Stereocontrolled Formation of Epoxy Peroxide FunctionalityAppended to a Lactam Ring

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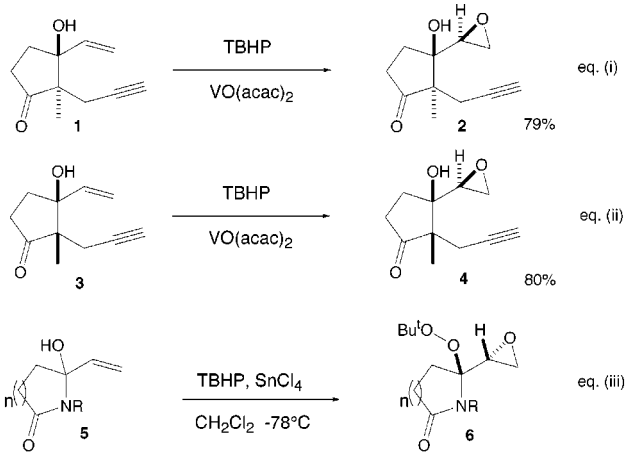
The action of *tert*-butyl hydroperoxide and tin(IV) chloride upon allylic alcohols containing a lactam ring leads mainly to epoxy alkyl peroxides with high diastereoselection. Both the stereochemistry and the products formed are in marked contrast to the reactions of the analogous carbocyclic allylic alcohols with *tert*-butyl hydroperoxide-$VO(acac)_2$.

The epoxidation of allylic alcohols has achieved outstanding importance, mainly because of their ease of enantioselective formation[1] and the variety of useful transformations that the resulting 2,3-epoxy alcohols can undergo.[2] Recently we employed diastereoselective epoxidations as part of new methodology for the stereocontrolled construction of polyoxygenated bicyclic systems (Scheme 1, eqs. i and ii).[3] We have also shown that such epoxidations take a markedly different course when the carbocyclic backbone is replaced by a lactam system (Scheme 1, eqs. iii),[4] the results of which are described in detail in this paper. Although it is unlikely that these epoxidations can readily be made enantioselective, the convenience of the procedure and the good diastereoselectivities are of benefit. Generally, our studies show that an allylic hydroxyl group, when adjacent to the nitrogen atom of an amidic linkage, is replaced by an alkyl peroxy group, usually with concomitant epoxidation of an exocyclic double bond, giving epoxy alkyl peroxides **6** as the major products. Considering that stereocontrol is also quite high, such processes could find use in the preparation of alkyl peroxide analogues to the many dialkyl peroxides of importance in nature (e.g. prostaglandin endoperoxides).[5] Endoperoxides possess potent physiological activity, and together with thromboxane A_2 and prostacyclin have been implicated in the control of platelet aggregation.[6] Additionally, the biological activity of dialkyl peroxides, formed in lipids by the action of reactive oxygen species on unsaturated lipid membranes, is of continuing interest.[7]

Scheme 1



The diastereoselective epoxidations (eqs. i and ii) shown in Scheme 1 are prerequisite to Lewis acid mediated cyclizations that furnish polyfunctionalized fused carbocycles.[3] The π-face selectivity exhibited by **1** and **3** is notable and in both cases the syn epoxy alcohols **2** and **4** result (in this context, we have found it useful to define the configuration by orienting the carbon framework as prior to a cyclization as in Scheme 1, and then to apply the terms syn and anti). With cyclizations[3] resulting in nitrogen heterocycles in mind, an investigation of the epoxidation of lactam analogues such as **5** was undertaken. Whereas **1** and **3** can be epoxidized using either *m*-CPBA in $CHCl_3$, or by *tert*-butyl hydroperoxide (TBHP) (1.5 eq., catalytic $VO(acac)_2$, benzene, 18 h reflux), neither of those methods was successful for **5**; instead attempted epoxidation led to fragmentation to the *N*-substituted cyclic imide, whose formation evidently reflects the increase in electron density of the quaternary center owing to the nitrogen atom.

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Table 1. Reaction of Allylic Alcohols with TBHP and $SnCl_4$

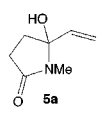
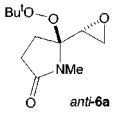
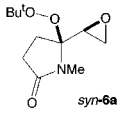
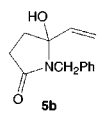
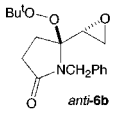
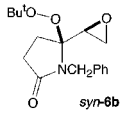
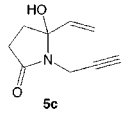
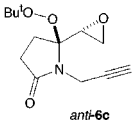
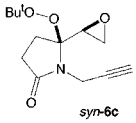
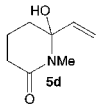
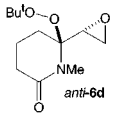
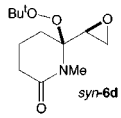
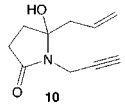
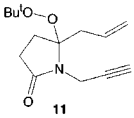
Entry	Allylic Alcohol	Products	Yield (ratio)
1	 **5a**	 *anti*-**6a**  *syn*-**6a**	69% (9:1)
2	 **5b**	 *anti*-**6b**  *syn*-**6b**	67% (9:1)
3	 **5c**	 *anti*-**6c**  *syn*-**6c**	80% (9:1)
4	 **5d**	 *anti*-**6d**  *syn*-**6d**	64% (7:1)
5	 **10**	 **11**	40%

