Syntheses of Substituted Succinimides by Radical β-Fragmentation of Bicyclic Carbinol Amides. A New Expeditious Synthesis of 2-[2-(Methoxycarbonyl)ethyl]-3-[(methoxycarbonyl)methyl]-3-methylsuccinimide, the Ring-B Imide of Vitamin B₁₂

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A mild and efficient synthesis of substituted succinimides by radical β-fragmentation of carbinol amides is described. The carbinol amides studied were generated by treatment of the corresponding α,β-unsaturated ketones with hydrogen cyanide and subsequent hydrolysis of the cyanide intermediates. Photolysis with visible light in the presence of (diacetoxyiodo)benzene (DIB) and iodine of azabicyclic carbinol amides of the types 1-hydroxy-2-azabicyclo[3.3.0]octan-3-one (e.g., 4, 6, and 7) and 1-hydroxy-2-azabicyclo[3.2.1]octan-3-one (e.g., 16, 17, and 21) led to the substituted succinimides in good yields. A novel and operationally simple synthesis of the ring-B imide 28 is described, employing this β-fragmentation reaction on the carbinol amide 7 as the key step. The transformation of the resulting succinimide 11 into the target 28 was accomplished in one step by oxidation of the primary iodide and the phenyl group with RuO₄.

Five-membered cyclic imides and their N-derivatives are of considerable interest because of their presence in structures of interesting naturally occurring compounds such as the antibiotics isohematinic acid[1] and showdomycin[2] and synthetic compounds such as azaprostaglandins[3] and because of their significance as building blocks for the synthesis of isobacteriochlorins.[4] They are also useful intermediates, via N-acyliminium ions, α-acylamino radicals, or intramolecular Wittig reactions, for the synthesis of pyrrolidizine alkaloids.[5]

The methods usually used to synthesize cyclic imides involve the formation of a carbon–nitrogen bond from a variety of bifunctional acyclic nitrogen derivatives such as diamides, dinitriles, and amidic acids.[6] These reactions sometimes require drastic cyclization conditions which are not compatible with many functional groups.

In this paper we describe further synthetic applications of β-fragmentation reactions, promoted by alkoxy radicals generated by reaction of the corresponding carbinol amides with hypervalent iodine reagents.[7] This methodology involves the treatment of the carbinol amides in dichloromethane with (diacetoxyiodo)benzene (DIB) and iodine under irradiation with visible light at 25 °C. These mild conditions make it possible to extent the reaction to the preparation of substituted imides not available by other methods. The synthesis of substituted succinimides from easily accessible carbinol amides of the types 1-hydroxy-2-azabicyclo[3.3.0]octan-3-one (e.g., 4, 6, and 7) and 1-hydroxy-2-azabicyclo[3.2.1]octan-3-one (e.g., 16, 17, and 21) by this method is described.

The process is expected to occur through the mechanism outlined in Scheme 1. The alkoxy radical **A** initially formed undergoes two types of β-fragmentation to give radicals **B** and **C**. Radical **B** was stabilized by trapping an iodine radical from the medium, while N-radical **C**

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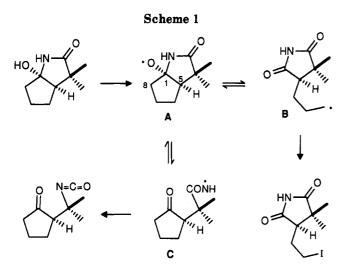
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Scheme 1

Scheme 2^a

suffers an amidyl rearrangement[8] to give the isocyanate. The other possible fragmentation through C_1–C_5 was not observed.

The intermediate carbinol amides can be prepared by a number of simple procedures from α,β-unsaturated ketones.[9] Substrates required for this study were synthesized by Michael addition of cyanide anion to the corresponding enone followed by hydrolysis.

Preliminary results to ascertain the feasibility of this approach were reported earlier.[10]
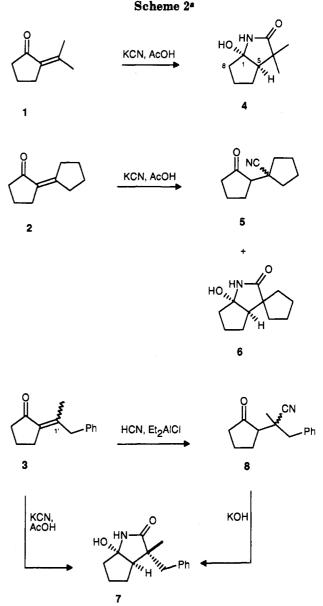
Results and Discussion

Fragmentation of 1-Hydroxy-2-azabicyclo[3.3.0]-octan-3-ones. The α,β-unsaturated ketones were prepared essentially following previously reported procedures.[11] Compounds 1[12] and 2[13] were obtained by aldol condensation of cyclopentanone with the corresponding ketone under basic conditions (Scheme 2). Enones 3Z and 3E were synthesized by a modified Mukaiyama[14] aldol addition of 1-[(trimethylsilyl)oxy]-1-cyclopentene[15] with benzyl methyl ketone in the presence of titanium tetrachloride and subsequent dehydration with p-toluene-sulfonic acid of the resulting crude reaction mixture of tertiary alcohols in 89% overall yield. The stereochemistry of the double bond was determined by ^{1}H NMR spectroscopy.[16] Thus, the 1'-Me in the 3Z isomer appears at 1.74 ppm (t, J = 1.4 Hz), while in the 3E isomer it is at 2.15 ppm (t, J = 2 Hz).

The racemic carbinol amides 4,[17] 6, and 7 were synthesized by reaction of the corresponding enones 1, 2, and 3E/Z utilizing the Lapworth procedure[18] by treatment with KCN in EtOH–H_2O–AcOH in 80, 53, and 85% yield, respectively. Intermediate nitriles, e.g., 5, were obtained

^{a} Products 4, 6, and 7 are racemic although single enantiomers are shown.
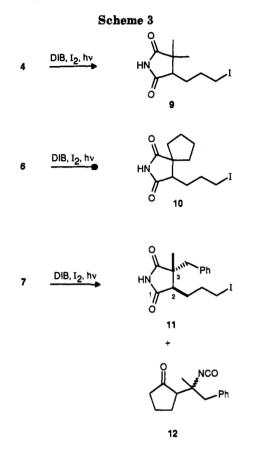
in some cases when the hydrolytic process was not completed. Alternatively, the carbinol amide 7 was prepared in a two-step sequence by hydrocyanation of the enone 3E/Z with hydrogen cyanide and diethylaluminum chloride following the procedure of Nagata et al.[19,20] and subsequent hydrolysis of the nitrile intermediate 8 with 4% KOH in EtOH–H_2O solution. This latter sequence produced a poorer overall yield. It is worth noting that in all cases only one isomer of the carbinol amides 4, 6, and 7 was obtained. In the case of the carbinol amide 7 this can be explained considering an equilibrium in the Michael addition with hydrolysis of the cyanide 8 placing the benzyl group in the more stable *exo* position.

