PERKIN 1

A new version of the reverse-Cope elimination initiated by the nucleophilic addition of allylamines to nitrones: a synthesis of vicinal diamines

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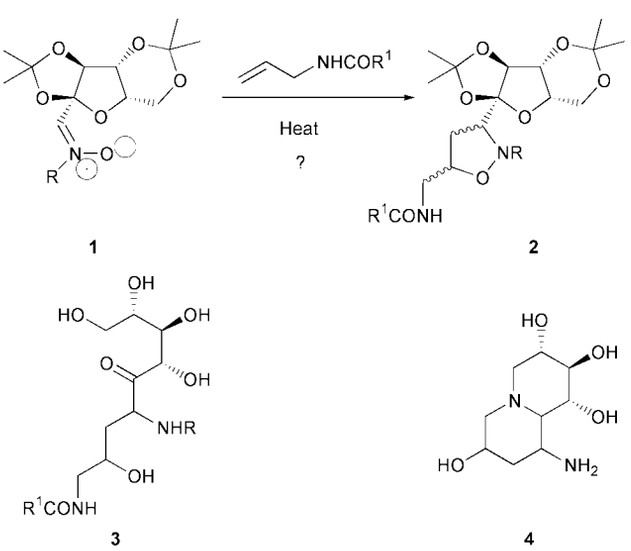
Attempts to utilize the sugar-derived nitrones **1** in enantioselective [1,3]dipolar cycloadditions with protected allylamines **6** are only partly successful, giving mixtures of the expected adducts **7**. However, reactions between nitrones **1** and unprotected allylamine **11** follow a different pathway involving sequential nucleophilic addition to the nitrone by the amine, reverse-Cope cyclization and Meisenheimer rearrangement leading to the 1,2,5-oxadiazinanes **12** and **13**. Similar reactions with the benzaldehyde derived nitrone **8** are successful, giving the *trans*-oxadiazinanes **24**, **33** and the stereoisomers **38** and **39** from linalylamine **37**, but only when the terminus of the allylamine is unsubstituted are the reactions efficient. A range of *N*-alkylallylamines **43**, **45**, **47** and **49**, however, react smoothly with nitrone **8**, as competing imine formation is precluded. Various mechanistic aspects are discussed, along with the effects of aryl substituents in *N*-benzylallylamines **57** and at the 4-position (**59**) of the nitrone **8**, none of which is found to enhance the overall reaction rate. The initial oxadiazinanes are useful as precursors to both amino-hydroxylamines **69** and vicinal diamine derivatives **70**.

Synthetic approaches to polyhydroxylated pyrrolizidines and indolizidines, along with similarly festooned pyrrolidines and piperidines, have attracted enormous interest during the past decade or so, stimulated especially by the prospects of discovering novel antiviral agents.[1] Obvious, but by no means exclusive, starting materials for these syntheses are natural sugars, a strategy most elegantly exemplified by the Fleet group.[2] A combination of this and our interest in nitrone chemistry[3] led us to speculate that nitrones **1** could be useful as precursors of a variety of bicyclic azasugars, following [1,3]dipolar cycloaddition to an allylamine derivative which we expected would proceed regioselectively to stereoisomers **2** (Scheme 1), given the usual propensity for the oxygen of the nitrone to add to the inner carbon of the dipolarophile,[4,5] with, hopefully, useful levels of stereocontrol induced by the sugar residue. Subsequent unmasking of the latent ketone function, along with N–O bond cleavage would lead to synthetic equivalents of the polyoxygenated diaminononanone array **3** and thence to a range of both mono- and bicyclic azasugars, such as the quinolizidine **4**. An attraction of this idea is that the precursor hexulofuranosonic acid **5a** is cheap and readily available, being both an intermediate in the industrial synthesis of Vitamin C as well as a powerful systemic plant growth regulator, marketed as its sodium salt under various names including 'Dikegulac', 'Atrinal' and 'Cutless'.[6] The idea of using carbohydrate-derived nitrones in this area is not new: for example, Vasella and co-workers[7] have used dipolar cycloadditions of a nitrone prepared from a mannose oxime to access chiral isoxazolidines which serve as proline analogues while the Kibayashi group[8] have employed a related nitrone, obtained from D-gulono-γ-lactone, in cycloadditions with protected allylamines as the key starting point in a total synthesis of (+)-negamycin.



Scheme 1

Results and discussion

The nitrones **1a–c** were obtained as summarized in Scheme 2. Previous methods for obtaining ester **5b** include the use of diazomethane on a small scale and KH–MeI on a larger scale,[9] along with a combination of MeI and potassium carbonate in DMF.[10] We found it more convenient to substitute 4-methylpentan-2-one as solvent and were able to secure a 95% isolated yield of the methyl ester **5b**. Direct reduction using diisobutylaluminium hydride (DIBAL) in hexanes at −78 °C provided convenient access to the required aldehyde **5c**, despite a typical conversion of around 60%, the remainder of the material being the separable ester **5b**. The aldehyde, which was isolated as a hydrate, was then converted into the nitrones **1a–c**, which turned out to be rather sensitive intermediates and which were

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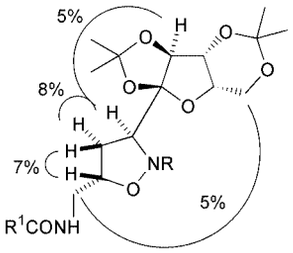
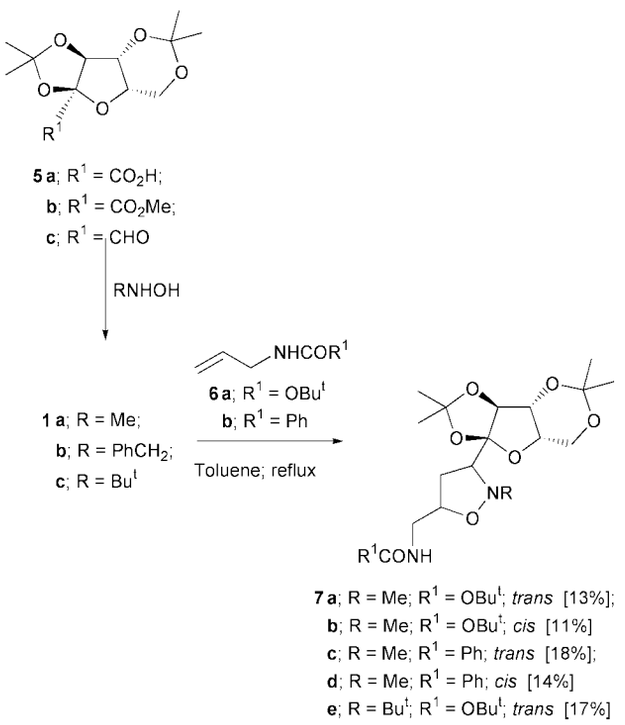
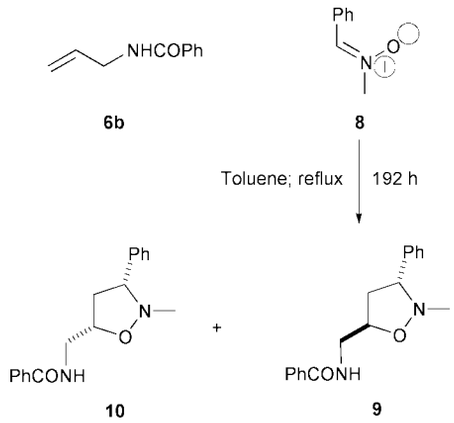


Fig. 1



Scheme 2



Scheme 3

therefore prepared as required. The [1,3]dipolar cycloadditions between the nitrones **1** and both *N*-Boc-allylamine **6a** and *N*-benzoylallylamine **6b** were carried out in refluxing toluene, as is typical of many such reactions.[3–5] TLC analysis indicated complete reaction after approximately 10 h but only poor returns of the isoxazolidines **7** were isolated with a dismal level of stereoselection, although the cycloadditions were highly regioselective, as expected.[3–5] In the case of the *N*-*tert*-butyl nitrone **1c**, a single isoxazolidine **7e** was isolated in poor yield; another isomer, presumably *cis*-**7e**, was visible in the ^{1}H NMR spectrum of the crude product. The structures were assigned particularly on the basis of the relatively high-field shifts of the 4-CH_2 protons in the ^{1}H NMR spectra of the isomeric products **7**, as well as by comparisons with known, related structures[3–5] and NOE data (Fig. 1). In view of the almost complete lack of stereoselection, this synthetic method was not pursued further.

In view of the poor yields of the isoxazolidines **7**, the relatively brief reaction time for the reactions to go to 'completion' no doubt reflected the instability of the nitrones **1** in refluxing toluene, rather than an acceleration of the cycloaddition reactions. By contrast, reaction between *N*-benzoylallylamine **6b** and the more robust nitrone **8**[11] had not gone to completion after 192 h, typical of such reactions (Scheme 3),[4,5] to give the *trans*- and *cis*-substituted isoxazolidines **9** and **10**[3] in 35 and 11% isolated yield, respectively, again with a relatively poor level of stereoselection. Returning to the original nitrones **1**, we wondered if a cycloaddition with allylamine itself might prove more successful, because of the smaller size of this dipolarophile and on the possibility that hydrogen bonding between the two reactants could enhance both the rate and stereoselectivity of the cycloaddition. While we were aware of the possibility that the free amine could attack the nitrone to give an aminal, the reversibility of this should still allow the desired cycloaddition to take place. In the event, however, the reaction took an entirely different pathway.[12] A solution of the nitrone **1a** and two equivalents of allylamine **11** was refluxed for 10 h until TLC and ^{1}H NMR analysis again indicated complete disappearance of the former. Two adducts were separated by column chromatography in 36 and 10% yield, respectively, which were evidently very different from the [1,3]dipolar cycloadducts **7** according to preliminary ^{1}H NMR analysis. Mass spectral data showed clearly that these were 1 : 1 adducts and NMR data showed that the sugar residue was intact. Spectacular differences in the ^{1}H NMR spectra of both products, relative to the dipolar cycloadducts **7**, included the appearance of methyl resonances as doublets [δ_H 0.88 and 1.17 (both *J* 6.3 Hz), respectively]. The major isomer also showed an apparent ABX system as part of a six-membered ring [d_H 2.67 (dd, *J* 13.7 and 10.6 Hz, H_{Aax}); 2.89 (dd, *J* 13.7 and 3.0 Hz, H_{Beq}); 2.41 (dqd, *J* 10.6, 6.3 and 3.0 Hz, H_{Xax})], suggestive of a partial structure -CH_2CH(Me)-. The appearance of an additional sharp singlet at δ_H 4.66 led us to speculate that the product was the *trans*-1,2,5-oxadiazinane **12a**, a proposal consistent with these data and ^{13}C NMR and some NOE data, and that the minor isomer was hence the corresponding *cis*-isomer **13a**. The latter showed much more indistinct resonances at ambient temperature, consistent with a not unreasonable conformational mobility. A third minor product, visible in ^{1}H NMR spectra of the crude product, was not isolated but was tentatively identified as the imine **14** on the basis of typical *N*-allyl group resonances and a singlet at δ_H 8.14 (RC*H*=NCH_2). Presumably, this was formed by an exchange reaction, initiated by nucleophilic attack of the allylamine **11** onto the nitrone **1a**, followed by expulsion of *N*-methylhydroxylamine (Scheme 4). This novel oxadiazinane synthesis was further exemplified by a similar reaction between allylamine **11** and nitrone **1b** which led to the related N^2-benzyl-1,2,5-oxadiazinanes **12b** and **13b**, in 56 and 19% isolated yield, respectively, along with traces of the imine **14**. In contrast, the *N*-*tert*-butyl nitrone **1c** failed to give more than traces of oxadiazinanes but instead gave only the imine **14**. Fortunately, crystallization of the minor isomer **13a** produced material suitable for X-ray analysis, as it seemed rather dangerous to propose the oxadiazinane structures **12** and **13** solely on the basis of spectroscopic analysis. The structure found is shown in Fig. 2 and confirms the foregoing assignments, although there still exists an uncertainty about which centre in the corresponding *trans*-isomers **12** has the opposite configuration with respect to the *cis*-isomers **13**.

