Synthesis of Aminocyclopentitols from Chromium Carbene Complex Derived Aminocyclobutanones

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Functionalized cyclopentenones were synthesized by the diazomethane ring expansion of cyclobutanones, produced by the photochemical reaction of vinyl oxazolidinones with chromium carbene complexes.

Introduction

Aminocyclohexitols (polyhydroxyaminocyclohexanes) have long been known as important antibiotics, among which are streptomycin, gentamycin, and tobramycin.[1] More recently, aminocyclopentitols have been recognized as being important biologically active compounds in their role as glycosidase inhibitors.[2] Important aminocyclopentitols include the potent α-D-mannoside inhibitors mannostatin A[3] (**1**) and cyclopentylamine **2**,[4] the chitinase inhibitor allosamidin **3**,[5] and the α,α-trehalase inhibitor trehazolin **4**[6] and its aglycon trehalamine **5**.[7]
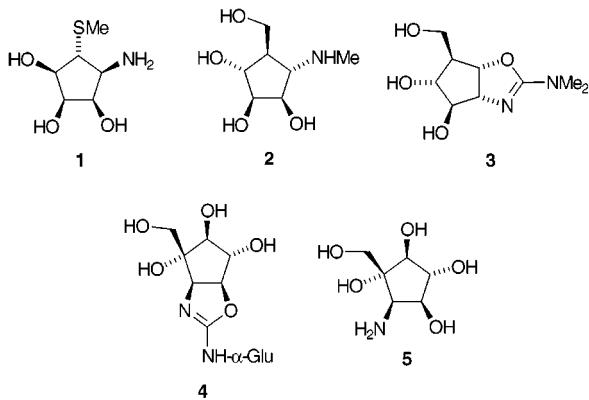
Because of the density of functionality as well as the presence of many contiguous chiral centers, aminocyclopentitols present a major synthetic challenge and continue to be the focus of substantial synthetic effort. The majority of syntheses of aminocyclopentitols involve

carbohydrate-derived starting materials,[8] with formation of the carbocyclic ring by radical,[9] aldol, or 1,3-dipolar cycloaddition strategies. More recently, synthetic approaches from relatively unfunctionalized cyclopentyl systems[2a] and *N*-alkylpyridinium salts[2b] have been developed. Particularly useful have been palladium(0)-catalyzed desymmetrization of *meso*-cyclopentene-1,4-diol derivatives[10] and heterocycloadditions to cyclopentadienes.[11,12]

Recent research in these laboratories has centered on the development of photochemical reactions of chromium carbene complexes for use in organic synthesis.[13] Utilizing this chemistry, an efficient synthesis of functionalized chiral cyclobutanones has been developed[14] along with Baeyer–Villiger ring expansion to chiral butenolides[15] for the synthesis of nucleoside analogues.[16] The cyclobutanone itself has been converted to (−)-cyclobut-A[17] and to carbovir and aristeromycin by an ylide-based carbocyclic ring expansion.[18] Diazomethane ring expansion of this same cyclobutanone proceeded with the regiochemistry found in the aminocyclopentitols. Studies directed toward introducing the additional functionality found

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(2) (a) For an excellent in-depth review of both the synthesis and biological activity of aminocyclopentitols, see: Bereubar, A.; Grandjean, C.; Siriwardena, A. *Chem. Rev.* **1999**, *99*, 779. (b) Acar, E. A.; Glarner, F.; Burger, U. *Helv. Chim. Acta* **1998**, *81*, 1095.

(3) Aoyagi, T.; Yamamoto, T.; Kojuiri, T.; Morishima, H.; Nagai, M.; Hamada, M.; Takeuchi, T.; Umezawa, H. *J. Antibiot.* **1989**, *42*, 883.

(4) Farr, R. A.; Peet, N. R.; Kang, M. S. *Tetrahedron Lett.* **1990**, *49*, 7109.

(5) Nishimoto, Y.; Sakuda, S.; Takayama, S.; Yamada, Y. *J. Antibiot.* **1991**, *44*, 716.

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(7) Ando, O.; Nakajima, M.; Hamano, K.; Itoi, K.; Takahashi, S.; Takamatsu, Y.; Sato, A.; Enokita, R.; Okazaki, T.; Haruyama, H.; Kinoshita, T. *J. Antibiot.* **1993**, *46*, 1116.

(8) (a) For a review, see: Ferrier, R. J.; Middleton, S. *Chem. Rev.* **1993**, *93*, 2779. (b) Mannostatin, A.; Knapp, S.; Dhar, T. G. M. *J. Org. Chem.* **1991**, *56*, 4096. (c) Allosamizoline: Simpkins, N. S.; Stokes, S.; Whittle, A. J. *J. Chem. Soc., Perkin Trans. 1* **1992**, 2471. (d) Cyclopentylamine **2**: Farr, R. A.; Peet, N. P.; Kang, M. S. *Tetrahedron Lett.* **1990**, *31*, 7109. (e) Trehazolin, trehalamine: Kobayashi, Y.; Miyayaki, H.; Shiozaki, M. *J. Am. Chem. Soc.* **1992**, *114*, 10065. (f) Kobayashi, Y.; Miyazaki, H.; Shiozaki, M. *J. Org. Chem.* **1994**, *59*, 813. (g) Kobayashi, Y.; Shiozaki, M.; Ando, O. *J. Org. Chem.* **1995**, *60*, 2570. (h) Miyazaki, H.; Kobayashi, Y.; Shiozaki, M.; Endo, O.; Nakajima, M.; Hanazawa, H.; Haruyama, H. *J. Org. Chem.* **1995**, *60*, 6103. (i) Kobayashi, Y.; Miyazaki, H.; Shiozaki, M.; Haruyama, H. *J. Antibiot.* **1994**, *47*, 932. (j) Shiozaki, M.; Kobayashi, Y.; Arai, M.; Haruyama, H. *Tetrahedron Lett.* **1994**, *35*, 887. (k) Elliot, R. P.; Hui, A.; Fairbanks, A. J.; Nash, R. J.; Winchestr, B. G.; Way, G.; Smith, C.; Lamont, R. B.; Storer, R.; Fleet, G. W. J. *Tetrahedron Lett.* **1993**, *34*, 7949. (l) Blaser, A.; Reymond, J.-L. *Helv. Chim. Acta* **1999**, *82*, 760.

(9) Marco-Contelles, J.; Destabel, C.; Chiara, J. L.; Bernabe, M. *Tetrahedron: Asymmetry* **1995**, *6*, 1547.

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(11) King, S. B.; Ganem, B. *J. Am. Chem. Soc.* **1994**, *116*, 562.

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(14) Hegedus, L. S.; Bates, R. W.; Söderberg, B. C. *J. Am. Chem. Soc.* **1991**, *113*, 923.

(15) (a) Miller, M.; Hegedus, L. S. *J. Org. Chem.* **1993**, *58*, 6779. (b) Reed, A. D.; Hegedus, L. S. *J. Org. Chem.* **1995**, *60*, 3787.

(16) Reed, A. D.; Hegedus, L. S. *Organometallics* **1997**, *16*, 2313.

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in these aminocyclopentitols and stereochemical features of the processes developed are presented below.

Results and Discussion

The planned approach to aminocyclopentitols involved synthesis of (alkoxy)(amino)cyclopentenones from the corresponding (alkoxy)(amino)cyclobutanones, followed by the development of stereoselective reduction/oxygenation of the cyclopentenone to introduce the remaining hydroxyl groups. Photolysis of chromium carbene complex **6** with chiral (racemic) vinyl oxazolidinone **7** produced cyclobutanone **8** in excellent yield as a single diastereoisomer. Treatment with diazomethane[19,20] resulted in a 4:1 mixture of cyclopentanones **9** and **10**, with migration of the *less* substituted terminus predominating. α-Selenation/oxidation/elimination[21] produced model cyclopentenone **11** in fair yield (eq 1).


(Eq. 1)
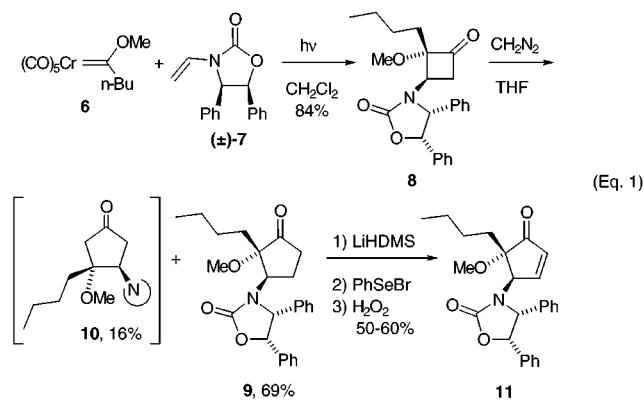
Reduction of the keto group, followed by epoxidation of the allylic alcohol and subsequent hydrolysis of the epoxide, should install all of the requisite functionality. The stereoselectivity of these processes was examined with cyclopentenone **11**. It was anticipated that reduction of the carbonyl group should occur from the face opposite the large butyl and oxazolidinone groups, perhaps in conjunction with coordination of the reducing agent to the methoxide group, giving the β-allyl alcohol. Surprisingly, sodium borohydride overreduced **11** to the saturated cyclopentanol, while lithium aluminum hydride, diisobutylaluminum hydride in methylene chloride, and sodium borohydride/cerium(III) chloride all reduced the carbonyl group from the β face to give exclusively the α-allylic alcohol **12** (assigned from NOE measurements; see the Experimental Section) (eq 2). This compound proved unreactive toward Mitsunobu inversion[22] using benzoic acid, perhaps because of the steric hindrance associated with neopentyl alcohols.

(Eq. 2)
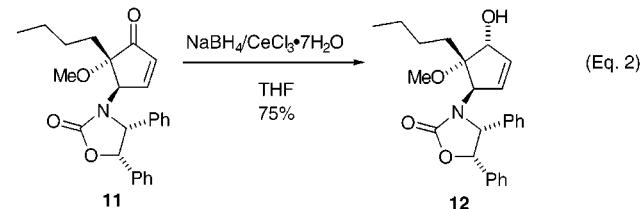
(19) Paquette, L. A., Ed. *Encyclopedia of Reagents for Organic Synthesis*; John Wiley & Sons: Chichester, 1995; p 1516 and references therein.

(20) Reeder, L. M.; Hegedus, L. S. *J. Org. Chem.* **1999**, *64*, 3306.