The β-fragmentation of carbinol amides 4, 6, and 7 proceeded smoothly by irradiation with visible light (two 100-W tungsten filament lamps) under mild conditions (25 °C, 45–60 min) in the presence of DIB (1.5 equiv) and

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Scheme 3

iodine (1 equiv) in dichloromethane to give the imides **9**, **10**, and **11**, respectively, in good yield (Scheme 3). Small amounts of isocyanates, e.g., **12**, could also be isolated by chromatography of the crude reaction mixture.
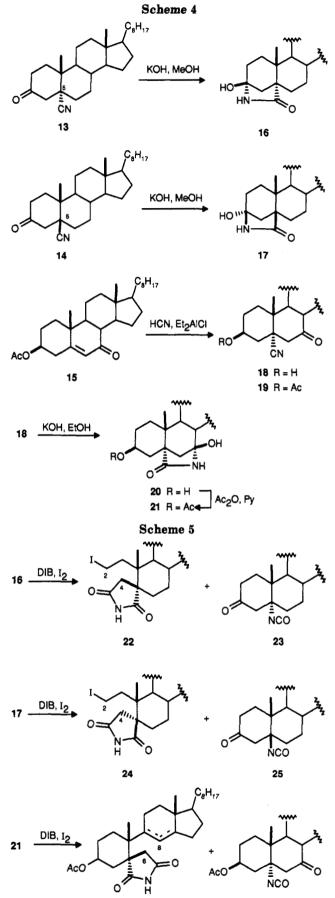
Although, as shown in Scheme 1, stabilization of the alkoxyl radical **A** can proceed by fragmentation of C_1–C_8 or C_1–C_5 bonds to give five- or eight-membered cyclic imides via stabilization of primary or secondary C-radicals, complete regioselectivity was observed in these cases. No medium-sized imides were detected; only the more stable five-membered imides were obtained. The isocyanate **12** was presumably formed by amidyl rearrangement.[8]

Fragmentation of 1-Hydroxy-2-azabicyclo[3.2.1]-octan-3-ones. Three different steroidal carbinol amides **16**, **17**, and **21** were prepared by hydrocyanation of the corresponding α,β-unsaturated ketones using the method of Nagata *et al.*[19,20] (Scheme 4). In the case of cholest-4-en-3-one a mixture of isomeric carbonitriles **13** and **14** was obtained. These were separated by chromatography and independently hydrolyzed to afford carbinol amides **16** and **17**. The hydrocyanation of 3β-acetoxycholest-5-en-7-one (**15**) occurred only from the α-side of the molecule to give a mixture of compounds **18** and **19**. The 5α-carbonitrile **18** was hydrolyzed and acetylated to the carbinol amide **21** in 89% overall yield.

Fragmentation of these carbinol amides promoted by DIB and iodine gave the spiroimides **22**, **24**, and **26** in 62, 63, and 38% yield, respectively (Scheme 5). The double bond position of **26** was not determined.

Again, complete regioselectivity was observed; however, significant amounts of isocyanates **23**, **25**, and **27** also formed.

Synthesis of the Ring-B Imide of Vitamin B$_{12}$. With the succinimide **11** in hand, we then addressed the synthesis of ring-B imide **28**[4] in racemic form (Scheme 6).
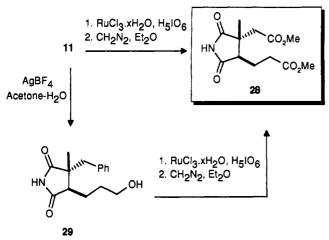
Scheme 4

Scheme 5

This compound has attracted considerable synthetic interest because it is the essential building block in the

Scheme 6[a]

[a] Products 28 and 29 are racemates although only one enantiomer is shown.

syntheses of isobacteriochlorins. Compound 28, which was first obtained in small amounts by degradation of vitamin B_{12}, was recently synthesized, first as a racemate and then in optically active form by multistep sequences.[4,21] We used a simple and straightforward approach to prepare the 2-[2-(methoxycarbonyl)ethyl] and 3-[(methoxycarbonyl)methyl] substituents of the ring-B imide. The conversion of phenyl groups into carboxylic acids has been well established.[22] Recently, we showed[23] that ruthenium tetraoxide, a widely recgonized oxidizing agent,[24] efficiently oxidizes primary alkyl iodides to carboxylic acids. Thus, when the succinimide 11 was treated with ruthenium tetraoxide and the crude reaction treated with ethereal diazomethane and chromatographed, the imide 28 was obtained in 54% yield. Compound 28 can also be obtained from 11 in a 42% overall yield by a two-step sequence by treatment with silver tetrafluoroborate[25] and subsequent oxidation of the resulting alcohol 29 with RuO_4. The mp, IR, and ^1H and ^{13}C NMR spectra of compound 28 were identical with those previously described.[21] The overall yield of 28 for the four operations from 1-[(trimethylsilyl)-oxy]-1-cyclopentene → 3 → 7 → 11 → 28 was 29%. This demonstrates that this reaction sequence constitutes a very feasible synthetic route to the racemic imide 28.

In summary, the DIB/I_2-assisted β-fragmentation of 4,4-substituted carbinol amides is a mild and simple method for the syntheses of 2-(3-iodopropanyl)-substituted succinimides. The iodine atom can be conveniently transformed into different useful functional groups, e.g., carboxylic acids, alcohols, etc. This method permitted a short and efficient synthesis of the ring-B imide 28 with good overall yield from simple commercially available starting materials. Syntheses of other biologically interesting *trans*-2,3-substituted succinimides by this method are in progress.

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Experimental Section

General. Melting points were determined with a Kofler hot-stage apparatus and are uncorrected. Optical rotation measurements were recorded at room temperature in $CHCl_3$ on Perkin-Elmer 141 or 142 polarimeters. IR spectra were recorded on a Perkin-Elmer 1605/FTIR spectrometer in $CHCl_3$ solutions. ^1H NMR (200 MHz) and ^{13}C NMR (50.3 MHz) spectra (δ) were recorded in $CDCl_3$ on a Bruker WP 200 SY spectrometer with Me_4Si as internal standard. Low-resolution mass spectra were determined with Hewlett-Packard 5930 A or VG Micromass ZAB-2F spectrometers and high-resolution mass spectra on a VG Micromass ZAB-2F spectrometer. Merck silica gel 60 PF_{254} and 60 (0.063–0.2 mm) were used for preparative thin-layer chromatography (TLC) and column chromatography, respectively. Circular layers of 1 mm of Merck silica gel 60 PF_{254} were used on a Harrison Chromatotron for centrifugally assisted chromatography. Commercial reagents and solvents were analytical grade or were purified by standard procedures prior to use. The spray reagent for TLC was vanillin (1 g) in H_2SO_4–EtOH (4:1, 200 mL). (Diacetoxyiodo)benzene (DIB) 98% was purchased from Aldrich. 2-Isopropylidenecyclopentanone (1)[12] and 2-cyclopentylidenecyclopentanone (2)[13] were prepared following previously reported procedures in 40 and 60% yield, respectively.

