, 1.73×10^{-5} mol) in anhydrous DMF (2.5 mL) in a thick-walled reaction vessel was flushed with argon and then sealed and left to stir at 80 °C in the dark for 24 h. The solution was then cooled to rt, diluted with CH_2Cl_2 (10 mL), washed with a half-saturated aqueous solution of NaCl (2 × 5 mL), dried ($MgSO_4$), and concentrated. Purification by column chromatography (40% ethyl acetate/hexane) gave the title alkene as a tan oil (64 mg, 83%).

(3′*R*)-(*E*)-4-[3′,4′-*O*-(3′-Pentylidene)-3′,4′-dihydroxybut-1′-enyl]-1-(ethoxymethyl)imidazole (14a). Using the procedure described above for the synthesis of **14b**, the title compound was obtained as a dark tan oil (46%) after purification by column chromatography (35% ethyl acetate/hexane), $[\alpha]^{25}{}_D$ −18.3° (*c* 0.82, MeOH). Spectral data are identical to those of **14b**.

(3′*S*)-(*E*)-2-Acetyl-4-[3′,4′-*O*-(3′-pentylidene)-3′,4′-dihydroxybut-1′-enyl]-1-(ethoxymethyl)imidazole (15b). The title compound was prepared from the alkene **14b** (345 mg, 1.23 mmol) using the method descibed above for the synthesis of **10b**. Purification by column chromatography (15% ethyl acetate/hexane) gave the title methyl ketone as a tan oil (255 mg, 65%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (1H, s); 6.61 (1H, d, J = 15.6 Hz); 6.37 (1H, dd, J = 7.2, 15.6 Hz); 5.75 (2H, s); 4.69−4.62 (1H, m); 4.16 (1H, dd, J = 6.0, 8.1 Hz); 3.66 (1H, t, J = 8.1 Hz); 3.53 (2H, q, J = 6.9 Hz); 2.68 (3H, s); 1.75−1.65 (4H, m); 1.19 (3H, t, J = 6.9 Hz); 0.96; 0.94 (2 × 3H, 2 × t, J = 7.5 Hz). ^{13}C NMR (75.6 MHz, $CDCl_3$) δ 190.9; 142.6; 139.5; 127.2; 124.0; 122.2; 113.3; 77.14; 77.10; 69.9; 64.9; 29.94; 29.67; 27.3; 14.8; 8.1. MS (CI positive): m/z 332 (M$^+$, 21); 293 (24); 277 (16); 265 (11); 236 (30); 177 (68); 161 (100). HRMS: calcd for $C_{17}H_{26}N_2O_4$ 322.1892, found 322.1891.

(3′*R*)-(*E*)-2-Acetyl-4-[3′,4′-*O*-(3′-pentylidene)-3′,4′-dihydroxybut-1′-enyl]-1-(ethoxymethyl)imidazole (15a). Using the procedure described above for the synthesis of **15b**, the title compound was obtained pure as a light tan oil (72%) after purification by column chromatography (15% ethyl acetate/hexane) with the starting alkene (19%) also recovered, $[\alpha]^{26}{}_D$ −39.0° (*c* 0.92, $CHCl_3$). Spectral data of **15a** are identical to those of **15b**.