Table 2. Reaction of 7a with TBHP and $SnCl_4$

entry	$SnCl_4$ (mol %)	peroxide **7b** (%)	diperoxide **8b** (%)	epoxy peroxide **6b** (%)
1	0.33	33	13	-
2	10	13	25	-
3	25	-	28	10
4	50	-	20	32
5	100	-	-	67
6	220	-	-	38

Products of the reaction of a variety of the amidic allylic alcohols **5** with TBHP in the presence of 2.5 mol eq. of $SnCl_4$ are given in Table 1. Good yields of the epoxy alkyl peroxides **6** were obtained for a variety of *N*-substituents, and for γ- and δ-lactam rings. This is notable since tertiary alcohols have been converted into the corresponding *tert*-butyl peroxides by reaction with trichloroacetonitrile followed by TBHP and $BF_3.OEt_2$, but in low yields.[8] The homoallylic alcohol **10** (entry 5) did not undergo epoxidation. However, it was converted into the peroxide **11**, suggesting that an allylic peroxide may be the means by which epoxy alkyl peroxides **6** are formed. Treatment of the allylic peroxide **7a** with TBHP in the presence of only 2.5 mol eq. of $SnCl_4$ indeed afforded peroxy epoxide **6a**, though in considerably lower yield (35%) than the one-pot reaction (Table 1, entry 1). A similar pattern was observed when **5b** was treated with *tert*-butyl hydroperoxide in dichloromethane and a widely varying stoichiometry of $SnCl_4$ (Table 2 and Scheme 3). The initial product was the α-peroxy amide **7b**, and the epoxy peroxide **6b** was the final product. At intermediate concentrations of $SnCl_4$, the diperoxide **8b** is formed, perhaps via consecutive addition of peroxide to the 1-azabutadienium cation (**9**) (Scheme 4). The catalytic effect of $SnCl_4$ on the formation of the allylic peroxides was also shown by treatment of **5a** and TBHP (2.2 eq.) in dichloromethane with 8 mol % of $SnCl_4$; the corresponding allylic peroxide **7a** was formed in 59%, whereas **5a** was recovered quantitatively when $SnCl_4$ was omitted (Scheme 2).

The good diastereoselection in the products of eq. iii was established by ^{1}H NMR spectroscopy. Thus, for the epoxy peroxides **6c** the methine hydrogen atom of the epoxide unit resonated at δ 3.32 (dd, J = 4.5 and 2.8 Hz) for the *anti*-diastereoisomer and at δ 3.37 (dd, J = 4.1 and 3.0 Hz) for the *syn*-diastereoisomer. For epoxy peroxides **6a** the methine hydrogen atom of the epoxide unit resonated at δ 3.11 (dd, J = 4.0 and 2.5 Hz) for the *anti*-diastereoisomer and at δ 3.18 (dd, J = 3.8 and 2.5 Hz) for the *syn*-diastereoisomer. The ^{1}H NMR spectrum of the reaction mixture for entry 3 (Table 1) indicated a 9:1 ratio of diastereoisomers that were subsequently shown to be anti-**6c** and syn-**6c** respectively. The major diastereoisomer anti-**6c** crystallized from ethyl acetate − 40−60 °C petroleum ether as cubes, mp 98−99 °C. Its relative configuration was confirmed by an X-ray determination on a single crystal. (For crystallographic data of **6a** see: Coles, S. J.; Hibbs, D. E.; Hursthouse, M. B. *Acta Cryst.* **2001**, *E57*, 066−067). The TBHP−$SnCl_4$ system is of particular significance, since reaction of *m*-CPBA (1.5 eq.) and $SnCl_4$ (2.0 eq.) with **5c** (CH_2Cl_2, 0 °C, 0.5 h) gave *N*-propargylsuccinimide (85%).

The above results are markedly different from epoxidations of the carbocyclic analogues in the presence of TBHP−$VO(acac)_2$, and suggest substantially different mechanisms. Tin(IV) alkyl peroxides are known to displace trifluoromethanesulfonates to give dialkyl peroxides,[9] and cyclic peroxides can be prepared from bis(trifluoromethanesulfonates) and bis(tri-*n*-butyltin)peroxide.[9] This well-established use of tin(IV) in the context of peroxides as nucleophiles is consistent with the catalytic formation of the α-peroxy lactams, which in turn strongly suggests an acyliminium intermediate, presumably **9** (Scheme 4), that could be subject to both α- and β-addition of nucleophiles (here peroxide). The addition of hydroperoxide to an acyliminium species rapidly results in an allyl peroxide,[10] and we consider that the peroxy amides **7** are formed by the analogous α-addition to **9**. A likely route to the diperoxides **8** proceeds via conjugate addition to the acyliminium species **9** followed by α-addition of a second molecule of peroxide (Scheme 4). The mechanism of formation of the epoxy peroxides **6** has not been established. While hydroxyl-directed (or peroxy-directed) epoxidations (of **5**) involving coordination to tin cannot currently be excluded, a plausible alternative route proceeds via intramolecular cyclization of enamide **12** giving **13**, followed by α-addition of peroxide.[10]