2-(1-Methyl-2-phenylethylidene)cyclopentanone (3). A solution of 1-[(trimethylsilyl)oxy]-1-cyclopentene (12 g, 0.77 mol) in CH_2Cl_2 (300 mL) was added dropwise to a stirred solution of benzyl methyl ketone (10.8 g, 0.81 mol) and $TiCl_4$ (15.36 g, 0.81 mol) in dry CH_2Cl_2 (150 mL), over 3–4-Å molecular sieves, under an argon atmosphere and at –78 °C. The resulting solution was allowed to reach room temperature and the stirring continued for 7 h, and then the solution was poured into H_2O (500 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried, filtered, and concentrated. The crude mixture in C_6H_6 (100 mL) was treated with *p*-toluenesulfonic acid (190 mg, 1 mmol) for 16 h at rt. To the mixture was added H_2O (200 mL), and it was extracted with CH_2Cl_2 (3 × 50 mL). The organic phase was washed with 5% NaOH (2 × 50 mL), 5% HCl (50 mL), and H_2O (50 mL), dried, and evaporated. The crude products were purified by column chromatography (hexane–ethyl acetate, 98:2) to yield 3 (13.69 g, 89%) as a mixture of Z- and E-olefins (2:1, ^1H NMR analysis). Chromatotron chromatography of a sample (233 mg) (C_6H_6–EtOAc, 99.7:0.3) gave 3Z enone (151 mg) and 3E enone (71 mg). Compound 3Z: amorphous; IR 1699, 1625, 1601, 1495, 1453, 1410, 1373 cm^{-1}; ^1H NMR 1.74 (3H, t, J = 1.4 Hz), 1.89 (2H, quintuplet, J = 7.5 Hz), 2.39 (2H, t, J = 8 Hz), 2.62 (2H, m), 4.13 (2H, br s), 7.1–7.4 (5H, m); ^{13}C NMR 19.13 (t), 21.66 (q), 29.62 (t), 38.20 (t), 40.72 (t), 125.99 (d), 128.26 (2 × d), 128.99 (2 × d), 131.57 (s) 139.58 (s), 148.56 (d), 207.38 (s); MS *m/z* (rel intensity) 200 (M$^+$, 100), 185 (16), 183 (30), 129 (63), 91 (72); HRMS calcd for $C_{14}H_{16}O$ 200.1201, found 200.1184. Compound 3E: amorphous; IR 1701, 1624, 1601, 1495, 1453, 1410, 1372 cm^{-1}; ^1H NMR 1.91 (2H, quintuplet, J = 7.4 Hz), 2.15 (3H, t, J = 2 Hz), 2.37 (2H, t, J = 7.9 Hz), 2.75 (2H, m), 3.47 (2H, br s), 7.1–7.4 (5H, m); ^{13}C NMR 18.48 (q), 19.56 (t), 29.62 (t), 40.59 (t), 43.81 (t), 126.44 (d), 128.58 (2 × d), 128.63 (2 × d), 132.00 (s), 137.97 (s), 148.33 (s), 208.06 (s); MS *m/z* (rel intensity) 200 (M$^+$, 100), 185 (14), 183 (25), 129 (61), 91 (78); HRMS calcd for $C_{14}H_{16}O$ 200.1201, found 200.1190.

(±)-(1S*,5R*)-4,4-Dimethyl-1-hydroxy-2-azabicyclo[3.3.0]-octan-3-one (4). To a solution of enone 1 (30 g, 0.242 mol) in ethanol (50 mL) was added a solution of KCN (16.15 g, 0.248 mol) in EtOH (700 mL) and water (38 mL). To the resulting mixture was added dropwise acetic acid (4.5 mL, 75 mmol) in EtOH (250 mL) and the mixture stirred at room temperature for 24 h and then poured into water (2 L) and extracted with CH_2Cl_2 (3 × 250 mL). The organic phase was washed with aqueous $NaHCO_3$ (2 × 50 mL) and water (50 mL), dried, and evaporated. The residue was purified by crystallization from EtOAc to give 4 (32.7 g, 80%): mp 118–120 °C (lit.[17] mp 117.5–118.5 °C); IR 3585, 3410, 1685 cm^{-1}; ^1H NMR 1.04 (3H, s), 1.29 (3H, s), 1.50–1.95 (6H, m), 2.23 (1H, m), 5.04 (1H, br s), 7.45 (1 H, br s); ^{13}C NMR 20.70 (q), 24.97 (t), 28.38 (t), 28.86 (q), 40.48 (t), 42.58 (s), 56.65 (d), 95.29 (s), 183.23 (s); MS *m/z* (rel intensity) 169 (M$^+$, 12), 154 (16), 151 (88), 136 (100), 127 (18), 122 (53), 111 (47), 108 (83).

(±)-(1*S**,5*R**)-1-Hydroxy-2-azabicyclo[3.3.0]octanespiro-4'-(cyclopentan)-3-one (6). Enone 2 (11.25 g, 75 mmol) in EtOH (400 mL) was treated as described previously and the resulting mixture stirred for 54 h at 65 °C Column chromatography of the residue (hexane–EtOAc, 1:1) gave the cyano derivative 5 (4.52 g, 34%) (mixture 4:1 ^{13}C NMR analysis) and the carbinol amide 6 (7.89 g, 54%). Compound 5: amorphous; IR 2210, 1735 cm^{-1}; ^{1}H NMR 1.4–2.3 (15-H, m); ^{13}C NMR 19.50 (t), 22.78 (t), 23.63 (t), 27.23 (t), 35.92 (t), 43.84, 43.75 (s, s), 54.17, 54.94 (d, d), 123.09 (s), 215.60 (s); MS *m/z* (rel intensity) 177 (M$^+$, 5), 149 (4), 136 (2), 134 (3), 121 (5), 108 (4), 106 (6), 93 (7), 84 (100); HRMS calcd for C$_{11}$H$_{15}$NO 177.1154, found 177.1165. Compound 6: mp 143–144 °C (acetone); IR 3580, 3410, 1680 cm^{-1}; ^{1}H NMR 1.3–2.1 (14H, m), 2.22 (1H, t, *J* = 7.4 Hz), 3.74 (1H, br s), 6.65 (1H, br s); ^{13}C NMR 24.44 (t), 24.94 (t), 24.98 (t), 29.21 (t), 31.25 (t), 40.20 (t), 40.70 (t), 53.73 (s), 56.58 (d), 95.39 (s), 182.83 (s); MS *m/z* (rel intensity) 195 (M$^+$, 28), 166 (57), 154 (84), 153 (21), 137 (100); HRMS calcd for C$_{11}$H$_{17}$NO$_2$ 195.1259, found 195.1256.