The 1,2,5-oxadiazinane ring system is relatively obscure; the first examples of such compounds were reported contemporaneously by Katritzky[13] and Riddell[14] and co-workers and were

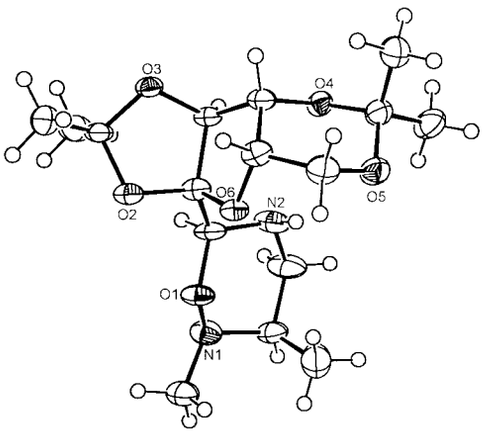
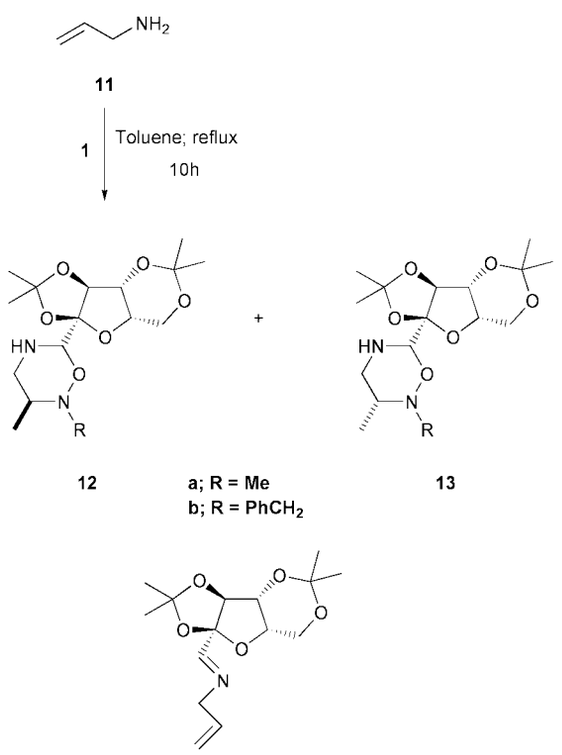
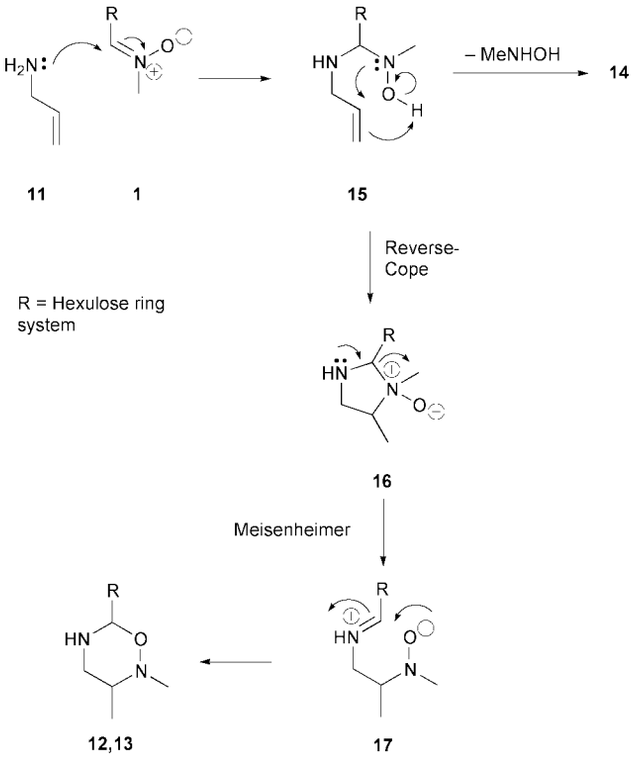


Fig. 2 X-ray molecular structure of compound **13a**.

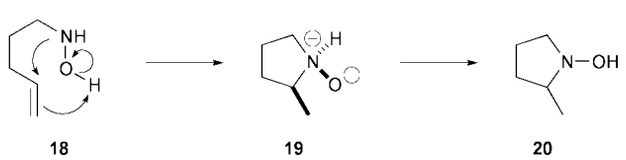


Scheme 4

prepared during a general survey of the NMR properties of the oxadiazinane ring system in general (see also Scheme 7 below). As for a mechanism for the formation of the 1,2,5-oxadiazinanes **12** and **13**, a tentative proposal is shown in Scheme 5. The expected and presumed reversible addition of allylamine **11** to the nitrones **1** (see above) leads to the unsaturated hydroxylamines **15**, which can react in two ways. First, expulsion of *N*-methylhydroxylamine gives the imine **14**, observed in varying amounts in each of the reactions of nitrones **1** with allylamine **11**. More productively, the intermediates **15** could undergo a reverse-Cope cyclization to give the *N*-oxides **16**, which are unstable with respect to ring opening to the iminium ions **17**. Finally, these reclose by a 6-endo process leading to the observed products **12** and **13**. The retro- or reverse-Cope reaction, as the name implies, is the reverse of the well known Cope elimination of tertiary amine *N*-oxides leading to a hydroxylamine and an alkene.[15] It was first discovered serendipitously by House and co-workers[16] and by Oppolzer's group[17] over twenty years ago. The latter report features the simplest version of this type of cyclization whereby *N*-pent-4-enylhydroxylamine **18** cyclizes at 40 °C to give *N*-hydroxy-2-methyl-



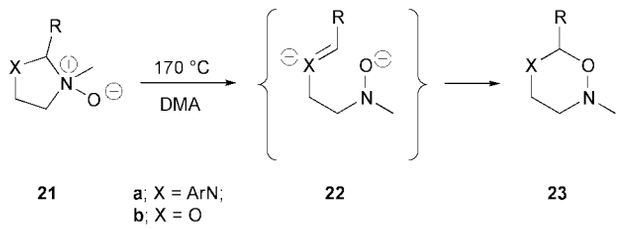
Scheme 5



Scheme 6

pyrrolidine **20**, presumably *via* the *N*-oxide **19** (Scheme 6). It was only in the 1990s that interest was renewed in this transformation, largely due to the extensive and definitive studies of Ciganek and his colleagues.[18] A further seminal report by the Oppolzer group[19] settled any doubt that the reaction is a thermal pericyclic process, belonging to the general class of 1,3-azaprotio cyclotransfer reactions, as defined by Grigg,[20] as well as providing elegant applications of the cyclization in alkaloid synthesis. Subsequent theoretical work[21] and further examples[22] strongly indicate that the five participating atoms must lie in a single plane; hence the depiction of the intermediate *N*-oxide **19** with the new methyl group *syn* to the N–O bond. In this respect, it seems likely that the intermediate *N*-oxides **16**, proposed but not observed in the present studies, are also formed as single diastereoisomers with the hexulose residue, the methyl group and the N–O bond all on the same face.[23] The reverse-Cope reaction can also be applied to alkynylhydroxylamines and indeed, given a choice, cyclization onto an alkyne occurs in preference to a similarly suitably positioned alkene.[24] In general,[16,18,19,23] substituents at the distal end of the participating alkene slow the cyclization, in some examples sufficiently to render the process not viable, as substrate or product decomposition takes preference. Although pyrrolidines are the typical products, the cyclization can also be used to obtain piperidines[16,25] but, as yet, there is no case known of a successful cyclization onto a terminally substituted alkene leading to a piperidine, *i.e.* the reaction can only be applied to a-methylpiperidine synthesis. One method recently found whereby reverse-Cope cyclizations can be activated is to position a hydroxy or derived ether group at an allylic position of the reacting alkene.[26] The second step of the proposed mechanism (Scheme 5) is a Meisenheimer rearrangement,[27] being the migration of an alkyl group from nitrogen to oxygen. The

accepted mechanism for this usually high-temperature process, which is also largely limited to the migration of allyl or benzyl groups, involves radical intermediates, to judge from the extensive studies carried out by the Schöllkopf group.[28] However, the present process represents a rather special case and clearly does not necessitate the evocation of radicals. Indeed, there is literature precedent for relatively simple Meisenheimer rearrangements involving α-aminoamine *N*-oxides.[29,30] Thus, direct support for this mechanism comes from the observation that rearrangement of the *N*-oxides **21a**, derived by peracid oxidation of the corresponding imidazolidines, occurs at ambient temperature to give the oxadiazinanes **23a**, presumably *via* the iminium species **22a** (Scheme 7).[30] Consistent with this is the

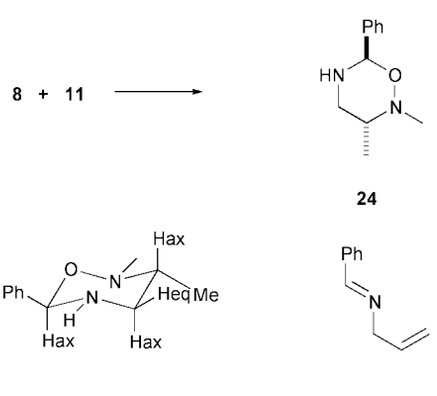


21 a; X = ArN; b; X = O **22** **23**

Scheme 7

finding that the corresponding oxazolidines **21b** undergo a similar rearrangement *via* the intermediates **22b**, to the 1,5,2-dioxazinanes **23b** but only when heated to 170 °C, presumably because the oxygen lone pair necessary to trigger the reaction is much more tightly bound.[31]

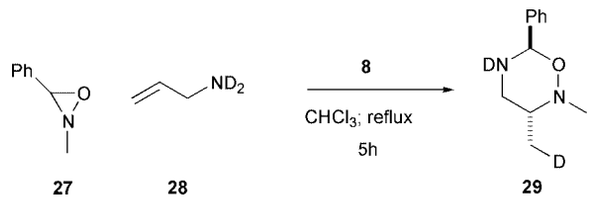
Naturally, we wondered if this sequence possessed any degree of generality. We were therefore delighted to find that when a solution of equal amounts of the benzaldehyde nitrone **8** and allylamine **11** in deuteriochloroform was monitored by ^{1}H NMR, a new set of signals slowly appeared, culminating in complete conversion to a new, single compound after approximately 7 days at ambient temperature. In the light of the foregoing, this was identified as the 1,2,5-oxadiazinane **24**, the *trans* stereochemistry being evident from coupling constant[13,14] and NOE data, which also indicated that the compound existed in the not unexpected chair conformation **25**, at least in chloroform at ambient temperature (Scheme 8). The reaction was



24 **25** **26**

Scheme 8

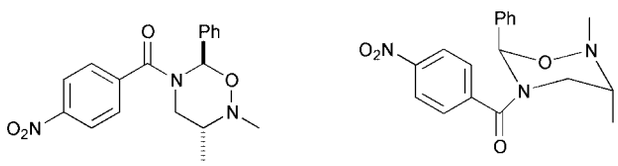
similarly efficient but took 36 h to go to completion at 45 °C, while in refluxing toluene conversion was complete in less than 17 h, but the product was accompanied by the benzaldehyde imine **26**, again formed by simple exchange of the amino groups. Under all conditions, only the *trans*-isomer **24** was formed but the proposed intermediate imidazolidine (*cf*. **16**; Scheme 5) was not observed; small transitory doublets around δ_H 1.1 indicated the formation of this and perhaps other species, but evidence better than this was not secured. The *trans*-stereochemistry in the product **24** is presumably established during the final 6-endo ring closure involving the proposed *anti*-iminium species (see Scheme 5), which would have a chair-like conformation with the new methyl group positioned equatorially. Two other mechanistic aspects have been investigated. First, it has been suggested[32] that the oxaziridine **27**, derived from rearrangement of the nitrone **8**, could be involved. However, experiments using independently prepared oxaziridine **27** in place of the nitrone clearly established that it was not an intermediate.[33] Secondly, when the deuteriated allylamine **28** was treated with nitrone **8**, only the deuteriated oxadiazinane **29** was formed (Scheme 9); hardly proof, but at least evidence