(1′*S*,2′*S*,3′*R*)-2-Acetyl-4-[3′,4′-*O*-(3′-pentylidene)-1′,2′,3′,4′ -tetrahydroxy-1′-butyl]-1-(ethoxymethyl)imidazole (16). General AD Procedure for Alkenes Using AD mix-*β*. Into a 25 mL round bottom flask were added AD mix-β[20] (1.09 g), $(DHQD)_2PHAL$ (24 mg, 3.09×10^{-5} mol), $K_2OsO_4 \cdot 2H_2O$ (2.8 mg, 9.75×10^{-6} mol), and methanesulfonamide (147 mg, 1.55 mmol). The reagents were dissolved in H_2O (4 mL) and *t*-BuOH (2 mL) and the solution cooled to 0 °C. The (*Z*)-alkene **11b** (250 mg, 7.76×10^{-4} mol) in *t*-BuOH (2 mL) was added in a single addition, and the reaction was allowed to stir for 48 h at 0 °C until complete by TLC. Sodium sulfite (1.2 g) was then added, and the reaction was warmed to rt and stirred for 1 h. The mixture was extracted with CH_2Cl_2 (4 × 5 mL) and ethyl acetate (5 mL), and the combined extracts were washed with a 2 M aqueous solution of KOH (7 mL), dried ($MgSO_4$), and concentrated. Purification by column chromatography (40% ethyl acetate/hexane) gave the title compounds as a pale yellow oil (200 mg, 72%). The ratio of **16:17** was 2.0:1 from ^{1}H NMR analysis.

16. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (1H, s); 5.77 (2H, d, J = 2.4 Hz); 4.82 (1H, dd, J = 4.0, 6.4 Hz); 4.56 (1H, d, J = 4.0 Hz); 4.23−4.18 (1H, m); 4.04−3.98 (1H, m); 3.85−3.73 (2H, m); 3.66 (1H, d, J = 3.6 Hz); 3.561 (2H, q, J = 7.2 Hz); 2.62 (3H, s); 1.74−1.59 (4H, m); 1.207 (3H, t, J = 7.2 Hz); 0.926; 0.881 (2 × 3H, 2 × t, J = 7.2 Hz). ^{13}C NMR (75.6 MHz, $CDCl_3$): δ 190.3; 142.8; 141.7; 122.4; 113.8; 77.8; 77.4; 75.5; 69.4; 68.2; 65.2; 29.6; 29.0; 27.3; 14.8; 8.13; 8.05. MS (ES positive): m/z 357 (M + H$^+$, 100). HRMS: calcd for $C_{15}H_{23}N_2O_6$ 327.1556, found 327.1556.

(1′*R*,2′*R*,3′*R*)-2-Acetyl-4-[3′,4′-*O*-(3′-pentylidene)-1′,2′,3′, 4′-tetrahydroxy-1′-butyl]-1-(ethoxymethyl)imidazole (17). General AD Procedure for Alkenes Using AD Mix-α. Into a 25 mL round bottom flask were added AD mix-α[20] (1.09 g), $(DHQ)_2PHAL$ (24 mg, 3.09×10^{-5} mol), $K_2OsO_4 \cdot 2H_2O$ (2.8 mg, 9.75×10^{-6} mol), and methanesulfonamide (147 mg, 1.55 mmol). The reagents were dissolved in H_2O (4 mL) and *t*-BuOH (2 mL), and the solution was then cooled to 0 °C. The (*Z*)-alkene **11b** (250 mg, 7.76×10^{-4} mol) in *t*-BuOH (2 mL) was added in a single addition, and the reaction was allowed to stir for 48 h at 0 °C until complete by TLC analysis. Sodium sulfite (1.2 g) was then added, and the reaction was warmed to rt and stirred for 1 h. The mixture was extracted with CH_2Cl_2 (4 × 5 mL) and ethyl acetate (5 mL), and the combined extracts were washed with a 2 M aqueous solution of KOH (7 mL), dried ($MgSO_4$), and concentrated. Purification by column chromatography (40% ethyl acetate/hexane) gave the final product as a pale yellow oil (200 mg, 72%). The ratio of **17:16** was 3.4:1 from ^{1}H NMR analysis.

17. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (1H, s); 5.76 (2H, d, J = 7.2 Hz); 4.76 (1H, t, J = 6.0 Hz); 4.32−4.27 (1H, m); 4.04−3.98 (1H, m); 3.85−3.73 (2H, m); 3.547 (2H, q, J = 7.2 Hz); 3.28 (1H, d, J = 6.8 Hz); 3.21 (1H, d, J = 6.4 Hz); 2.643 (3H, s); 1.74−1.60 (4H, m); 1.200 (3H, t, J = 7.2 Hz); 0.929; 0.880 (2 × 3H, 2 × t, J = 7.2 Hz). ^{13}C NMR (75.6 MHz, $CDCl_3$): δ 190.6; 142.7; 142.0; 122.1; 113.1; 77.3; 76.0; 73.5; 69.8; 66.5; 65.2; 29.6; 27.0; 27.3; 14.8; 8.13; 8.05. MS (ES positive): m/z 357 (M + H$^+$, 100). HRMS: calcd for $C_{15}H_{23}N_2O_6$ 327.1556, found 327.1546.

(1′*R*,2′*R*,3′*S*)-2-Acetyl-4-[3′,4′-*O*-(3′-pentylidene)-1′,2′, 3′,4′ -tetrahydroxy-1′-butyl]-1-(ethoxymethyl)imidazole (20). Using the general procedure described above for the synthesis of **17** except that the (*Z*)-alkene **11a** (225 mg, 6.98 × 10^{-4} mol) was used, the title compound was obtained as a pale yellow oil (235 mg, 95%) after purification by column chromatography (40% ethyl acetate/hexane). The ratio of **20:21** was 1.9:1 from ^{1}H NMR analysis. Spectral data of **20** and **21** are identical to those of **16** and **17**, respectively.

(1′*S*,2′*S*,3′*S*)-2-Acetyl-4-[3′,4′-*O*-(3′-pentylidene)-1′,2′,3′,4′-tetrahydroxy-1′-butyl]-1-(ethoxymethyl)imidazole (21). Using the general procedure described above for the synthesis of **16** except that (*Z*)-alkene **11a** (225 mg, 6.98 × 10^{-4} mol)

was used, the title compound was obtained as a pale yellow oil (225 mg, 91%) after purification by column chromatography (40% ethyl acetate/hexane). The ratio of **20:21** was 1:1.1 from ^{1}H NMR analysis. Spectral data of **20** and **21** are identical to those of **16** and **17**, respectively.

Dihydroxylation of the (*E*)-Alkene 15b in the Absence of a Chiral Ligand: (1′*R*,2′*S*,3′*R*)-2-Acetyl-4-[3′,4′-*O*-(3′-pentylidene)-1′,2′,3′,4′ -tetrahydroxy-1′-butyl]-1-(ethoxymethyl)imidazole (24) and (1′*S*,2′*R*,3′*R*)-2-Acetyl-4-[3′,4′-*O*-(3′-pentylidene)-1′,2′,3′,4′-tetrahydroxy-1′-butyl]-1-(ethoxymethyl)imidazole (25). To a solution of the (*E*)-alkene **15b** (20 mg, 6.21×10^{-5} mol) in *t*-BuOH/H_2O (1:1, 2 mL) were added $K_3Fe(CN)_6$ (62 mg, 1.86×10^{-4} mol), K_2CO_3 (26 mg, 1.86×10^{-4} mol), methanesulfonamide (12 mg, 1.2×10^{-4} mol), and $K_2OsO_4 \cdot 2H_2O$ (1 mg, $3.48 \times {}^{-6}$ mol), and the solution was cooled to 0 °C and stirred vigorously for 3 days until complete by TLC analysis. Sodium sulfite (200 mg) was added, and the reaction was warmed to rt and stirred for 1 h. The mixture was diluted with H_2O (2 mL) and extracted with CH_2Cl_2 (4 × 5 mL), and the combined extracts were washed with a 2 M aqueous solution of KOH (6 mL), dried ($MgSO_4$), and concentrated. The residue was purified by preparative layer chromatography (50% ethyl acetate/hexane) and the diastereomeric mixture taken into deuterated acetone for ^{1}H NMR analysis. The ratio of **24:25** was 3.5:1 from ^{1}H NMR analysis. Spectral data for **24** and **25** are given below.