(±)-(1*S**,4*R**,5*R**)-4-Benzyl-4-methyl-1-hydroxy-2-azabicyclo[3.3.0]octan-3-one (7). Enones 3*Z* and 3*E* (2:1, ^{1}H NMR analysis) (13.0 g, 65 mmol) were treated as described above for 72 h at rt. Column chromatography of the residue (hexane–EtOAc, 1:1, EtOAc) gave the carbinol amide 7 (13.54 g, 85%): mp 156–157 °C (acetone); IR 3534, 3415, 1694, 1602, 1496, 1448, 1409 cm^{-1}; ^{1}H NMR 1.23 (3H, s), 1.4–1.8 (6H, m), 2.35 (1H, m), 2.51 (1H, d, *J* = 13 Hz), 3.19 (1H, d, *J* = 13 Hz), 6.46 (1H, m), 7.2–7.4 (5H, m); ^{13}C NMR 20.82 (q), 24.99 (t), 28.74 (t), 39.71 (t), 46.24 (t), 47.92 (s), 52.03 (d), 94.76 (s), 127.23 (d), 128.56 (2 × d), 130.53 (2 × d), 137.62 (s), 180.77 (s); MS *m/z* (rel intensity) 245 (M$^+$, 42), 230 (8), 227 (43), 213 (6), 202 (5), 199 (11), 154 (27), 91 (100); HRMS calcd for C$_{15}$H$_{19}$NO$_2$ 245.1416, found 245.1421. Alternatively, to a solution of 3*Z* (110 mg, 0.55 mmol) in THF (10 mL), at 0 °C and with stirring, were added 8.64 M HCN (97 μL, 0.84 mmol) and 2.87 M Et$_2$AlCl (0.34 mL, 0.98 mmol) THF solutions. The resulting mixture was allowed to reach room temperature and the stirring continued for 24 h. The product was then poured into a 5% NaOH aqueous solution (10 mL) that was precooled and vigorously stirred in an ice bath. The product was extracted with CH$_2$Cl$_2$ (3 × 10 mL), and the organic layers were dried, evaporated, and chromatographed on a chromatotron (hexane–EtOAc, 9:1) to yield starting material 3*Z* and 3*E* (53.5 mg, 1:1, ^{1}H NMR analysis) and the cyano derivatives 8a and 8b (18.3 and 17.1 mg, 30 and 28%, respectively, from starting material conversion). Less polar isomer 8a: amorphous; IR 2236, 1733, 1604, 1597, 1455, 1405, 1381 cm^{-1}; ^{1}H NMR 1.39 (3H, s), 1.7–2.4 (7H, m), 2.96 (1H, d, *J* = 13.5 Hz), 3.32 (1H, d, *J* = 13.5 Hz), 7.1–7.4 (5H, m); ^{13}C NMR 19.76 (t), 20.53 (q), 27.39 (t), 39.14 (s), 39.94 (t), 42.78 (t), 51.73 (t), 122.74 (s), 127.39 (d), 128.43 (2 × d), 130.44 (2 × d), 135.34 (s), 215.97 (s); MS *m/z* (rel intensity) 227 (M$^+$, 6) 198 (2), 91 (100); HRMS calcd for C$_{15}$H$_{17}$NO 227.1310, found 227.1310. More polar isomer 8b: amorphous; IR 2236, 1738, 1603, 1500, 1454, 1405, 1381 cm^{-1}; ^{1}H NMR 1.31 (3H, s), 1.7–2.4 (5H, m), 3.08 (1H, d, *J* = 13.4 Hz), 3.32 (1H, d, *J* = 13.4 Hz), 7.1–7.4 (5H, m); ^{13}C NMR 19.68 (t), 22.58 (q), 26.94 (t), 38.63 (s), 39.20 (t), 41.86 (t), 53.59 (d), 122.66 (s), 127.33 (d), 128.36 (2 × d), 130.68 (2 × d), 135.08 (s), 216.03 (s); MS *m/z* (rel intensity) 227 (M$^+$, 8), 198 (1), 91 (100); HRMS calcd for C$_{15}$H$_{17}$NO 227.1310, found 227.1307. Enone 3*E* (51 mg, 0.25 mmol) was hydrocyanated as described previously to give 8a (16 mg, 28%) and 8b (6.3 mg, 11%).

Hydrolysis of Cyanides. A solution of compound 8a (18 mg, 0.08 mmol) in 4% KOH in EtOH–H$_2$O (3:1) (4 mL) was stirred at room temperature for 23 h and then poured into water (20 mL) and the resulting aqueous solution acidified with 5% HCl and extracted with CH$_2$Cl$_2$ (3 × 15 mL). The organic phase was dried, evaporated, and purified by chromatotron chromatography (hexane–EtOAc, 1:1) to give 7 (16.9 mg, 87%). Similarly, 8b (18 mg) gave 7 (15.4 mg, 89%).

(±)-2-(3-Iodopropanyl)-3,3-dimethylsuccinimide (9). A solution of the carbinol amide 4 (169 mg, 1 mmol) in CH$_2$Cl$_2$ (50 mL) (dried over 3–4-Å molecular sieves), containing DIB (483 mg, 1.5 mmol) and I$_2$ (254 mg, 1 mmol), was irradiated with 2 × 100-W tungsten-filament lamps for 1 h at 25 °C. The reaction mixture was then poured into aqueous saturated sodium thiosulfate (25 mL) and extracted with CH$_2$Cl$_2$ (3 × 50 mL), dried, and concentrated. Chromatotron chromatography of the residue

(hexane–EtOAc, 85:15) gave 9 (180 mg, 61%): mp 68–69 °C (acetone–pentane); IR 3395, 1775, 1718 cm^{-1}; ^{1}H NMR 1.24 (3H, s), 1.35 (3H, s), 1.5–2.2 (4H, m), 2.51 (1H, t, *J* = 7.1 Hz), 3.26 (2H, m), 8.16 (1H, m); ^{13}C NMR 6.07 (t), 21.36 (q), 24.89 (q), 27.11 (t), 31.57 (t), 45.14 (s), 51.09 (d), 178.41 (s), 182.77 (s); MS *m/z* (rel intensity) 295 (M$^+$, 26), 280 (1), 225 (1), 168 (100), 140 (18), 127 (45), 112 (17), 97 (98); HRMS calcd for C$_9$H$_{14}$INO$_2$ 295.0071, found 295.0067.

(±)-2-(3-Iodopropanyl)succinimidespiro-3'-cyclopentane (10). Carbinol amide 6 (250 mg, 1.28 mmol) was treated as above to give, after chromatography (hexane–EtOAc, 4:1), the succinimide 10 (292 mg, 71%): mp 97–98 °C (acetone–pentane); IR 3390, 1770, 1720 cm^{-1}; ^{1}H NMR 1.5–2.2 (12H, m), 2.53 (1H, t, *J* = 6.9 Hz), 3.19 (2H, t, *J* = 6.5 Hz), 9.26 (1H, br s); ^{13}C NMR 6.42 (t), 25.36 (t), 25.67 (t), 28.48 (t), 30.72 (t), 31.11 (t), 38.79 (t), 50.05 (d), 54.92 (s), 179.67 (s), 183.98 (s); MS *m/z* (rel intensity) 322 (M$^+$ + 1, 2), 280 (4), 194 (100); HRMS calcd for C$_{11}$H$_{17}$INO$_2$ 322.0306, found 322.0206.