(21) Meyers, A. I.; Tschantz M. A.; Brengel, G. P. *J. Org. Chem.* **1995**, *60*, 4359.

Attempted epoxidation of cyclopentenone **11** using basic hydrogen peroxide or *t*-BuOOLi resulted in extensive decomposition. Sodium hypochlorite was the most efficient epoxidizing agent, although the substrate was prone to overoxidation to the Baeyer−Villiger lactone **14** (eq 3). Excess hypochlorite resulted in complete conversion of **11** to **14**, while use of 0.5 equiv led to an inseparable mixture of enone **11** and epoxide **13**. Portionwise addition of 1 equiv of sodium hypochlorite to enone **11** at 0 °C over 1 h resulted in complete conversion of **11** to a separable mixture of **13** and **14** in reasonable yield. (The stereochemistry of epoxidation was assigned by analogy to that from the X-ray structures of **27** and **29**, vide infra.)

(Eq. 3)
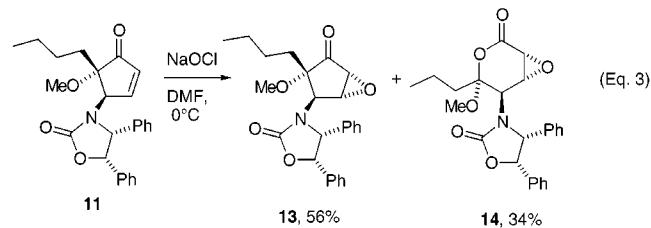
Attempted reduction of the keto group of **13** with both sodium borohydride[23] and tributyltin hydride/TBAF,[24] systems reported to efficiently reduce α-epoxyketones, led instead to decomposition and intractable mixtures of compounds. In contrast, lactone **14** underwent clean DIBAL-H reduction/acetylation[25] to produce a single anomer (stereochemistry unassigned) of lactol acetate **15** (eq 4).

(Eq. 4)
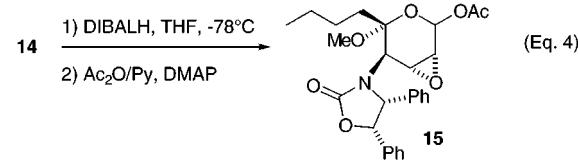
With these model studies in hand, attention was turned to analogue **16**, having the protected hydroxymethyl group common to most aminocyclopentitols in place and available in good yield by recently developed[16] methodology. Again, diazomethane ring expansion of the cyclobutanone favored migration of the *less* substituted terminus to give cyclopentanone **17** (eq 5). α-Selenation/

(Eq. 5)
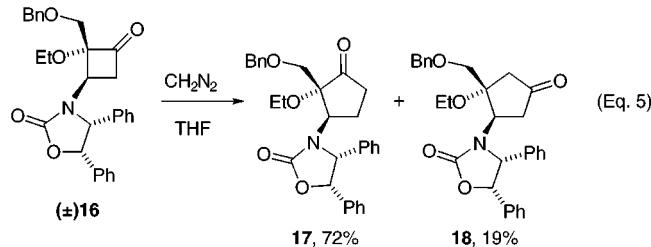
oxidation/elimination gave cyclopentenone **19** in fair yield. Reduction with sodium borohydride/CeCl$_3$·7H$_2$O again occurred from the more hindered β-face to give

(22) Hughes, D. L. *Org. React.* **1992**, *42*, 335.

(23) Weissenberg, M.; Glotter, E. *J. Chem. Soc., Perkin Trans. 1* **1978**, 568.

(24) Kawakami, T.; Shibata, I.; Baba, A.; Matsuda, H.; Sonoda, N. *Tetrahedron Lett.* **1994**, *35*, 8625.

(25) Dahanakar, V. H.; Rychnovsky, S. D. *J. Org. Chem.* **1996**, *61*, 8317.

α-allyl alcohol **20** as a single isomer. (Because assignment of stereochemistry by ^{1}H NMR/NOE techniques proved difficult, an X-ray crystal structure of **20** was obtained.) In contrast, reduction with diisobutyl aluminum hydride in THF gave a β-allylic alcohol **21** in good yield together with the 1,4-reduction product, cyclopentanone **17** in 22% yield (eq 6).

(Eq. 6)
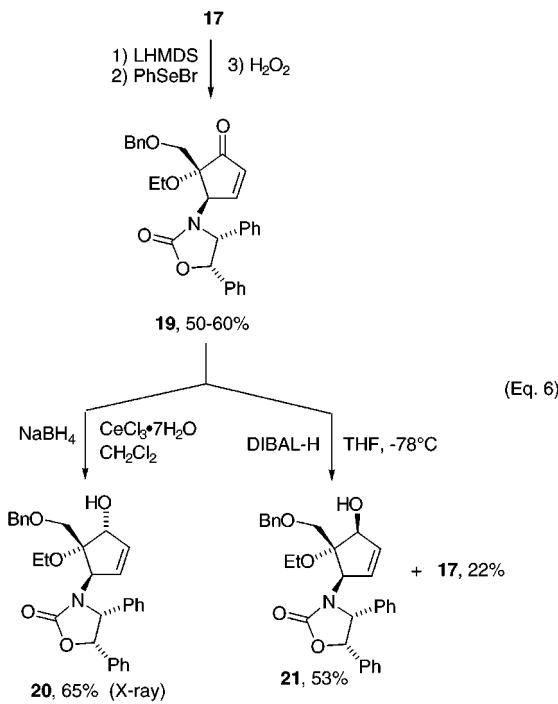
Attempted epoxidation of **21** with metachloroperbenzoic acid resulted instead in reoxidation of **21** to ketone **19**, as did Sharpless epoxidation conditions.[26] In contrast, the use of dimethyl dioxirane[27] resulted in decomposition of the starting material, while the use of *tert*-butyl hydroperoxide/VO(acac)$_2$ resulted in no reaction. Protection of the free hydroxyl group with MOM chloride followed by oxidation with either metachloroperbenzoic acid or dimethyl dioxirane resulted in oxidative debenzylation[28] of the benzyloxymethyl side chain rather than the desired epoxidation (eq 7). To circumvent this, the redox sequence was reversed.

(Eq. 7)
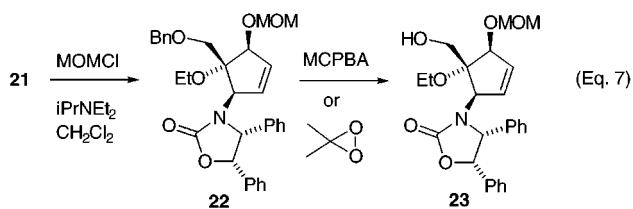
Epoxidation of enone **19** with sodium hypochlorite in aqueous THF[29] resulted in attack from the less hindered face to give α-epoxide **24**. Overoxidation to lactone **25** (a potential precursor to aminohexoses) occurred when the reaction was run to completion. This lactone could be

efficiently produced using an excess of oxidant. By using only 0.75 equiv of oxidant, good yields of **24** were obtained after separation from unreacted starting material (eq 8).

(Eq. 8)
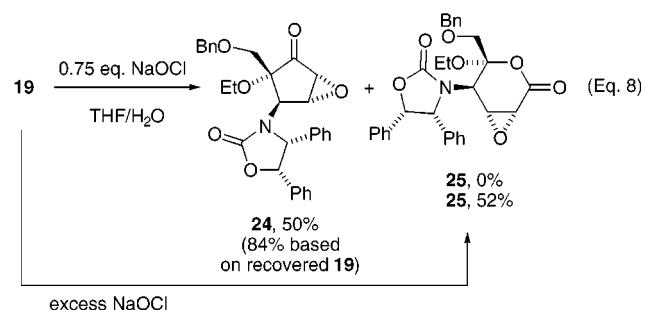
Reduction of **24** with diisobutylaluminum hydride in methylene chloride occurred from the face opposite the epoxide to give **26**, which upon aqueous acidic opening of the epoxide with HClO$_4$ followed by acetylation of the free OH groups gave oxazolidinone **27**, the stereochemistry of which was assigned on the basis of an X-ray crystal structure. This expected trans opening of the epoxide placed an hydroxyl group cis to the oxazolidinone, and transacylation of the oxazolidinone occurred to give ring-fused oxazolidinone **27** (eq 9). This compound is a protected form of trehalostatin **2a** (5-epi-trehezolin).

(Eq. 9)
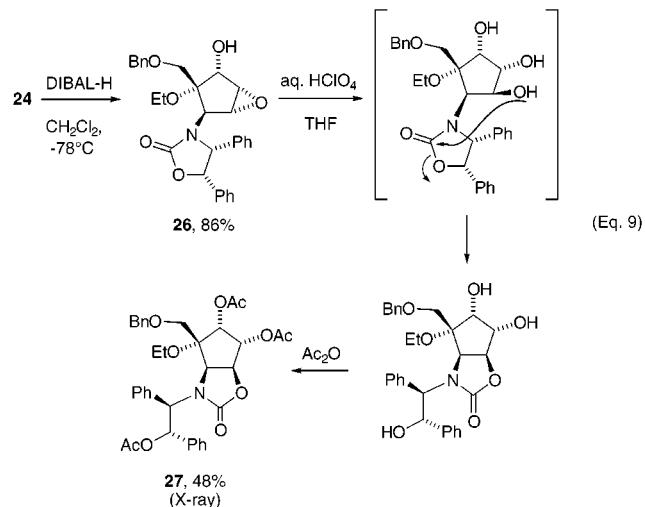
In contrast, reduction of keto epoxide **24** with diisobutylaluminum hydride in THF occurred from the *same* face as the epoxide to give predominantly epimer **28** (28:26 ≈ 4:1). Acid-catalyzed epoxide ring opening of **28** (aqueous TFA in dioxane) followed by acetylation gave **29**, the product from cis epoxide opening. Again, the stereochemistry was established by X-ray crystallography. This unexpected stereochemical outcome is likely the result of initial epoxide interchange (Payne rearrangement[30]) not possible with epoxide **26** because of the cis disposition of the epoxide and the free hydroxyl group (eq 10).

In an attempt to block this Payne rearrangement during the planned acid-catalyzed epoxide ring opening, the free hydroxyl group was protected as its acid-stable allyl ether.[31] Treatment of a 1:3 mixture of epimers of

(26) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974.