(1′*R*,2′*S*,3′*R*)-2-Acetyl-4-[3′,4′-*O*-(3′-pentylidene)-1′,2′, 3′,4′ -tetrahydroxy-1′-butyl]-1-(ethoxymethyl)imidazole (24). Using the general procedure described above for the synthesis of **16** except that the (*E*)-alkene **15b** (70 mg, 2.17×10^{-4} mol) was used and additional osmium catalyst excluded, the title compound was obtained as a thick pale oil (62 mg, 80%, de > 99%) after purification by column chromatography (50% ethyl acetate/hexane), $[\alpha]^{23}_D$ +3.7° (*c* 2.10, MeOH). ^{1}H NMR (400 MHz, acetone-d_6): δ 7.48 (1H, d, J = 0.4 Hz); 5.77 (1H, d, J_{AB} = 10.4 Hz); 5.74 (1H, d, J_{AB} = 10.4 Hz); 4.84 (1H, d, J = 2.0 Hz; 4.23 (1H, dd, J = 6.4, 13.2 Hz); 4.08 (1H, dd, J = 6.0, 8.0 Hz); 3.91 (1H, dd, J = 6.4, 8.0 Hz); 3.85 (1H, dd, J = 2.4, 7.6 Hz); 3.53 (2H, q, J = 6.8 Hz); 2.53; 1.66−1.56 (4H, m); 1.12 (3H, t, J = 6.8 Hz; 0.89; 0.86 (2 × 3H, 2 × t, J = 7.6 Hz). ^{13}C NMR (75.6 MHz, acetone-d_6): δ 190.6; 145.1; 142.6; 124.0; 113.2; 77.5; 76.4; 75.6; 68.7; 68.2; 65.1; 29.4; 29.0; 27.2; 15.1; 8.5; 8.3. MS (ES positive): m/z 379 (M + Na^+, 100). HRMS: calcd for $C_{17}H_{28}N_2O_6$ 356.1947, found 356.1942.

(1′*S*,2′*R*,3′*R*)-2-Acetyl-4-[3′,4′-*O*-(3′-pentylidene)-1′,2′, 3′,4′ -tetrahydroxy-1′-butyl]-1-(ethoxymethyl)imidazole (25). Using the general procedure described above for the synthesis of **17** except that the (*E*)-alkene **15b** (70 mg, 2.17×10^{-4} mol) was used and additional osmium catalyst excluded, the title compound was obtained as a thick pale oil (52 mg, 67%, de = 96%) after purification by column chromatography (50% ethyl acetate/hexane), $[\alpha]^{23}_D$ +4.4° (*c* 2.40, MeOH). ^{1}H NMR (400 MHz, acetone-d_6): δ 7.47 (1H, s); 5.73; (2H, ABq, J = 10.4 Hz); 4.72 (1H, d, J = 4.4 Hz); 4.25 (1H, s(b)); 4.21 (1H, ddd, J = 5.2, 6.8, 11.2 Hz); 3.97 (1H, dd, J = 6.4, 8.0 Hz); 3.96−3.92 (1H, s(b)); 3.84−3.77 (2H, m); 3.52 (2H, q, J = 7.2 Hz); 2.54 (3H, s); 1.66−1.54 (4H, m); 1.15 (3H, t, J = 7.2 Hz); 0.88; 0.84 (2 × 3H, 2 × t, J = 7.2 Hz). ^{13}C NMR (100 MHz, acetone-d_6): δ 190.6; 144.2; 142.7; 124.2; 113.0 77.9; 77.5; 74.5; 70.4; 67.0; 65.0; 30.4; 30.0; 27.2; 15.1; 8.3. MS (ES positive): m/z 379 (M + Na^+, 100). HRMS: calcd for $C_{17}H_{28}N_2O_6$ 356.1947, found 356.1942.