(±)-(2*R**,3*R**)-2-(3-Iodopropanyl)-3-benzyl-3-methylsuccinimide (11). Carbinol amide 7 (1.2 g, 4.9 mmol) was irradiated for 45 min at 25 °C as described previously to give, after chromatography (hexane–EtOAc, 85:15), the isocyanate 12 (120 mg, 10%) and the succinimide 11 (1.31 g, 72%). Compound 12: amorphous; IR 2247, 1734, 1603, 1454, 1405, 1379 cm^{-1}; ^{1}H NMR 1.31 (3H, s), 1.6–2.4 (7H, m), 3.13 (1H, d, *J* = 13.2 Hz), 3.21 (1H, d, *J* = 13.2 Hz), 7.2–7.4 (5H, m); ^{13}C NMR 19.62 (t), 26.39 (t), 29.46 (q), 39.81 (t), 45.47 (t), 55.00 (d), 61.50 (s), 119.98 (s), 126.87 (d), 128.11 (2 × d), 130.77 (d), 130.85 (d), 136.18 (s), 217.15 (s); MS *m/z* (rel intensity) 243 (M$^+$, 9), 200 (31), 152 (49), 91 (65), 81 (100); HRMS calcd for C$_{15}$H$_{17}$NO$_2$ 243.1259, found 243.1312. Compound 11: mp 116–117 °C (EtOAc–pentane); IR 3400, 1778, 1718, 1605, 1496, 1454, 1382 cm^{-1}; ^{1}H NMR 1.32 (3H, s), 1.4–2.3 (4H, m), 2.59 (1H, t, *J* = 6.8 Hz), 2.62 (1H, d, *J* = 13.8 Hz), 3.39 (1H, d, *J* = 13.8 Hz), 3.18 (2H, m), 7.1–7.3 (5H, m); ^{13}C NMR 6.12 (t), 21.35 (q), 26.58 (t), 31.58 (t), 42.17 (t), 45.56 (d), 50.18 (s), 127.29 (d), 128.77 (2 × d), 130.11 (2 × d), 135.15 (s), 178.88 (s), 182.04 (s); MS *m/z* (rel intensity) 371 (M$^+$, <1), 356 (1), 280 (1), 244 (41), 91 (100); HRMS calcd for C$_{15}$H$_{18}$INO$_2$ 371.0385, found 371.0375.

3-Oxocholestane-5α-carbonitrile (13) and -5β-carbonitrile (14). Preparation of these compounds essentially followed a previously reported procedure.[19] Compound 13: mp 181–183 °C (from MeOH); [α]$_D$ = +46° (CHCl$_3$, c = 0.264); IR 2225, 1715 cm^{-1}; ^{1}H NMR 0.69 (3H, s), 0.87 (6H, d, *J* = 6.6 Hz), 0.91 (3H, d, *J* = 6.6 Hz), 1.14 (3H, s), 2.46 (1H, d, *J* = 16.0 Hz), 2.52 (1H, d, *J* = 16.0 Hz); ^{13}C NMR 12.17 (q), 12.46 (q), 18.78 (q), 21.61 (t), 22.68 (q), 22.94 (q), 23.97 (t), 24.19 (t), 28.12 (d), 28.12 (d), 28.19 (t), 28.30 (t), 31.72 (t), 34.26 (t), 34.92 (d), 35.87 (d), 36.23 (t), 37.28 (t), 37.97 (s), 39.61 (t), 39.61 (t), 42.67 (s), 47.38 (s), 47.49 (t), 49.47 (d), 55.68 (d), 56.24 (d), 122.32 (s), 206.41 (s); MS *m/z* (rel intensity) 411 (M$^+$, 61), 396 (5), 256 (100); HRMS calcd for C$_{28}$H$_{45}$NO 411.3498, found 411.3496. Compound 14: mp 125–127 °C (from MeOH); [α]$_D$ = +26° (CHCl$_3$, c = 0.248); IR 2230, 1715 cm^{-1}; ^{1}H NMR 0.69 (3H, s), 0.86 (6H, d, *J* = 6.4 Hz), 0.91 (3H, d, *J* = 6.5 Hz), 1.26 (3H, s), 2.37 (1H, d, *J* = 15.9 Hz), 3.00 (1H, d, *J* = 15.9 Hz); ^{13}C NMR 12.00 (q), 18.66 (q), 19.48 (q), 21.36 (t), 22.53 (q), 22.76 (q), 23.79 (t), 24.00 (t), 25.59 (t), 27.95 (d), 28.14 (t), 31.26 (t), 33.43 (t), 34.43 (d), 35.67 (d), 36.10 (t), 36.54 (t), 37.13 (s), 39.47 (t), 39.78 (t), 40.22 (d), 42.53 (s), 44.24 (t), 45.82 (s), 56.14 (d), 56.22 (d), 122.72 (s), 206.72 (s); MS *m/z* (rel intensity) 411 (M$^+$, 64), 396 (8), 383 (12), 256 (100); HRMS calcd for C$_{28}$H$_{45}$NO 411.3498, found 411.3483.

3β-Hydroxycholestane-5α,3α-carbolactam (16). A solution of 5α-carbonitrile 13 (380 mg, 0.92 mmol) in ethanol (60 mL) was treated with KOH (2.4 g) at rt for 20 h as described previously to give the lactam 16[20] (309 mg, 78%): mp 248–251 °C (from MeOH); [α]$_D$ = +12° (CHCl$_3$, c = 0.48); IR 3570, 3405, 1680 cm^{-1}; ^{1}H NMR 0.65 (3H, s), 0.86 (6H, d, *J* = 6.4 Hz), 0.89 (3H, d, *J* = 7.0 Hz), 0.98 (3H, s), 3.25 (1H, m), 5.92 (1H, m); ^{13}C NMR 12.13 (q), 13.05 (q), 18.88 (q), 21.49 (t), 22.71 (q), 22.94 (q), 24.08 (t), 24.41 (t), 27.40 (t), 28.16 (d), 28.32 (t), 28.39 (t), 32.01 (t), 34.59 (d), 34.67 (t), 35.99 (d), 36.05 (s), 36.79 (t), 39.72 (t), 39.92 (t), 42.61 (s), 46.97 (d), 47.82 (t), 53.23 (s), 56.13 (d), 56.44 (d), 86.28 (s), 180.02 (s); MS *m/z* (rel intensity) 429 (M$^+$, 100), 414 (8), 411 (8), 385 (32), 372 (28), 316 (44); HRMS calcd for C$_{28}$H$_{47}$NO$_2$ 429.3607, found 429.3606.

3α-Hydroxycholestane-5β,3β-carbolactam (17). To a solution of 5β-carbonitrile 14 (0.5 g, 1.21 mmol) in ethanol (100 mL) was added KOH (4 g), and the mixture was stirred at rt for 24 h. The mixture was then poured into 5% hydrochloric acid and extracted with CHCl₃. The organic extracts were washed with water, dried with Na₂SO₄, and concentrated under reduced pressure. The residue was purified by chromatotron chromatography (benzene–EtOAc, 1:1) to give the lactam 17[20] (412 mg, 79%): mp 202–205 °C (from MeOH); $[\alpha]_D$ = +33° (CHCl₃, c = 0.246); IR 3570, 3410, 1690 cm⁻¹; ¹H NMR 0.66 (3H, s), 0.87 (6H, d, J = 6.7 Hz), 0.90 (3H, d, J = 7.0 Hz), 0.95 (3H, s), 4.27 (1H, br s), 6.46 (1H, br s); ¹³C NMR 12.45 (q), 18.80 (q), 18.98 (q), 22.46 (t), 22.70 (q), 22.95 (q), 24.04 (t), 24.20 (t), 26.66 (t), 26.90 (t), 28.15 (d), 28.47 (t), 31.80 (t), 32.41 (t), 35.77 (d), 35.83 (s), 35.94 (d), 36.30 (t), 39.65 (t), 40.39 (t), 43.01 (s), 43.13 (d), 46.80 (t), 55.42 (s), 56.48 (d), 56.77 (d), 87.03 (s), 179.02 (s); MS m/z (rel intensity) 429 (M⁺, 61), 414 (7), 411 (2), 385 (98), 372 (57), 316 (100); HRMS calcd for C₂₈H₄₇NO₂ 429.3607, found 429.3606.

