PHOTO-OXIDATIVE CLEAVAGE OF A FURAN-AZETIDINONE CARBON-CARBON BOND: A SYNTHESIS OF 4-ACETOXYAZETIDINONE

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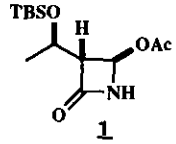
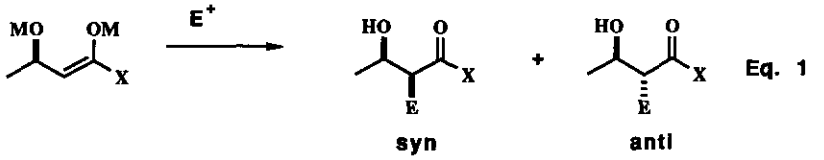
Abstact-A stereoselective synthesis of the 4-acetoxyazetidinione(1)from methyl 3(R)-hydroxybutyrate is reported. The synthesis involved stereoselective preparation of a 4-(2-furanyl)azetidinone that was allowed to react with singlet oxygen. The resulting endoperoxide intermediates underwent direct rearrangement to an acyloxyazetidinone that on reaction with sodium acetate gave 1 in modest yield. An improved yield of 1 was obtained by treatment of the endoperoxides with hydrogen peroxide followed by acetic anhydride to give an α-alkoxy acylperoxide that underwent thermal rearrangement to 1.

The 4-acetoxyazetidinone (1) is well recognized as a versatile building block for the synthesis of β-lactam antibiotics particularly carbapenems[1] and β-methylcarbapenems[2] and as such has been the object of intense investigation during the last ten years.[3] We wish to report a stereoselective synthesis of 1 from methyl 3(R)-hydroxybutyrate (2) which involves a novel oxidative cleavage of an azetidinone C-4 furan carbon-carbon bond.

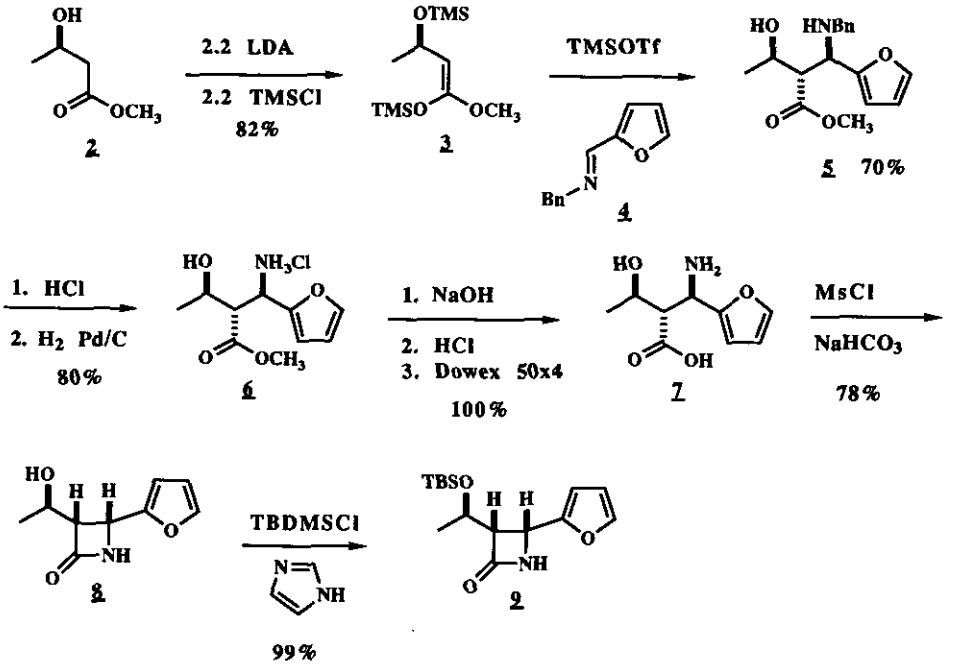


1

Any synthesis of 1 must address two key issues: control of stereochemistry and introduction of the sensitive acetal oxidation state of C-4. The ready availability of enantiomerically pure methyl 3-hydroxybutyrate and the well-precedented stereo-directing effect of an adjacent hydroxyl group makes 2 an ideal starting material. The enol or enolate derivatives of 3-hydroxybutyric acid are known to undergo electrophilic substitution with good control of relative stereochemistry to give either syn[4] or anti[5] products (equation 1). Both modes of stereocontrol have been exploited in the synthesis of 3-(1-hydroxyethyl)azetidinones.[3 ~ 5] We prepared the



