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On the use of anomeric hydroxylamines in the reverse-Cope cyclisation

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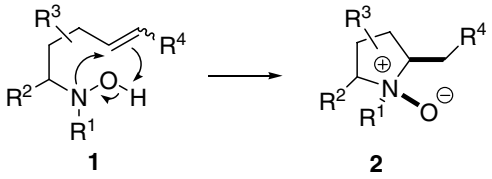
Abstract—Reverse-Cope cyclisations of unsaturated hydroxylamines, when the latter are anomeric, are shown to be a viable approach to a variety of hexahydrofuro[2,3-*b*]pyrrole 6-oxides.

The reverse-Cope cyclisation, as the name suggests,[1] is a reaction wherein an unsaturated hydroxylamine **1** undergoes a thermally-induced cyclisation to give a pyrrolidine N-oxide **2**, or *N*-hydroxypyrrolidine when $R^1 = H$ (Scheme 1).[2] All available evidence supports a thermally allowed $2\pi + 2\sigma + 2n$ concerted mechanism, requiring a planar transition state conformation.

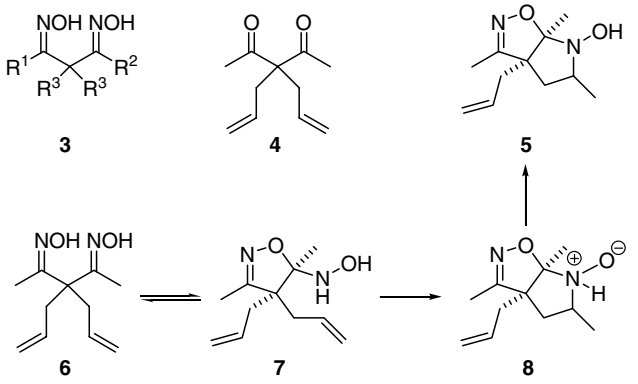
Six-membered ring formation is less favoured[3] but, on the positive side, the cyclisations are usually highly stereocontrolled, as expected given the likely mechanism. A number of additional heteroatoms can also be incorporated into the newly-formed heterocyclic ring.[3,4] Suitable hydroxylamines also cyclise very productively onto alkynes leading to cyclic nitrones; a notable application of this chemistry is its use as a key step in a recent synthesis of (+)-histrionicotoxin.[5]

Most advances in the area of reverse-Cope cyclisations have been initiated by serendipitous discovery rather than rational design.[2] This was the case in the first documented example of a reverse-Cope cyclisation, which arose during the synthesis of a series of bis-oximes **3** from the corresponding 1,3-diketones, reported by House and co-workers in 1976.[6] The chemistry was uneventful until the bis-allylated diketone **4** was the precursor, when the product isolated was the novel bicyclic system **5** (Scheme 2). This seemingly bizarre outcome can be rationalised if it is assumed that the desired bis-oxime **6** is in tautomeric equilibrium with the cyclic form **7**, which can undergo a reverse-Cope cyclisation to give N-oxide **8**; proton transfer then gives the observed product **5**.

Little was subsequently heard of this reaction but it was saved from obscurity by the extremely thorough scope



Scheme 1.



Scheme 2.

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and limitations studies carried out by Ciganek et al.,[7] along with subsequent contributions from ourselves[8] and the O'Neil Group,[9] amongst others.[2,10] It was against this background that we wondered whether there could be any synthetic utility in House's original observation,[6] outlined in Scheme 2, if this were to be applied to simpler analogues, that is, reduced to its basic features of an alkene and an *anomeric* hydroxylamine. Herein, we report our preliminary studies in this area, which reveal some useful methodology and also some associated limitations.