(27) Adam, W.; Chan, Y.-Y.; Cremer, D.; Gauss, J.; Schautzow, D.; Schindler, M. *J. Org. Chem.* **1987**, *52*, 2800.

(28) Csuk, R.; Dorr, P. *Tetrahedron* **1994**, *50*, 9983.

(29) Reed, A. D.; Hegedus, L. S. *J. Org. Chem.* **1995**, *60*, 3787.

(30) Payne, G. B. *J. Org. Chem.* **1962**, *27*, 3819.

(31) Grigg, R.; Conant, R. *Carbohydr. Res.* **1982**, *100*, C5.

28, 46%

(Eq. 10)

29, 36%
(X-ray)
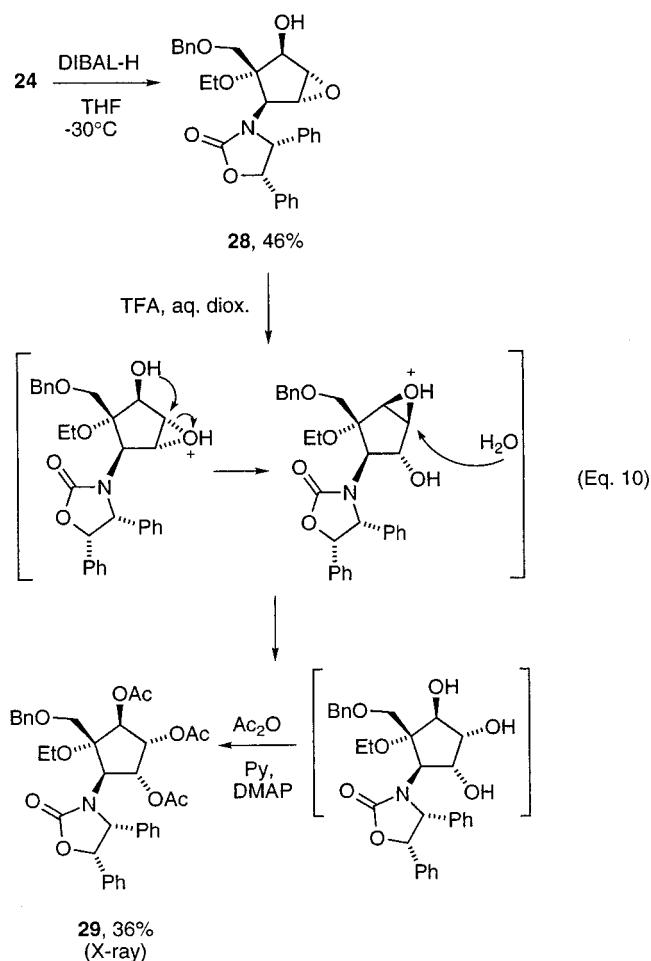
the epoxyalcohols **26** and **28** with excess allyl bromide and NaHMDS at −78 °C produced three compounds (eq 11).

1:3 / **26, 28**

30, 26%

(Eq. 11)

31, 1.5%   **32**, 70%
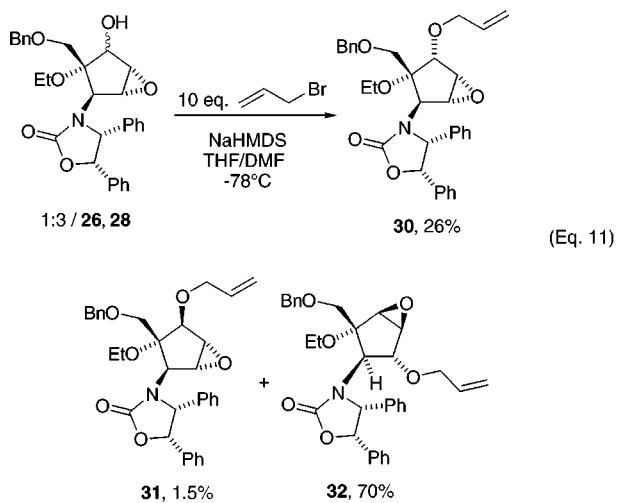
Compound **30**, from the α alcohol **26** was readily identified by comparison with material previously prepared from pure **26**. (Since the epoxide and alcohol are on the same face of the ring, Payne rearrangement is not possible.) Distinguishing between **31** and **32** was more difficult, since they are regioisomeric and have similar ^{1}H and ^{13}C NMR spectra. To be sure that structural

assignments were correct, extensive NMR studies[32] (^{1}H, ^{13}C, DEPT, COSY, HMQC, HMBC, NOE) were performed on these and related compounds (see the Supporting Information for data). The final key to assigning the structure to **32** was a 1% NOE interaction between the methine proton on the carbon bearing the oxazolidinone with the methylene proton on the *O*-allyl group.

Under the mistaken initial impression that epoxide **32** was actually epoxide **31** (the structure was not obvious from a cursory inspection of the physical data), it was treated with barium hydroxide to open the oxazolidinone ring,[33] producing epoxide **33** (eq 12). Removal of the protecting group by rhodium(I)-catalyzed rearrangement of the allyl ether to the enol ether, followed by hydrolysis of the enol ether with aqueous hydrochloric acid, gave epoxy alcohols **34** and **35** in 44% overall yield in a 1:1 ratio.

(Eq. 12)

35   **34**
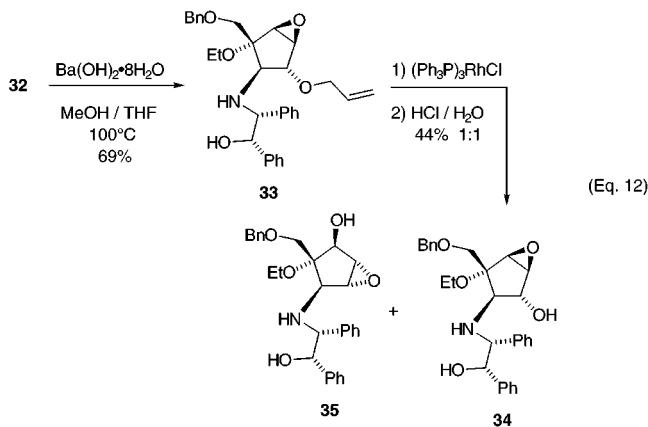
These experiments demonstrate the remarkable propensity of systems such as these to undergo the Payne rearrangement and the difficulty in ensuring the regio- and stereochemical integrity of centers during transformations involving trans epoxy alcohols.

Experimental Section

General Methods. The 300-MHz ^{1}H and 75-MHz ^{13}C NMR spectra were recorded in CDCl$_3$, and chemical shifts (δ) were given in ppm relative to Me$_4$Si (0 ppm, ^{1}H) and CDCl$_3$ (77 ppm, ^{13}C). Radial-layer chromatography (Chromatotron Model 7924) was performed using silica gel 60 PF$_{254}$ (with gypsum, E. Merck Science), and flash chromatography was performed with ICN 32−63 μm, 60 A silica gel. Elemental analyses were performed by M−H−W Laboratories, Phoenix, AZ. The photoreactions were carried out using a 450-W Conrad-Hanovia 7825 medium-pressure mercury lamp immersed in a water-cooled well and Pyrex pressure tube (from Ace Glass) equipped with a pressure head capable of withstanding 150 psi. All solids were recrystallized from mixtures of ethyl acetate and hexane.

Cyclobutanone 8. A pressure tube charged with chromium carbene complex **6** (1.00 g, 0.14 mmol), (±)vinyl oxazolidinone **7**[34] (0.91 g, 3.4 mmol), and degassed CH$_2$Cl$_2$ was flushed with CO gas, and CO pressure was kept at 80 psi. The reaction mixture in this pressure tube was irradiated for about 20 h at 0 °C. The CO pressure was slowly released, and the solvent of the reaction mixture was removed. The residue was placed in a sublimation apparatus and heated to 50 °C under reduced

(32) The authors thank Dr. Chris Rithner for his help in acquiring and interpreting these data.

(33) Takacs, J. M.; Jaber, M. R.; Vellekoop, A. S. *J. Org. Chem.* **1998**, *63*, 2742.

(34) Akiba, T.; Tamura, O.; Terashima, S. *Org. Synth.* **1997**, *75*, 45.

pressure (ca. 1 mmHg) to remove all chromium hexacarbonyl. The remaining crude mixture was washed with Et_2O followed by recrystallization with EtOAc at $-20\ °C$ to produce cyclobutanone **8** (1.1 g, 84%) as a white solid: ^{1}H NMR δ 0.95 (t, $J =$ 7 Hz, 3H), 1.38 (m, 3H), 1.50 (m, 1H), 1.77 (m, 1H), 2.09 (m, 1H), 2.47 (dd, $J =$ 10.2, 18 Hz, 1H), 2.82 (dd, $J =$ 9.6, 18 Hz, 1H), 3.42 (s, 3H), 4.65 (t, $J =$ 9.9 Hz, 1H), 5.08 (d, $J =$ 7.5 Hz, 1H), 5.92 (d, $J =$ 7.5 Hz, 1H), 6.85 (m, 2H), 7.00 (m, 2H), 7.11 (m, 6H); ^{13}C NMR δ 13.9, 22.9, 25.1, 28.8, 43.5, 47.4, 52.5, 65.7, 80.1, 98.5, 126.0, 126.8, 127.8, 128.1, 128.5, 133.3, 134.6, 158.1, 205.2; IR (thin film) ν 1788, 1747 cm^{-1}; mp $168-170\ °C$. Anal. Calcd for $C_{24}H_{27}NO_4$: C, 73.26; H, 6.92; N, 3.56. Found: C, 73.17; H, 7.02; N, 3.60.

General Procedure for Preparation of Cyclopentanones. To a test tube charged with Diazald and EtOH concd was added slowly aqueous KOH. Diazomethane was generated at once and bubbled via Tygon tubing into a second test tube containing a THF solution of the cyclobutanone cooled with an ice bath. The reaction mixture was allowed to stand at 0 °C for an appropriate amount of time. AcOH was added to each test tube. The reaction mixture was diluted with CH_2Cl_2, and $NaHCO_3$ (saturated) was used to neutralize the excess AcOH. The aqueous and organic layers were separated, and the aqueous layer was extracted with CH_2Cl_2 ($3\times$). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Recrystallization from EtOAc or flash chromatography with hexane/ CH_2Cl_2/ethyl acetate gave the cyclopentanone.