4-furanylazetidinone (9) as a single stereoisomer as shown in Scheme 1. The Z silylketeneacetal (3) was obtained as a single isomer by reaction of 2 with 2.2 equivalents of LDA followed by 2.2 equivalents of TMS-Cl.[6] Reaction of 3 with the imine from furfural and benzylamine (4) according to the method of Guanti[3] gave the β - amino ester (5) in 70% yield (after silica gel chromatography, SGC). The major by-products of this reaction were methyl crotonate and unreacted imine; no other stereoisomers of 5 were detected.

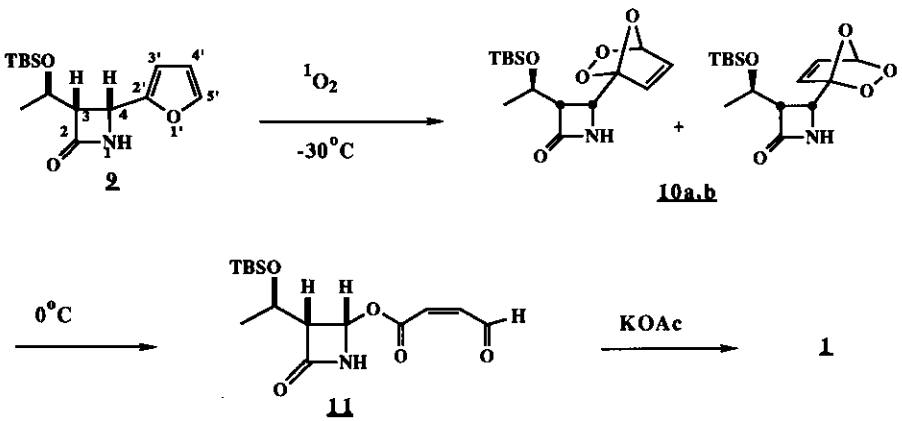


Scheme 1

Hydrogenation of the hydrochloride salt of 5 at atmospheric pressure gave the primary amine hydrochloride (6) in 80% yield following crystallization from 2-propanol/ ether. The hydrogenolysis was monitored carefully to prevent hydrogenation of the furan to the tetrahydrofuran. Saponification of 6 likewise had to be carefully controlled at pH=12.5 to avoid epimerization at C-2 while maintaining an acceptable rate of hydrolysis. The amino acid (7) was obtained in quantitative yield after desalting on Dowex 50X4 resin and crystallization from 2-propanol. Dehydration of 7 with methanesulfonyl chloride and sodium bicarbonate[7] gave the *cis*-azetidinone (8) (78%) which was silylated to give 9 in nearly quantitative yield.

Singlet oxygen addition to furans is known to give unstable endoperoxide products that may undergo a variety of rearrangements depending on their structure and the exact experimental conditions.[8] Due to the anti-

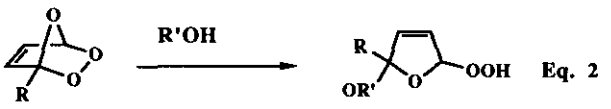
periplanar alignment of the C2'-substituent bond with the oxygen-oxygen bond (as in 10a,b, Scheme 2) a Baeyer-Villiger like rearrangement is possible. A number of examples of C-C bond cleavage involving a C-2' substituent have been reported; in each case the C-2' substituent contained an α-heteroatom capable of stabilizing a positive charge.[9] Thus 9 appeared as an ideal candidate for such a rearrangement. Exposure of the furanylazetidinone (9) to singlet oxygen (generated photochemically from O_2 with methylene blue as sensitizer) at -30 °C led to the formation of a 3:2 mixture of two products whose nmr spectra were consistent with the diastereomeric endoperoxides (10a,b)[6] (Scheme 2). These endoperoxides were stable overnight at