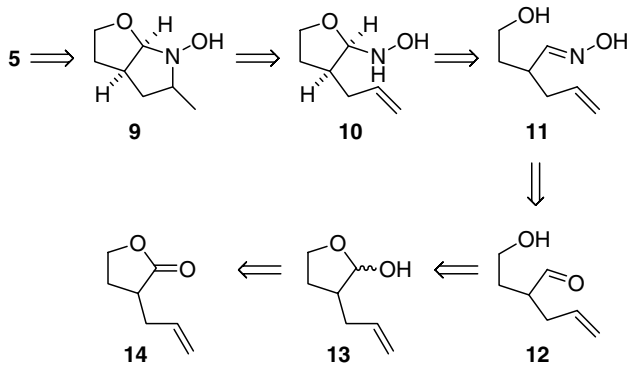
Our idea was to extract the key features, in terms of the reverse-Cope reaction, of the chemistry leading to the eventual product **5**, which in our view was the annulated tetrahydrofuran **9**, which should be formed by cyclisation of the anomeric hydroxylamine **10** (Scheme 3). This, we reasoned, should be in equilibrium with the open chain hydroxy-oxime **11**, whose precursor should be aldehyde **12**, itself in equilibrium with lactol **13**, derived from the corresponding lactone **14**. We therefore began our investigations with butyrolactone, partly because various functionalisations, especially α-allylation and reduction to the corresponding lactols are known to work well and partly, of course, because this ring size most accurately reflected that involved in House's original discovery.[6]

Starting with butyrolactone, sequential α-allylation (LDA, allyl bromide, −78 °C) and reduction using Dibal–H gave the known lactol **13** in good yield.[11] Unfortunately, in our hands, reactions between this lactol and hydroxylamine under a wide variety of conditions and using many solvents failed to initiate the anticipated cascade of reactions suggested in Scheme 3. We therefore turned to the idea of using an *N*-alkylhydroxylamine in the knowledge that anomeric *N*-alkylhydroxylamines have been obtained as synthetic intermediates from the corresponding lactols on a number of occasions[12] and also that, in general, reverse-Cope cyclisations are facilitated by the presence of an alkyl group on the nitrogen of the hydroxylamine.[2] We were therefore delighted to discover, after a survey of solvents, reaction times, temperatures and reagent quantities, that heating lactol **13** with 2.5 equiv of *N*-methylhydroxylamine hydrochloride and 10 equiv of anhydrous potassium carbonate in dry hexanes under nitrogen for 16 h resulted in near quantitative conversion into the N-oxide **15** (Scheme 4).[13] Also formed was a small quantity of azaoxacine **16**, the structure of which was proposed on the basis of both mechanistic speculation (Scheme 6) and spectroscopic data.

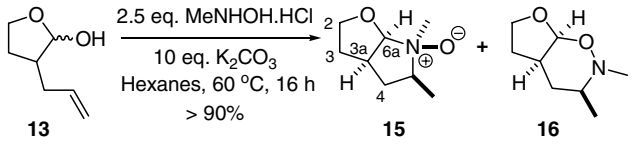
The highly polar nature of N-oxide **15** initially made its purification difficult until we employed this very property: filtration of the cooled hexane suspension through a silica gel column packed using the same solvent was followed by elution with chloroform, which removed excess hydroxylamine and some minor impurities, and finally by methanol to remove N-oxide **15** as a pale brown oil and a single diastereoisomer. Its richly detailed ^{1}H NMR spectrum was almost first order and was fully assigned, using a combination of coupling constant measurements and COSY experiments.[13,14]

The cis-ring fusion expected of such a 5/5 system was supported by the coupling constant, $J = 5.6$ Hz, between the two ring junction protons, H_{3a} and H_{6a}, which is consistent with such a geometry and contrasts with a higher value of ~11 Hz for a trans-ring fusion.[15] For reasons unknown, NOE experiments were ineffective in providing useful data but fortunately NOESY spectra gave good correlations which, when combined with the coupling constant data, allowed us to deduce the stereochemistry shown in structure **15**. These data formed the basis of all the subsequent structural assignments. We therefore conclude that the detailed mechanism is as shown in Scheme 5.