The diastereoselective peroxidation with concomitant epoxidation processes herein described are a new means

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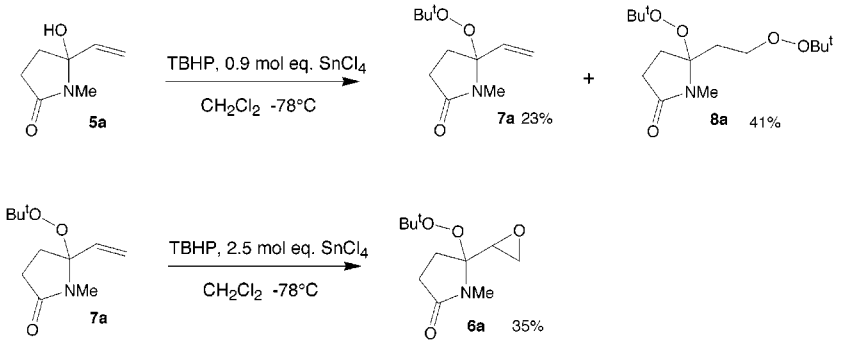
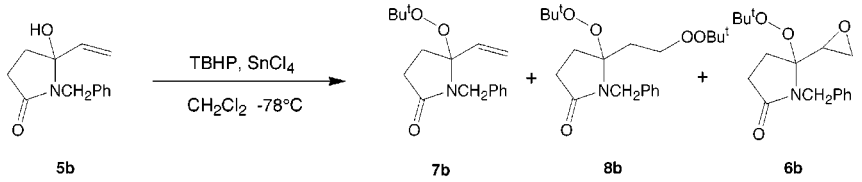
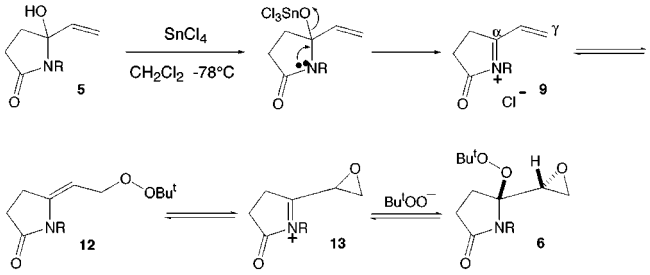
Scheme 2



Scheme 3



Scheme 4



of difunctionalization that could find use in the synthesis of polyoxygenated natural products. Unsymmetrical dialkyl peroxides can be prepared, but often in modest yields, by other methods.[8,9,11] The ability to cleave peroxides reductively would provide access to the corresponding alcohols. In the context of methods of epoxidation, these peroxidations mediated by tin(IV) are noteworthy, as is the "direct" replacement of an hydroxy group by peroxyalkyl, related cases requiring activation of the hydroxyl group, e.g., as the trichloroacetimidate.[8]

Experimental Section

General. Melting points were determined on a microscope hot-stage apparatus. ^{1}H and ^{13}C NMR spectra were obtained at 250 and 68.8 MHz, respectively. Thin-layer chromatography was performed on Merck 0.2 mm aluminum-backed silica gel 60 F_{254} plates and visualized using an alkaline $KMnO_4$ spray or by ultraviolet light. Flash column chromatography was performed using Merck 0.040 to 0.063 mm, 230 to 400 mesh silica gel. Petroleum ether (40−60 °C fraction) and ethyl acetate were distilled before use; tetrahydrofuran was distilled from sodium and benzophenone; dichloromethane was distilled from calcium hydride. Evaporation refers to the removal of solvent under reduced pressure.

5-Hydroxy-1-methyl-5-vinyl-2-pyrrolidinone **5a**[12] and 1-benzyl-5-hydroxy-5-vinyl-2-pyrrolidinone **5b**[13] were prepared according to literature procedures. Anhydrous TBHP was prepared and handled according to the safety procedures previously described.[14]

***N*-Methylglutarimide.** A mixture of glutarimide (1.00 g, 8.84 mmol), methyl iodide (1.51 g, 10.6 mmol), and anhydrous potassium carbonate (1.47 g, 10.6 mmol) was heated at reflux in anhydrous acetone (20 mL) for 16 h. After cooling, more methyl iodide (1.60 g, 4.42 mmol) and potassium carbonate (0.61 g, 4.42 mmol) were added, and the mixture was again heated at reflux for a further 7.5 h. After cooling to 0 °C, the mixture was filtered and the acetone evaporated to give an orange oil which was subjected to Kugelrohr distillation to give *N*-methylglutarimide as prisms (1.10 g, 98%); bp 115 °C/0.25 mmHg, mp 30−31 °C, lit.[15] mp 30 °C; ^{1}H NMR (D_2O) δ 3.12 (3H, s), 2.75 (4H, t, J = 6.5 Hz), 2.00 (2H, quint., J = 6.5 Hz); ^{13}C NMR (D_2O) δ 176.7 (s), 32.0 (q), 26.2 (q), 16.3 (t).