Scheme 2

-30 °C but decomposed on warming to 0 °C (95% conversion at 0 °C over 16 h). The nmr spectrum revealed the formation of a major product in the decomposed mixture; filtration through a short plug of silica gel provided a small amount of the labile 4-acyloxyazetidinone (11) sufficiently purified to allow assignment of its ^1H and ^{13}C nmr spectra.[6] The migration of the azetidinone proceeded with retention of configuration at C-4 (J_{H3-H4}=4.4 Hz), consistent with a Baeyer-Villiger mechanism. A comparison of the integration values of the vinyl signals with those of the *t*-butyl signals in the nmr of the crude reaction mixture suggested that 11 was formed in 35% yield. When the crude reaction mixture was treated with potassium acetate the acetoxy-azetidinone (1) was formed and was isolated (SGC) in 22% yield (from 9). The photo-oxidation of 9 was equally effective in a number of solvents (acetone, CH_2Cl_2, CH_3CN, DMF, *t*-butanol) but the yield of 11 was relatively insensitive to solvent changes. Attempts to catalyze the rearrangement with Lewis acids gave only intractable material (perhaps due to the lability of 11).

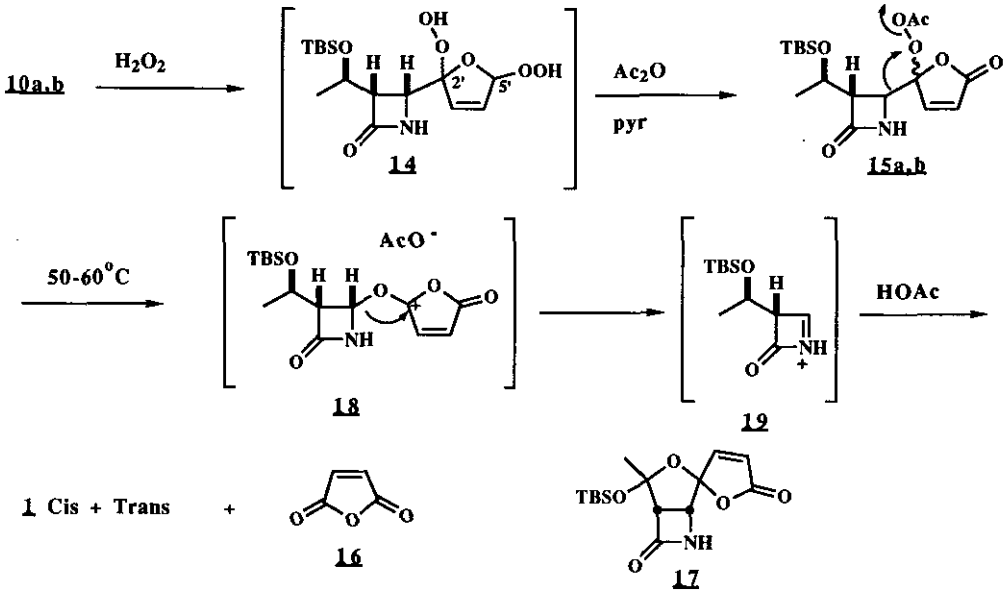
Having failed at all attempts to significantly improve the yield of 11 from 10, we attempted to control this interesting oxidation of the carbon-carbon bond by exploring an alternate approach. Schreiber has shown that a Baeyer-Villiger like rearrangement of an α-alkoxy hydroperoxide can be affected by acylation of the hydroperoxy group.[10] It is also well known that endoperoxides such as 12 undergo regioselective alcoholysis to give a hydroperoxide (13) resulting from attack of the alcohol at that carbon more able to accommodate a positive charge (equation 2). However, for the purpose of oxidatively cleaving the azetidinone-furan bond of 9 this would place the hydroperoxy group at C-5 rather than at the requisite C-2 of the furan.