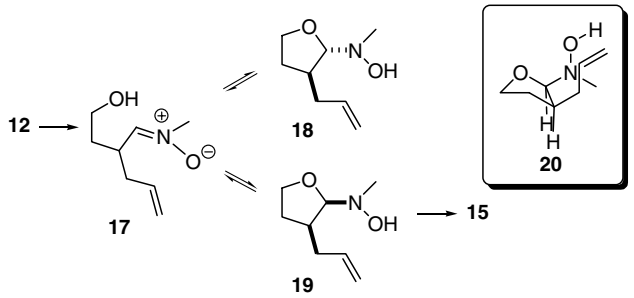
Equilibration of lactol **13** with its open chain form **12** (Scheme 3) would provide an aldehyde for conversion into the corresponding hydroxy-nitrone **17**. This should then be in equilibrium with both *trans*-**18** and *cis*-**19** isomers of the anomeric ring-closed hydroxylamines, only the latter of which can undergo productive cyclisation to give the observed product **15**. The requirement for a planar transition state in reverse-Cope cyclisations suggests the involvement of conformation **20**. This established feature[2,16] of the reverse-Cope cyclisation means



Scheme 3.



Scheme 4.



Scheme 5.

that the new methyl group and the N–O bond must be cis to each other. Hence, the stereochemical arguments in products **15** and relatives simplify as to whether these two substituents are cis or trans to the ring junction protons 3_a-H and 6_a-H.

A very minor product in the initial crude mixture appeared to be a single diastereomer and was tentatively assigned structure **16** (Scheme 4) on the basis of incomplete ^{1}H NMR data. These included a doublet ($J = 6.2$ Hz) centred on δ_H 0.98 due to the C(H)Me group, a methyl singlet at δ_H 2.60 (NMe) and a doublet ($J = 7.4$ Hz) at δ_H 5.11 due to the 'acetal' methine proton at the ring junction. Other resonances were partly or completely obscured and hence the possibility that this was an epimer of N-oxide **15** cannot be ruled out, although its removal with chloroform during the relatively insensitive chromatographic purification method outlined above militated against this. Its formation (Scheme 6) is best explained by a Meisenheimer rearrangement[2] wherein a lone pair on the tetrahydrofuran oxygen initiates loss of the positively charged nitrogen to generate the oxide **21**, which then recloses by nucleophilic attack of the oxide onto the resulting oxonium ion.[17] Such a product was not wholly unexpected, as there are a number of examples known where an initial reverse-Cope product undergoes such a Meisenheimer rearrangement (formally, an N→O alkyl transfer by thermolysis of an N-oxide).[2,4]

Initial attempts to apply this chemistry to the homologous α-methyl lactol **22** met with almost complete failure, with only traces of the expected N-oxide **23** being observed by ^{1}H NMR analysis of crude products. Changing the solvent to more polar chloroform, as usually recommended for reverse-Cope cyclisations, was ineffective as was the use of the higher boiling solvents toluene and xylene. It was only when we again used a large excess of anhydrous potassium carbonate in hexanes that conversion into N-oxide **23** occurred almost completely (Scheme 7), accompanied by small traces (<5%) of what could have been the Meisenheimer product (cf **16**, Schemes 4 and 6). Structural assignment was made on the basis of comparisons with the foregoing data. The reason for the requirement of such a large excess of potassium carbonate is unclear; it is as if the solid is acting as a catalyst for the cyclisation, as other siccatives are not so effective. Despite the additional methyl substituent, the cyclisation leading to N-oxide **23** was apparently not faster due to steric compression.

In a similar fashion, the *trans*-3,5-disubstituted lactol **24**[18] was converted into N-oxide **25** in high yield (Scheme 8).

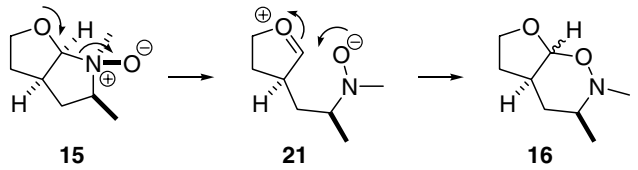
Extensive NMR and NOSEY analysis and comparisons with the spectroscopic data described above established the structure shown, which was accompanied by a trace (ca. 5%) of a second, possibly epimeric compound and a miniscule amount of a likely Meisenheimer product showing a characteristic methyl doublet centred on δ_H 0.90.