(1′*S*,2′*R*,3′*S*)-2-Acetyl-4-[3′,4′-*O*-(3′-pentylidene)-1′,2′, 3′,4′ -tetrahydroxy-1′-butyl]-1-(ethoxymethyl)imidazole (28). Using the general procedure described above for the synthesis of **17** except that the (*E*)-alkene **15a** (150 mg, 4.66×10^{-4} mol) was used and additional osmium catalyst excluded, the title compound was obtained as a thick pale oil (130 mg, 78%, de = 94%) after purification by column chromatography (45% ethyl acetate/hexane), $[\alpha]^{23}_D$ −3.3° (*c* 1.3, MeOH). Spectral data are identical to those of **24**.

(1′*R*,2′*S*,3′*S*)-2-Acetyl-4-[3′,4′-*O*-(3′-pentylidene)-1′,2′, 3′,4′ -tetrahydroxy-1′-butyl]-1-(ethoxymethyl)imidazole (29). Using the general procedure described above for the synthesis of **16** except that the (*E*)-alkene **15a** (150 mg, 4.66×10^{-4} mol) was used and additional osmium catalyst excluded, the title compound was obtained as a pale oil (155 mg, 93%, de = 90%) after purification by column chromatography (45% ethyl acetate/hexane), $[\alpha]^{23}_D$ −5.3° (*c* 1.55, MeOH). Spectral data are identical to those of **25**.

(1′*R*,2′*S*,3′*R*)-2-Acetyl-4-(1′,2′,3′,4′-tetrahydroxy-1′-butyl)imidazolium Chloride (26). To a solution of imidazole **24** (120 mg, 3.37×10^{-4} mol) in ethanol/H_2O (1:1, 8 mL) was added concd aqueous HCl (4 mL), and the reaction was stirred at 80 °C for 90 min. The solution was then cooled to rt, filtered, and concentrated by freeze drying to give the title compound as a tan solid (90 mg, 100%). ^{1}H NMR (300 MHz, D_2O): δ 7.60 (1H, s); 5.21 (1H, s); 3.83−3.60 (4H, m); 2.66 (3H, s). This coumpound was identical to the hydrochloride salt of THI (**1**) that was prepared by an independent route.[6]

(1′*S*,2′*R*,3′*R*)-2-Acetyl-4-(1′,2′,3′,4′-tetrahydroxy-1′-butyl-)imidazolium Chloride (27). Using the general procedure described above for the synthesis of **26**, compound **27** was obtained from the hydrolysis of **25** as a tan solid in quantitative yield (100%). ^{1}H NMR (300 MHz, D_2O): δ 7.61 (1H, s); 5.04 (1H, d, J = 4.8 Hz); 3.83−3.57 (4H, m); 2.64 (3H, s). ^{13}C NMR (75.6 MHz, D_2O): δ 184.7; 139.4; 136.6; 119.5; 72.7; 71.3; 66.1; 62.5; 26.4. MS (LSIMS positive): m/z 231 (M + H^+, 100). HRMS: calcd for $C_9H_{15}N_2O_5$ 231.0981, found 231.0975.

(1′*S*,2′*R*,3′*S*)-2-Acetyl-4-(1′,2′,3′,4′-tetrahydroxy-1′-butyl-)imidazolium Chloride (30). Using the general procedure described above for the synthesis of **26**, compound **30** was obtained as a glassy yellow solid (100%), mp 174−178 °C dec, $[\alpha]^{27}_D$ +14.9° (*c* 0.70, H_2O). ^{1}H NMR (300 MHz, D_2O): δ 7.60 (1H, s); 5.21 (1H, s); 3.82−3.61 (4H, m); 2.66 (3H, s). ^{13}C NMR (100 MHz, D_2O): δ 187.2; 141.7; 140.2; 121.6; 75.2; 73.1; 67.3; 65.4; 28.9. MS (ES positive): m/z 231 (M + H^+, 100); 213(64); 200 (23).