***N*-Propargylsuccinimide.** A mixture of succinimide (2.0 g, 20.2 mmol), propargyl bromide (3.17 g, 22.2 mmol, 80% w/w in toluene) and anhydrous potassium carbonate (3.35 g, 24.2 mmol) was heated at reflux in anhydrous acetone (30 mL) for 6 h. A fine, milky precipitate of potassium bromide formed. After cooling to 20 °C the mixture was filtered and the acetone evaporated to give an orange oil which was subjected to Kugelrohr distillation to give *N*-propargylsuccinimide as a clear oil (2.70 g, 97%), bp 163 °C/1.0 mmHg, lit.[16] bp 120 °C/0.03 mmHg; ^{1}H NMR ($CDCl_3$): δ 4.20 (2H, d, J = 4.7 Hz), 2.70 (4H, s), 2.16 (1H, t, J = 4.7 Hz); ^{13}C NMR ($CDCl_3$): δ 175.9 (s), 76.7 (s), 71.3 (d), 28.2 (t), 27.6 (t).

5-Hydroxy-1-prop-2-ynyl-5-vinyl-2-pyrrolidinone (5c). To *N*-propargylsuccinimide (2.32 g, 16.9 mmol) in THF (140 mL), cooled to −78 °C, was added vinylmagnesium bromide (22.0 mL, 22.0 mmol, 1 M solution in THF) dropwise, and when the addition was complete the mixture was then stirred at 20 °C for 1.5 h. It was then poured onto saturated ammonium chloride (100 mL), the layers were separated, and the aqueous layer was extracted with diethyl ether (2 × 30 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated to give an orange oil which was purified by column chromatography (55:45 ethyl acetate:40−60 °C petroleum ether) to give **5c** (1.71 g, 62%) as prisms, mp 71−72 °C (ethyl acetate/petroleum ether); IR ν_{max} (KBr disk) 3280, 1675 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.90 (1H, dd, J = 17.0, 10.0 Hz), 5.56 (1H, dd, J = 17.0, 1.0 Hz), 5.35 (1H, dd, J = 10.0, 1.0 Hz), 4.08 (1H, dd, J = 17.5 Hz, J = 2.5 Hz), 3.81 (1H, dd, J = 17.5 Hz, J = 2.5

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Hz), 2.70−2.05 (5H, m); ^{13}C NMR ($CDCl_3$) δ 174.8 (s), 138.4 (d), 117.4 (t), 98.1 (s), 79.7 (s), 71.2 (d), 34.3 (t), 28.9 (t), 28.0 (t); *m*/*z* (EI): 165 (M^+, 32%), 147 (16%), 138 (34%), 119 (27%), 111 (38%), 83 (37%), 55 (100%); HRMS, M^+ found 165.0794, $C_9H_{11}NO_2$ requires 165.0790; and **4-oxohex-5-enoic acid prop-2-ynylamide**, (0.73 g, 26%), as prisms, mp 66−67 °C (ethyl acetate/petroleum ether); IR ν_{max} (KBr disk) 3300, 3230, 1650 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.30 (1H, d, J = 9.8 Hz), 6.28 (1H, d, J = 2.0 Hz), 5.84 (1H, dd, J = 9.8, 2.0 Hz), 3.98 (2H, dd, J = 5.5, 2.5 Hz), 2.95 (2H, t, J = 6.5 Hz), 2.47 (2H, t, J = 6.5 Hz), 2.19 (1H, t, J = 2.5 Hz); ^{13}C NMR ($CDCl_3$) δ 199.6 (s), 171.8 (s), 136.2 (d), 128.9 (t), 79.7 (s), 71.5 (d), 34.6 (t), 29.6 (t), 29.2 (t); *m*/*z* (EI): 165 (M^+, 12%), 137 (14%), 111 (43%), 83 (34%), 55 (100%). HRMS, calcd for $C_9H_{11}NO_2$ 165.0790, found 165.0792.

1-Methyl-6-hydroxy-6-vinyl-2-piperidinone (5d). To *N*-methylglutarimide (0.3 g, 2.36 mmol) in THF (20 mL), cooled to −78 °C, was added vinylmagnesium bromide (3.1 mL, 3.1 mmol, 1 M solution in THF) dropwise. When the addition was complete, the mixture was stirred at 20 °C for 16 h. Since TLC indicated the presence of starting material, additional vinylmagnesium bromide (1.2 mL, 1.2 mmol) was then added and the mixture stirred for an additional 50 min. It was then poured onto saturated ammonium chloride (10 mL), the layers were separated, and the aqueous layer was extracted with ether (2 × 8 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated to give an orange oil whose ^{1}H NMR showed a 3:7 mixture of **5d: 5-oxo-hept-6-enoic acid methylamide** (0.18 g, 49%). This mixture was treated directly with TBHP−$SnCl_4$, since attempted purification of the mixture by column chromatography (80:20 ethyl acetate: 40−60 °C petroleum ether) resulted solely in 5-oxohept-6-enoic acid methylamide as an oil; IR ν_{max} (thin film) 3305, 1650 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.34 (NH, bs), 6.31−6.07 (2H, m), 5.75 (1H, dd, J = 10.0, 2.0 Hz), 2.67 (3H, d, J = 4.8 Hz), 2.57 (2H, t, J = 7.5 Hz), 2.30 (2H, t, J = 7.5 Hz), 1.83 (2H, quint., J = 7.5 Hz); ^{13}C NMR ($CDCl_3$) δ 200.6 (s), 173.3 (s), 136.3 (d), 128.5 (t), 38.4 (t), 35.1 (t), 26.1 (q), 19.8 (t); *m*/*z* (EI): 156 (MH^+, 79%), 138 (10%), 125 (100%), 97 (20%), 58 (11%). HRMS, calcd for $C_8H_{13}NO_2$ 155.0948, found 155.0957.