27 **28** **29**

Scheme 9

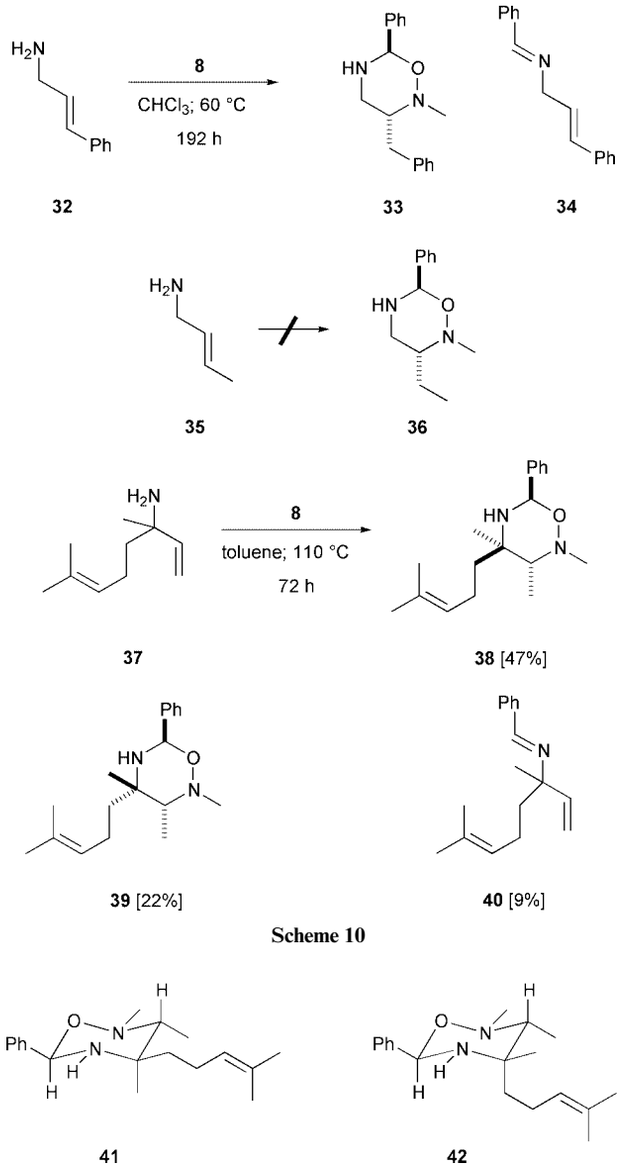
that a pathway totally different to that shown in Scheme 5 is probably not involved. Finally, the oxadiazinane structure **24** was further confirmed by conversion into the crystalline 4-nitrobenzoyl derivative **30**. The understandably sensitive nature



30 **31**

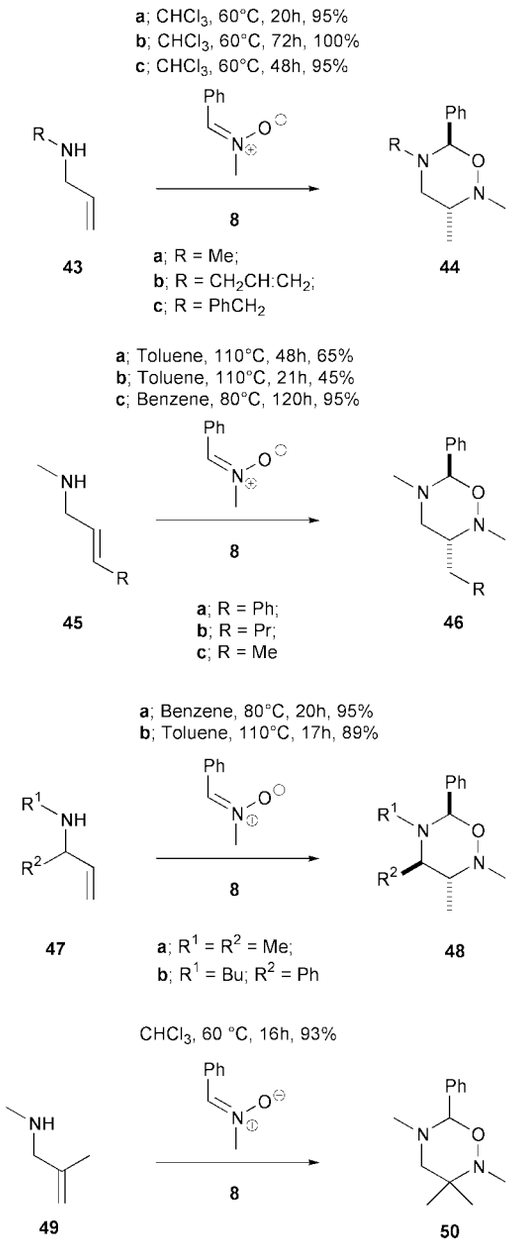
of oxadiazinane **24** meant that Hunig's base, rather than triethylamine, had to be used in this derivatization and it was essential to add this prior to the acid chloride. The amide **30** turned out to be highly rotameric at ambient temperature, presumably due to rotation about the new amide bond, but usable NMR data could be obtained at 63 °C, which suggested that 3-H was now equatorial ($J_{3,4eq}$ 4.1 Hz), and hence the conformation **31**, a known phenomenon in the case of N-acylated 2-substituted piperidines,[34] engendered by the avoidance of $A^{(1,2)}$ strain, present if the 2-substituent is positioned equatorially.

As mentioned above, substituents at the distal end of participating alkenes retard the reverse-Cope cyclization.[17–19] Hence, it was not surprising that reaction between nitrone **8** and (*E*)-cinnamylamine **32**[35] was very slow in refluxing chloroform, an optimum solvent for reverse-Cope cyclization,[18] and gave only a 40% isolated yield of the oxadiazinane **33**, accompanied by a similar amount of the exchange product, the imine **34**. Even worse, similar reactions between nitrone **8** and (*E*)-crotonylamine **35** gave only the corresponding imine and very little oxadiazinane **36**. By contrast, reaction between nitrone **8** and linalylamine **37**,[36] although slow, gave good yields of the separable oxadiazinanes **38** and **39**, accompanied by only 9% of the related imine **40** (Scheme 10). The stereochemistry of the two isomers was confirmed by NOE measurements as being the expected chair conformations **41** and **42**; the stereoselection was presumably controlled by the larger homoprenyl residue. The success of this transformation, despite the crowded nature of the allylamine **37**, is not too surprising, as the reverse-Cope cyclization is known to benefit from the Thorpe–Ingold effect; the latter is crucial to the success of many examples.[18] Attempts to use other benzaldehyde nitrones were not productive. Reaction between *N*-benzyl-*C*-phenylnitrone was some seven times slower with allylamine in chloroform at ambient temperature while the corresponding *N*-*tert*-butyl nitrone showed very little reaction.



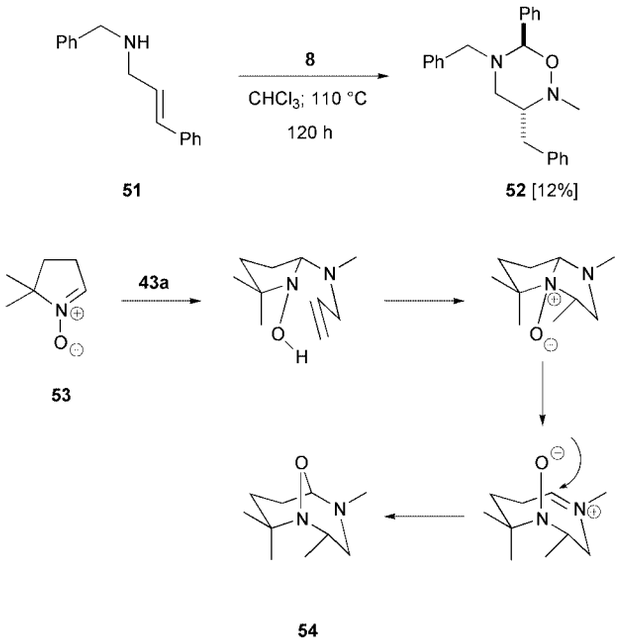
Scheme 10

We reasoned that to extend this chemistry, it might be an idea to use a secondary allylamine, hence preventing the exchange reaction with the nitrone partner leading to the corresponding imines; any equilibrium between the reactants and an iminium salt and a hydroxylamine should lie very much on the side of the former. However, the evident sensitivity of the reverse-Cope cyclization to substituent effects made us uncertain if this idea would be successful. In the event, we were delighted to observe that *N*-methylallylamine **43a** reacted slowly with the nitrone **8** at ambient temperature to give the 1,2,5-oxadiazinane **44a**. Subsequently, heating in chloroform for 16 h delivered essentially a quantitative yield of the *trans*-isomer **44a**; no evidence for formation of the corresponding *cis*-isomer was visible in ^{1}H NMR spectra of the crude product. Fortunately, the products of this and other equally efficient cyclizations were generated with sufficient purity to be used in further transformations as losses were considerable during chromatographic purification. Similarly, the *N*-allyl- and *N*-benzylallylamine **43b** and **43c** were converted into the oxadiazines **44b** and **44c**, respectively, but both reactions took considerably longer to reach completion (Scheme 11), indicating a rate retardation associated with these substituents in this position. Again, substituents at the distal end of the alkene function also retarded such reverse-Cope cyclizations: reactions between the substituted *N*-methylallylic amines **45** and nitrone **8** gave the oxadiazinanes **46**, again as single *trans*-isomers, but in lower yields and after considerably increased reactions times. However, incorporation of a



Scheme 11

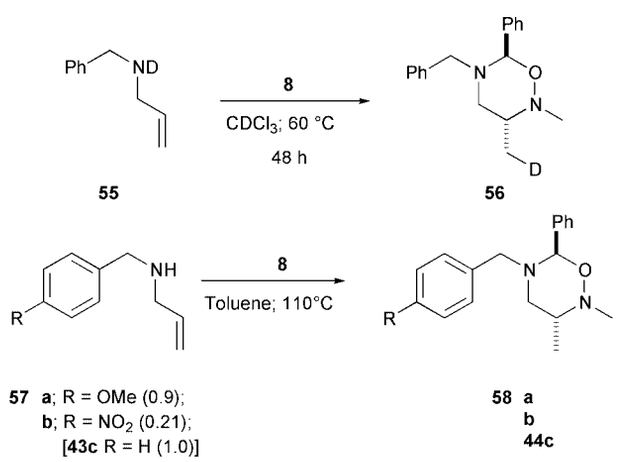
substituent adjacent to the amine group led to excellent yields under relatively mild conditions during the formation of trisubstituted oxadiazinanes **48**, as the single diastereoisomers shown, from amines **47**. Again, the stereochemistry of these is presumably set during the initial reverse-Cope cyclization and is controlled by the substituent R^2 adopting a pseudoequatorial position.[22] The internally substituted allylic amine **49** also reacted smoothly to provide an excellent yield of the dimethyl derivative **50**, despite the apparent steric crowding. A limitation of this scheme was reached when two deactivating groups were present in the allylic amine: reaction between *N*-benzylcinnamylamine **51** and nitrone **8** gave a mere 12% isolated yield of the oxadiazinane **52** and only after prolonged reaction times. Interestingly, however, the pyrrolidine nitrone **53** reacted smoothly, if slowly, with *N*-methylallylamine **43a** to provide excellent yields of the 1,4-diazabicyclo[3.3.1]nonane **54**, as a single diastereoisomer of undetermined stereochemistry (Scheme 12), thus providing more evidence of the validity of the proposed overall mechanism (Scheme 5). Once again, the proposed intermediates (Scheme 12) were not observed by NMR; the delicate nature of the nitrone **53** and especially that of the product **54** precluded further thermal acceleration and also successful reactions with distally substituted allylic amines.