Eq. 2

12 13

We chose then to react the endoperoxide mixture (10a,b) with aqueous hydrogen peroxide which should place a hydroperoxy group at C-2' (as well as at C-5'). After an aqueous work-up to remove excess hydrogen peroxide the reaction mixture, presumably containing the bis-hydroperoxide (14), was directly acetylated to give the acetylperoxides (15a,b) (Scheme 3).[6] Although these diastereomers were separated by column chromatography, they were found to be unstable at room temperature, slowly rearranging to the acetoxyazetidinone (1) (as a mixture of *cis* and *trans* isomers) and maleic anhydride (16). The yield of 15a,b as determined by hplc was 75%; however, only a 58% combined yield was obtained following chromatography. Although the more polar isomer (tlc) (15b) was clearly the major product in the crude nmr spectrum, it was isolated in lower yield than the earlier eluting 15a. Consistent with the lower yield was the observation that 15b rearranged to 1 at a faster rate than did 15a. Warming of 15b at 50 °C in acetonitrile gave 1 (79% 1.2: 1 *trans*: *cis*) and maleic anhydride as the only identifiable products. Treatment of 15a under the same conditions gave 1 (52%), 16, and a third component (22%) tentatively assigned as structure (17) by its ^{1}H and ^{13}C nmr spectra.



Scheme 3

The fact that a substantial amount of *cis* (1) was formed suggests that some internal return of acetate is occurring during rearrangement. Both S_N2 reaction of acetate on ion(18)or addition of acetic acid to imine(19) would give exclusively (>99%) *trans* (1). Interestingly 17 was formed as a single diastereomer and may arise from homolytic cleavage of the peroxide bond. The resulting oxygen radical could then abstract a proton from the silyloxyethyl sidechain followed by oxidation to give the oxygen stabilized carbonium ion that collapses to 17. The fact that 15b does not give rise to 17 and more readily rearranges to 1 suggests that it can more easily

adopt that conformation in which the breaking C-C bond is antiperiplanar to O-O bond of the peroxide.

Although not applicable to large scale preparation of 1 due to the inherent dangers associated with hydroperoxide compounds, the photo-oxidative cleavage of the furan group represents an interesting and unique method to introduce the acetal oxidation state at C-4 of an azetidinone.

EXPERIMENTAL

General: nmr spectra were recorded on a Bruker AM300 or WM250 spectrometer in $CDCl_3$ unless otherwise stated; chemical shifts (δ) are reported relative to residual $CHCl_3$ (δ=7.27) in ^1H and to $CDCl_3$ (δ=77.0) in the ^{13}C spectra. Ir spectra were recorded on a Perkin-Elmer 281 B spectrophotometer. Characteristic bands are reported as s (strong), m (medium) and/or br(broad). Rotations were recorded on a Perkin-Elmer 241 polarimeter equipped with a Lauda RC3 constant temperature bath. Melting points are uncorrected. All reactions were run under nitrogen unless otherwise stated. Solvents and reagents were used as received from the vendor. Where specified, dry solvent refers to sieve dried solvents with a Karl Fisher titer of less than 20 μg/mL H_2O.

(R)-1-Methoxy-1,3-bis(trimethylsilyloxy)-1-butene, 3: n-BuLi (1.5M, 60.0 ml, 92.4 mmol) was added to a cold (-78°C) solution of diisopropylamine (9.42 g, 93.1 mmol) in dry THF (180 ml). (R)-Methyl 3-hydroxybutyrate (5.02 g, 42.4 mmol) in dry THF (85 ml) was added dropwise at a rate such that the temperature did not exceed -70°C . After 30 min TMSCl (10.10 g, 93 mmol) in dry THF (85 ml) was added while maintaining the temperature at less than -70°C. The solution was stirred at -78°C for 2 h and was then removed from the cold bath and allowed to warm slowly to room temperature. The solution was concentrated (rotovapor), diluted with hexanes (500 ml) and reconcentrated. The residue was resuspended in hexanes (170 ml), stirred at room temperature for 1 h, filtered, concentrated, and distilled (kugelrohr, bp 70-80°C/0.25 mm) giving a clear colorless liquid, 9.10 g (82%). ^1H Nmr: 4.63 (m, 1H); 3.62 (d, J= 9 Hz, 1H); 3.48 (s, 3H); 1.22 (d, J= 7 Hz, 3H); 0.21 (s, 9H); 0.10 (s, 9H). ^{13}C Nmr: 156.7, 82.0, 64.7, 54.5, 26.0, 0.43, 0.36. A 7% NOE was observed at the vinyl ^1H signal (3.62 ppm) on irradiation of the methoxy singlet at 3.48 ppm.