7-Oxo-3β-hydroxycholestane-5α-carbonitrile (18). To a solution of compound 15 (2 g, 4.52 mmol) in dry THF (28 mL) was added a solution (1.5 M) of cyanhydric acid in dry THF (8.8 mL, 9 mmol) and a solution (1.5 M) of diethyl aluminum chloride in dry THF (12 mL) at 0 °C under argon. The mixture was stirred at rt for 4 h and then poured into water, neutralized with aqueous 2% NaOH, and extracted with CH₂Cl₂. The organic layer was washed with water, dried over Na₂SO₄, and concentrated under reduced pressure. The residue was purified by column chromatography (hexane–EtOAc, 7:3) to give the title compound 18 (1.36 g, 70%) and a small amount of the 7-oxo-3β-acetoxycholestane-5α-carbonitrile (19) (156 mg, 7%). Compound 18: mp 179–181 °C (from benzene–CHCl₃); $[\alpha]_D$ = –50° (CHCl₃, c = 0.106); IR 3600, 2220, 1700 cm⁻¹; ¹H NMR 0.65 (3H, s), 0.86 (6H, d, J = 6.5 Hz), 0.91 (3H, d, J = 6.5 Hz), 1.24 (3H, s), 2.33 (1H, d, J = 13.4 Hz), 2.64 (1H, d, J = 13.4 Hz), 4.11 (1H, m); ¹³C NMR 12.22 (q), 13.21 (q), 18.89 (q), 22.12 (t), 22.66 (q), 22.90 (q), 23.92 (t), 25.19 (t), 28.09 (d), 28.52 (t), 30.04 (t), 32.84 (t), 35.75 (d), 36.23 (s), 38.42 (t), 38.55 (t), 39.42 (t), 39.58 (t), 42.93 (s), 48.51 (t), 48.75 (s), 48.99 (d), 50.31 (d), 50.69 (d), 54.96 (d), 67.33 (d), 121.47 (s); MS m/z (rel intensity) 427 (M⁺, 100), 409 (27), 342 (8), 324 (8); HRMS calcd for C₂₈H₄₅NO₂ 427.3450, found 427.3458. Compound 19: mp 194–195 °C (from benzene–*n*-pentane); $[\alpha]_D$ = –36 °C (CHCl₃, c = 1.07); IR 2217, 1738, 1719 cm⁻¹; ¹H NMR 0.64 (3H, s), 0.85 (6H, d, J = 6.6 Hz), 0.90 (3H, d, J = 6.4 Hz), 1.25 (3H, s), 2.03 (3H, s), 2.34 (1H, d, J = 13.5 Hz), 2.60 (1H, d, J = 13.5 Hz), 5.10 (1H, m); ¹³C NMR 12.11 (q), 12.96 (q), 18.79 (q), 21.00 (q), 21.97 (t), 22.50 (q), 22.71 (q), 23.82 (t), 25.10 (t), 26.21 (t), 27.94 (t), 28.35 (t), 32.45 (t), 35.61 (d), 35.81 (t), 36.14 (t), 38.27 (s), 38.49 (t), 39.48 (t), 42.88 (s), 48.30 (t), 48.30 (s), 48.99 (d), 50.18 (d), 50.34 (d), 54.94 (d), 69.58 (d), 120.68 (s), 169.72 (s).

3β,7β-Dihydroxycholestane-5α,7α-carbolactam (20). To a solution of compound 18 (550 mg, 1.288 mmol) in ethanol (80 mL) was added a solution of NaOH (3.2 g) in water (5 mL) and the mixture stirred at 55 °C for 5 h. The lactam 20 was isolated as previously described (530 mg, 92%): amorphous; $[\alpha]_D$ = –24 °C (CHCl₃, c = 0.242); IR 3575, 3400, 1680 cm⁻¹; ¹H NMR 0.71 (3H, s), 0.86 (6H, d, J = 6.7 Hz), 0.90 (3H, d, J = 7.3 Hz), 0.98 (3H, s), 3.14 (1H, br s), 4.65 (1H, m), 7.27 (1H, br s); ¹³C NMR 12.62 (q), 16.08 (q), 19.04 (q), 21.79 (t), 22.71 (q), 22.95 (q), 24.09 (t), 26.54 (t), 28.22 (d), 28.96 (t), 30.31 (t), 32.68 (t), 35.73 (d), 35..99 (s), 36.39 (t), 37.38 (t), 39.68 (t), 40.25 (t), 43.82 (d), 44.89 (s), 49.29 (t), 51.28 (d), 52.20 (d), 54.35 (s), 55.44 (d), 66.47 (d), 88.32 (s), 179.43 (s); MS m/z (rel intensity) 445 (M⁺, 100), 427 (5), 386 (9), 384 (9), 314 (23); HRMS calcd for C₂₈H₄₇NO₃ 445.3556, found 445.3540.

3β-Acetoxy-5β-hydroxycholestane-5α,7α-carbolactam (21). To a solution of alcohol 20 (520 mg, 1.168 mmol) in pyridine (40 mL) was added acetic anhydride (6 mL) and the mixture stirred at rt for 4 h, quenched with ice, and extracted with CH₂Cl₂ (3 × 50 mL). The combined CH₂Cl₂ layers were then washed with 5% HCl (3 × 25 mL), water (3 × 25 mL), and 5% aqueous NaHCO₃ (25 mL), dried (Na₂SO₄), filtered, and evaporated. The resulting residue was purified by crystallization to give the title compound 21 (553 mg, 97%): mp 199.5–200.5 °C (from acetone); $[\alpha]_D$ = –50° (CHCl₃, c = 0.24); IR 3570, 3400, 1700, cm⁻¹; ¹H NMR 0.70 (3H, s), 0.85 (6H, d, J = 6.7 Hz), 0.89 (3H, d, J = 7.8 Hz), 0.98

(3H, s), 1.98 (3H, s), 3.21 (1H, s), 5.66 (1H, m), 7.25 (1H, s); ¹³C NMR 12.58 (q), 16.00 (q), 19.01 (q), 21.55 (q), 21.76 (t), 22.70 (q), 22.97 (q), 24.08 (t), 26.47 (t), 26.47 (t), 28.20 (d), 28.89 (t), 32.40 (t), 33.21 (t), 35.70 (d), 35.80 (s), 36.32 (t), 39.61 (t), 40.19 (t), 43.67 (d), 44.79 (s), 48.91 (t), 51.25 (d), 52.10 (d), 53.99 (s), 55.34 (d), 70.17 (d), 88.31 (s), 166.46 (s), 170.42 (s), 179.25 (s); MS m/z (rel intensity) 487 (M⁺, 56), 444 (100), 427 (32), 412 (11), 384 (29), 368 (21), 314 (37); HRMS calcd for C₃₀H₄₉NO₄ 487.3661, found 487.3646.