Cyclopentanone 9 and 10. Diazald (3.80 g, 17.7 mmol) in EtOH was treated with aqueous KOH (3.80 g) to generate diazomethane, which was bubbled into a THF solution of cyclobutanone **8** (0.68 g, 1.7 mmol). Cyclopentanone **9** was obtained as a white solid (0.48 g, 69%), along with cyclopentanone **10** also as a white solid (0.11 g, 16%). **Cyclopentanone 9**: ^{1}H NMR δ 0.95 (t, $J =$ 7.1 Hz, 3H), 1.36-1.64 (m, 6H), 1.88 (m, 2H), 2.12 (m, 2H), 3.26 (s, 3H), 4.64 (t, $J =$ 6.6 Hz, 1H), 4.80 (d, $J =$ 7.5 Hz, 1H), 5.81 (d, $J =$ 7.5 Hz, 1H), 6.91 (m, 2H), 6.98 (m, 2H), 7.10 (m, 6H); ^{13}C NMR δ 14.0, 22.1, 23.3, 24.1, 27.1, 34.2, 51.5, 55.5, 65.1, 80.5, 85.9, 126.1, 127.4, 127.9, 128.1, 128.3, 128.6, 133.5, 135.3, 158.2, 213.2; mp $225-227\ °C$; IR (thin film) ν 1751 cm^{-1}. Anal. Calcd for $C_{25}H_{29}NO_4$: C, 73.69; H, 7.17; N, 3.44. Found: C, 73.63, H, 7.10; N, 3.44. **Cyclopentanone 10**: δ 0.96 (t, $J =$ 6.7 Hz, 3H), 1.20-1.50 (m, 5H), 1.65 (m, 1H), 1.92 (m, 1H), 2.07 (m, 1H), 2.43 (d, $J =$ 18.3 Hz, 1H), 2.52 (m, 1H), 2.59 (d, $J =$ 18.6 Hz, 1H), 3.14 (s, 3H), 4.61 (d, $J =$ 8.7 Hz, 1H), 4.84 (d, $J =$ 7.5 Hz, 1H), 5.84 (d, $J =$ 7.5 Hz, 1H), 6.85 (m, 2H), 6.98 (m, 2H), 7.09 (m, 6H); ^{13}C NMR δ 14.0, 23.0, 25.6, 30.4, 40.3, 48.2, 49.5, 54.9, 65.0, 80.2, 85.6, 125.8, 125.9, 126.0, 127.5, 127.8, 128.0, 128.2, 128.4, 128.5, 128.7, 133.6, 134.9, 158.2, 213.6.

Cyclopentenone 11. Cyclopentanone **9** (0.20 g, 0.50 mmol) was dissolved in 50 mL of freshly distilled THF and was treated with LiHMDS [prepared from n-BuLi (0.75 mmol) and HMDS (0.18 mL, 0.83 mmol) at room temperature] at $-78\ °C$ for 2.5 h. PhSeBr (0.18 g, 0.75 mmol) in THF was added at $-78\ °C$, and the reaction mixture was stirred at that temperature for 2.5 h. Saturated aqueous NH_4Cl solution was added, and the reaction mixture was allowed to warm to room temperature. The aqueous and organic layers were separated, and the aqueous layer was extracted with CH_2Cl_2 ($3\times$). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Flash chromatography with hexane/CH_2Cl_2/ethyl acetate (14:3:2) gave an oily foamlike compound that was taken in CH_2Cl_2 and was treated with 30% H_2O_2 (0.17 mL) at 0 °C to room temperature overnight. The reaction mixture was washed with 1 N HCl ($2\times$) and brine. It was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Flash chromatography with hexane/CH_2Cl_2/ ethyl acetate (4:2:1) gave cyclopentenone **11** (0.10 g, 51%) as a white solid: ^{1}H NMR δ 0.99 (t, $J =$ 7.0 Hz, 3H), 1.43 (m, 2H), 1.57 (m, 2H), 1.82 (m, 2H), 3.23 (s, 3H), 4.81 (d, $J =$ 7.5 Hz, 1H), 5.31 (t, $J =$ 2.1 Hz, 1H), 5.84 (d, $J =$ 7.5 Hz, 1H), 6.06 (dd, $J =$ 2.1, 6.3 Hz, 1H), 6.86 (dd, $J =$ 2.4, 6.3 Hz, 1H), 6.98 (m, 2H), 7.09-7.16 (m, 8H); ^{13}C NMR δ 14.0, 23.4, 24.0, 30.7, 52.3, 59.4, 65.3, 80.4, 85.6, 126.0, 128.0, 128.2, 128.6,

128.8, 133.3, 133.7, 135.6, 156.5, 157.9, 203.7; IR (thin film) ν 1749, 1718 cm^{-1}; mp $127.5-128.5\ °C$. Anal. Calcd. for $C_{25}H_{27}$-NO_4: C, 74.05; H, 6.71; N, 3.45. Found: C, 74.16; H, 6.79; N, 3.47.

Allylic Alcohol 12. Cyclopentenone **11** (20 mg, 0.05 mmol) and $CeCl_3\cdot7H_2O$ (30 mg, 0.08 mmol) were dissolved in 1.5 mL of a mixture of MeOH and CH_2Cl_2 (2:1) at 0 °C and were stirred for 30 min at that temperature. $NaBH_4$ (3.0 mg, 0.08 mmol) was added, and the reaction mixture was stirred at room temperature for 2.5 h. AcOH-MeOH (10% v/v) was added, and the mixture was stirred vigorously for 15 min at room temperature, diluted with CH_2Cl_2, and washed with saturated $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 ($3\times$). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Flash chromatography with hexane/CH_2Cl_2/EtOAc (14: 3:2) gave the allylic alcohol **12** (15 mg, 75%) as a white solid: ^{1}H NMR δ 1.00 (t, $J =$ 7.2 Hz, 3H), 1.46 (m, 4H), 1.63 (m, 1H), 2.15 (m, 1H), 3.25 (d, $J =$ 9.3 Hz, 1H), 3.46 (s, 3H), 4.54 (d, $J = 7.5$ Hz, 1H), 4.65 (dd, $J =$ 9.3, 1.2 Hz, 1H), 5.02 (bs, 2H), 5.66 (dd, $J =$ 4.8, 1.5 Hz, 1H), 5.78 (d, $J =$ 7.5 Hz, 1H), 6.97 (m, 3H), 7.10 (m, 7H); ^{13}C NMR δ 14.2, 23.4, 25.2, 30.8, 50.6, 63.1, 64.2, 80.6, 81.1, 83.2, 126.0, 127.8, 128.0, 128.1, 128.2, 133.6, 136.5, 138.5, 158.2; IR (thin film) ν 3518, 1738 cm^{-1}; mp $195-196\ °C$. Anal. Calcd. for $C_{25}H_{29}NO_4$: C, 73.69; H, 7.17; N, 3.44. Found: C, 73.85; H, 7.20; N, 3.22. The structure was assigned on the basis of the following NOE data.
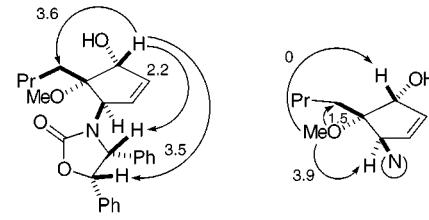
Epoxycyclopentanone 13. To a solution of cyclopentenone **11** (50 mg, 0.13 mmol) in a mixture of DMF and CH_2Cl_2 at 0 °C was added 10% aqueous NaOCl solution in portions. The reaction was monitored by TLC and quenched with 5% aqueous $Na_2S_2O_3$ when no starting enone **11** was remained. The organic and aqueous layers were separated, and the aqueous layer was extracted with CH_2Cl_2 ($3\times$). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Flash chromatography with hexane/CH_2Cl_2/EtOAc (12:5:2) gave epoxy ketone **13** (34 mg, 56%), along with epoxy lactone **14** (19 mg, 34%). Epoxy ketone **13**: ^{1}H NMR δ 0.95 (t, $J =$ 6.9 Hz, 3H), 1.33-1.46 (m, 5H), 2.13 (m, 1H), 2.98 (s, 3H), 3.31 (d, $J =$ 2.4 Hz, 1H), 3.52 (d, $J =$ 2.1 Hz, 1H), 4.29 (s, 1H), 4.91 (d, $J =$ 7.8 Hz, 1H), 5.82 (d, $J =$ 8.1 Hz, 1H), 6.88 (m, 2H), 6.97 (m, 2H), 7.14 (m, 6H); ^{13}C NMR δ 14.0, 23.4, 24.0, 27.8, 51.8, 54.6, 54.7, 57.2, 66.0, 80.3, 83.1, 125.9, 128.0, 128.2, 128.3, 128.4, 128.5, 129.3, 133.6, 134.2, 158.2, 204.0; IR (thin film) ν 1754 cm^{-1}; mp $151-152.5\ °C$. Anal. Calcd for $C_{25}H_{27}NO_5$: C, 71.24; H, 6.46; N, 3.32. Found: C, 71.36; H, 6.44; N, 3.35. **Epoxylactone 14**: ^{1}H NMR δ 0.99 (t, $J =$ 6.9 Hz, 3H), 1.43 (m, 4H), 1.75 (m, 1H), 2.18 (m, 1H), 2.34 (d, $J =$ 3.3 Hz, 1H), 3.05 (dd, $J =$ 3.3, 2.7 Hz, 1H), 3.33 (s, 3H), 4.83 (d, $J =$ 7.5 Hz, 1H), 5.04 (d, $J =$ 2.4 Hz, 1H), 5.86 (d, $J =$ 7.2 Hz, 1H), 7.03-7.16 (m, 10H); ^{13}C NMR δ 13.7, 22.7, 24.3, 33.1, 47.2, 49.6, 50.4, 53.0, 63.2, 80.8, 108.6, 125.6, 128.1, 128.6, 129.2, 132.8, 135.4, 157.5, 166.8; IR (thin film) ν 1749 cm^{-1}; mp $187-189\ °C$; HRMS calcd for $C_{25}H_{27}NO_6$ M + H 438.1917, found M + H 438.1920.