Scheme 12

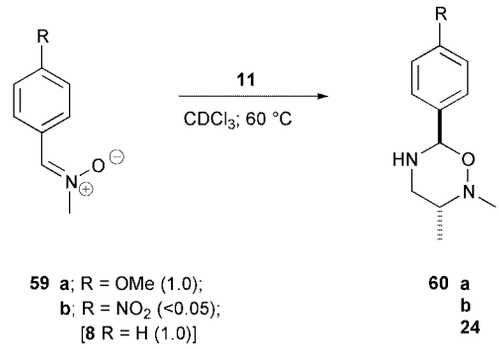
As a final mechanistic check, the *N*-deuteriated allylamine **55** was treated with nitrone **8** in hot deuteriochloroform and provided only the monodeuteriated product **56**; the absence of deuterium elsewhere in the product again precludes many alternative pathways. Throughout these experiments and despite the sometimes lengthy reaction times, no products from [1,3]dipolar cycloadditions were observed.

In an effort to define more reactive components, we briefly examined some homologues of the two starting materials. Competition experiments between the *para*-substituted *N*-benzylallylamines **57** leading to the oxadiazinanes **58**, carried out using equimolar amounts of the allylamines **57a,b** and **43c** and the nitrone **8** with ^{1}H NMR monitoring, revealed the relative rates shown in Scheme 13. In a similar fashion, the *para*-



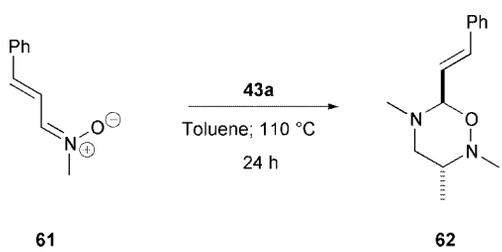
Scheme 13

substituted nitrones **59** gave the oxadiazinanes **60** at the relative rates shown (Scheme 14). While the effect of the *p*-methoxy group in allylamine **57a** is almost negligible, it was unexpected that the reaction would be slower, as one might expect acceleration of the initial nucleophilic attack (Scheme 5); presumably, this step is much slower in allylamine **57b** where the *p*-nitro group renders the amine less nucleophilic. Similarly odd was the finding (Scheme 14) that a *p*-methoxy group in the nitrone **59a** had very little effect on the overall rate whereas a *p*-nitro group slowed the reaction greatly, meaning that the oxadiazinane



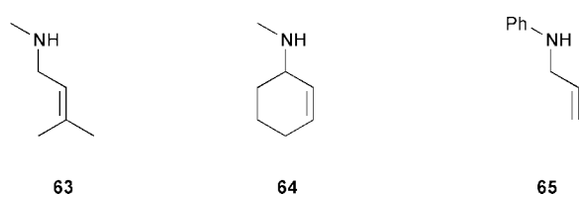
Scheme 14

60b was not isolated from similar reactions of nitrone **59b**, despite the fact that this group should significantly accelerate the initial nucleophilic attack by allylamine **11**. Presumably, in the latter case, the *p*-nitro group destabilizes the intermediates involved in the later Meisenheimer rearrangement. Two features are evident: first, and not surprisingly, more than one rate-determining step is probably involved in the sequence, and secondly, and disappointingly, incorporation of these electronically extreme functions in either reactant did not result in useful rate increases but rather made no difference or, worse, reduced the overall rate significantly. Not unexpectedly, the effect of the phenyl group in nitrone **8** can be transmitted by an alkene link. Thus, the cinnamylnitrone **61** reacted in a similar manner to give a good yield of the rather sensitive 6-styryloxadiazinane **62** (Scheme 15). In view of the foregoing

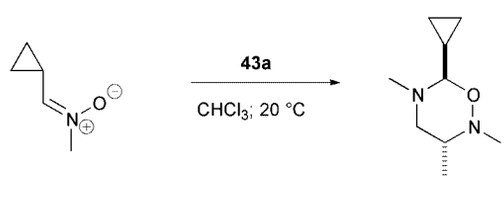


Scheme 15

together with Ciganek's results,[18] it came as no surprise that the allylic amines **63** and **64** failed to react with the nitrone **8**; the *N*-phenyl derivative **65** was similarly recalcitrant, pre-



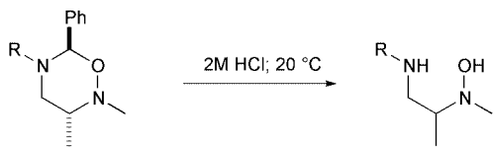
sumably by reason of reduced nucleophilicity at nitrogen. Finally, we had a tantalizing insight into a future direction for this chemistry, which has subsequently been successfully exploited:[33] the *C*-cyclopropyl nitrone **66** underwent reaction with *N*-methylallylamine **43a** at ambient temperature to provide a quantitative return of the *trans*-oxadiazinane **67** (Scheme 16).



Scheme 16

The same compound **67** was even obtained after storage of a solution of the two reactants in chloroform at −20 °C for a few days. Hence, a final conclusion is that the *C*-phenyl nitrone **8**, attractive as a test substrate by reason of its stability and crystallinity, is not the most reactive system in this chemistry, for reasons which are, as yet, not entirely clear.

Overall, a main interest in the overall sequence (Scheme 5) is that a carbon–nitrogen bond is formed, effectively by the uncatalysed addition of an amine to an alkene, unactivated in a Michael sense. We have briefly examined some further reactions of the initial oxadiazinanes in order to emphasize this feature. First, exposure of four representative oxadiazinanes to dilute hydrochloric acid led to good yields of the aminohydroxylamines **69** (Scheme 17). These might well find use as ligands and

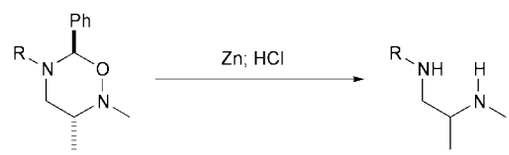


44b (R = CH_2:$CHCH_2$);
44c (R = $PhCH_2$);
58a (R = *p*-$MeOC_6H_4CH_2$);
68 (R = *p*-MeC_6H_4CO)

69 a; R = CH_2:$CHCH_2$;
b; R = $PhCH_2$;
c; R = *p*-$MeOC_6H_4CH_2$;
d; R = *p*-MeC_6H_4CO.

Scheme 17

synthetic intermediates and are not too easy to obtain in other ways; the ease of preparation of the monoacylated derivative **69d** is also of note. Finally, zinc reduction led to similarly good isolated yields of the diamines **70** (Scheme 18); again, this



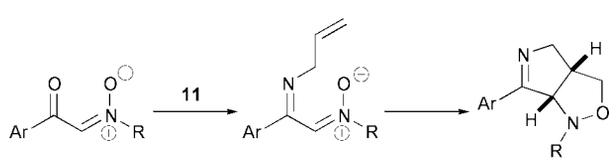
44c (R = $PhCH_2$);
68 (R = *p*-MeC_6H_4CO.

70 a; R = $PhCH_2$;
b; R = *p*-MeC_6H_4CO.

Scheme 18

provides access to a monoacylated derivative **70b** which is also not easily accessible by alternative routes.

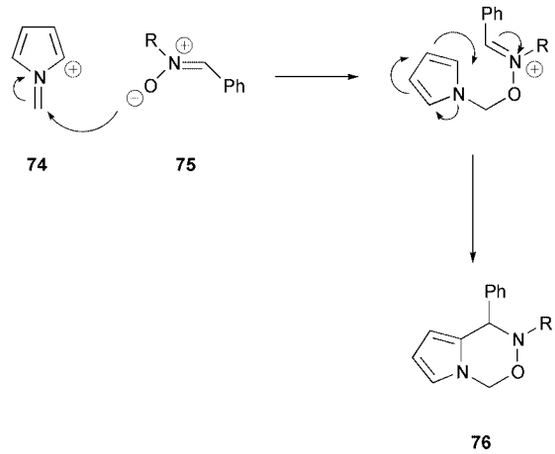
There are three footnotes to this work. First, this is not the first report of a reaction between a nitrone and allylamine: Black has reported that the acyl nitrones **71** react with allylamine **11** in refluxing diethyl ether to give the products **73** of a particularly simple intramolecular [1,3]dipolar cycloaddition of the intermediate imines **72** (Scheme 19).[37] Evidently, the



71 **72** **73**

Scheme 19

amine prefers to react with the carbonyl group in these distorted nitrones rather than with the nitrone function itself; if the latter had occurred, this would presumably have led to chemistry related to that described above. Secondly, the oxadiazinane ring system **76** has been obtained from a nitrone previously, but by a rather different pathway (Scheme 20).[38] Formally, or perhaps in reality, this is a [6π + 4π] process, or one which features a double Mannich reaction between the pyrrole iminium salt **74** and the nitrone **75**, triggered by



74 **75** **76**

Scheme 20

nucleophilic addition of the nitrone oxygen. Finally, we have reported that similar but more limited chemistry can be carried out using allylthiols in place of allylamines.[23]

Experimental

General details

Melting points were determined on a Köfler hot-stage apparatus and are uncorrected. Optical rotations were measured using a JASCO DIP-370 instrument; $[\alpha]_D$-values are given in units of 10^{-1} deg cm^2 g^{-1}. IR spectra were recorded using a Perkin-Elmer 1720 series Fourier transform spectrometer using thin films between sodium chloride plates, unless otherwise stated. ^{1}H NMR spectra were determined using a Bruker WM-250 or a Bruker AM-400 spectrometer. ^{13}C NMR spectra were determined using a JEOL EX270 spectrometer operating at 67.8 MHz or the Bruker AM-400 instrument operating at 100 MHz. Unless otherwise stated, all spectra were determined using dilute solutions in deuteriochloroform and tetramethylsilane as internal standard. *J*-Values are expressed in Hertz. Relative molecular masses and mass spectra were measured using a VG 7070E instrument, operating in the electron-impact mode.

Unless otherwise stated, all reactions were carried out under an atmosphere of dry nitrogen in anhydrous solvents which were obtained by the usual methods.[39] All organic solutions from work-ups were dried by brief exposure to anhydrous magnesium sulfate followed by filtration. Solvents were removed by rotary evaporation. CC refers to column chromatography over Sorbsil C60-H (40–60 μm) silica gel using the eluants specified. Light petroleum (LP) refers to the fraction with distillation range 40–60 °C. Ether refers to diethyl ether. The benzaldehyde-derived nitrone **8** was prepared by an established method.[11,40]

Methyl 2,3:4,6-di-*O*-isopropylidene-α-L-*xylo*-hex-2-ulofurano-sonate 5b

Iodomethane (21.3 ml, 48.55 g, 342 mmol) was added to 4-methylpent-2-anone (500 ml), anhydrous potassium carbonate (23.5 g, 171 mmol) and 2,3:4,6-di-*O*-isopropylidene-L-*xylo*-hex-2-ulosonic acid monohydrate **5a** (50 g, 171 mmol; Aldrich) and the resulting mixture was stirred and refluxed for 4 h, then cooled and filtered. The solid was washed thoroughly with acetone and the combined filtrates were evaporated. The residual viscous oil was dissolved in ether (100 ml) and the resulting solution was washed successively with saturated aq. sodium hydrogen carbonate (50 ml) and brine (50 ml), then dried and evaporated to leave the crude ester as a viscous yellow oil. CC (EtOAc–hexane, 1:2), collection of the fraction with R_f 0.24 (visualized using anisaldehyde spray) and crystallization from hexane gave the *ester* **5b** (46.8 g, 95%) as colour-

less needles, mp 47 °C (lit.[9] 46–47 °C); $[\alpha]_D^{20}$ −155.6 (*c* 1, $CHCl_3$) (Found: C, 54.1; H, 6.8. Calc. for $C_{13}H_{20}O_7$: C, 54.1; H, 7.0%); ν_{max}/cm^{-1} 1750; δ_H (250) 1.35 (3H, s), 1.43 (6H, s, 2 × Me), 1.53 (3H, s), 3.86 (3H, s, OMe), 4.10 (1H, d, *J* 2.0, 6-H[a]), 4.11 (1H, d, *J* 1.0, 4-H), 4.17 (1H, ddd, *J* 2.0, 2.0 and 1.0, 5-H), 4.31 (1H, d, *J* 2.0, 6-H[b]) and 4.84 (1H, s, 3-H); δ_C (67.8) 18.4, 25.3, 26.5, 28.4 (all Me), 52.6 (OMe), 59.3 (CH_2), 72.2, 73.5, 87.2 (all CH), 97.1, 109.9, 113.6 (all C) and 167.0 (CO); *m*/*z* 273 (M^+ − 15, 50%), 229 (8), 215 (14), 187 (11), 171 (25), 158 (17), 143 (27), 59 (32) and 43 (100) (Found: M^+ − Me, 273.0973. $C_{12}H_{17}O_7$ requires *m*/*z*, 273.0974).