Fragmentation of 3β-Hydroxycholestane-5α,3α-carbolactam (16). A solution of carbinol amide 16 (150 mg, 0.35 mmol), DIB (170 mg, 0.52 mmol), and iodine (90 mg, 0.35) in CH₂Cl₂ (60 mL) was irradiated as above for 1 h at 25 °C to give, after chromatotron chromatography (hexane–EtOAc, 9:1), the isocyanate 23 (28.3 mg, 19%) and the imide 22 (122 mg, 63%). Compound 23: amorphous; IR 2225, 1705 cm⁻¹; ¹H NMR 0.68 (3H, s), 0.86 (6H, d, J = 6.7 Hz), 0.91 (3H, d, J = 6.4 Hz), 1.16 (3H, s), 2.30 (1H, d, J = 15.2 Hz), 2.68 (1H, d, J = 15.2 Hz); ¹³C NMR 12.24 (q), 14.73 (q), 18.81 (q), 21.64 (t), 22.71 (q), 22.96 (q), 23.96 (t), 24.25 (t), 26.93 (t), 28.15 (d), 28.33 (t), 33.47 (t), 34.83 (d), 35.20 (t), 35.93 (d), 36.27 (t), 37.66 (t), 39.64 (t), 39.87 (t), 42.74 (s), 47.22 (d), 51.59 (t), 55.97 (d), 56.30 (d), 68.98 (s), 122.63 (s), 208.46 (s) only 27 carbons can be observed; MS m/z (rel intensity) 427 (M⁺, 20), 412 (4), 384 (100), 369 (32); HRMS calcd for C₂₈H₄₅NO₂ 427.3451, found 427.3467. Compound 22: mp 159–161 °C (from MeOH); $[\alpha]_D$ = –8° (CHCl₃, c = 0.33); IR 3390, 1770, 1710 cm⁻¹; ¹H NMR 0.67 (3H, s), 0.86 (6H, d, J = 6.5 Hz), 0.91 (3H, d, J = 6.2 Hz), 0.89 (3H, s), 2.21 (1H, d, J = 18.5 Hz), 2.88 (1H, d, J = 18.5 Hz), 3.12 (2H, t, J = 9.0 Hz), 8.14 (1H, br s); ¹³C NMR 1.23 (t), 12.07 (q), 16.41 (q), 18.74 (q), 22.67 (t), 22.67 (q), 22.92 (q), 23.88 (t), 24.22 (t), 26.46 (t), 28.08 (d), 28.27 (t), 34.31 (t), 34.61 (d), 35.83 (d), 36.21 (t), 39.59 (t), 39.85 (t), 42.00 (t), 42.37 (s), 42.88 (t), 43.75 (d), 43.82 (s), 51.85 (t), 55.77 (d), 56.20 (d), 176.34 (s), 181.90 (s); MS m/z (rel intensity) 555 (M⁺, 13), 540 (8), 442 (7), 428 (90), 400 (58), 372 (100); HRMS calcd for C₂₈H₄₆INO₂ 555.2575, found 555.2549.

Fragmentation of 3α-Hydroxycholestane-5β,3β-carbolactam (17). A solution of carbinol amide 17 (100 mg, 0.233 mmol), DIB (113 mg, 0.345 mmol), and iodine (59 mg, 0.232) in CH₂Cl₂ (50 mL) was irradiated as above for 1.5 h at 25 °C to give, after chromatotron chromatography (benzene–EtOAc, 96.4), 3-oxacholestan-5β-isocyanate (25) (20.5 mg, 20%) and the imide 24 (82.7 mg, 62%). Compound 25: amorphous; IR 2230, 1710 cm⁻¹; ¹H NMR 0.68 (3H, s), 0.86 (6H, d, J = 6.6 Hz), 0.91 (3H, d, J = 6.5 Hz), 1.06 (3H, s), 2.19 (1H, d, J = 15.2 Hz), 3.11 (1H, d, J = 15.2 Hz); ¹³C NMR 12.17 (q), 17.90 (q), 18.77 (q), 22.11 (t), 22.68 (q), 22.94 (q), 23.95 (t), 24.23 (t), 28.13 (d), 28.30 (t), 28.38 (t), 32.15 (t), 34.68 (d), 35.86 (d), 36.24 (t), 36.94 (t), 37.16 (t), 39.61 (t), 39.95 (t), 40.30 (t), 42.66 (s), 42.69 (t), 49.05 (t), 56.30 (d), 56.51 (d), 68.75 (s), 123.45 (s), 209.12 (s); MS m/z (rel intensity) 427 (M⁺, 22), 412 (6), 384 (100), 369 (11), 366 (22); HRMS calcd for C₂₈H₄₅NO₂ 427.3451, found 427.3444. Compound 24: mp 110–113 °C (from MeOH); $[\alpha]_D$ = +11° (CHCl₃, c = 0.522); IR 3395, 1765, 1715 cm⁻¹; ¹H NMR 0.66 (3H, s), 0.85 (6H, d, J = 6.7 Hz), 0.90 (3H, d, J = 6.6 Hz), 1.27 (3H, s), 2.56 (1H, d, J = 18.8 Hz), 2.78 (1H, d, J = 18.8 Hz), 3.11 (2H, m), 8.24 (1H, br s); ¹³C NMR 0.65 (t), 11.96 (q), 13.44 (q), 18.60 (q), 21.58 (t), 22.50 (q), 22.74 (q), 23.77 (t), 24.04 (t), 26.79 (t), 27.94 (t), 28.09 (d), 31.62 (t), 34.17 (t), 35.67 (d), 36.08 (t), 38.11 (t), 39.46 (t), 39.79 (t), 42.27 (t), 43.80 (t), 44.36 (t), 49.21 (d), 53.12 (t), 56.12 (d), 56.19 (d), 175.79 (s), 182.35 (s); MS m/z (rel intensity) 555 (M⁺, 1), 540 (2), 442 (2), 428 (100), 400 (61), 372 (10); HRMS calcd for C₂₅H₄₆INO₂ 555.2575, found 555.2546.