5-(*tert*-Butylperoxy)-1-methyl-5-oxiranyl-2-pyrrolidinone (6a). To a solution of **5a** (0.2 g, 1.42 mmol) in dichloromethane (30 mL), cooled to −78 °C, was added tin(IV) chloride (0.36 mL, 3.12 mmol) dropwise followed by *tert*-butyl hydroperoxide (0.57 mL, 3.12 mmol, 5.46 M solution in dichloromethane). The mixture was then stirred at −78 °C for 2 h and poured onto ice (30 mL), and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 10 mL), and the combined organic extracts were washed with brine (20 mL), dried ($MgSO_4$), and evaporated. This gave **6a** (9 anti: 1 syn) as a colorless oil (0.22 g, 69%) which required no further purification; IR ν_{max} (thin film) 3475, 1702 cm^{-1}; ^{1}H NMR ($CDCl_3$; *anti*-**6a**) δ 3.11 (1H, dd, J = 4.0, 2.5 Hz), 2.86 (3H, s), 2.81 (1H, dd, J = 5.0, 4.0 Hz), 2.73 (1H, dd, J = 5.0, 2.5 Hz), 2.60−2.40 (1H, m), 2.40−2.10 (2H, m), 2.05−1.80 (1H, m), 1.20 (9H, m); ^{1}H NMR ($CDCl_3$; *syn*-**6a**) δ 3.18 (1H, dd, J = 4.0, 2.4 Hz), 2.86 (3H, s), 2.81 (1H, m), 2.65−2.40 (2H, m), 2.35−2.05 (2H, m), 2.00−1.70 (1H, m), 1.19 (9H, s); ^{13}C NMR ($CDCl_3$) δ 176.3 (s), 96.4 (s), 80.3 (s), 53.1 (d), 42.7 (t), 29.8 (t), 26.4 (q), 25.8 (q), 25.0 (t); *m*/*z* (CI): 230 ($M - H^+$, 100%), 172 (21%), 158 (15%), 140 (77%), 128 (16%), 114 (52%), 57 (51%). HRMS, calcd for $C_{11}H_{20}NO_4$ 230.1392, found 230.1398.

1-Benzyl-5-(*tert*-butylperoxy)-5-oxiranyl-2-pyrrolidinone (6b). A solution of **5b** (0.2 g, 0.92 mmol) in dichloromethane (20 mL) was cooled to −78 °C and treated dropwise with tin(IV) chloride (0.11 mL, 0.92 mmol) to give a cloudy solution to which was added *tert*-butyl hydroperoxide (0.35 mL, 2.12 mmol, 6.08 M solution in dichloromethane) dropwise. The mixture was then stirred at −78 °C for 1.25 h and poured onto ice (20 mL), and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 5 mL), and the combined organic extracts were dried ($MgSO_4$) and evaporated. The residue was purified by column chromatography (23:77 ethyl acetate: 40−60 °C petroleum ether) to give **6b** (9 anti: 1 syn) as a colorless oil (133 mg, 67%); IR ν_{max} (KBr disk) 3394, 1704 cm^{-1}; ^{1}H NMR ($CDCl_3$; *anti*-**6b**) δ 7.40−7.15 (5H, m), 4.91 (1H, d, J = 15.5 Hz), 4.19 (1H, d, J = 15.5 Hz), 2.89 (1H, dd, J = 4.5, 2.8 Hz), 2.80−2.50 (1H, m), 2.45−2.15 (4H, m), 1.90−1.70 (1H, m), 1.22 (9H, s); ^{1}H NMR ($CDCl_3$; *syn*-**6b**) δ 7.40−7.15 (5H, m), 4.88 (1H, d, J = 15.3 Hz), 4.24 (1H, d, J = 15.3 Hz), δ 2.73 (1H, dd, J = 5.0, 2.5 Hz), 2.70−2.50 (1H, m), 2.45−2.10 (4H, m), 2.92−2.13 (1H, m), 1.20 (9H, s); ^{13}C NMR ($CDCl_3$) δ 176.3 (s), 138.6 (s), 128.4 (d), 128.1 (d), 127.2 (d), 96.9 (s), 80.4 (s), 53.1 (d), 43.2 (t), 49.8 (t), 29.7 (t), 26.5 (q), 24.7 (t); *m*/*z* (FAB): 306 (MH^+, 89%), 216 (100%), 190 (84%). HRMS, calcd for $C_{17}H_{24}NO_4$ 306.1705, found 306.1720.