The related 5,5-dimethyl lactol **26**,[19] by contrast, underwent equally smooth cyclisation but only required ca. 4 h to achieve complete conversion into the now expected product **27** (Scheme 9).

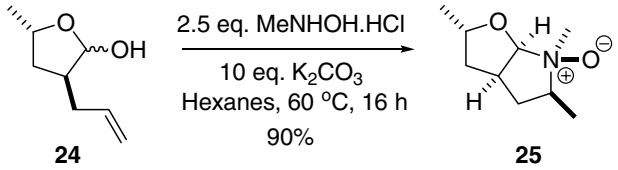
Presumably, the *gem*-dimethyl group provides significant steric compression, thereby favouring the ring closed forms, and hence facilitates the cyclisation.

A typical feature of the reverse-Cope cyclisation is that it is greatly retarded by alkyl substituents at the distal end of the reacting alkene.[2,6c] Numerous examples attest to this phenomenon, which often results in failure, as the necessarily higher temperatures required cause thermal destruction of either or both the starting material or product. Unfortunately, the present chemistry was no exception: under the usual conditions, lactol **28** derived from (*E*)-crotyl bromide delivered less that 20% of the hoped-for N-oxide **29**, which was obtained as a component of a gross mixture and neither fully separated or characterised (Scheme 10).

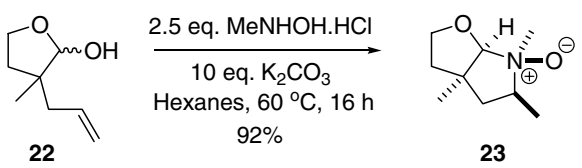
Perhaps precursor **28** is too simple; more substituted examples may respond better. Attempts using higher boiling (toluene or xylene) or more polar (chloroform) solvents failed to improve the yield. However, during



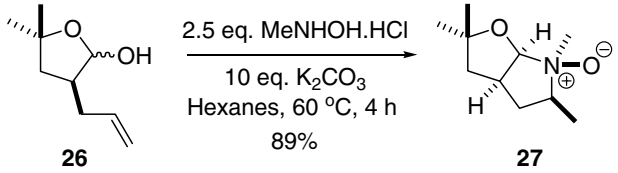
Scheme 6.



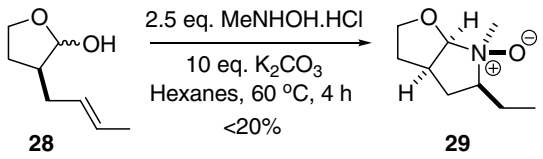
Scheme 8.



Scheme 7.



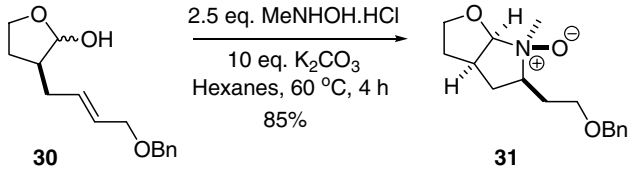
Scheme 9.



Scheme 10.

an earlier target synthesis,[20] we discovered that if the substituent at the distal end of the alkene carries an oxygen atom (OH or OR) at the allylic position, then there is a distinct rate *enhancement*. We were pleased to find that this feature also operated in this type of cyclisation: in contrast to the hydroxylamine derived from lactol **28**, the benzyloxy derivative **30** underwent quite clean cyclisation during 16 h to give N-oxide **31** in ca. 85% isolated yield (Scheme 11). Characterisation was again largely on a comparative basis. Hence, it is possible to incorporate at least some functionality in the new side chains of such N-oxides.