Fragmentation of 3β-Acetoxy-7β-hydroxycholestane-5α,7α-carbolactam (21). A solution of carbinol amide 21 (200 mg, 0.41 mmol), DIB (250 mg, 0.77 mmol), and iodine (120 mg, 0.47 mmol) in CH₂Cl₂ (60 mL) was irradiated as described above for 90 min at 25 °C to give, after chromatotron chromatography (hexane–EtOAc, 98:2), the isocyanate 27 (63 mg, 32%) and the imide 26 (75 mg, 38%). Compound 27: amorphous; IR 2250, 1725 cm⁻¹; ¹H NMR 0.66 (3H, s), 0.86 (6H, d, J = 6.6 Hz), 0.91 (3H, d, J = 6.4 Hz), 1.27 (3H, s), 2.03 (3H, s), 2.26 (1H, d, J = 13.0 Hz), 2.80 (1H, d, J = 13.0 Hz), 5.61 (1H, m); ¹³C NMR 12.26 (q), 15.41 (q), 18.91 (q), 21.32 (q), 22.00 (t), 22.67 (q), 22.90 (q),

23.89 (t), 25.08 (t), 26.40 (t), 28.09 (d), 28.54 (t), 31.17 (t), 35.75 (d), 36.24 (t), 38.83 (t), 39.59 (t), 39.82 (t), 39.88 (s), 42.92 (s), 48.95 (d), 49.07 (d), 50.41 (d), 52.67 (t), 55.02 (d), 69.67 (d), 70.05 (s), 123.29 (s), 170.30 (s), 207.96 (s); MS m/z (rel intensity) 485 (M^+, 90), 470 (6), 467 (33), 443 (18), 424 (15), 382 (100), 364 (21), 277 (36), 228 (30); HRMS calcd for $C_{30}H_{47}NO_4$ 485.3505, found 485.3480. Compound **26**: mp 157–158 °C (from MeOH), $[\alpha]_D$ = +27° (CHCl$_3$, c = 0.26); IR 3395, 1765, 1720 cm^{-1}; ^{1}H NMR 0.49 (3H, s), 0.86 (6H, d, J = 6.5 Hz), 0.87 (3H, d, J = 6.4 Hz), 1.17 (3H, s), 2.19 (1H, d, J = 18.4 Hz), 2.96 (1H, d, J = 18.4 Hz), 5.37 (1H, m), 2.01 (3H, s), 5.62 (1H, m), 7.59 (1H, m); ^{13}C NMR 11.02 (q), 18.20 (q), 20.19 (q), 21.17 (q), 22.49 (q), 22.71 (q), 23.63 (t), 26.55 (t), 27.96 (d), 28.21 (t), 29.08 (t), 29.63 (t), 31.21 (t), 35.70 (d), 36.15 (t), 37.62 (t), 39.51 (t), 39.93 (s), 41.47 (t), 42.26 (s), 42.57 (t), 46.60 (d), 52.54 (s), 56.23 (d), 69.16 (d), 125.73 (d), 138.70 (s), 170.04 (s), 174.99 (s), 180.52 (s); MS m/z (rel intensity) 485 (M^+, 48), 470 (4), 425 (56), 410 (16), 372 (25), 312 (100), 247 (80); HRMS calcd for $C_{30}H_{47}NO_4$ 485.3505, found 485.3501.

(±)-(2R*,3R*)-2-[2-(Methoxycarbonyl)ethyl]-3-[(methoxycarbonyl)methyl]-3-methylsuccinimide (Ring-B Imide) (28). Method A. Periodic acid (1.02 g, 4.4 mmol, 22.4 equiv) was added to a stirred solution of **11** (74.2 mg, 0.2 mmol) in carbon tetrachloride (0.5 mL), acetonitrile (0.5 mL), and water (0.75 mL), under positive pressure of dry Ar. After 15 min, ruthenium trichloride hydrate (1 mg, 0.02 equiv) was added and the stirring continued for 6 h at room temperature. The reaction mixture was cooled to 0 °C with an ice bath, and ether (2 mL) was added. Vigorous stirring was continued for 10 min, and the product was then extracted with ether (3 × 10 mL). The combined organic layers were washed with brine (3 × 10 mL) and water (10 mL), dried, filtered, and concentrated. The crude product dissolved in Et$_2$O (3 mL) was treated with excess ethereal diazomethane and purified by chromatotron chromatography (hexane–EtOAc, 7:3) to give the dimethyl ester imide **28** (29.3 mg, 54%): mp 115–115.5 °C (EtOAc–hexane) (lit.[20] mp 111.5–113.5 °C); IR 3401, 1782, 1729, 1719 cm^{-1}; ^{1}H NMR 1.23 (3H, s), 1.7–2.1 (2H, m), 2.54–2.84 (2H, m), 2.63 (1H, d, J = 17.6 Hz), 2.90

(1H, d, J = 17.6 Hz), 2.96 (1H, dd, J = 9.5, 4.2 Hz), 3.68 (3H, s), 3.69 (3H, s), 9.02 (1H, br s); ^{1}H NMR (C$_6$D$_6$) 0.67 (3H, s), 1.34–1.79 (2H, m), 2.20 (1H, d, J = 17.5 Hz), 2.59 (1H, d, J = 17.5 Hz), 2.44 (2H, m), 2.96 (1H, dd, J = 9.1, 5.1 Hz), 3.21 (3H, s), 3.28 (3H, s), 7.97 (1H, br s); ^{13}C NMR 20.45 (t), 20.63 (q), 32.03 (t), 39.31 (t), 45.99 (s), 46.96 (d), 51.59 (q), 51.87 (q), 171.11 (s), 173.27 (s), 178.76 (s), 181.55 (s); MS m/z (rel intensity) 271 (M^+, 5), 240 (75), 211 (33), 198 (41), 185 (40), 180 (34), 166 (100); HRMS calcd for $C_{12}H_{17}NO_6$ 271.1056, found 271.1078.

Method B. Silver tetrafluoroborate (204 mg, 1.05 mmol) was added to a solution of **11** (259 mg, 0.7 mmol) in acetone (9 mL) and water (1 mL), and the mixture was stirred in the dark for 30 min, at room temperature, and then poured into water (30 mL) and extracted with CH$_2$Cl$_2$ (3 × 15 mL). The combined CH$_2$Cl$_2$ layers were dried, filtered, and evaporated. Chromatography of the residue (hexane–EtOAc, 7:3) gave the hydroxyimide **29** (151 mg, 83%): amorphous; IR 3614, 3401, 1776, 1714, 1600, 1495, 1453, 1380 cm^{-1}; ^{1}H NMR 1.31 (3H, s), 1.60–1.90 (4H, m), 2.29 (1H, m), 2.64 (1H, d, J = 13.8 Hz), 3.27 (1H, d, J = 13.8 Hz), 2.64 (1H, t, J = 6.7 Hz), 3.63 (2H, m), 7.1–7.3 (5H, m), 8.88 (1H, m); ^{13}C NMR 21.05 (q), 21.88 (t), 30.95 (t), 42.19 (t), 46.24 (d), 50.15 (s), 61.98 (t), 127.06 (d), 128.55 (2 × d), 130.13 (2 × d), 136.25 (s), 179.92 (s), 182.67 (s); MS m/z (rel intensity) 261 (M^+, 3), 243 (3), 231 (2), 202 (7), 170 (9), 152 (13), 91 (100); HRMS calcd for $C_{15}H_{19}NO_3$ 261.1364, found 261.1362. A solution of **29** (124 mg, 0.48 mmol) in CCl$_4$ (1 mL), CH$_3$CN (1 mL), and H$_2$O (1.5 mL) when treated with H$_5$IO$_6$ (1.86 g, 8.1 mmol, 14 equiv) and RuCl$_3$·xH$_2$O (2.4 mg, 0.02 equiv) as described previously for **11** afforded **28** (65.7 mg, 51%).

Supplementary Material Available: ^{1}H NMR and ^{13}C NMR spectra of compounds **3Z**, **3E**, **5–16**, **19–26**, **28**, and **29** and ^{1}H NMR spectrum of compound **27** (49 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.