Methyl 2(S)-[(R)-benzenemethylamino-(furan-2-yl)methyl]-3(R)-hydroxybutyrate 5: Furfural (3.30 g, 34.3 mmol) was added to benzylamine (3.68 g, 34.3 mmol) in CH_2Cl_2 (25 ml) at 0°C. Molecular sieves (3Å, 10 g) were added and the mixture was stirred for 2 h at 20°C. The mixture was filtered, concentrated, and then redissolved in dry CH_2Cl_2 (40 ml). The solution was cooled to -20°C and TMSOTf (0.76 g, 3.4 mmol) was added followed by addition of silyl keteneacetal (3). The solution was stirred at -20°C for 20 h and then was allowed to warm to 20°C. Hexanes (25 ml) and 2N HCl (50 ml) were added and the mixture was stirred vigorously. The layers were separated and the aqueous layer was extracted with 1:1 hexane: ethyl acetate (25 ml). The aqueous layer was neutralized with 5N NH_4OH (75 ml) and was then extracted with CH_2Cl_2 (2 X 50 ml). The CH_2Cl_2 layer was dried (Na_2SO_4), filtered and concentrated to a dark brown oil. Silica gel chromatography (3: 2 hexane: ethyl acetate) provided a yellow oil, 7.34 g (70.4%). ^1H Nmr: 7.41 (J≈2 Hz, 1H); 7.30 (m, 5H); 6.32 (dd, J= 8, 7 Hz, 1H); 4.11 (d, J= 10 Hz, 1H); 3.74 (d(AB), J=13 Hz, 1H); 3.57 (d(AB), J=13

Hz, 1H); 3.45 (s, 3H); 2.78 (dd, J=8, 10 Hz, 1H); 1.15 (d, J=8 Hz, 3H). ^{13}C Nmr: 171.8, 152.4, 142.5, 138.2, 128.7, 128.5, 127.6, 110.1, 108.2, 70.3, 58.4, 57.4, 51,6, 51.2, 21.7. Ir ($CDCl_3$): 3400-2800 br, 1730 s. Anal. Calcd for $C_{17}H_{21}NO_4$: C, 67.31; H, 6.98; N, 4.62. Found: C, 67.46; H, 7.24; N, 4.58.

Methyl 2(S)-[(R)-aminofuran-2-ylmethyl]-3(R)-hydroxybutyrate hydrochloride, 6: Benzylamino ester (5) (12.15 g, 40.05 mmol) was dissolved in acetonitrile (500 ml) and 2N HCl (20.1 ml, 40.2 mmol) was added. The solution was concentrated to a yellow foam and the dry salt thus formed was dissolved in methanol (120 ml). The solution was hydrogenated over 10% Pd/C at 2 psig at 20°C until 1 eq. of H_2 had been absorbed (5 h). The mixture was filtered and concentrated to a yellow solid which was dissolved in 2-propanol (70 ml); ether (150 ml) was added dropwise giving fine white needles. The product was filtered, washed with 2:1 ether:2-propanol and dried to give 6.49 g. The mother liquors were concentrated and the residue was taken up in 2-propanol (25 ml), ether (75 ml) was added giving a second crop, 1.47 g. Total 7.96 g, 79.6%. Anal. Calcd for: $C_{10}H_{16}NO_4Cl$: C, 48.10; H, 6.46; N, 5.61. Found: C, 47.95; H, 6.45; N, 5.66. Spectral analyses were performed on the free base obtained by dissolving the hydrochloride in $CDCl_3$, washing with 5N NH_4OH, and filtering through Na_2SO_4. ^1H Nmr: 7.33 (m, 1H); 6.24 (m, 1H); 6.07 (m, 1H); 4.32 (d, J=11 Hz, 1H); 4.19 ((dq, J=8, 7 Hz, 1H); 3.50 (s, 3H); 2.68 (dd, J=11, 8 Hz, 1H); 1.13 (d, J=7 Hz, 3H). ^{13}C Nmr: 172.1, 155.8, 142.0, 110.2, 105.1, 70.2, 57.5, 52.7, 51.6, 21.6. Ir ($CDCl_3$): 3380 m, 1730 s, 1120 s. mp 165°C (decomp.). $[\alpha]_D^{25}$= -38.5° (c 1.026, CH_3OH).