A 'transannular' version of this type of reverse-Cope cyclisation was also attempted, starting with lactol **32**.[21] However, by far the dominant pathway proved to be an intramolecular [1,3]-dipolar cycloaddition during which the 'anomeric' hydroxylamine component **33** was in equilibrium with the open chain nitrone **34**, which evidently underwent much faster cyclisation to give the observed product **35** in 88% yield (Scheme 12). If the expected reverse-Cope product **36** was indeed formed, this was only to a very minor extent (ca. <5%), only perhaps certain evidence being the appearance of a methyl doublet at δ_H 1.23 in the ^{1}H NMR spectrum of the crude product. This observation was not especially surprising in view of the success of related cyclisations reported by Shing et al.[22]



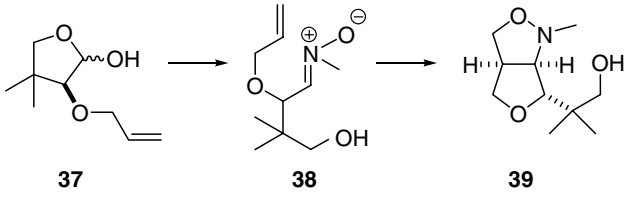
Scheme 11.

Similarly, the *O*-allyl lactol **37** derived from pantolactone gave only the [1,3]-dipolar cycloadduct **39** derived from nitrone **38** when heated with *N*-methylhydroxylamine and excess potassium carbonate (Scheme 13).

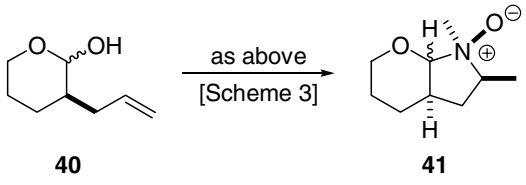
Again, the relative reluctance of the reverse-Cope cyclisation to give six-membered rings is probably a crucial factor, despite that the *gem*-dimethyl group might be expected to favour formation of the ring-closed hydroxylamine.

Finally, we were able to show that lactols with larger ring sizes can also participate in reverse-Cope cyclisations. Thus, lactol **40**[23] derived from δ-valerolactone,[24] when heated for 16 h in hexanes with MeNHOH·HCl and excess potassium carbonate gave a respectable 88% return of the highly polar N-oxides **41**, now as a 1:1 mixture of cis- and trans-fused isomers (Scheme 14).

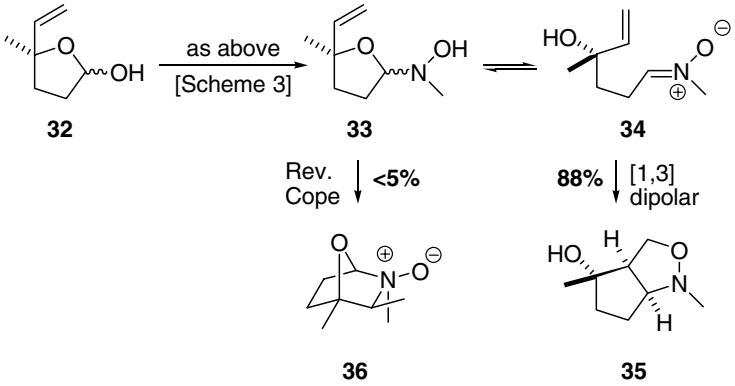
There were two significant differences in the corresponding chemistry of the seven-membered, caprolactone-derived 'lactol'.[24] Firstly, the latter existed very largely in its open form **42**, at least in deuteriochloroform. More significantly, under the usual conditions (Scheme 15), the only isolated product **43** was that of a Meisenheimer



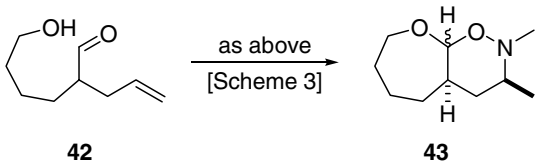
Scheme 13.



Scheme 14.

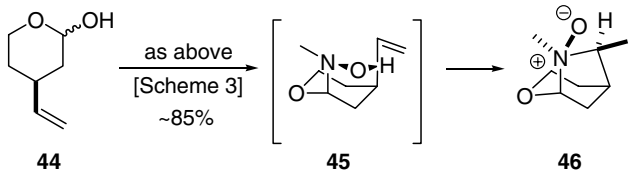


Scheme 12.