2,3:4,6-Di-*O*-isopropylidene-α-L-*xylo*-hex-2-ulose monohydrate 5c

A stirred solution of the ester **5b** (8.34 g, 28.4 mmol) in hexane (500 ml) was maintained at −78 °C during the dropwise addition of DIBAL (31.8 ml of a 1 M solution in hexanes, 31.8 mmol). Stirring at this temperature was continued for 5.5 h, then the reaction was quenched by the addition of aq. methanol (9:1; 2.5 ml). The resulting suspension was filtered through a pad of silica gel (20 g) with an upper layer of dried magnesium sulfate (10 g). The solid was washed with ethyl acetate (200 ml) and the combined filtrates were evaporated. CC (EtOAc–hexane–Et_3N, 1:1:0.02) of the residue separated the *aldehyde monohydrate* **5c** (4.36 g, 58%), R_f 0.10, as a colourless solid, mp 46 °C; $[\alpha]_D^{20}$ −147 (*c* 1, $CHCl_3$); ν_{max}/cm^{-1} 3700–3200 and 1768; δ_H (250) 1.28 (3H, s), 1.38 (3H, s), 1.43 (3H, s), 1.50 (3H, s), 4.05 (1H, d, *J* 2.0, 6-H[a]), 4.06 (1H, d, *J* 1.0, 4-H), 4.18 (1H, ddd, *J* 2.0, 2.0 and 1.0, 5-H), 4.30 (1H, d, *J* 2.0, 6-H[b]), 4.48 (1H, s, 3-H) and 9.62 (1H, s, CHO); *m*/*z* 229 (M^+ − CHO, 49%), 185 (12), 171 (63), 157 (7), 113 (33), 59 (34) and 43 (100) (Found: M^+ − CHO, 229.1042. $C_{11}H_{17}O_5$ requires *m*/*z*, 229.1076).

Earlier fractions contained the ester **5b** (3.25 g, 39% recovery).

N-(1-Deoxo-2,3:4,6-di-*O*-isopropylidene-α-L-*xylo*-hex-2-ul-1-ylidene)methylamine *N*-oxide 1a

N-Methylhydroxylamine (0.15 g, 3.1 mmol) was added to a stirred mixture of the aldehyde monohydrate **5c** (0.80 g, 3.1 mmol), dried magnesium sulfate (3.0 g) and methanol (0.5 ml) in ether (30 ml) maintained at 0 °C. After 1 h, the mixture was warmed to ambient temperature and filtered. The solid was washed with ether and the combined filtrates were evaporated to leave the *nitrone* **1a** (0.90 g, 95%) as colourless crystals, mp 35 °C; ν_{max}/cm^{-1} 1605; δ_H (250) 1.33 (3H, s), 1.43 (3H, s), 1.52 (3H, s), 1.65 (3H, s), 3.76 (3H, s, NMe), 4.04 (1H, d, *J* 2.0, 6-H[a]), 4.07 (1H, d, *J* 1.0, 4-H), 4.15 (1H, ddd, *J* 2.0, 2.0 and 1.0, 5-H), 4.36 (1H, d, *J* 2.0, 6-H[b]) 5.21 (1H, s, 3-H) and 6.92 (1H, s, CHN); *m*/*z* 287 (M^+, 3%), 272 (12), 243 (15), 229 (21), 171 (31), 142 (14), 126 (9), 113 (18), 101 (20), 85 (21), 69 (23), 59 (48) and 48 (100).

The sample showed no carbonyl stretch in the IR spectrum and was used promptly and not further purified due to its limited stability.

N-(1-Deoxo-2,3:4,6-di-*O*-isopropylidene-α-L-*xylo*-hex-2-ul-1-ylidene)benzylamine *N*-oxide 1b

N-Benzylhydroxylamine (0.647 g, 5.26 mmol) was added in one portion to a stirred solution of the aldehyde monohydrate **5c** (1.35 g, 5.26 mmol) in ether (30 ml) maintained at 0 °C. After 1 h, the mixture was warmed to ambient temperature, dried and evaporated to leave the *nitrone* **1b** (1.88 g, 98%) as a colourless glass, ν_{max}/cm^{-1} 1600; δ_H (250) 1.27 (3H, s), 1.40 (3H, s), 1.52 (3H, s), 1.64 (3H, s), 4.01 (1H, d, *J* 2.0, 6-H[a]), 4.06 (1H, d, *J* 1.0, 4-H), 4.14 (1H, ddd, *J* 2.0, 2.0 and 1.0, 5-H), 4.34 (1H, d, *J* 2.0, 6-H[b]), 4.89 (1H, d, *J* 10.8, PhCH[a]), 4.99 (1H, d, *J* 10.8, PhCH[b]), 5.16 (1H, s, 3-H), 6.97 (1H, s, CHN) and 7.28–7.44 (5H, m, Ph); *m*/*z* 243 (28%), 229 (36), 171 (51), 113 (26), 91 (90), 77 (4) and 48 (100).

The sample showed no carbonyl stretch in the IR spectrum and was used promptly and not further purified due to its limited stability.

N-(1-Deoxo-2,3:4,6-di-*O*-isopropylidene-α-L-*xylo*-hex-2-ul-1-ylidene)-*tert*-butylamine *N*-oxide 1c

N-*tert*-Butylhydroxylamine hydrochloride (0.97 g, 7.75 mmol) was added to a stirred solution of sodium methoxide (0.42 g, 7.75 mmol) in methanol (50 ml) and the resulting mixture was stirred for 0.5 h, then cooled to 0 °C. The aldehyde **5c** (2.00 g, 7.75 mmol) as a solution in toluene (20 ml) was added dropwise and the resulting solution was stirred at ambient temperature without further cooling for 16 h, then was dried and evaporated. The residue was dissolved in dry ether, the solution was filtered and the filtrate evaporated to leave the *nitrone* **1c** (2.42 g, 95%) as a colourless glass, ν_{max}/cm^{-1} 1580; δ_H (250) 1.47 (3H, s), 1.55 (3H, s), 1.66 (9H, s), 1.67 (3H, s), 1.82 (3H, s), 4.18 (1H, d, *J* 2.0, 6-H[a]), 4.25 (1H, d, *J* 1.0, 4-H), 4.30 (1H, app. q, *J* 2.0, 5-H), 4.47 (1H, d, *J* 2.0, 6-H[b]), 5.32 (1H, s, 3-H) and 7.13 (1H, s, CHN); *m*/*z* 329 (4%), 314 (9), 243 (19), 229 (29), 171 (33), 157 (11), 113 (24) and 57 (100).

(+)-(3*R*,5*R*)- and (−)-(3*R*,5*S*)-5-(*tert*-Butoxycarbonylaminomethyl)-3-(2-deoxy-3,5-*O*-isopropylidene-1,2-isopropylidenedioxy-β-L-*xylo*-furanosyl)-2-methylisoxazolidine 7a and 7b

A solution of *N*-*tert*-butoxycarbonylprop-2-en-1-amine **6a** (0.272 g, 1.74 mmol) and the *N*-methyl nitrone **1a** (0.50 g, 1.74 mmol) in toluene (20 ml) was refluxed for 10 h then cooled and evaporated. CC (EtOAc–hexane–Et_3N, 1:4:0.01) of the residue separated (i) the (3*R*,5*R*)-isoxazolidine **7a** (99 mg, 13%), R_f 0.58 (EtOAc–hexane–Et_3N, 1:2:0.1), as a colourless oil, $[\alpha]_D^{20}$ +1.7 (*c* 0.36, $CHCl_3$); ν_{max}/cm^{-1} 3360 and 1705; δ_H (250) 1.37 (3H, s), 1.43 (3H, s), 1.44 (9H, s, Bu[t]), 1.45 (3H, s), 1.48 (3H, s), 2.10 (1H, ddd, *J* 12.7, 10.3 and 10.3, 4-H[a]), 2.67 (1H, ddd, *J* 12.7, 6.4 and 4.0, 4-H[b]), 2.85 (3H, s, NMe), 3.31 (1H, dd, *J* 10.3 and 4.0, 3-H), 3.43 (1H, m, 6-H), 4.04–4.14 (5H, m), 4.27 (1H, d, *J* 2.5), 4.53 (1H, s) and 4.85 (1H, t, *J* 4.0, NH); *m*/*z* 388 ($M^+ + H - Bu^t$, 7%), 159 (100), 141 (19), 115 (13), 98 (15), 84 (9), 68 (9), 59 (28) and 57 (25) (Found: $M^+ + H - Bu^t$, 388.1819. $C_{17}H_{28}N_2O_8$ requires *m*/*z*, 388.1846) and (ii) the (*3R*,*5S*)-*isoxazolidine* **7b** (84 mg, 11%), R_f 0.40 (EtOAc–hexane–Et_3N, 1:2:0.1), as a colourless oil, $[\alpha]_D^{20}$ −34.4 (*c* 0.46, $CHCl_3$); ν_{max}/cm^{-1} 3360 and 1708; δ_H (250) 1.36 (3H, s), 1.43 (6H, s, 2 × Me), 1.44 (9H, s, Bu[t]), 1.51 (3H, s), 2.12 (1H, ddd, *J* 12.5, 9.5 and 9.5, 4-H[a]), 2.59 (1H, ddd, *J* 12.5, 5.9 and 2.6, 4-H[b]), 2.80 (3H, s, NMe), 3.18 (1H, dd, *J* 9.5 and 2.6, 3-H), 3.25 (1H, m, CH[a]NH), 3.45 (1H, m, CH[b]NH), 4.05–4.08 (3H, m), 4.07 (1H, d, *J* 2.0), 4.27 (1H, d, *J* 1.9), 4.38 (1H, s) and 4.85 (1H, t, *J* 5.0, NH); *m*/*z* 388 ($M^+ + H - Bu^t$, 9%), 159 (100), 141 (17), 115 (15), 98 (11), 84 (7), 68 (10), 59 (18) and 57 (22) (Found: $M^+ + H - Bu^t$, 388.1842).