5-(*tert*-Butylperoxy)-1-prop-2-ynyl-5-oxiranyl-2-pyrrolidinone (6c). To a solution of **5c** (0.15 g, 0.91 mmol) in dichloromethane (30 mL), cooled to −78 °C, was added tin(IV) chloride (0.31 mL, 2.66 mmol) dropwise to give a cloudy solution. To this was added *tert*-butyl hydroperoxide (0.42 mL, 2.29 mmol, 5.46 M solution in dichloromethane) and the mixture stirred at −78 °C for 1.5 h then poured onto ice (30 mL). The layers were separated, the aqueous layer was extracted with dichloromethane (3 × 10 mL), and the combined organic extracts were washed with brine (20 mL) and then dried ($MgSO_4$). Evaporation gave an oil which was purified by column chromatography (15:85 ethyl acetate: 40−60 °C petroleum ether) to give a mixture of two diastereoisomers (9 anti: 1 syn) of **6c** (172 mg, 80%) as an oily solid. To this mixture was added hot petroleum (40−60 °C), followed by ethyl acetate added dropwise until a homogeneous mixture was obtained. On standing, the solution deposited *anti*-**6c** as cubes, mp 98−99 °C (the X-ray crystallographic sample); IR ν_{max} (thin film) 3240, 2588, 1707, cm^{-1}; ^{1}H NMR ($CDCl_3$; *anti*-**6c**) δ 4.36 (1H, dd, J = 18.0, 2.0 Hz), 3.82 (1H, dd, J = 18.0, 2.0 Hz), 3.32 (1H, dd, J = 4.5, 2.8 Hz), 2.78 (1H, t, J = 5.0 Hz), 2.69 (1H, dd, J = 5.0, 2.8 Hz), 2.60−2.16 (4H, m), 2.15 (1H, t, J = 2.0 Hz), 1.18 (9H, s); ^{1}H NMR ($CDCl_3$; syn-**6c**) δ 4.33 (1H, dd, J = 18.0, 2.0 Hz), 3.82 (1H, m), 3.38 (1H, dd, J = 4.6, 3.0 Hz), 2.86 (1H, t, J = 5.0 Hz), 2.69 (1H, m), 2.60−1.75 (5H, m), 1.18 (9H, s); ^{13}C NMR ($CDCl_3$) δ 175.2 (s), 96.4 (s), 80.6 (s), 79.5 (s), 75.5 (d), 52.8 (d), 43.6 (t), 29.4 (t), 28.5 (t), 26.4 (q), 24.6 (t). Anal. Calcd for C 61.63, H 7.58, N 5.53. Found C 61.68, H 7.45, N 5.28%.

5-(*tert*-Butylperoxy)-1-methyl-5-oxiranyl-2-piperidinone (6d). To the 3:7 mixture (360 mg) described above (equivalent to 108 mg, 0.70 mmol of pure **5d**) in dichloromethane (26 mL), cooled to −78 °C, was added tin(IV) chloride (0.45 mL, 3.86 mmol) dropwise to give a cloudy solution. To this was added *tert*-butyl hydroperoxide (0.78 mL, 4.25 mmol), the mixture was stirred at −78 °C for 2 h and then poured onto ice (20 mL), and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 5 mL), and the combined organic extracts were washed with brine (15 mL) and then dried ($MgSO_4$). Evaporation gave an oil which was purified by column chromatography (20:80 ethyl acetate: 40−60 °C petroleum ether) to give two diastereoisomers (7 anti: 1 syn) of **6d** as a colorless oil (109 mg, 64%); IR ν_{max} (thin film) 3476, 1659 cm^{-1}; ^{1}H NMR ($CDCl_3$; *anti*-**6d**) δ 3.20 (1H, dd, J = 4.0, 2.9 Hz), 2.94 (3H, s), 2.70 (1H, dd, J = 5.0, 4.0 Hz), 2.54 (1H, dd, J = 5.0, 2.9 Hz), 2.50−1.50 (6H, m), 1.18 (9H, m); ^{1}H NMR ($CDCl_3$; *syn*-**6d**) δ 3.11 (1H, dd, J = 4.1, 2.9 Hz), 2.92 (3H, s), 2.78 (1H, dd, J = 5.2, 4.1 Hz), 2.60 (1H, dd, J = 5.2, 2.9 Hz), 2.90−2.50 (6H, m), 1.20 (9H, m); ^{13}C NMR ($CDCl_3$) δ 171.7 (s), 91.2 (s), 80.2 (s), 54.9 (d), 32.0 (t), 28.7 (q), 28.0 (t), 26.5 (t), 16.9 (t); *m*/*z* (EI): 209 (21%), 170 (16%), 154 (100%), 126 (22%), 55 (10%).

5-(*tert*-Butylperoxy)-1-methyl-5-vinyl-2-pyrrolidinone (7a) and 5-(*tert*-Butylperoxy)-5-(2-*tert*-butylperoxyethyl)-1-methyl-2-pyrrolidinone (8a). A solution of **5a** (0.15 g, 1.06 mmol) in dichloromethane (24 mL) was cooled to