(1′*R*,2′*S*,3′*S*)-2-Acetyl-4-(1′,2′,3′,4′-tetrahydroxy-1′-butyl-)imidazolium Chloride (31). Using the general procedure described above for the synthesis of **26**, the title compound was obtained as a light tan solid after concentration by freeze drying (95%), $[\alpha]^{26}_D$ −11.3° (*c* 0.70, H_2O). Spectral data are identical to those of **27.**

(1′*S*,2′*S*,3′*R*)-2-Acetyl-4-(1′,2′,3,′4′-tetrahydroxy-1′-butyl-)imidazolium Chloride (18). Using the general procedure described above for the synthesis of **26**, the title compound was obtained as a mixture of **18** and **19** (*ca.* 2:1) from the hydrolysis of a 2:1 mixture of **16** and **17.** Concentration by freeze drying gave a light tan solid (85%), mp 161−168 °C dec. ^{1}H NMR (300 MHz, D_2O): δ 7.61 (1H, s); 5.12 (1H, d, J = 4.8 Hz); 3.95−3.56 (4H, m); 2.65 (3H, s). ^{13}C NMR (75.6 MHz, D_2O): δ 184.6; 139.1; 135.6; 119.7; 72.9; 71.8; 65.9; 62.5; 26.4. MS (ES positive): m/z 231 (M + H^+, 100); 213 (24). HRMS: calcd for $C_9H_{15}N_2O_5$ 231.0981, found 231.0976.

(1′*R*,2′*R*,3′*R*)-2-Acetyl-4-(1′,2′,3′,4′-tetrahydroxy-1′-butyl)-imidazolium Chloride (19). Using the general procedure described above for the synthesis of **26**, the title compound was obtained as a mixture of **19** and **18** (*ca.* 3:1) from hydrolysis of a mixture (3.4:1) of **17** and **16** as a light tan solid (90%) after concentration by freeze drying, mp 168−174 °C dec. ^{1}H NMR (300 MHz, D_2O): δ 7.60 (1H, s); 4.89 (1H, d, J = 8.4 Hz); 3.92−3.60 (4H, m); 2.64 (3H). ^{13}C NMR (75.6 MHz, D_2O): δ 184.6; 139.1; 137.4; 119.5; 72.2; 69.9; 65.0; 62.8; 26.4. MS (ES negative): m/z 229 (M − H^-, 100). HRMS: calcd for $C_9H_{15}N_2O_5$ 231.0981, found 231.0970.

(1′*R*,2′*R*,3′*S*)-2-Acetyl-4-(1′,2′,3′,4′-tetrahydroxy-1′-butyl-)imidazolium Chloride (22) and (1′*S*,2′*S*,3′*S*)-2-Acetyl-4-(1′,2′,3′,4′-tetrahydroxy-1′-butyl)imidazolium Chloride (23). Using the general procedure described above for the synthesis of **26**, the title compounds were obtained as a mixture (**22**:**23** *ca.* 2:1) from hydrolysis of a mixture (1.9:1) of **20** and **21** as a light tan solid after concentration by freeze drying (85%), mp 177−182 °C dec. Spectral data of **22** and **23** are identical to those of **18** and **19**, respectively.

(1′*R*,2′*S*,3′*R*)-2-Acetyl-4(5)-(1′,2′,3′,4′-tetrahydroxy-1′-butyl)imidazole (THI, 1). To a solution of the imidazolium salt **26** (155 mg, 0.59 mmol) in H_2O (3 mL) was added solid K_2CO_3 (82 mg, 0.59 mmol). The solution was then cooled to near freezing for 3 days and the precipitated THI collected after centrifuging the solution. The precipitate was washed with H_2O to remove salts and then dried under high vacuum to give

the title compound as a light yellow solid (33 mg, 24%), mp 240−244 °C (lit.[6] mp 234−236 °C), $[\alpha]^{23}_D$ −14.9° (*c* 0.09, H_2O) (lit.[6] $[\alpha]^{25}_D$ −12°, *c* 1.17, 1 N HCl). ^{1}H NMR (300 MHz, D_2O/DCl): δ 7.30 (1H, s); 4.91 (1H, s); 3.51−3.32 (4H, m); 2.35 (3H, s). Spectral data are identical to those of an authentic sample of THI (**1**).[6]