($\pm$)-Cyclobutanone 16. In a pressure tube with ($\pm$)-ene carbamate **7** (5.1 g, 19.2 mmol) and (benzyloxymethyl)(ethoxy)-chromium carbene complex (3.2 g, 8.6 mmol) under argon was added degassed CH_2Cl_2 via cannula. The pressure tube was then equipped with a pressure head, CO was flushed (80 psi), and the CO pressure was maintained at 80 psi. The pressure tube was placed in a $-35\ °C$ cold bath and irradiated for 4 days. The solvent was evaporated, and $Cr(CO)_6$ was recovered

by sublimation at reduced pressure (high vacuum pump) and elevated temperature (about 50 °C). Flash chromatography with CH_2Cl_2/hexane (4:1) gave ene carbamate **7** (3.0 g) and CH_2Cl_2/ethyl acetate (4:1) gave cyclobutanone **16** as a white solid (2.7 g, 67%): ^1H NMR (300 MHz, $CDCl_3$) δ 1.23 (t, $J = 7.5$ Hz, 3H), 2.45 (dd, $J = 10.6, 18$ Hz, 1H), 2.71 (dd, $J = 9.6$, 18 Hz, 1H), 3.75 (m, 2H), 3.87 (d, $J = 9$ Hz, 1H), 4.06 (d, $J = 9$ Hz, 1H), 4.55 (d, $J = 11.1$ Hz, 1H), 4.70 (d, $J = 11.1$ Hz, 1H), 4.81 (t, $J = 10.2$ Hz, 1H), 5.03 (d, $J = 7.8$ Hz, 1H), 5.59 (d, $J = 7.5$ Hz, 1H), 6.54 (bs, 1H), 6.78 (m, 2H), 7.03 (m, 6H), 7.42 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.6, 46.1, 48.0, 61.6, 64.8, 69.0, 74.4, 80.3, 97.7, 125.9, 126.7, 127.7, 127.9, 128.0, 128.1, 128.3, 128.7, 133.6, 135.5, 137.2, 158.5, 206.4; mp 170−172 °C; IR (thin film) ν 1791 cm^{-1}, 1752 cm^{-1}. Anal. Calcd for $C_{29}H_{29}NO_5$: C, 73.87; H, 6.20; N, 2.97. Found: 73.66; H, 6.12; N, 2.94.

Cyclopentanone 17 and 18. According to the general procedure to make cyclopentanones, cyclobutanone **16** (0.66 g, 1.4 mmol) in THF was treated with diazomethane generated from treatment of Diazald (3.0 g, 14 mmol) in EtOH with concd aqueous KOH. Flash chromatography with hexane/CH_2Cl_2/ethyl acetate (14:3:2) gave cyclopentanone **17** (0.49 g, 72%) as a white solid and the regioisomer **18** (0.19 g, 19%). **Cyclopentanone 17**: ^1H NMR δ 1.20 (t, $J = 6.9$ Hz, 3H), 1.62 (m, 1H), 1.78 (m, 1H), 2.08 (dt, $J = 9.9, 19.5$ Hz, 1H), 2.32 (ddd, $J = 2.4, 9.0, 19.5$ Hz, 1H), 3.32 (quin, $J = 6.9$ Hz, 1H), 3.73 (d, $J = 9.3$ Hz, 1H), 3.81 (quin, $J = 6.9$ Hz, 1H), 3.98 (d, $J = 9$ Hz, 1H), 4.47 (d, $J = 11.4$ Hz, 1H), 4.64 (d, $J = 11.7$ Hz, 1H), 4.95 (dd, $J = 7.8, 11.1$ Hz, 1H), 4.99 (d, $J = 7.2$ Hz, 1H), 5.58 (d, $J = 7.2$ Hz, 1H), 6.81 (m, 3H), 7.05 (m, 7H), 7.34−7.43 (m, 5H); ^{13}C NMR δ 15.5, 22.3, 36.7, 54.7, 59.9, 64.1, 71.7, 74.6, 80.6, 84.1, 126.1, 127.7, 127.9, 128.1, 128.3, 128.7, 133.6, 136.4, 136.9, 158.6, 215; IR (thin film) ν 1751 cm^{-1}; mp 181−183 °C. Anal. Calcd for $C_{30}H_{31}NO_5$: C, 74.21; H, 6.43; N, 2.88. Found: C, 74.17; H, 6.49; N, 2.86. **Cyclopentanone 18**: ^1H NMR δ 1.18 (t, $J = 6.9$ Hz, 3H), 2.08 (dd, $J = 7.5, 18.6$ Hz, 1H), 2.23 (dd, $J = 9.3, 18.9$ Hz, 1H), 2.62 (d, $J = 18.6$ Hz, 1H), 2.69 (d, $J = 18.6$ Hz, 1H), 3.56 (m, 2H), 3.67 (d, $J = 9.6$ Hz, 1H), 4.05 (d, $J = 9.6$ Hz, 1H), 4.56 (d, $J = 11.7$ Hz, 1H), 4.66 (d, $J = 11.4$ Hz, 1H), 4.72 (d, $J = 7.2$ Hz, 1H), 4.98 (dd, $J = 9.3, 8.1$ Hz, 1H), 5.51 (d, $J = 7.5$ Hz, 1H), 6.72 (m, 3H), 7.04 (m, 6H), 7.38 (m, 6H).

Cyclopentenone 19. Cyclopentanone **17** (0.49 g, 1.0 mmol) was dissolved in 25 mL of freshly distilled THF and was treated with LiHMDS (prepared from *n*-BuLi (1.52 mmol) and HMDS (0.35 mL, 1.67 mmol) at room temperature) at −78 °C for 2.5 h. PhSeBr (0.36 g, 1.52 mmol) in THF was added at −78 °C, and the reaction mixture was stirred at that temperature for 2.5 h. Saturated aqueous NH_4Cl solution was added, and the reaction mixture was allowed to warm to room temperature. The aqueous and organic layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3×). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Flash chromatography with hexane/CH_2Cl_2/ethyl acetate (14:3:2) gave an oily foamlike compound that was taken up in CH_2Cl_2 and treated with 30% H_2O_2 (0.34 mL) at 0 °C for 2 h. The reaction mixture was washed with 1 N HCl (aqueous) and brine. It was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Flash chromatography with hexane/CH_2Cl_2/ethyl acetate (14:3:2) gave cyclopentenone **19** (0.29 g, 60%) as a white solid: ^1H NMR δ 1.20 (t, $J = 6.9$ Hz, 3H), 3.61 (m, 2H), 3.97 (d, $J = 9.3$ Hz, 1H), 4.08 (d, $J = 9.3$ Hz, 1H), 4.54 (d, $J = 10.8$ Hz, 1H), 4.66 (d, $J = 10.8$ Hz, 1H), 4.88 (d, $J = 7.5$ Hz, 1H), 5.40 (t, $J = 2.4$ Hz, 1H), 5.48 (d, $J = 7.5$ Hz, 1H), 6.20 (dd, $J = 6.3, 2.4$ Hz, 1H), 6.54 (m, 2H), 6.81 (dd, $J = 6.3, 2.7$ Hz, 1H), 6.96−7.08 (m, 8H), 7.38 (m, 5H); ^{13}C NMR δ 15.7, 60.1, 60.8, 64.1, 70.3, 74.5, 80.8, 83.2, 125.7, 127.6, 127.7, 127.8, 128.1, 128.2, 128.3, 128.5, 128.7, 133.6, 135.0, 136.8, 137.4, 157.9, 158.2, 204.1; mp 160−161.5 °C; IR (thin film) ν 1755, 1724 cm^{-1}. Anal. Calcd for $C_{30}H_{29}NO_5$: C, 74.52; H, 6.04; N, 2.90. Found: C, 74.36; H, 6.02; N, 2.97.

Allylic Alcohol 20. Cyclopentenone **19** (24.4 mg, 0.05 mmol) and $CeCl_3 \cdot 7H_2O$ (30 mg, 0.08 mmol) were dissolved in 1.5 mL of a mixture of MeOH and CH_2Cl_2 (2:1) at 0 °C and

were stirred for 30 min at that temperature. $NaBH_4$ (3 mg, 0.08 mmol) was added, and the reaction mixture was stirred at room temperature for 2.5 h. AcOH−MeOH (10% v/v) was added, and it was stirred vigorously for 15 min at room temperature. It was diluted with CH_2Cl_2 and was washed with saturated $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (3×). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Flash chromatography with hexane/CH_2Cl_2/ EtOAc (14:3:2) gave the allylic alcohol **20** (16 mg, 65%) as a white solid: ^1H NMR δ 1.21 (t, $J = 6.9$ Hz, 3H), 3.16 (bd, 1H), 3.71 (m, 1H), 3.82 (d, $J = 9.6$ Hz, 1H), 3.98 (m, 1H), 4.10 (d, $J = 9.6$ Hz, 1H), 4.48 (d, $J = 7.8$ Hz, 1H), 4.63 (d, $J = 11.1$ Hz, 1H), 4.74 (d, $J = 11.1$ Hz, 1H), 4.99 (m, 1H), 5.18 (b, 2H), 5.28 (d, $J = 7.5$ Hz, 1H), 5.71 (d, $J = 6.0$ Hz, 1H), 6.43 (m, 2H), 7.01 (m, 7H), 7.42 (m, 6H); ^{13}C NMR δ 16.1, 59.7, 62.4, 64.0, 68.9, 74.3, 76.8, 80.5, 82.8, 125.9, 127.5, 127.6, 127.7, 127.9, 128.0, 128.1, 128.2, 128.8, 133.9, 137.0, 137.7, 138.2, 158.6; mp 108−110 °C; IR (thin film) ν 3525, 1747 cm^{-1}. Anal. Calcd for $C_{30}H_{31}NO_5$: C, 74.21; H, 6.43; N, 2.88. Found: C, 74.40; H, 6.55; N, 2.90.