2(S)-[(R)-Aminofuran-2-ylmethyl]-3(R)-hydroxybutyric acid 7: The amine hydrochloride (6) (41.74 g, 167.2 mmol) was dissolved in water (150 ml); 5N NaOH was added to give pH=12.5. The pH was maintained at pH=12.5 +/- 0.1 using a pH meter controlled pump which added 5N NaOH when needed. After 21 h, the solution was acidified to pH=2 with 12N HCl and the aqueous solution was passed through a Dowex 50X4 column (700ml) which had previously been washed with 2N HCl (2.1 l) and then water (2.1 l). The column was eluted with water (1.4 l) to remove NaCl and was then eluted with 1.5N NH_4OH (2.1 l) collecting 450 ml fractions. Those fractions containing the amino acid (#2 and #3) were concentrated (rotovapor) to a paste. 2-Propanol was added and the mixture was heated to reflux with stirring. After cooling to room temperature the product was collected as an off-white solid on a filter, was washed with 2-propanol and dried at 50°C/1.0 mm for 2 days, 34.26 g (103% ,still contaminated with 2-propanol by nmr). Further drying at 75°C/1.0 mm for 3 days provided an analytical sample. ^1H Nmr (D_2O): 7.53 (br s, 1H); 6.51 (d, J≈3 Hz, 1H); 6.45 (br s, 1H); 4.75 (d, J=9 Hz, 1H); 4.15 (m, 1H); 2.83 (t, J=9 Hz, 1H); 1.30 (d, J=7 Hz, 3H). ^{13}C Nmr (D_2O): 177, 148, 145, 112, 111, 71, 58, 53, 23. Ir (KBr): 3460 s, 3200-2400 s. Anal. Calcd for $C_9H_{13}NO_4$: C, 54.26; H, 6.58; N, 7.03. Found: C, 54..13, H, 6.52; N, 7.01. mp 135-140°C (decomp.). $[\alpha]_D^{25}$ -35.0° (c 1.000, H_2O).

4(R)-Furan-2-yl-3(S)-(1(R)-hydroxyethyl)-2-azetidinone, 8: $NaHCO_3$ (50.7 g, 60.3 mmol) was added to dry 1-propanol (1.0 l) at 45°C followed by addition of methanesulfonyl chloride (8.7ml, 112 mmol). Amino acid (7) (5.00 g, 25.1 mmol) was added and after 30 min a second portion of 7 (5.00 g, 25.1 mmol) was added. The mixture was stirred at 45°C for 4 h and then at 20°C overnight. Methanol (25 ml) and water (25 ml) were added and the mixture was stirred 1 h. It was then filtered and concentrated ; the residue was dissolved in ethyl acetate and refiltered. Concentration gave an oil, 12.1 g, which was chromatographed on silica gel (1:2

hexane:ethyl acetate) giving an oil which crystallized on trituration with 3:1 hexane:ethyl acetate (80 ml). The solid was collected on a filter, washed, and dried 7.05 g (77.5%). ^{1}H Nmr: 7.42 (m, 1H); 6.8 (br s, 1H); 6.39 (m,2H); 4.83 (d, J=5 Hz, 1H); 3.92 (m, 1H); 3.43 (ddd, J=1.5, 4.9, 6.4 Hz, 1H); 1.9 (br s, 1H); 1.26 (d, J=7 Hz, 3H). ^{13}C Nmr: 168.0, 151.4, 143.2, 111.0, 109.0, 64.9, 63.9, 48.4 21.1. Ir ($CDCl_3$): 3600 m, 3400 m, 1767 s. Anal. Calcd for $C_9H_{11}NO_3$: C, 59.66; H, 6.12; N, 7.73. Found: C, 59.38; H, 6.08; N, 7.65. mp 90-92°C. $[\alpha]_D^{25}$= +70.0° (c 1.001, CH_3CN).