−78 °C and treated dropwise with tin(IV) chloride (22.8 mg, 0.088 mmol) followed by *tert*-butyl hydroperoxide (0.43 mL, 2.33 mmol, 5.46 M solution in dichloromethane) and the stirring continued at −78 °C for 2.5 h. The mixture was then poured onto ice (15 g), the layers were separated, and the aqueous layer was extracted with dichloromethane (3 × 10 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated, and the residue was purified by column chromatography (30:70 ethyl acetate: 40−60 °C petroleum ether) to give **7a** as a colorless oil (52 mg, 23%); IR ν_{max} (thin film) 1707 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.68 (1H, dd, J = 18.0, 11.0 Hz), 5.24 (1H, dd, J = 18.0, 1.0 Hz), 5.23 (1H, dd, J = 11.0, 1.0 Hz), 2.69 (3H, s), 2.60−1.90 (4H, m), 1.16 (9H, s); ^{13}C NMR ($CDCl_3$) δ 176.4 (s), 135.7 (d), 117.7 (t), 97.8 (s), 79.9 (s), 30.6 (t), 30.2 (t), 26.5 (s), 26.3 (s); *m*/*z* (EI): 214 (MH^+, 97%), 172 (15%), 158 (42%), 142 (88%), 124 (100%), 114 (39%), 73 (27%), 57 (41%); HRMS, calcd for $C_{11}H_{20}NO_3$ 214.1443, found 214.1442; and **8a** as a colorless oil (125 mg, 41%); IR ν_{max} (thin film): 1707 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.69 (2H, dt, J = 7.0, 2.0 Hz), 2.71 (3H, s), 2.60−1.79 (6H, m), 1.17 (9H, s), 1.13 (9H, s); ^{13}C NMR ($CDCl_3$) δ 176.3 (s), 97.5 (s), 80.3 (s), 79.7 (s), 69.9 (t), 32.9 (t), 30.2 (t), 28.1 (t), 26.5 (q), 26.3 (q), 24.8 (q); *m*/*z* (EI): 304 (MH^+, 76%), 214 (100%), 158 (69%), 140 (43%), 124 (28%), 111(54%), 73 (24%), 57 (40%). HRMS calcd for $C_{15}H_{30}NO_5$ 304.2124, found 304.2140.

Reaction of 5-(*tert*-Butylperoxy)-1-methyl-5-vinyl-2-pyrrolidinone (7a) with Tin(IV) Chloride. A solution of **7a** (251 mg, 1.18 mmol) in dichloromethane (30 mL) was cooled to −78 °C and treated dropwise with tin(IV) chloride (0.28 mL, 2.36 mmol) followed by *tert*-butyl hydroperoxide (0.48 mL, 2.60 mmol, 5.46 M solution in dichloromethane). The mixture was then stirred at −78 °C for 2 h and poured onto ice (20 g), and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 5 mL), and the combined organic extracts were dried ($MgSO_4$) and evaporated. The residue was then purified by column chromatography (36:64 ethyl acetate: 40−60 °C petroleum ether) to give **6a** as a colorless oil (70 mg, 35%); with spectral data identical with those given above.

1-Benzyl-5-(*tert*-butylperoxy)-5-(2-*tert*-butylperoxyethyl)pyrrolidin-2-one (8b) and 1-Benzyl-5-(*tert*-butylperoxy)-5-vinyl-2-pyrrolidinone (7b). A solution of **5b** (0.3 g, 1.38 mmol) in dichloromethane (20 mL) was cooled to −78 °C and treated dropwise with tin(IV) chloride (118 mg, 0.45 mmol) followed by *tert*-butyl hydroperoxide (0.52 mL, 3.18 mmol, 6.08 M solution in dichloromethane). The reaction mixture was then stirred at −78 °C for 2 h and poured onto ice (15 g), and the layers were separated. The aqueous phase was extracted with dichloromethane (3 × 10 mL), and the combined organic extracts were dried ($MgSO_4$) and evaporated to give an oil which was purified by column chromatography (14:86 ethyl acetate: 40−60 °C petroleum ether) to give **8b** as a colorless oil (69 mg, 13%); IR ν_{max} (thin film) 1707 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35−7.10 (5H, m), 4.79 (1H, d, J = 15.5 Hz), 4.12 (1H, d, J = 15.5 Hz), 3.87 (2H, t, J = 13.5 Hz), 2.70−1.70 (6H, m), 1.20 (9H, s), 1.15 (9H, s); ^{13}C NMR ($CDCl_3$) δ 177.0 (s), 138.6 (s), 128.4 (d), 127.7 (d), 127.0 (d), 98.2 (d), 80.1 (s), 79.9 (s), 69.8 (t), 42.8 (t), 34.7 (t), 30.2 (t), 28.7 (t), 26.5 (q), 26.3 (q); *m*/*z* (FAB): 380 (MH^+, 100%), 290 (90%), 234 (14%), 216 (16%), 190 (65%); HRMS calcd for $C_{21}H_{34}NO_5$ 380.2437, found 380.2450; and **7b** as a colorless oil (136 mg, 33%); ^1H NMR ($CDCl_3$) δ 7.40−7.20 (5H, m), 5.62 (1H, dd, J = 17.5 Hz, J = 11.0 Hz), 5.35 (1H, dd, J = 17.5, 1.5 Hz), 5.16 (1H, dd, J = 11.0, 1.5 Hz), 4.63 (1H, d, J = 15.5 Hz), 4.16 (1H, d, J = 15.5 Hz), 2.55−2.35 (2H, m), 2.20−2.00 (2H, m), 1.15 (9H, s); ^{13}C NMR ($CDCl_3$) δ 177.0 (s), 138.5 (s), 136.2 (d), 128.6 (d), 127.9 (d), 127.3 (d), 117.7 (d), 97.6 (s), 80.0 (s), 43.4 (t), 32.0 (t), 30.7 (t), 26.6 (q); *m*/*z* (FAB): 290 (MH^+, 100%), 234 (18%), 216 (31%), 190 (67%). HRMS calcd for $C_{17}H_{24}NO_3$ 290.1756, found 290.1770.