Allylic Alcohol 21. To a solution of cyclopentenone **19** (50 mg, 0.10 mmol) in 4 mL of THF cooled to −78 °C was added a solution of DIBAL-H (0.1 mL, 1 M in hexane) in 4 mL of THF. This reaction mixture was allowed to stir at −78 °C for 4 h, and another portion of DIBAL-H (0.12 mL, 1 M) in 3 mL of THF was added. After the reaction mixture stirred for another 4 h, aqueous AcOH (10% v/v) was added, and the mixture was allowed to warm to room temperature. It was stirred until the mixture became clear (∼30 min). It was extracted with CH_2Cl_2 (5×). The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered. The solvent was removed. Chromatography with hexane/CH_2Cl_2/EtOAc (14:3:2) gave allylic alcohol **21** as a white solid (22 mg, 53% vs recovered starting material), along with a clean 1:1 (18 mg) mixture of cyclopentanone **17** (22% vs recovered starting material) and starting cyclopentenone **19**. Allylic alcohol **21**: ^1H NMR δ 1.19 (t, $J = 6.9$ Hz, 3H), 2.93 (b, 1H), 3.69 (m, 1H), 3.78 (m, 1H), 3.79 (d, $J = 10.5$ Hz, 1H), 3.98 (d, $J = 10.5$ Hz, 1H), 4.52 (broad, 1H), 4.55 (d, $J = 12$ Hz, 1H), 4.78 (d, $J = 7.5$ Hz, 1H), 4.82 (d, $J = 11.7$ Hz, 1H), 4.86 (broad, 1H), 5.17 (dd, $J = 2.7, 5.7$ Hz, 1H), 5.47 (d, $J = 7.5$ Hz, 1H), 5.81 (broad, 1H), 6.85 (m, 2H), 7.06 (m, 7H), 7.43 (m, 6H); ^{13}C NMR δ 15.9, 59.4, 62.6, 63.5, 66.4, 73.9, 80.7, 81.0, 87.7, 125.9, 127.8, 127.9, 128.1, 128.3, 128.4, 128.5, 128.8, 131.5, 133.7, 135.2, 136.4, 137.1, 157.9; IR (thin film) ν 1748, 3426 cm^{-1}; HRMS Calcd for $C_{30}H_{31}NO_5$: M+H = 486.2280. Found: M+H = 486.2281. Anal. Calcd for $C_{30}H_{31}NO_5$: C, 74.21; H, 6.43; N, 2.88. Found: C, 74.05; H, 6.42; N, 2.97.

O-MOM allylic alcohol 22. Allylic alcohol **21** and MOMCl in a 1:1 mixture of $^iPr_2NEt$ and CH_2Cl_2 were stirred at room temperature for 4 days and a dark red solution resulted. The solvent was removed. The residue was poured into H_2O and extracted with diethyl ether. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Chromatography with hexane/CH_2Cl_2/EtOAc gave the product **22** as a white solid. ^1H NMR δ 1.19 (t, $J = 6.9$ Hz, 3H), 3.34 (s, 3H), 3.76 (d, $J = 10.5$ Hz, 1H), 3.77 (m, 2H), 3.89 (d, $J = 10.2$ Hz, 1H), 4.27 (d, $J = 2.7$ Hz, 1H), 4.60 (d, $J = 11.7$ Hz, 1H), 4.62 (d, $J = 6.3$ Hz, 1H), 4.71 (d, $J = 11.7$ Hz, 1H), 4.82 (d, $J = 7.5$ Hz, 1H), 4.85 (d, $J = 6.3$ Hz, 1H), 4.99 (broad s, 1H), 5.16 (dd, $J = 2.7, 5.7$ Hz, 1H), 5.46 (d, $J = 7.5$ Hz, 1H), 5.78 (broad, 1H), 6.88 (m, 3H), 7.05 (m, 7H), 7.33−7.44 (m, 5H); ^{13}C NMR δ 15.9, 55.3, 59.4, 61.8, 63.3, 66.2, 74.1, 80.6, 85.2, 87.0, 97.2, 126.0, 126.2, 127.7, 127.9, 128.0, 128.3, 128.4, 131.9, 133.9, 134.8, 136.9, 137.7, 157.9.

Primary Alcohol 23. Dimethyldioxirane was distilled from the reaction mixture of oxone (25 g), acetone (13 mL), H_2O (20 mL), and $NaHCO_3$ (12 g) at reduced pressure with a water aspirator. A 3.5-mL portion of the above acetone solution of dimethyldioxirane was added to a CH_2Cl_2 solution of compound **22**. This reaction mixture was allowed to stir overnight. The solvent was removed to give primary alcohol **23** as a white solid: ^1H NMR δ 1.21 (t, $J = 6.9$ Hz, 3H), 3.42 (s, 3H), 3.73 (m, 2H), 4.02 (d, $J = 12.3$ Hz, 1H), 4.05 (d, $J = 12.3$ Hz, 1H),

4.41 (d, $J = 2.4$ Hz, 1H), 4.76 (d, $J = 6.6$ Hz, 1H), 4.85 (d, $J = 6.6$ Hz, 1H), 5.00 (d, $J = 7.2$ Hz, 1H), 5.10 (t, $J = 2.4$ Hz, 1H), 5.22 (dd, $J = 2.7$, 6 Hz, 1H), 5.78 (dt, $J = 2.1$, 6 Hz, 1H), 5.83 (d, $J = 7.5$ Hz, 1H), 6.97–7.07 (m, 10 H); ^{13}C NMR δ 11.5, 51.1, 54.8, 55.6, 57.4, 59.2, 76.3, 80.7, 84.1, 92.4, 121.6, 123.3, 123.4, 123.5, 123.7, 127.8, 129.1, 129.3, 132.4, 153.7.

Epoxy Ketone 24. Cyclopentenone **19** (0.25 g, 0.52 mmol) was dissolved in 2 mL of THF and 1 mL of H_2O, followed by the addition of 10% aqueous solution of NaOCl (0.29 mL, 0.39 mmol). It was allowed to stir for 6.5 h at 0 °C and quenched by adding 5% aqueous $Na_2S_2O_3$. The organic and aqueous layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3×). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Flash chromatography with CH_2Cl_2/hexane (4:1) gave epoxy ketone **24** (0.13 g, 50%, (84% vs recovered starting material)) as a white solid, and CH_2Cl_2/EtOAc (4:1) gave the starting cyclopentenone (0.11 g): ^{1}H NMR δ 1.16 (t, $J = 7$ Hz, 3H), 3.36 (d, $J = 2.1$ Hz, 1H), 3.40 (dd, $J = 0.9$, 2.1 Hz, 1H), 3.50 (m, 2H), 3.84 (d, $J = 9.4$ Hz, 1H), 4.03 (d, $J = 9.4$ Hz, 1H), 4.51 (d, $J = 11$ Hz, 1H), 4.64 (d, $J = 11$ Hz, 1H), 4.82 (broad, 1H), 4.97 (d, $J = 7.5$ Hz, 1H), 5.49 (d, $J = 7.5$ Hz, 1H), 6.56 (m, 2H), 6.75 (broad, 1H), 6.98–7.05 (m, 7H), 7.36–7.44 (m, 5H); ^{13}C NMR δ 15.5, 54.1, 55.2, 56.8, 61.0, 64.8, 71.0, 74.6, 80.8, 84.4, 125.8, 127.1, 127.7, 127.8, 128.0, 128.4, 128.5, 128.6, 128.8, 133.5, 136.2, 137.1, 158.5, 203.7; IR (thin film) ν 1753 cm^{-1}; mp 152–153 °C. Anal. Calcd for $C_{30}H_{29}NO_6$: C, 72.13; H, 5.85; N, 2.8. Found: C, 71.97; H, 5.74; N, 2.78.

Epoxylactone 25. Cyclopentenone **19** (100 mg, 0.21 mmol) was dissolved in 3 mL of a mixture of THF and H_2O (2:1). It was treated with 10% NaOCl aqueous solution (0.44 mL, 0.64 mmol) overnight. It was quenched by adding 5% aqueous NaS_2O_3. The organic and aqueous layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3×). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Flash chromatography with CH_2Cl_2/hexane (3:1) to CH_2Cl_2 gave epoxy lactone **25** as a white solid (56 mg, 52%): ^{1}H NMR δ 1.22 (t, $J = 6.9$ Hz, 3H), 2.48 (d, $J = 3.6$ Hz, 1H), 3.01 (dd, $J = 3.6$, 2.7 Hz, 1H), 3.64 (d, $J = 11.4$ Hz, 1H), 3.69 (m, 2H), 3.84 (d, $J = 11.4$ Hz, 1H), 4.62 (d, $J = 10.8$ Hz, 1H), 4.67 (d, $J = 8.1$ Hz, 1H), 4.78 (d, $J = 11.1$ Hz, 1H), 5.03 (d, $J = 7.8$ Hz, 1H), 5.13 (d, $J = 2.4$ Hz, 1H), 6.62 (m, 3H), 6.98 (m, 4H), 7.06 (broad, 3H), 7.31 (m, 1H), 7.41 (t, $J = 7.2$ Hz, 2H), 7.50 (d, $J = 6.9$ Hz, 2H); ^{13}C δ 15.3, 47.3, 51.5, 53.1, 58.6, 63.2, 68.2, 74.8, 80.0, 105.5, 125.7, 127.7, 128.4, 128.5, 128.8, 129.2, 133.3, 136.2, 136.6, 157.9, 166.8; mp 181–183 °C; IR (thin film) ν 1754 cm^{-1}. Anal. Calcd for $C_{30}H_{29}NO_7$: C, 69.89; H, 5.67; N, 2.72. Found: C, 69.66; H, 5.82; N, 2.89.

Epoxy Alcohol 26. Epoxy ketone **24** (0.29 g, 0.58 mmol) was dissolved in 3 mL of CH_2Cl_2 and treated with DIBAL-H (0.87 mL, 0.87 mmol) at −78 °C for 2.5 h. Aqueous AcOH (10%) was added, and the reaction mixture was stirred vigorously at room temperature for 30 min. The organic layer and aqueous layer were separated, and the aqueous layer was extracted with CH_2Cl_2 (6×). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Flash chromatography with hexane/CH_2Cl_2/EtOAc (12:3:2) gave epoxy alcohol **26** as a white solid (0.25 g, 86%): ^{1}H NMR δ 1.19 (t, $J = 6.9$ Hz, 3H), 2.90 (broad d, $J = 1.5$ Hz, 1H), 3.18 (d, $J = 9.9$ Hz, 1H), 3.40 (broad s, 1H), 3.55 (m, 1H), 3.59 (d, $J = 9.6$ Hz, 1H), 3.75 (m, 1H), 3.97 (d, $J = 9.6$ Hz, 1H), 4.61 (d, $J = 9.9$ Hz, 1H), 4.66–4.75 (m, 4H), 5.38 (d, $J = 8.1$ Hz, 1H), 6.44 (d, $J = 7.5$ Hz, 2H), 6.95–7.04 (m, 8H), 7.44 (m, 5H); ^{1}H NMR (300 MHz, acetone-d_6) δ 1.08 (t, $J = 6.9$ Hz, 3H), 2.81 (broad d, $J = 9$ Hz, 1H), 2.89 (d, $J = 2.4$ Hz, 1H), 3.33 (s, 1H), 3.56 (m, 2H), 3.72 (d, $J = 9.9$ Hz, 1H), 3.89 (d, $J = 10.2$ Hz, 1H), 4.54 (s, 1H), 4.62 (s, 1H), 4.69 (s, 2H), 5.16 (d, $J = 7.8$ Hz, 1H), 5.65 (d, $J = 8.1$ Hz, 1H), 6.74 (m, 2H), 6.99–7.09 (m, 8H), 7.42 (m, 3H), 7.52 (d, $J = 9.0$ Hz, 2H); ^{13}C NMR δ 16.0, 53.4, 56.3, 59.4, 59.6, 64.6, 69.4, 73.2, 74.4, 80.5, 82.6, 125.7, 127.6, 127.7, 127.9, 128.0, 128.3, 128.4, 128.6, 128.9, 133.7, 136.5, 137.4, 158.5; mp 146–147.5 °C; IR (thin film) ν 3495, 1751 cm^{-1}; HRMS calcd for $C_{30}H_{31}NO_6$ M + H 502.2230, found 502.2229. Anal. Calcd for $C_{30}H_{31}NO_6$: C, 71.84; H, 6.23; N, 2.79. Found: C, 72.00; H, 6.13; N, 2.78.