(+)-(3*R*,5*R*)- and (−)-(3*R*,5*S*)-5-(Benzoylaminomethyl)-3-(2-deoxy-3,5-*O*-isopropylidene-1,2-isopropylidenedioxy-β-L-*xylo*-furanosyl)-2-methylisoxazolidine 7c and 7d

By the foregoing method, reaction between the *N*-methyl nitrone **1a** (0.727 g, 2.53 mmol) and *N*-prop-2-enylbenzamide **6b** (0.41 g, 2.53 mmol) in toluene (30 ml) followed by CC (EtOAc–hexane–Et_3N, 1:4:0.1) separated (i) the (3*R*,5*R*)-isoxazolidine **7c** (204 mg, 18%), R_f 0.39, as a colourless solid, mp 151 °C (Found: C, 61.6; H, 7.3; N, 6.3. $C_{23}H_{32}N_2O_7$ requires C, 61.6; H, 7.2; N, 6.3%) $[\alpha]_D^{20}$ +13.9 (*c* 0.42, $CHCl_3$); ν_{max}/cm^{-1} 3350 and 1640; δ_H (250) 1.35 (3H, s), 1.43 (3H, s), 1.45 (3H, s), 1.48 (3H, s), 2.17 (1H, ddd, *J* 12.8, 10.0 and 10.0, 4-H[a]), 2.73 (1H, ddd, *J* 12.8, 6.1 and 3.7, 4-H[b]), 2.89 (3H, s, NMe), 3.34 (1H, dd, *J* 10.0 and 3.7, 3-H), 3.47 (1H, ddd, *J* 14.0, 7.3 and 5.2, CH[a]NH), 3.88 (1H, ddd, *J* 14.0, 6.1 and 3.1, CH[b]NH), 4.06

(1H, d, *J* 2.3), 4.11 (1H, d, *J* 2.3), 4.20–4.25 (2H, m), 4.28 (1H, d, *J* 2.0), 4.52 (1H, s), 6.49 (1H, m, NH), 7.45–7.51 (3H, m) and 7.78–7.84 (2H, m); *m*/*z* 448 (M^+, 12%), 219 (72), 172 (25), 134 (9), 105 (100), 98 (26), 84 (19), 77 (22), 70 (9), 59 (23), 48 (40) and 43 (29) (Found: M^+, 448.2203. $C_{23}H_{32}N_2O_7$ requires *M*, 448.2209) and (ii) the (3*R*,5*S*)-isoxazolidine **7d** (159 mg, 14%), R_f 0.31 (EtOAc–hexane–Et_3N, 1:2:0.1), as a colourless glass, ν_{max}/cm^{-1} 3550 and 1640; δ_H (250) 1.35 (3H, s), 1.42 (6H, s, 2 × Me), 1.49 (3H, s), 2.17 (1H, m, 4-H^a), 2.69 (1H, ddd, *J* 12.5, 6.1 and 2.6, 4-H^b), 2.85 (3H, s, NMe), 3.22 (1H, dd, *J* 9.4 and 2.6, 3-H), 3.52 (1H, ddd, *J* 14.0, 5.6 and 3.5, CH^aNH), 3.85 (1H, ddd, *J* 14.0, 6.1 and 3.5, CH^bNH), 4.06 (1H, s), 4.18–4.24 (2H, m), 4.27 (1H, d, *J* 2.0), 4.37 (1H, s), 4.38 (1H, s), 6.47 (1H, t, *J* 3.5, NH), 7.43–7.51 (3H, m) and 7.77–7.80 (2H, m); *m*/*z* 448 (M^+, 20%), 219 (89), 172 (24), 134 (6), 105 (100), 98 (18), 84 (11), 77 (22), 70 (12), 59 (11), 48 (14) and 43 (24) (Found: M^+, 448.2211).

(3*RS*,5*RS*)- and (3*RS*,5*SR*)-5-Benzoylaminomethyl-2-methyl-3-phenylisoxazolidine 9 and 10

A solution of *N*-2-propen-1-ylbenzamide **6b** (1.20 g, 7.40 mmol) and the benzaldehyde-derived nitrone **8** (1.00 g, 7.40 mmol) in toluene (40 ml) was refluxed for 192 h, then cooled and evaporated. CC (EtOAc–LP, 1:1] of the residue separated (i) the (3*RS*,5*RS*)-*trans*-*isoxazolidine* **9** (770 mg, 35%), R_f 0.27, as a colourless solid, mp 99–100 °C (Found: C, 72.9; H, 7.1; N, 9.4. $C_{18}H_{20}N_2O_2$ requires C, 72.9; H, 6.8; N, 9.5%), ν_{max}/cm^{-1} 3330 and 1635; δ_H (250) 2.15 (1H, ddd, *J* 12.7, 8.0 and 5.6, 4-H^a), 2.60 (3H, s, 2-Me), 2.83 (1H, ddd, *J* 12.7, 8.0 and 8.0, 4-H^b), 3.56 (1H, dd, *J* 8.0 and 8.0, 3-H), 3.69 (1H, ddd, *J* 13.9, 3.7 and 3.7, CH^aNH), 3.74 (1H, ddd, *J* 13.9, 5.3 and 3.7, CH^bNH), 4.47 (1H, m, 5-H), 7.21–7.29 (5H, m), 7.40–7.45 (3H, m) and 7.78–7.83 (2H, m); δ_C (67.8) 42.4 (4-CH_2), 43.0 (2-Me), 44.5 (1′-CH_2), 73.5 (3-CH), 75.0 (5-CH), 127.0, 127.5, 128.0, 128.5, 128.7 (Ph CH), 131.4, 138.4 (Ph C) and 167.6 (CO); *m*/*z* 296 (M^+, 33%), 251 (14), 160 (39), 147 (41), 120 (76), 106 (23), 105 (100), 91 (16) and 77 (98) (Found: M^+, 296.1512. $C_{18}H_{20}N_2O_2$ requires *M*, 296.1525) and ii) the (3*RS*,5*SR*)-*cis*-*isoxazolidine* **10** (250 mg, 11%), R_f 0.17, as a colourless solid, mp 83–85 °C (Found: C, 72.8; H, 6.8; N, 9.3), ν_{max}/cm^{-1} 3307 and 1641; δ_H (250) 2.38–2.44 (2H, m, 4-CH_2), 2.58 (3H, s, 2-Me), 3.44–3.50 (1H, m, 3-H), 3.61 (1H, ddd, *J* 13.0, 5.9 and 5.9, CH^aNH), 3.74 (1H, ddd, *J* 13.0, 5.9 and 3.6, CH^bNH), 4.44–4.49 (1H, m, 5-H), 6.93 (1H, br res, NH), 7.32–7.42 (8H, m) and 7.78–7.83 (2H, m); δ_C (67.8) 42.2 (4-CH_2), 42.7 (2-Me), 43.1 (1′-CH_2), 73.1 (3-CH), 75.7 (5-CH), 126.9, 127.5, 127.8, 128.5, 128.7 (Ph CH), 131.3, 138.6 (Ph C) and 167.6 (CO); *m*/*z* 296 (M^+, 3%), 147 (11), 120 (12), 106 (9), 105 (100), 91 (8) and 77 (46) (Found: M^+, 296.1526).

(+)-*trans*- and (−)-*cis*-6-(2-deoxy-3,5,-*O*-isopropylidene-1,2-isopropylidenedioxy-β-L-*xylo*-furanosyl)-2,3-dimethyl-1,2,5-oxadiazinane 12a and 13a

A solution of allylamine **11** (0.198 g, 3.48 mmol) and the *N*-methyl nitrone **1a** (0.318 g, 1.74 mmol) in toluene (30 ml) was refluxed for 10 h, then was cooled and evaporated. CC (EtOAc–hexane–Et_3N, 1:1:0.1) of the residue separated (i) the *trans*-1,2,5-*oxadiazinane* **12a** (213 mg, 36%), R_f 0.20, as a colourless solid, mp 71 °C (from ether–LP) (Found: C, 55.6; H, 8.4; N, 7.8. $C_{16}H_{28}N_2O_6$ requires C, 55.8; H, 8.2; N, 8.1%) $[\alpha]_D^{20}$ +10.4 (*c* 1.06, $CHCl_3$); ν_{max}/cm^{-1} 3320; δ_H (250) 0.88 (3H, d, *J* 6.3, 3-Me), 1.31 (3H, s), 1.33 (3H, s), 1.36 (3H, s), 1.41 (3H, s), 2.41 (1H, dqd, *J* 10.6, 6.3 and 3.0, 3-H), 2.60 (3H, s, 2-Me), 2.67 (1H, dd, *J* 13.7 and 10.6, 4-H^{ax}), 2.89 (1H, dd, *J* 13.7 and 3.0, 4-H^{eq}), 3.98 (1H, d, *J* 2.2), 4.01 (2H, app. d, *J* 2.5), 4.18 (1H, d, *J* 2.2), 4.52 (1H, s) and 4.66 (1H, s, 6-H); δ_C (67.8) 15.4 (3-Me), 18.4, 26.2, 27.1, 28.6 [all MeC(O)O], 43.5 (2-Me), 50.2 (4-CH_2), 59.6 (6′-CH_2), 61.6 (3-CH), 72.1, 73.1, 85.2 (all CHO), 88.9 (6-CH), 97.1, 112.0 and 112.5 (all C); *m*/*z* 344 (M^+, 18%), 183 (7), 171 (8), 155 (11), 136 (13), 126 (6), 115 (22), 83 (14), 74 (100), 69 (23), 58 (68), 43 (42) and 30 (20) (Found: M^+, 344.1945. $C_{16}H_{28}N_2O_6$ requires *M*, 344.1947) and (ii) the *cis*-1,2,5-*oxadiazinane* **13a** (62 mg, 10%), R_f 0.14, as a colourless solid, mp 83 °C (Found: C, 55.6; H, 8.5; N, 7.8%) $[\alpha]_D^{20}$ −65.5 (*c* 0.49, $CHCl_3$); ν_{max}/cm^{-1} 3320; δ_H (250) 1.13 and 1.17 (3H, d, *J* 6.3, 3-Me), 1.38 (3H, s), 1.40 (3H, s), 1.43 (3H, s), 1.45 (3H, s), 2.38 (1H, br s, NH), 2.56 and 2.57 (3H, s, 2-Me), 2.67 (1H, m, 4-H^{ax}), 2.75 (1H, br, 3-H), 2.81 (1H, dd, *J* 13.7 and 4.8, 4-H^{eq}), 4.05–4.14 (3H, m), 4.26 (1H, m), 4.61 (1H, s) and 4.74 (1H, s, 6-H); *m*/*z* 344 (M^+, 47%), 329 (8), 256 (10), 155 (16), 136 (17), 115 (32), 74 (100), 69 (29) and 58 (52) (Found: M^+, 344.1924).