42 43

Scheme 15.



44 45 46

Scheme 16.

rearrangement of the presumed initial N-oxide. Key evidence was its relative lack of polarity (eluted from silica gel using dichloromethane; all the foregoing N-oxides required methanol) and characteristic differences in its NMR data, especially associated with the chemical shifts of the methyl groups, along with infrared and mass spectrometric data consistent with the proposed structure. However, as product **43** was isolated as an isomeric mixture, this assignment is not absolutely certain.

A last example featured an alternative 'transannular' version in which lactol **44** derived from dihydropyranone[24] was heated overnight with MeNHOH as usual and gave very largely a single N-oxide (Scheme 16). In view of previous examples carried out by us and involving the corresponding carbocyclic derivatives,[25] we assigned structure **46** to this product. Structural assignment was based on the conformation **45** of the likely transition state, which would allow a planar juxtaposition of the five centres involved in the cyclisation,[16] and on NMR analysis, which was complicated by multiple peak overlaps. However, the methyl and other visible resonances fitted in well with the initial example **15**.[13]

Our conclusion is therefore that the original reverse-Cope method can be extended to include many less substituted examples. It seems likely that many, more highly substituted bicyclic N-oxides can be prepared in a similar manner, which could serve as precursors to a wide range of substituted pyrrolidines, within the stated limitations of this chemistry.

Acknowledgement

We thank the EPSRC and AstraZeneca Ltd, for financial support.