Triacetate 27. Epoxy alcohol **26** (60 mg, 0.12 mmol) in a mixture of 2 mL of THF and 1 mL of 44% aqueous $HClO_4$ was heated at reflux for 2.5 h. The reaction mixture was diluted with CH_2Cl_2 and washed with H_2O (3×). The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered, and the solvent was removed. The residue was dissolved in 2 mL of pyridine, followed by the addition of acetic anhydride (0.14 mL, 1.4 mmol) and DMAP (15 mg, 0.12 mmol). The reaction mixture was stirred at room temperature overnight. EtOH was added, and the mixture was stirred for 30 min. The reaction mixture was concentrated under reduced pressure and diluted with EtOAc. The EtOAc solution was washed with 1 N HCl (3×), and the organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Chromatography with hexane/CH_2Cl_2/EtOAc (14:3:2) gave triacetate **27** as a white solid (37 mg, 48%): ^{1}H NMR δ 1.13 (t, $J = 7$ Hz, 3H), 1.72 (s, 3H), 1.95 (s, 3H), 2.05 (s, 3H), 2.73 (d, $J = 11.1$ Hz, 1H), 2.82 (d, $J = 11.1$ Hz, 1H), 3.32 (m, 2H), 3.59 (d, $J = 10.5$ Hz, 1H), 3.92 (d, $J = 12$ Hz, 1H), 4.07 (d, $J = 12$ Hz, 1H), 4.17 (dd, $J = 4.5$, 10.5 Hz, 1H), 4.55 (d, $J = 11.1$ Hz, 1H), 5.16 (t, $J = 4.2$ Hz, 1H), 5.64 (d, $J = 4.2$ Hz, 1H), 6.86 (d, $J = 11.1$ Hz, 1H), 7.10 (m, 2H), 7.26–7.43 (m, 9H), 7.61–7.73 (m, 4H); ^{13}C NMR δ 15.9, 20.3, 20.6, 20.7, 61.4, 65.4, 69.2, 69.7, 72.6, 73.3, 73.4, 75.4, 79.6, 84.5, 127.7, 127.8, 128.4, 128.5, 128.7, 128.9, 129.3, 136.3, 137.7, 137.8, 157.1, 168.9, 169.0, 169.4; IR (thin film) ν 1754 cm^{-1}; mp 161–163 °C. Anal. Calcd for $C_{36}H_{39}NO_{10}$: C, 66.96; H, 6.09; N, 2.17. Found: C, 67.02; H, 6.18; N, 2.19.

Epoxy Alcohol 28. Epoxy ketone **24** (195 mg, 0.39 mmol) was dissolved in THF and treated with DIBAL-H (0.59 mL, 0.59 mmol) at −35 °C for 10 h. Aqueous acetic acid (10%) was added, and the reaction mixture was stirred vigorously at room temperature for 30 min. The organic layer and aqueous layer were separated, and the aqueous layer was extracted with CH_2Cl_2 (5×). The combined organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Flash chromatography with hexane/CH_2Cl_2/EtOAc (12:3:2) gave the epoxy alcohol **28** as a white solid (90 mg, 46%): ^{1}H NMR δ 1.22 (t, $J = 6.9$ Hz, 3H), 2.16 (d, $J = 10.8$ Hz, 1H), 3.39 (d, $J = 2.4$ Hz, 1H), 3.69 (d, $J = 10.2$ Hz, 1H), 3.70 (m, 1H), 3.80 (d, $J = 2.4$ Hz, 1H), 3.83 (d, $J = 11.1$ Hz, 1H), 3.90 (m, 1H), 3.98 (d, $J = 10.8$ Hz, 1H), 4.45 (s, 1H), 4.62 (d, $J = 12$ Hz, 1H), 4.75 (d, $J = 12$ Hz, 1H), 5.05 (d, $J = 7.5$ Hz, 1H), 5.38 (d, $J = 7.5$ Hz, 1H), 6.80 (m, 2H), 7.03–7.10 (m, 8H), 7.38–7.44 (m, 5H); ^{13}C NMR δ 15.7, 56.8, 57.7, 59.1, 63.8, 64.1, 66.5, 72.4, 73.7, 80.6, 86.8, 125.9, 127.7, 127.8, 127.9, 128.0, 128.2, 128.3, 128.4, 128.5, 133.5, 136.1, 137.5, 158.4; IR (thin film) ν 1743, 3430 cm^{-1}; mp 144–145 °C. Anal. Calcd for $C_{30}H_{31}NO_6$: C, 71.84; H, 6.23; N, 2.79. Found: C, 71.67; H, 6.31; N, 2.88.

Triacetate 29. Epoxy alcohol **28** (90 mg, 0.18 mmol) in a mixture of 3 mL of dioxane and 1.5 mL of 30% CF_3CO_2H was refluxed for 3 days. It was diluted with CH_2Cl_2 and washed with H_2O (3×). The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered, and the solvent was removed. The residue was dissolved in 2 mL of pyridine, followed by the addition of acetic anhydride (0.20 mL, 2.2 mmol) and DMAP (22 mg, 0.18 mmol). The reaction mixture was stirred at room temperature overnight and then diluted with EtOAc. The EtOAc solution was washed with saturated $NaHCO_3$ (3×). The combined aqueous layers were extracted with EtOAc (4×), and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Chromatography with hexane/CH_2Cl_2/EtOAc (14:3:2) gave triacetate **29** as a white solid (36.8 mg, 36% vs recovered starting material), along with O-acetyl epoxy alcohol (10.3 mg), which corresponded to unreacted epoxy alcohol (9.5 mg): ^{1}H NMR δ 1.17 (t, $J = 6.9$ Hz, 3H), 1.68 (s, 3H), 1.90 (s, 3H), 2.05 (s, 3H), 3.51 (m, 1H), 3.68 (broad, 2H), 3.86 (m, 1H), 4.66 (d, $J = 12.0$ Hz, 1H), 4.82 (d, $J = 12$ Hz, 1H), 4.89 (t, $J = 9.0$ Hz, 1H), 5.02 (d, $J = 10.2$ Hz, 1H), 5.03 (d, $J = 6.9$ Hz, 1H), 5.49 (dd, $J =$

6.9, 9.0 Hz, 1H), 5.12 (d, $J = 6.9$ Hz, 1H), 5.71 (d, $J = 7.2$ Hz, 1H), 6.85 (m, 4H), 7.04 (m, 6H), 7.47 (m, 5H); ^{13}C NMR δ 15.2, 19.8, 20.5, 20.8, 56.5, 58.0, 63.6, 67.5, 68.1, 70.0, 73.8, 74.4, 80.8, 82.7, 125.9, 127.7, 127.9, 128.2, 128.5, 128.6, 128.9, 133.3, 135.1, 136.5, 158.1, 168.6, 169.3, 169.9; IR (thin film) ν 1752; mp 175−176 °C. Anal. Calcd for $C_{36}H_{39}NO_{10}$: C, 66.96; H, 6.09; N, 2.17. Found: C, 66.76; H, 5.98; N, 2.13.