(+)-*trans*- and (−)-*cis*-2-Benzyl-6-(2-deoxy-3,5-*O*-isopropylidene-1,2-isopropylidenedioxy-β-L-*xylo*-furanosyl)-3-methyl-1,2,5-oxadiazinane 12b and 13b

A solution of allylamine **11** (0.270 g, 5.17 mmol) and the *N*-benzyl nitrone **1b** (1.88 g, 5.17 mmol) in toluene (30 ml) was refluxed for 10 h then, was cooled and evaporated. CC (EtOAc–hexane–Et_3N, 1:1:0.1) of the residue separated (i) the *trans*-1,2,5-*oxadiazinane* **12b** (1.23 g, 56%), R_f 0.45, as a colourless solid, mp 98 °C (from ether–LP) (Found: C, 62.8; H, 7.7; N, 6.7. $C_{22}H_{32}N_2O_6$ requires C, 62.8; H, 7.7; N, 6.7%), $[\alpha]_D^{20}$ +74 (*c* 1, $CHCl_3$); ν_{max}/cm^{-1} 3300; δ_H (250) 1.02 (3H, d, *J* 5.7, 3-Me), 1.31 (3H, s), 1.40 (3H, s), 1.41 (3H, s), 1.42 (3H, s), 2.82 (1H, ddq, *J* 8.7, 8.7 and 5.7, 3-H), 2.83 (1H, dd, *J* 8.7 and 8.7, 4-H^{ax}), 3.00 (1H, app. d, *J* 8.7, 4-H^{eq}), 3.69 (1H, d, *J* 14.7, $PhCH^a$), 3.86 (1H, d, *J* 14.7, $PhCH^b$), 4.03 (1H, d, *J* 2.8), 4.05 (1H, d, *J* 1.9), 4.14 (1H, d, *J* 1.9), 4.16-4.19 (1H, m), 4.53 (1H, s), 4.73 (1H, s, 6-H), 7.23–7.32 (3H, m) and 7.38–7.45 (2H, m); δ_C (67.8) 15.9 (3-Me), 18.6, 26.3, 27.3, 28.8 [all *Me*C(O)O], 51.0 (4-CH_2), 58.8 (5′-CH_2), 59.5 (3-CH), 59.9 ($PhCH_2$), 72.5, 72.9, 84.9 (all CHO), 89.0 (6-CH), 97.1, 112.2, 112.6 (all C), 126.4, 127.8, 128.2 (all Ph CH) and 138.0 (Ph C); *m*/*z* 420 (M^+, 9%), 175 (20), 150 (29), 134 (12), 91 (100) and 59 (15) (Found: M^+, 420.2258. $C_{22}H_{32}N_2O_6$ requires *M*, 420.2260) and (ii) the *cis*-1,2,5-*oxadiazinane* **13b** (420 mg, 19%), R_f 0.58, as a colourless glass (Found: C, 62.4; H, 7.8; N, 6.3%) $[\alpha]_D^{20}$ −30.8 (*c* 1.01, $CHCl_3$); ν_{max}/cm^{-1} 3340; δ_H (250) 1.00 (3H, d, *J* 6.9, 3-Me), 1.38 (3H, s), 1.42 (9H, s), 2.82 (1H, dqd, *J* 10.1, 6.9 and 2.6, 3-H), 2.85 (1H, dd, *J* 13.1 and 10.1, 4-H^{ax}), 3.01 (1H, dd, *J* 13.1 and 2.6, 4-H^{eq}), 4.02–4.11 (4H, m), 4.21 (1H, d, *J* 13.1, $PhCH^a$), 4.23 (1H, d, *J* 13.1, $PhCH^b$), 4.50 (1H, s), 4.90 (1H, s, 6-H), 7.25–7.32 (3H, m) and 7.41–7.45 (2H, m); δ_C (67.8) 15.9 (3-Me), 18.7, 26.0, 27.4, 28.6 [all *Me*C(O)O], 50.8 (4-CH_2), 59.2 (5′-CH_2), 59.8 (3-CH), 60.1 ($PhCH_2$), 72.3, 72.9, 84.7 (all CHO), 88.4 (6-CH), 97.3, 112.4, 113.2 (all C), 127.7, 128.1, 128.2 (all Ph CH) and 138.1 (Ph C); *m*/*z* 420 (M^+, 14%), 175 (9), 150 (90), 134 (10) and 91 (100) (Found: M^+, 420.2246).

trans-2,3-Dimethyl-6-phenyl-1,2,5-oxadiazinane 24

(i) A solution of the nitrone **8** (100 mg, 0.74 mmol) and allylamine **11** (42 mg, 0.74 mmol) in deuteriochloroform (1 ml) was stirred at ambient temperature for 7 days (NMR monitoring), then evaporated to leave the oxadiazinane **24** (142 mg, 100%) as a pale yellow oil which exhibited spectral data identical to the sample described below in (iii) and which was pure according to NMR analysis (see below).

(ii) A solution of the nitrone **8** (100 mg, 0.74 mmol) and allylamine **11** (42 mg, 0.74 mmol) in deuteriochloroform (1 ml) was stirred at 45 °C for 36 h (NMR monitoring), then evaporated to leave the oxadiazinane **24** (142 mg, 100%) as a pale yellow oil which exhibited spectral data identical to the sample below and which was pure according to NMR analysis (see below).

(iii) A solution of the benzaldehyde nitrone **8** (1.0 g, 7.4 mmol) and allylamine **11** (0.55 ml, 7.4 mmol) in toluene (30 ml) was refluxed for 17 h, then cooled and evaporated. CC (EtOAc–hexane, 1:2) of the residue gave the *oxadiazinane* **24** (1.14 g,

80%), R_f 0.48, as a pale yellow oil; ν_{max}/cm^{-1} 3301 and 915; δ_H (400) 1.00 (3H, d, *J* 6.3, 3-Me), 2.49 (1H, dqd, *J* 10.4, 6.3 and 4.1, 3-H^{ax}), 2.71 (3H, s, 2-Me), 2.87 (1H, dd, *J* 13.8 and 10.4, 4-H^{ax}), 3.05 (1H, dd, *J* 13.8 and 4.1, 4-H^{eq}), 5.53 (1H, s, 6-H^{ax}), 7.19–7.35 (3H, m) and 7.41–7.50 (2H, m); δ_C (100) 16.3 (3-Me), 44.3 (2-Me), 51.8 (4-CH$_2$), 62.4 (3-CH), 90.0 (6-CH), 126.3, 128.6, 128.8 (all Ph CH) and 139.1 (Ph C); *m*/*z* 192 (M$^+$, 59%), 175 (9), 146 (30), 118 (54), 106 (12), 105 (36), 91 (40), 77 (38) and 74 (100) (Found: M$^+$, 192.1234. $C_{11}H_{16}N_2O$ requires *M*, 192.1263).

NOE data: 2-Me ~ 3-Me (1.7%); 3-Me ~ 4-H^{ax} (1.0%); 3-H^{ax} ~ 4-H^{eq} (3.5%); 4-H^{ax} ~ 6-H^{ax} (3.0%); all other enhancements were < 1%.

The crude reaction mixture from the latter experiment in toluene also contained approximately 20% of the imine **26**, formed from benzaldehyde and allylamine, identified by δ_H (250) 4.20 (2H, d, *J* 6.1, C*H*$_2$CH=), 5.12 (1H, d, *J* 10.6, =CH^c), 5.23 (1H, d, *J* 16.0, =CH′), 6.04 (1H, ddt, *J* 16.0, 10.6 and 6.1, =CH) and 8.18 (1H, s, CHN).

trans-5-Deuterio-3-deuteriomethyl-2-methyl-6-phenyl-1,2,5-oxadiazinane 29

Allylamine **11** (2.0 g, 35 mmol) was stirred in deuterium oxide (25 ml) for 1 h, then the solution was treated with solid sodium hydroxide (3.0 g) and, after complete dissolution of the solid, was extracted with chloroform (2 × 20 ml). The combined extracts were dried and filtered and the filtrate was added to the benzaldehyde nitrone **8** (1.60 g, 11.7 mmol). NMR analysis showed approximately 50% deuterium incorporation at the amino function. The resulting solution was refluxed for 5 h, then was cooled and evaporated. Last traces of allylamine were removed under high vacuum to leave the deuteriated *oxadiazinane* **29** (2.27 g, 99% based on the nitrone). Approximately 50% deuterium incorporation was evident from δ_H (250) 0.90–1.05 (2H, m, 3-CH$_2$D) and δ_C (67.8) 15.1 (t, *J* 19.5, 3-CH$_2$D); *m*/*z* M$^+$, 194.1379. $C_{11}H_{14}D_2N_2O$ requires *M*, 194.1388. There was no other evidence for deuterium incorporation.

trans-2,3-Dimethyl-5-(4-nitrobenzoyl)-6-phenyl-1,2,5-oxadiazinane 30

A solution of 4-nitrobenzoyl chloride (0.96 g, 5.2 mmol) in dichloromethane (20 ml) was slowly added to a stirred solution of the oxadiazinane **24** (1.00 g, 5.2 mmol) and diisopropylethylamine (0.67 g, 5.2 mmol) in dichloromethane (50 ml) cooled in an ice bath. After 1 h, the solvent was evaporated. CC (EtOAc–LP, 2:1) of the residue and collection of the fraction with R_f 0.54 gave the *benzoyloxadiazinane* **30** (1.61 g, 91%) as yellow crystals, mp 171–173 °C (from ether–LP) (Found: C, 63.1; H, 5.8; N, 12.5. $C_{18}H_{19}N_3O_4$ requires C, 63.3; H, 5.6; N, 12.3%); ν_{max}(KBr)/cm^{-1} 1630 and 931; δ_H (400; 63 °C, sealed tube) 1.20 (3H, d, *J* 6.3, 3-Me), 2.59 (3H, s, 2-Me), 2.92 (1H, br m, 4-H^{ax}), 3.64 (1H, dd, *J* 12.8 and 4.1, 4-H^{eq}), 4.00 (1H, br m, 3-H), 6.52 (1H, br s, 6-H), 7.32–7.39 (5H, m), 7.59 (2H, d, *J* 8.6) and 8.20 (2H, d, *J* 8.6); δ_C (100; 63 °C, sealed tube) 10.5 (br, 3-Me), 42.4 (2-Me), 45.9 (br, 4-CH$_2$), 58.3 (br, 3-CH), 86.8 (br, 6-CH), 123.9, 126.5, 128.2, 128.5, 128.8 (all Ph CH), 137.6, 141.8, 148.9 (all Ph C) and 169.5 (CO); *m*/*z* 341 (M$^+$, 3%), 224 (33), 223 (100), 175 (51), 118 (11), 106 (14), 105 (20), 91 (16) and 77 (19) (Found: M$^+$, 341.1371. $C_{18}H_{19}N_3O_4$ requires *M*, 341.1375).

trans-3-Benzyl-2-methyl-6-phenyl-1,2,5-oxadiazinane 33

A solution of the nitrone **8** (0.31 g, 2.3 mmol) and (*E*)-cinnamylamine[35] **32** (0.31 g, 2.3 mmol) in chloroform (50 ml) was refluxed for 192 h, then was cooled and evaporated. Rapid CC (EtOAc) separated the *oxadiazinane* **33** (0.25 g, 40%) as a pale yellow oil; ν_{max}/cm^{-1} 3600–3200, 1958, 1644 and 911; δ_H (250) 2.45–2.90 (5H, m), 2.75 (3H, s, 2-Me), 6.50 (1H, s, 6-H) and 7.10–7.50 (10H, m); δ_C (67.5) 36.8 (4-CH$_2$), 44.3 (2-Me), 62.7 (Ph*C*H$_2$), 67.2 (3-CH), 89.2 (6-CH), 126.2, 127.2, 128.0, 128.3, 129.1, 130.3 (all Ph CH), 130.6 and 131.2 (both Ph C); *m*/*z* 341 (M$^+$, 3%), 224 (33), 223 (100), 175 (51), 118 (11), 106 (14), 105 (20), 91 (16) and 77 (19) (Found: M$^+$, 341.1371. $C_{18}H_{19}N_3O_4$ requires *M*, 341.1375).

In the crude product, the imine **34** was present to an extent of *ca*. 40%; δ_H (80) 4.15 (2H, d, *J* 5, NCH$_2$), 6.20 (1H, dd, *J* 16 and 5, =CH), 6.45 (1H, d, *J* 16, =CH), 7.60–7.70 (2H, m) and 8.13 (1H, s, =CHN).