4(R)-Furan-2-yl-3(S)-1(R)-t-butyldimethylsilyloxyethyl-2-azetidinone, 9: *t*-Butyldimethylchlorosilane (3.58 g, 23.7 mmol) was added to azetidinone 8 (3.91 g, 21.6 mmol) and imidazole (2.21 g, 32.5 mmol) in dry DMF (15 ml) at 20°C. After 1 h, gc analysis indicated complete reaction (30M DB-17, 180°C to 280°C at 10°C/min; 8, 5.6 min; 9, 7.4 min). Methylene chloride (75 ml), hexanes (75 ml), and water (150 ml) were added and the mixture was stirred vigorously. The organic layer was then washed with 0.5N HCl (150 ml), 3% $NaHCO_3$ (150 ml), and water (150 ml). It was dried ($MgSO_4$), filtered, and concentrated to a yellow oil that was homogeneous by tlc (3:1 hexane: ethyl acetate Rf=0.6) 6.33 g (99%) . ^{1}H Nmr: 7.41(m, 1H); 6.38 (dd, J=3.4, 2.0 Hz, 1H); 6.1 (br s, 1H); 4.83 (d, J=5.4 Hz, 1H); 4.18 (dq, J=8.8, 6.4 Hz, 1H); 3.50 (ddd, J=7.8, 5.4, 1.0 Hz , 1H); 1.33 (d, J= 6.4 Hz, 3H); 0.77(s, 9H); -0.08 (s, 3H); -0.29 (s, 3H). ^{13}C Nmr: 168.5, 151.3, 142.6, 110.7, 109.3, 65.3, 64.3, 48.9, 25.8, 22.4, 17.8, -3.9, -5.1. Ir ($CDCl_3$) : 3400 m, 1760 s. Anal. Calcd for $C_{15}H_{25}NO_3Si$: C, 60.98; H, 8.53; N,4.74. Found: C, 60.63; H, 8.87; N, 4.51. $[\alpha]_D^{25}$= -3.5° (c 1.02 CH_3CN).

Photo-oxygenation of 9:

Endoperoxides 10a,b Methylene blue (1 mg) was added to the silylated azetidinone (9) (295 mg, 1.00 mmol) in dry acetone-d_6 (5 ml). The dark blue solution was cooled to -30°C and O_2 was bubbled through the solution while irradiating with a 400W halogen lamp. After 1.5 h tlc indicated no starting material remained (3:1 hexane: ethyl acetate). The solution was cooled to -78°C and a 0.6 ml aliquot was removed for nmr analysis. ^{13}C Nmr (acetone-d_6, T=-30°C) : Diastereomers present, ratio 3/2: Major 167.4, 133.4, 131.7, 113.4, 104.8, 66.2, 62.9, 49.0, 26.2, 22.9, 18.5, -3.5, -3.7; minor 167.5, 133.7, 131.9, 113.7, 104.6, 65.7, 62.8, 47.5, 26.4, 22.7, 18.5, -3.3, -3.8; Due to severe overlap in the ^{1}H spectrum useful data could not be reported.

4-Acyloxyazetidinone 11: After sampling, the above solution was allowed to warm to 20°C and was stirred overnight. The solution was concentrated, dissolved in 1:1 hexane: ethyl acetate (1ml) and was passed through a 1in column of silica gel. The eluent (1:1 hexane: ethyl acetate) was concentrated to an oil (37 mg, 12%). Attempts to isolate pure 11 by more careful chromatography lead to complete decomposition. ^{1}H Nmr: 10.53 (d, J= 7.3 Hz, 1H); 6.92 (br s, 1H); 6.63 (d, J= 11.7 Hz, 1H); 6.42 (dd, J= 11.7, 7.3 Hz, 1H); 6.02 (d, J=4.4 Hz, 1H); 4.36 (m, 1H); 3.45 (ddd, J= 8.8, 4.4, 1.9 Hz, 1H); 1.37 (d, J= 7.5 Hz, 3H); 0.83 (s, 9H); 0.09 (s, 3H); 0.05 (s, 3H). ^{13}C Nmr: 191.7, 166.4, 164.4, 142.1, 132.0, 76.5, 64.2, 63.0, 25.7, 22.3, 17.9, -3.7, -4.7.