References and notes

1. Nomenclature in this area is no simple matter: the reaction has variously been referred to over the years as the Reverse or Retro Cope cyclisation, elimination or reaction (with or without a hyphen) and, more recently, the House–Cope reaction, in recognition of their important initial contributions.[2]
2. For a review, see: Cooper, N. J.; Knight, D. W. *Tetrahedron* **2004**, *60*, 243–269; See also: Gallagher, B. M.; Pearson, W. H. *Chemtracts-Org. Chem.* **1996**, 126–127; Oppolzer, W. *Gazz. Chim. Ital.* **1995**, *125*, 207–213.
3. O'Neil, I. A.; Southern, J. M. *Tetrahedron Lett.* **1998**, *39*, 9089–9092; O'Neil, I. A.; Cleator, E.; Southern, J. M.; Hone, N.; Tapolczay, D. J. *Synlett* **2000**, 695–697; O'Neil, I. A.; Cleator, E.; Ramos, V. E.; Chorlton, A. P.; Tapolczay, D. J. *Tetrahedron Lett.* **2004**, *45*, 3655–3658; See also: O'Neil, I. A.; Ramos, V. E.; Ellis, G. L.; Cleator, E.; Chorlton, A. P.; Tapolczay, D. J.; Kalindjian, S. B. *Tetrahedron Lett.* **2004**, *45*, 3659–3661.
4. Bell, K. E.; Coogan, M. P.; Gravestock, M. B.; Knight, D. W.; Thornton, S. R. *Tetrahedron Lett.* **1997**, *38*, 8545–8548; Coogan, M. P.; Gravestock, M. B.; Knight, D. W.; Thornton, S. R. *Tetrahedron Lett.* **1997**, *38*, 8549–8552; Gravestock, M. B.; Knight, D. W.; Malik, K. M. A.; Thornton, S. R. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3292–3305.
5. Holmes, A. B.; Smith, A. L.; Williams, S. F.; Hughes, L. R.; Lidert, Z.; Swithenbank, C. *J. Org. Chem.* **1991**, *56*, 1393–1405; Davison, E. C.; Holmes, A. B.; Forbes, I. T. *Tetrahedron Lett.* **1995**, *36*, 9047–9050; Williams, G. M.; Roughley, S. D.; Davies, J. E.; Holmes, A. B. *J. Am. Chem. Soc.* **1999**, *121*, 4900–4901; Smith, C. J.; Holmes, A. B.; Press, N. J. *Chem. Commun.* **2002**, 1214–1215, and references cited therein.
6. (a) House, H. O.; Manning, D. T.; Melillo, D. G.; Lee, L. F.; Hayes, O. R.; Wilkes, B. E. *J. Org. Chem.* **1976**, *41*, 855–863; (b) House, H. O.; Lee, L. F. *J. Org. Chem.* **1976**, *41*, 863–869; (c) Black, D. St. C.; Doyle, J. E. *Aust. J. Chem.* **1978**, *31*, 2317–2322.
7. Ciganek, E. *J. Org. Chem.* **1995**, *60*, 5803–5807; Ciganek, E., ; Read, J. M., Jr.; Calabrese, J. C. *J. Org. Chem.* **1995**, *60*, 5795–5802.
8. Wheildon, A. R.; Knight, D. W.; Leese, M. P. *Tetrahedron Lett.* **1997**, *38*, 8553–8556; Hanrahan, J. R.; Knight, D. W.; Salter, R. *Synlett* **2001**, 1587–1589; Hanrahan, J. R.; Knight, D. W. *Chem. Commun.* **1998**, 2231–2232.
9. O' Neil, I. A.; Cleator, E.; Hone, N.; Southern, J. M.; Tapolczay, D. J. *Synlett* **2000**, 1408–1410; O'Neil, I. A.; Woolley, J. C.; Southern, J. M.; Hobbs, H. *Tetrahedron Lett.* **2001**, *42*, 8243–8245; See also: Palmer, A. M.; Jäger, V. *Synlett* **2000**, 1405–1407.
10. Serendipity continued to inspire: instances include Ciganek and Oppolzer (attempted nitrone formation from an unsaturated hydroxylamine), Holmes (generation of an alkynyl hydroxylamine) and us (additions of allylamines to nitrones and unexpected cyclisation of the resulting hydroxylamines).[2] O'Neil however has used design from the outset.[2,3,9]
11. Walton, R.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1991**, *113*, 5791–5799.
12. For previous applications of 'anomeric' hydroxylamines, see, for example, Huber, R.; Vasella, A. *Tetrahedron* **1990**, *46*, 33–58; Dondoni, A.; Perrone, D. *Tetrahedron Lett.* **1999**, *40*, 9375–9378; Cicchi, S.; Corsi, M.; Marradi, M.; Goti, A. *Tetrahedron Lett.* **2002**, *43*, 2741–2743.
13. A general procedure is as follows: (5*RS*,6*SR*,7*SR*,8*SR*)-*5,6-Dimethylhexahydrofuro[2,3-b]pyrrole 6-oxide* **15**: The β-allyl-lactol **13** (0.50 g, 3.9 mmol), *N*-methylhydroxylamine hydrochloride (0.36 g, 4.29 mmol) and finely powdered anhydrous potassium carbonate (1.62 g, 11.7 mmol) were added to degassed dry hexane (15 ml) and the resulting mixture stirred at reflux under nitrogen for 16 h. The cooled mixture was then filtered and the solids

thoroughly washed with chloroform. The combined filtrates were evaporated and the brown residue separated by silica gel column chromatography, eluting first with hexanes, followed by dichloromethane and finally with methanol to give N-oxide **15** as a pale brown oil (0.51 g, 84%), ν_{max} (film) 2976, 1654, 1448, 1111, 1069, 923 cm^{-1}, δ_H (400 MHz, $CDCl_3$) 4.98 (1H, d, *J* 5.6 Hz, 6a-H), 4.00 (1H, app. td, *J* 8.6 and 1.8 Hz, 2-H_β), 3.84 (1H, ddd, *J* 12.1, 8.6 and 5.6 Hz, 2-H_α), 3.25–3.12 (2H, m, 3a- and 5-H_α), 2.93 (3H, s, NMe), 2.39 (1H, ddd, *J* 13.1, 12.3 and 10.0 Hz, 4-H_α), 2.11 (1H, dddd, *J* 12.7, 12.1, 8.1 and 1.8 Hz, 3-H_α), 1.77 (1H, dddd, *J* 12.7, 8.6, 5.6 and 1.8 Hz, 3-H_β), 1.50 (1H, ddd, *J* 13.1, 6.7 and 1.6 Hz, 4-H_β), 1.27 (3H, d, *J* 6.1 Hz, 5-Me), δ_c (100 MHz, $CDCl_3$) 11.9 (5-Me), 33.9 (3-CH_2), 37.8 (4-CH_2), 39.3 (3a-CH), 49.3 (NMe), 68.6 (5-CH), 70.8 (2-CH_2), 111.5 (6a-CH), *m/z* (ES) 158 ($M+H^+$, 100%), 157 (30). [Found: $M+H^+$, 158.1182. $C_8H_{16}NO_2$ requires M, 158.1181].