Allyl Ethers 30−32. A 1:3 mixture of epimeric alcohols **26** and **28** (125 mg, 0.25 mmol) was dissolved in 3.0 mL of dry THF and cooled to −78 °C. Allyl bromide (0.22 mL, 2.5 mmol), NaHMDS (1.0 M in THF, 0.37 mL, 0.37 mmol), and DMF (dry, 0.2 mL) were added. The reaction mixture stirred at −78 to +20 °C over 17 h. The reaction mixture was quenched with saturated aqueous NH_4Cl. The aqueous and organic layers were separated, and the aqueous layer was extracted with CH_2-Cl_2 (4×). The combined organic layers were washed with brine, dried with $MgSO_4$, filtered, and concentrated under reduced pressure to give a yellow oil. Flash chromatography with hexane/CH_2Cl_2/EtOAc (15:1:1) gave allyl ethers **30** (37 mg, 26%), **31** (2 mg, 1.5%), and **32** (98 mg, 70%) as clear oils. Allyl ether **30**: ^{1}H NMR (CDCl$_3$) δ 1.23 (t, $J = 6.9$ Hz, 3H), 2.92 (d, $J = 2.7$ Hz, 1H), 3.47 (s, 1H), 3.63 (m, 1H), 3.72 (d, $J = 9.3$ Hz, 1H), 3.82 (m, 1H), 4.07 (d, $J = 9.9$ Hz, 1H), 4.34 (d, $J = 5.7$ Hz, 2H), 4.67 (d, $J = 1.6$ Hz, 1H), 4.68 (m, 2H), 4.75 (d, $J = 7.8$ Hz, 1H), 4.86 (s, 1H), 5.3 (dd, $J = 1.2, 10.2$ Hz, 1H), 5.41 (dd, $J = 1.5, 17.4$ Hz, 1H), 5.42 (d, $J = 8.1$ Hz, 1H), 6.07 (m, 1H), 6.47 (d, $J = 6.6$ Hz, 2H), 6.80 (m, 1H), 6.97 (m, 7H), 7.48 (m, 5H); ^{13}C NMR (CDCl$_3$) δ 16.5, 52.8, 57.2, 57.4, 59.8, 64.9, 70.6, 71.8, 74.4, 79.1, 80.7, 84.4, 117.8, 126.0, 127.8, 127.9, 128.0, 128.5, 128.6, 129.1, 134.0, 135.4, 136.9, 137.7, 158.8; IR (thin film) ν 1750 cm^{-1}; HRMS (FAB$^+$) calcd for $C_{33}H_{36}NO_6$ 542.2543, found 542.2531. Allyl ether **31**: ^{1}H NMR (CDCl$_3$) δ 1.18 (t, $J = 7.0$ Hz, 3H), 2.74 (d, $J = 2.0$ Hz, 1H), 3.17 (d, $J = 2.0$ Hz, 1H), 3.60 (m, 1H), 3.65 (m, 1H), 3.69 (d, $J = 9.6$ Hz, 1H), 3.73 (d, $J = 10.0$ Hz, 1H), 3.80 (s, 1H), 4.19 (ddt, $J = 1.2, 6.0, 12.8$ Hz, 1H), 4.28 (ddt, $J = 1.2, 5.2, 12.8$ Hz, 1H), 4.54 (d, $J = 12.0$ Hz, 1H), 4.66 (d, $J = 12.0$ Hz, 1H), 4.69 (s, 1H), 4.05 (d, $J = 7.6$ Hz, 1H), 5.30 (m, 2H), 5.40 (d, $J = 7.6$ Hz, 1H), 5.93 (m, 1H), 6.60 (m, 1H), 6.92 (m, 3H), 7.08 (m, 4H), 7.19 (m, 2H), 7.35 (m, 5H); ^{13}C NMR (CDCl$_3$) δ 15.9, 56.1, 56.4, 57.7, 59.0, 63.3, 66.2, 73.2, 74.2, 80.7, 81.6, 90.4, 117.4, 126.0, 128.1, 128.2, 128.6, 128.7, 133.9, 134.7, 137.2, 137.8, 158.1; IR (thin film) ν 1750 cm^{-1}; HRMS (FAB$^+$) calcd for $C_{33}H_{36}NO_6$ 542.2543, found 542.2558. Allyl ether **32**: ^{1}H NMR (CDCl$_3$) δ 1.22 (t, $J = 7.2$ Hz, 3H), 3.38 (d, $J = 2.4$ Hz, 1H), 3.54 (ddt, $J = 1.2, 5.6, 12.4$ Hz, 1H), 3.63 (d, $J = 10.0$ Hz, 1H), 3.64 (d, $J = 1.2$ Hz, 1H), 3.67 (m, 1H), 3.74 (dd, $J = 1.0, 2.2$ Hz, 1H), 3.76 (ddt, $J = 1.4, 5.6, 11.4$ Hz, 1H), 3.84 (d, $J = 10.0$ Hz, 1H), 3.85 (m, 1H), 4.53 (s, 1H), 4.59 (d, $J = 12.0$ Hz, 1H), 4.78 (d, $J = 12.0$ Hz, 1H), 4.89 (d, $J = 7.2$ Hz, 1H), 4.99 (m, 2H), 5.34 (d, $J = 7.6$ Hz, 1H), 5.61 (m, 1H), 6.58 (broad, 1H), 6.77 (m, 3H), 7.00−7.22 (m, 6H), 7.43 (m, 5H). ^{13}C NMR (CDCl$_3$) δ 16.0, 56.9, 59.2, 60.0, 63.6, 64.2, 67.7, 71.0, 74.1, 78.8, 81.0, 86.9, 117.9, 126.1, 127.9, 128.0, 128.1, 128.4, 128.7, 128.8, 133.8, 133.9, 136.9, 138.0, 158.4; IR (thin film) ν 1750 cm^{-1}; HRMS (FAB$^+$) calcd for $C_{33}H_{36}NO_6$ 542.2543, found 542.2550.

Amino Alcohol 33. The protected epoxy alcohol **32** (137 mg, 0.25 mmol) was dissolved in 1.2 mL of THF and 2.0 mL of MeOH in a small pressure tube, and $Ba(OH)_2 \cdot 8H_2O$ was added (775 mg, 2.5 mmol). The reaction mixture was sealed and heated to 100 °C for 24 h. The reaction mixture was cooled to room temperature, and additional $Ba(OH)_2 \cdot H_2O$ (100 mg, 0.32 mmol) was added. The pressure tube was sealed and heated for an additional 24 h at 100 °C. The reaction mixture was cooled to room temperature, quenched with saturated aqueous NH_4Cl, and diluted with CH_2Cl_2. The aqueous and organic layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (4×). The combined organic layers were washed with brine, dried with $MgSO_4$, filtered, and concen-

trated under reduced pressure. Flash chromatography with hexane/CH_2Cl_2/EtOAc (15:1:1) gave the amino alcohol **33** as a clear oil (36.1 mg, 69% based on recovered starting material) along with the starting material **32** (80.1 mg, 0.14 mmol): ^{1}H NMR (CDCl$_3$) δ 0.92 (t, $J = 5.1$ Hz, 3H), 1.45 (bs, 1H), 2.28 (bs, 1H), 2.66 (s, 1H), 2.92 (m, 1H), 3.29 (m, 1H), 3.47 (d, $J = 2.1$ Hz, 1H), 3.55 (s, 1H), 3.59 (d, $J = 2.4$ Hz, 1H), 3.66 (d, $J = 11.1$ Hz, 1H), 3.76 (d, $J = 11.4$ Hz, 1H), 3.81 (d, $J = 6.6$ Hz, 1H), 3.84 (d, $J = 3.9$ Hz, 2H), 4.52 (d, $J = 6.3$ Hz, 1H), 4.60 (s, 2H), 5.16 (d, $J = 11.6$ Hz, 1H), 5.20 (d, $J = 17.2$ Hz, 1H), 5.79 (m, 1H), 7.2−7.4 (m, 15H); ^{13}C NMR (CDCl$_3$) δ 15.9, 57.3, 58.2, 60.5, 62.8, 67.4, 68.7, 70.5, 73.8, 78.1, 82.0, 85.5, 117.4, 127.1, 127.8, 128.0, 128.3, 128.4, 128.5, 128.6, 129.0, 134.7, 138.6, 139.3, 140.4; IR (thin film) ν 3456 cm^{-1}; HRMS (FAB$^+$) calcd for $C_{32}H_{38}NO_5$ 516.2745, found 516.2744.

Diols 34 and 35. The allyl ether **33** (38.4 mg, 0.069 mmol) was dissolved in ethanol (95%, 1.0 mL), and then RhCl(PPh$_3$)$_3$ (2.6 mg, 0.0028 mmol) and DABCO (1.5 mg, 0.013 mmol) were added. The red solution was heated at reflux for 3 h. The reaction mixture was cooled to room temperature, poured into water (10 mL), and diluted with CH_2Cl_2. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (4×). The combined organic layers were washed with brine, dried with $MgSO_4$, filtered, and concentrated under reduced pressure to give a clear oil. The oil was dissolved in CH_2Cl_2 (4 mL), 1 N aqueous HCl (0.1 mL) was added, and the mixture was heated to reflux. After 24 h, six drops of concd HCl was added, and the mixture continued to heat at reflux. After 24 h, the mixture was neutralized with saturated aqueous $NaHCO_3$ and diluted with CH_2Cl_2. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (4×). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated under reduced pressure to give a dark yellow oil. Preparative layer chromatography with hexane/EtOAc (2:1 × 3) gave **34** (7.2 mg, 22%) and **35** (7.3 mg, 22%) as clear oils. Diol **34**: ^{1}H NMR (C$_6$D$_6$) δ 0.90 (t, $J = 6.9$ Hz, 3H), 1.34 (bs, 1H), 2.12 (bs, 2H), 3.13 (m, 2H), 3.24 (d, $J = 4.8$ Hz, 1H), 3.63 (d, $J = 12.4$ Hz, 1H), 3.72 (d, $J = 12.4$ Hz, 1H), 3.81 (t, $J = 5.7$ Hz, 1H), 4.05 (s, 2H), 4.14 (d, $J = 8.1$ Hz, 1H), 4.33 (d, $J = 6.0$ Hz, 1H), 4.39 (dd, $J = 6.9, 8.1$ Hz, 1H), 4.77 (d, $J = 6.3$ Hz, 1H), 6.95−7.36 (m, 15H); ^{13}C NMR (CDCl$_3$) δ 16.1, 59.2, 65.7, 66.1, 66.8, 67.7, 74.0, 74.5, 77.9, 81.5, 84.2, 127.2, 127.9, 128.1, 128.2, 128.3, 128.5, 128.8, 129.0, 137.2, 139.5, 140.9; IR (thin film) ν 3441 cm^{-1}; HRMS (FAB$^+$) calcd for $C_{29}H_{34}NO_5$ 476.2437, found 476.2445. Diol **35**: ^{1}H NMR (CDCl$_3$, D$_2$O) δ 1.00 (t, $J = 6.9$ Hz, 3H), 2.52 (s, 1H), 3.10 (m, 1H), 3.43 (m, 1H), 3.50 (s, 1H), 3.68 (s, 1H), 3.76 (d, $J = 11.4$ Hz, 1H), 3.83 (s, 1H), 3.87 (d, $J = 11.4$ Hz, 1H), 3.90 (d, $J = 6.9$ Hz, 1H), 4.54 (d, $J = 7.2$ Hz, 1H), 4.62 (d, $J = 16.0$ Hz, 1H), 4.68 (d, $J = 16.4$ Hz, 1H), 7.2−7.6 (m, 15H); ^{13}C NMR (CDCl$_3$) δ 15.8, 57.3, 58.2, 58.6, 63.9, 67.3, 67.7, 73.7, 73.9, 78.2, 86.0, 127.1, 128.1, 128.3, 128.4, 128.5, 128.6, 129.1, 138.2, 139.3, 140.5; IR (thin film) ν 3441 cm^{-1}; HRMS (FAB$^+$) calcd for $C_{29}H_{34}NO_5$ 476.2437, found 476.2434.

Supporting Information Available: ^{1}H NMR data supporting structural assignments for compounds **30−35**. X-ray crystal structural data for **20** and **29**. This material is available free of charge via the Internet at http://pubs.acs.org.