4-Acetoxyazetidinone 1: Potassium acetate (980 mg, 10 mmol) was added to a solution of 10a,b generated as above . The mixture was stirred for 1.5 h and was then diluted with CH_2Cl_2 (20 ml). The solution was washed with water (2x 5 ml), dried (Na_2SO_4), and concentrated to a dark blue oil (255 mg). Silica gel chromatography

(2:1 hexane: ethyl acetate) gave 1 as a white solid (63 mg, 22%).

Acetylperoxides 15a,b: Hydrogen peroxide (30%, 1 ml) was added to a solution of the endoperoxides (10a,b) obtained as above at -20°C and the solution was allowed to warm to 0°C. After stirring 1 h, the solution was diluted with ether (20 ml) and washed with water (3X 5ml). The ether layer was dried ($MgSO_4$), filtered, and concentrated to 5 ml . Methylene chloride (30 ml) was added and the solution was again concentrated to 5 ml. It was cooled to 0°C and acetic anhydride (0.300 ml) and then pyridine (0.280 ml) were added. The solution was stirred at 0°C for 1 h and was then allowed to warm to 20°C. The solution was diluted with CH_2Cl_2 (10 ml), washed with 2N HCl (5 ml), 3% $NaHCO_3$ (5 ml) and was then dried ($MgSO_4$) and concentrated to an oil 385 mg which was chromatographed on silica gel (2:3 hexane: ethyl acetate) giving 15a (101 mg, 27%) and 15b (90mg, 24%) and a mixed fraction (23 mg, 6%).
15a: ^1H Nmr ($CDCl_3$) 7.92 (d, J=5.8, 1 H), 6.37 (br s, 1 H), 6.27 (d, J=5.8, 1 H), 4.45 (qd, J=6.3, 5.5, 1 H), 4.33 (d, J=5.5, 1 H), 3.53 (td, J=5.5, 2.0, 1 H), 2.04 (s, 3 H), 1.44 (d, J=6.3, 3 H), 0.89 (s, 9 H), 0.14 (s, 3 H), 0.10 (s, 3 H). ^{13}C Nmr: 168.4, 167.3, 166.3, 150.1, 125.6, 112.9, 65.1, 62.3, 53.3, 25.8, 21.7, 18.1, 17.1, -4.3, -4.7.
15b: ^1H Nmr ($CDCl_3$) d 7.52 (d, J=5.5, 1 H), 6.33 (d, J=5.5, 1 H), 6.29 (br s, 1 H), 4.77 (dq, J=9.0, 6.3, 1 H), 4.04 (d, J=5.1, 1 H), 3.47 (ddd, J=9.0, 5.1, 0.8, 1 H), 2.03 (s, 3 H), 1.44 (d, J=6.3, 3 H), 0.89 (s, 9 H), 0.14 (s, 3 H), 0.11 (s, 3 H). ^{13}C Nmr: 168.3, 167.5, 166.7, 149.5, 126.3, 111.8, 65.7, 62.8, 54.4, 26.0, 22.8, 18.2, 17.1, -3.1, -3.7.

4-Acetoxyazetidinone 1: The acetyl peroxide 15b (68 mg, 0.18 mmol) was dissolved in CH_3CN (1 ml) and was heated at 50°C for 18h. The solution was concentrated and chromatographed on silica gel (2:1 hexane: ethyl acetate) giving a white solid 42 mg . ^1H Nmr showed both cis and trans 1 in a ratio of 1:1.2.
15a (96 mg, 0.26 mmol) in CH_3CN (1 ml) was likewise heated at 60°C for 18 h. Concentration and silica gel chromatography gave cis and trans 1 (39 mg, 52%) and the mixed ketal(17)(18 mg, 22%).
17: ^1H Nmr: 7.25 (d, J=5.5, 1 H), 6.55 (br s, 1 H), 6.31 (d, J=5.5, 1 H), 4.33 (d, J=3.9, 1 H), 3.90 (dd, J=3.9, 3.1, 1 H), 1.73 (s, 3 H), 0.91 (s, 9 H), 0.16 (s, 6 H). ^{13}C Nmr: 169.2, 165.5, 149.0, 126.1, 111.1, 107.0, 68.5, 60.0, 25.7, 25.2, 17.9, -2.6, -2.9.

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