14. The proton coupling constants, quoted in Hertz, showed an internally consistent set of values: $J_{2\alpha,2\beta} = 8.6$; $J_{2\alpha,3\alpha} = 12.1$; $J_{2\alpha,3\beta} = 5.6$; $J_{2\beta,3\alpha} = 1.8$; $J_{2\beta,3\beta} = 8.6$; $J_{3\alpha,3a\alpha} = 8.1$; $J_{3\alpha,3\beta} = 12.7$; $J_{3\beta,3a\alpha} = 1.8$; $J_{3a\alpha,\ 4\alpha} = 10.0$; $J_{3a\alpha,4\beta} = 1.6$; $J_{4\alpha,4\beta} = 13.1$; $J_{4\alpha,5\alpha} = 12.3$; $J_{4\beta,5\alpha} = 6.7$; $J_{3a\alpha,\ 6a\alpha} = 5.6$; $J_{5\alpha,5Me} = 5.5$. NOSEY data: NMe ↔ 6a-H_α and 5-H_α confirming both 5-Me_α and 3a-H_α and the cis-ring fusion; 3a-H_α ↔ 3-H_α and 4-H_α; 5-Me_β ↔ 4-H_β; 6a-H_α ↔ 2-H_α and 3-H_α; 2-H_α ↔ 3-H_α; 2-H_β ↔ 3-H_β.
15. See, for example, Barks, J. M.; Weingarten, G. G.; Knight, D. W. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3469–3476.
16. Komaromi, I.; Tronchet, J. M. J. *Phys. Chem.* **1997**, *101*, 3554–3560; For an excellent proof of the concertedness and of the likely planarity of alignment in reverse-Cope cyclisations, see: Oppolzer, W.; Spivey, A. C.; Bochet, C. G. *J. Am. Chem. Soc.* **1994**, *116*, 3139–3140.
17. For somewhat related examples and references to previously reported rearrangements of this type, see: O'Neil, I. A.; Potter, A. J. *Chem. Commun.* **1998**, 1487–1488.
18. Jalali, M.; Boussac, G.; Lellemand, J.-Y. *Tetrahedron Lett.* **1983**, *24*, 4307–4310.
19. Atkinson, R. S.; Malpass, J. R.; Skinner, K. L.; Woodthorpe, K. L. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1905–1912.
20. Knight, D. W.; Salter, R. *Tetrahedron Lett.* **1999**, *40*, 5915–5918.
21. Trost, B. M.; Yasukata, T. *J. Am. Chem. Soc.* **2001**, *123*, 7162–7163; Carda, M.; Murga, J.; Marco, J. A. *Tetrahedron Lett.* **1994**, *35*, 3359–3360.
22. Shing, T. K. M.; Elsley, D. A.; Gillhouley, J. G. *J. Chem. Soc. Commun.* **1989**, 1280–1282; See also Bernet, B.; Vasella, A. *Helv. Chim. Acta* **1979**, *62*, 1990–2016.
23. Bailey, W. F.; Khanolkar, A. D. *Tetrahedron Lett.* **1990**, *31*, 5993–5996.
24. For syntheses of both six- and seven-membered α-allyl lactones, as well as of β-vinyl-δ-valerolactone, see: Molander, G. A.; Harris, C. R. *J. Am. Chem. Soc.* **1995**, *117*, 3705–3716.
25. Coogan, M. P.; Knight, D. W. *Tetrahedron Lett.* **1996**, *37*, 6417–6420.