5-Allyl-5-hydroxy-1-prop-2-ynyl-2-pyrrolidinone (10) and 5-Allylidene-1-prop-2-ynyl-2-pyrrolidinone. Preparation of Allylzinc Bromide. Zinc powder was washed three times with dilute hydrochloric acid and then filtered under vacuum before washing initially with water and then with acetone. The zinc was then flame-dried under nitrogen in the reaction flask. To this activated zinc (1.91 g, 29.2 mmol), covered by THF, was added neat allyl bromide (3.53 g, 29.2 mmol; CAUTION: TOXIC) dropwise to initiate the reaction. Once the reaction had been initiated, the remaining solution of allyl bromide in THF (30 mL; CAUTION: TOXIC) was added dropwise, maintaining gentle reflux. When the addition was complete the mixture was heated at reflux for a further 0.5 h and then allowed to cool to 20 °C to give a solution of allylzinc bromide.

To *N*-propargylsuccinimide (1.00 g, 7.29 mmol), cooled in an ice−salt bath, was added dropwise a solution of allylzinc bromide (30 mL, 29.2 mmol, 0.97 M solution in THF) prepared as described above. The mixture was then stirred at 20 °C for 75 min and poured onto saturated ammonium chloride (15 mL), and the layers were separated. The aqueous layer was extracted with diethyl ether (2 × 10 mL), dried ($MgSO_4$), and evaporated to give the crude title compound as a reddish-brown oil (1.85 g). Attempted purification of the crude **10** by column chromatography (50:50 ethyl acetate: 40−60 °C petroleum ether) induced dehydration to give **5-allylidene-1-prop-2-ynyl-2-pyrrolidinone** as a colorless oil (0.59 g, 50%); IR ν_{max} (thin film) 1655 cm^{-1};^1H NMR ($CDCl_3$) δ 6.34 (1H, ddd, J = 20.0, 17.0, 12.0 Hz), 5.62 (1H, dt, J = 12.0, 2.5 Hz), 5.01 (1H, dd, J = 17.0, 1.0 Hz), 4.95 (1H, d, J = 12.0 Hz), 4.24 (2H, d, J = 3.0 Hz), 2.80 (2H, m), 2.53 (2H, m), 2.18 (1H, t, J = 3.0 Hz); ^{13}C NMR ($CDCl_3$) δ 174.8 (s), 141.0 (s), 131.3 (d), 113.8 (t), 103.8 (d), 77.0 (s), 71.8 (d), 29.3 (t), 28.5 (t), 21.5 (t); *m*/*z* (EI): 162 (MH^+, 85%), 138 (100%), 106 (27%), 95 (27%), 84 (78%), 56 (66%); HRMS calcd for $C_{10}H_{12}NO$ 162.0919, found 162.0910.

5-Allyl-5-(*tert*-butylperoxy)-1-prop-2-ynyl-2-pyrrolidinone (11). To a solution **10** (0.30 g, 1.67 mmol, crude) in dichloromethane (30 mL), cooled to −78 °C, was added tin(IV) chloride (0.59 mL, 5.01 mmol) dropwise to give a cloudy solution. To this was added *tert*-butyl hydroperoxide (0.77 mL, 4.18 mmol, 5.46M solution in dichloromethane) and the mixture stirred at −78 °C for 1.5 h, then poured onto ice (30 mL). The layers were separated and the aqueous layer extracted with dichloromethane (3 × 10 mL) and the combined organic extracts dried ($MgSO_4$). Evaporation gave an oil which was purified by column chromatography (10:90 ethyl acetate: 40−60 °C petroleum ether) to give **11** as a colorless oil (168 mg, 40%); IR ν_{max} (thin film) 3286, 1694 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.77 (1H, m), 5.15 (2H, m), 4.30 (1H, dd, J = 18.0, 1.6 Hz), 3.73 (1H, dd, J = 18.0, 1.6 Hz), 2.70−1.95 (7H, m), 1.15 (9H, s); ^{13}C NMR ($CDCl_3$) δ 175.9 (s), 131.4 (d), 119.7 (t), 98.2 (s), 79.9 (s), 70.6 (d), 40.1 (t), 29.9 (t), 27.8 (t), 27.5 (t), 26.5 (q); *m*/*z* (EI): 252 (MH^+, 12%), 220 (20%), 204 (39%), 162 (100%). HRMS calcd for $C_{14}H_{22}NO_3$ 252.1600, found 252.1610.

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Supporting Information Available: Copies of ^1H and ^{13}C NMR spectra of methyl glutarimide, propargyl succinimide, **5c**, byproduct of **5c**, byproduct of **5d**, **6a**−**d**, **7a**, **8a**, **8b**, byproduct of **10**, and **11**; ORTEP of *anti*-**6c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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