(1′*R*,2′*S*,3′*R*)-2-Acetyl-4(5)-(1′,2′,3′,4′-tetraacetoxy-1′-butyl)imidazole (32). General Procedure. From Authentic THI.[6] To a stirred solution of acetic anhydride (3.0 mL) and glacial acetic acid (5.0 mL) was added THI (**1**) (200 mg, 0.87 mol). A perchloric acid/acetic anhydride catalyst was added (4 drops, prepared by addition of 1.0 g of 70% $HClO_4$ to 2.3 g of acetic anhydride at 0 °C), and the reaction was stirred for 1 h at 60 °C. The mixture was poured into H_2O/ice (30 mL) and extracted with ethyl acetate (3 × 20 mL). The combined extracts were dried ($MgSO_4$) and concentrated to give a thick tan oil. Recrystallization from ethyl acetate gave the title compound as a white powder (190 mg, 55%), mp 153−154 °C, $[\alpha]^{24}_D$ −22.6° (*c* 0.58, CH_3CN).

From THI Synthesized in This Project. Using the general procedure descibed above, THI synthesized in this study was converted to the tetraacetate. Purification by preparative layer chromatography (60% ethyl acetate/hexane) gave the title compound as a white solid (47%), $[\alpha]^{24}_D$ −20.0° (*c* 0.09, CH_3CN). Spectral data are identical to those of the tetraacetate synthesized from authentic THI above. ^{1}H NMR (400 MHz, CD_3CN): δ 7.27 (1H, s); 6.05 (1H, d, J = 4.8 Hz); 5.56 (1H, dd, J = 5.2, 7.2 Hz); 5.18 (1H, ddd, J = 2.8, 5.6, 8.8 Hz); 4.25 (1H, dd, J = 3.2, 12.4 Hz); 4.11 (1H, dd, J = 6.0, 12.4 Hz); 2.51 (3H, s); 2.04; 2.02; 2.00; 1.98 (4 × 3H, 4 × s). ^{13}C NMR (100 MHz, CD_3CN): δ 188.7; 170.3; 169.7; 169.6; 169.5; 145.0; 138.5; 120.2; 70.8; 68.7; 67.5; 61.5; 24.7; 20.00; 19.93; 19.88; 19.86. MS (ES positive): *m*/*z* 399 (M + H$^+$, 100); 339 (71). HRMS: calcd for $C_{17}H_{23}N_2O_9$ 399.1402, found 399.1398. Anal. Calcd for $C_{17}H_{22}N_2O_9$: C, 51.26; H, 5.57; N, 7.03. Found: C, 51.09; H, 5.66; N, 6.65.

(1′*S*,2′*R*,3′*R*)-2-Acetyl-4(5)-(1′,2′,3′,4′-tetraacetoxy-1′-butyl)imidazole (33). Using the general procedure described above for the synthesis of **32**, the title compound was obtained as a glassy solid (23%) after purification by preparative layer chromatography (60% ethyl acetate/hexane). ^{1}H NMR (400 MHz, CD_3CN): δ 7.29 (1H, s); 5.98 (1H, d, J = 8.4 Hz); 5.70 (1H, dd, J = 3.6, 8.0 Hz); 5.01 (1H, ddd, J = 3.6, 5.2, 8.8 Hz); 4.18 (1H, dd, J = 5.2, 11.6 Hz); 4.00 (1H, dd, J = 6.4, 11.6 Hz); 2.52 (3H, s); 2.08; 2.05; 2.00; 1.96 (4 × 3H, 4 × s). ^{13}C NMR in part (100 MHz, CD_3CN): δ 181.7; 170.2; 169.8; 169.7; 145.1; 71.2; 68.7; 68.2; 61.6; 24.7; 20.1; 20.0; 19.9; 19.8. MS (ES positive): *m*/*z* 399 (M + H$^+$, 100); 339 (82). HRMS: calcd for $C_{17}H_{23}N_2O_9$ 399.1402, found 399.1409.

(1′*S*,2′*R*,3′*S*)-2-Acetyl-4(5)-(1′,2′,3′,4′-tetraacetoxy-1′-butyl)imidazole (34) and (1′*R*,2′*R*3′*S*)-2-Acetyl-4(5)-(1′,2′,3′,4′-tetraacetoxy-1′-butyl)imidazole (35) from 30. Using the general procedure described above for the synthesis of **32** and a reaction time of 6 h at 60 °C, a mixture of the tetraacetates **34** and **35** was obtained as a tan solid (71%, ratio **34:35** = 5.3:1) after purification by preparative layer chromatography (60% ethyl acetate/hexane). Separation of the diastereomers by preparative HPLC (30% ethyl acetate/hexane) gave the title compounds as single diastereomers, **34**. $[\alpha]^{24}_D$ +19.4° (*c* 0.06, CH_3CN), spectral data of **34** are identical to those of **32**. **Data for 35.** ^{1}H NMR (300 MHz, CD_3CN) δ 7.31 (1H, s); 6.01 (1H, d, J = 5.1 Hz); 5.61 (1H, dd, J = 5.1, 6.3 Hz); 5.12 (1H, ddd, J = 3.0, 6.0, 9.3 Hz); 4.34 (1H, dd, J = 3.3, 12.3 Hz); 4.13 (1H, dd, J = 6.0, 12.3 Hz); 2.49 (3H, s); 2.05; 2.01; 2.00; 1.99 (4 × 3H, 4 × s). ^{13}C NMR (75.6 MHz, CD_3CN): δ 188.7; 170.37; 169.62; 169.61; 169.60; 144.7; 138.6; 119.7; 70.4; 69.5; 68.9; 61.6; 24.6; 20.09; 20.06; 19.88. MS (ES positive): *m*/*z* 399 (M + H$^+$, 78); 339 (100). HRMS: calcd for $C_{17}H_{23}N_2O_9$ 399.1402, found 399.1389.

(1′*R*,2′*S*,3′*S*)-2-Acetyl-4(5)-(1′,2′,3′,4′-tetraacetoxy-1′-butyl)imidazole (36) and (1′*S*,2′*S*,3′*S*)-2-Acetyl-4(5)-(1′,2′,3′,4′-tetraacetoxy-1′-butyl)imidazole (37). Using the general procedure described above for the synthesis of **32** and a reaction time of 6 h at 60 °C, a mixture of the tetraacetates **36** and **37** was obtained as a cream solid (93%, ratio **36:37** = 1.3:1) after purification by preparative layer chromatography (60% ethyl acetate/hexane). HPLC separation of the diastereomers (30% ethyl acetate/hexane) gave the title compounds as single diastereomers. Spectral data of **36** were identical to those of **33**. **Data for 37.** ^{1}H NMR (300 MHz, CD_3CN) δ 7.29 (1H, s); 5.89 (1H, d, J = 7.8 Hz); 5.62 (1H, dd, J = 3.9, 7.8 Hz); 5.42 (1H, ddd, J = 4.8, 6.9, 8.4 Hz); 4.20 (1H, dd, J = 4.5, 12.0 Hz); 4.11 (1H, dd, J = 6.6, 11.7 Hz); 2.50 (3H, s); 2.03; 2.01; 1.99; 1.94 (4 × 3H, 4 × s). ^{13}C NMR (75.6 MHz, CD_3CN): δ 188.7; 170.3; 169.9, 169.6; 169.5; 144.8; 139.1; 119.9; 70.9; 68.5; 67.4; 62.2; 24.6; 20.1; 19.9; 19.8. MS (ES positive): *m*/*z* 399 (M + H$^+$, 57%); 339 (100). HRMS: calcd for $C_{17}H_{23}N_2O_9$ 399.1402, found 399.1407.

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Supporting Information Available: ^{1}H NMR of compounds **1**, **8b**, **10b**, **11a**, **13b**, **15b**, **16**−**19**, **24**−**26**, and **31**−**40** (18 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS; see any current masthead page for ordering information.

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