(3*RS*,4*RS*,6*RS*)- and (3*RS*,4*SR*,6*RS*)-2,3,4-Trimethyl-4-(4-methylpent-3-enyl)-6-phenyl-1,2,5-oxadiazinane 38 and 39

A solution of nitrone **8** (0.96 g, 7.12 mmol) and linalylamine[36] **37** (1.09 g, 7.12 mmol) in toluene (50 ml) was refluxed for 3 days, then was cooled and evaporated. CC (ether–pentane, 1:15) of the residue separated (i) the (*3RS,4RS,6RS*)-*oxadiazinane* **38** (0.97 g, 47%), R_f 0.12, as a colourless oil; ν_{max}/cm^{-1} 3310 and 1607; δ_H (400) 0.96 (3H, d, *J* 6.6, 3-Me), 1.28 (3H, s, 4-Me), 1.25–1.35 (1H, m, 1′-H^a), 1.54–1.61 (1H, m, 1′-H^b), 1.61 (3H, s, MeC=), 1.67 (3H, s, MeC=), 2.12–2.32 (2H, m, 2′-CH$_2$), 2.41 (1H, q, *J* 6.6, 3-H), 2.65 (3H, s, 2-Me), 5.11 (1H, tt, *J* 7.1 and 1.0, 3′-H), 5.70 (1H, s, 6-H), 7.25–7.36 (3H, m) and 7.46–7.48 (2H, m); δ_C (100) 13.1 (4-Me), 17.7 (MeC=), 18.0 (1′-CH$_2$), 21.2 (3-Me), 25.7 (MeC=), 40.4 (2′-CH$_2$), 44.2 (2-Me), 54.5 (4-C), 69.2 (3-CH), 85.1 (6-CH), 124.4 (3′-CH:), 126.0, 128.3 (both Ph CH), 131.8 (4′-C=) and 139.2 (Ph C); *m*/*z* 288 (M$^+$, 6%), 215 (20), 146 (100), 91 (14) and 77 (9) (Found: M$^+$, 288.2203. $C_{18}H_{28}N_2O$ requires *M*, 288.2202), (ii) the (*3RS,4SR,6RS*)-*oxadiazinane* **39** (0.46 g, 22%), R_f 0.21, as a colourless oil; ν_{max}/cm^{-1} 3310 and 1607; δ_H (400) 0.93 (3H, d, *J* 6.7, 3-Me), 1.08 (3H, s, 4-Me), 1.20–1.30 (1H, m, 1′-H^a), 1.35–1.44 (1H, m, 1′-H^b), 1.63 (3H, s, MeC=), 1.69 (3H, s, MeC=), 1.94–2.01 (1H, m, 2′-H), 2.22–2.26 (1H, m, 2′-H), 2.37 (1H, q, *J* 6.7, 3-H), 2.65 (3H, s, 2-Me), 5.20 (1H, tt, *J* 7.1 and 1.0, 3′-H), 5.61 (1H, s, 6-H), 7.25–7.35 (3H, m) and 7.41–7.47 (2H, m); δ_C (100) 13.1 (4-Me), 17.7 (*Me*C=), 21.8 (1′-CH$_2$), 25.2 (3-Me), 25.8 (MeC=), 29.9 (2′-CH$_2$), 41.2 (2-Me), 54.2 (4-C), 72.0 (3-CH), 85.0 (6-CH), 124.4 (3′-CH=), 126.0, 128.2, 128.3 (all Ph CH), 131.1 (4′-C=) and 139.2 (Ph C); *m*/*z* 288 (M$^+$, 7%), 215 (20), 146 (100), 91 (21) and 77 (15) (Found: M$^+$, 288.2207) and (iii) the *imine* **40** (0.16 g, 9%), R_f 0.46, as a colourless oil; ν_{max}/cm^{-1} 1693; δ_H (250) 1.33 (3H, s, 3-Me), 1.58 (3H, s, MeC=), 1.66 (3H, s, MeC=), 1.71–1.75 (2H, m, 4-CH$_2$), 2.04 (2H, q, *J* 7.5, 5-CH$_2$), 5.16 (1H, dd, *J* 17.4 and 1.4, 1-H′), 5.20 (1H, dd, *J* 10.9 and 1.4, 1-H^c), 5.92 (1H, dd, *J* 17.4 and 10.9, 2-H), 5.12 (1H, m, 6-H), 7.37–7.42 (3H, m), 7.73–7.79 (2H, m) and 8.24 (1H, s, NCH); δ_C (100) 17.6 (MeC=), 22.8 (4-CH$_2$), 24.1 (3-Me), 25.6 (MeC=), 42.3 (5-CH$_2$), 63.9 (3-C), 113.7 (1-CH$_2$), 124.7 (6-CH=), 127.9, 128.4, 130.2 (all PhCH), 131.1 (C=),137.0 (Ph C), 144.1 (2-CH) and 157.5 (CHN); *m*/*z* 241 (M$^+$, 12%), 226 (20), 159 (100), 118 (15), 106 (18), 104 (61), 91 (13), 81 (15) and 77 (10) (Found: M$^+$, 241.1879. $C_{17}H_{23}N$ requires *M*, 241.1830).

NOE data (3*RS*,4*RS*,6*RS*)-**38**: 2-Me ~ 3-H^{ax} (2%); 3-Me ~ 4-Me^{ax} (9%); 4-Me^{ax} ~ 3′-:CH (16%); 4-Me^{ax} ~ 6-H^{ax} (4%); all other enhancements were <1%. (3RS, 4SR, 6RS)-**39**: 3-H^{ax} ~ 4-Me^{eq} (13%); 6-H^{ax} ~ 1′-CH$_2$ (11%); 6-H^{ax} ~ 2′-CH$_2$ (10%); 3-H^{ax} ~ Ph (3%); all other enhancements were ⩽1%.

trans-2,3,5-Trimethyl-6-phenyl-1,2,5-oxadiazinane 44a

A solution of the nitrone **8** (1.90 g, 14.1 mmol) and *N*-methylallylamine **43a** (1.00 g, 14.1 mmol) in chloroform (5 ml) was stirred and heated at 60 °C for 20 h, then was cooled and evaporated to leave the oxadiazinane **44a** (2.76 g, 95%) as a colourless oil which was essentially a single compound according to ^{1}H NMR analysis. Attempted CC resulted in considerable loss of material, although TLC analysis (EtOAc–LP, 1:1) indicated a single product with R_f 0.27. The product showed ν_{max}/cm^{-1} 918; δ_H (400) 1.00 (3H, d, *J* 6.2, 3-Me), 1.98 (3H, s, 5-Me), 2.40 (1H, dd, *J* 11.0 and 10.7, 4-H^{ax}), 2.66 (3H, s, 2-Me), 2.90 (1H, dqd, *J* 10.7, 6.2 and 2.8, 3-H^{ax}), 2.94 (1H, dd, *J* 11.0 and 2.8,

4-H^{eq}), 4.81 (1H, s, 6-H), 7.29–7.35 (3H, m, Ph) and 7.44–7.47 (2H, m, Ph); δ_C (100) 16.1 (3-Me), 38.8 (5-Me), 43.2 (2-Me), 59.3 (3-CH), 61.4 (4-CH_2), 97.3 (6-CH), 127.8, 128.1, 128.7 (all Ph CH) and 137.4 (Ph C); *m*/*z* 206 (M^+, 28%), 132 (100), 118 (73), 91 (12) and 77 (19) (Found: M^+, 206.1456. $C_{12}H_{18}N_2O$ requires *M*, 206.1419).

trans-2,3-Dimethyl-6-phenyl-5-(prop-2-enyl)-1,2,5-oxadiazinane 44b

The nitrone **8** (3.00 g, 22.2 mmol) and diallylamine **43b** (2.16 g, 22.2 mmol) were refluxed together in chloroform (100 ml) for 72 h. Evaporation of the cooled solution left the *N-allyloxadiazinane* **44b** (5.16 g, 100%) as a colourless oil; ν_{max}/cm^{-1} 1642 and 916; δ_H (400) 1.00 (3H, d, *J* 6.4, 3-Me), 2.35 (1H, dd, *J* 11.9 and 10.4, 4-H^{ax}), 2.60 (1H, dd, *J* 13.8 and 6.5, 1′-H^a), 2.67 (3H, s, 2-Me), 2.88 (1H, dqd, *J* 10.4, 6.4 and 2.9, 3-H^{ax}), 3.03 (1H, ddt, *J* 13.8, 5.5 and 1.6, 1′-H^b), 3.05 (1H, dd, *J* 11.9 and 2.9, 4-H^{eq}), 5.06 (1H, br d, *J* 10.0, 3′-H^c), 5.08 (1H, s, 6-H), 5.09 (1H, ddd, *J* 17.1, 3.0 and 1.6, 3′-H′), 5.72 (1H, dddd, *J* 17.1, 10.0, 6.5 and 5.5, 2′-H), 7.27–7.36 (3H, m, Ph) and 7.46–7.50 (2H, m, Ph); δ_C (100) 16.3 (3-Me), 43.5 (2-Me), 53.5 (4-CH_2), 57.5 (1′-CH_2), 59.2 (3-CH), 96.1 (6-CH), 117.2 (3′-CH_2), 128.0, 128.3, 128.8 (all Ph CH), 135.0 (2′-CH) and 137.6 (Ph C); *m*/*z* 232 (M^+, 12%), 186 (27), 159 (51), 158 (66), 144 (54), 118 (100), and 91 (62) (Found: M^+, 232.1597. $C_{14}H_{20}N_2O$ requires *M*, 232.1576).

trans-5-Benzyl-2,3-dimethyl-6-phenyl-1,2,5-oxadiazinane 44c

A solution of the nitrone **8** (100 mg, 0.74 mmol) and *N*-benzylallylamine[41] **43c** (108 mg, 0.74 mmol) in chloroform (2 ml) was kept at 60 °C for 48 h, then was cooled and evaporated to leave essentially pure product, according to ^{1}H NMR analysis, as a viscous yellow oil in 95% yield. CC (EtOAc–LP, 1:5) and collection of the fraction with R_f 0.29, gave the *N-benzyloxadiazinane* **44c** (198 mg, 56%) as a colourless solid, mp 63–64 °C (Found: C, 76.8; H, 7.9. $C_{18}H_{22}N_2O$ requires C, 76.7; H, 7.9%); ν_{max}/cm^{-1} 917; δ_H (400) 0.95 (3H, d, *J* 6.3, 3-Me), 2.32 (1H, dd, *J* 12.0 and 10.4, 4-H^{ax}), 2.69 (3H, s, 2-Me), 2.86 (1H, dd, *J* 12.0 and 2.0, 4-H^{eq}), 2.90 (1H, dqd, *J* 10.4, 6.3 and 2.0, 3-H), 3.06 (1H, d, *J* 13.5, 1′-H^a), 3.61 (1H, d, *J* 13.5, 1′-H^b), 5.20 (1H, s, 6-H), 7.19–7.61 (10H, m, Ph); δ_C (100) 16.3 (3-Me), 43.6 (2-Me), 54.5 (1′-CH_2), 57.5 (4-CH_2), 59.2 (3-CH), 96.4 (6-CH), 126.9, 128.1, 128.3, 128.6, 128.7, 129.0 (all Ph CH), 137.9 and 138.7 (both Ph C); *m*/*z* 282 (M^+, 21%), 265 (4), 236 (6), 209 (18), 208 (13), 194 (11), 189 (9), 146 (7), 118 (91), 105 (8), 91 (100) and 77 (9) (Found: M^+, 282.1738. $C_{18}H_{22}N_2O$ requires *M*, 282.1732).

trans-3-Benzyl-2,5-dimethyl-6-phenyl-1,2,5-oxadiazinane 46a

The nitrone **8** (208 mg, 1.54 mmol) and (*E*)-*N*-methylcinnamylamine[41] **45a** (200 mg, 1.54 mmol) were refluxed in toluene (20 ml) for 48 h. The cooled solution was evaporated and the residue separated by CC (ether) to give the *3-benzyloxadiazinane* **46a** (265 mg, 65%) as an oil, R_f 0.60; ν_{max}/cm^{-1} 900; δ_H (250) 1.91 (3H, s, 5-Me), 2.34 (1H, dd, *J* 11.7 and 10.3, 4-H^{ax}), 2.79 (3H, s, 2-Me), 2.80 (1H, m, 4-H^{eq}), 3.15 (1H, m, 3-H), 3.16 (1H, m, 1′-H^a), 3.24 (1H, m, 1′-H^b), 4.76 (1H, s, 6-H) and 7.20–7.55 (10H, m, Ph); δ_C (67.8) 37.2 (PhCH$_2$), 39.2 (5-Me), 44.0 (2-Me), 59.2 (4-CH_2), 65.4 (3-CH), 97.7 (6-CH), 128.1, 128.3, 128.4, 128.5, 128.9, 129.1 (all Ph CH), 137.6 and 138.4 (both Ph C); *m*/*z* 282 (M^+, 41%), 265 (7), 191 (25), 175 (100), 132 (99), 118 (63) and 91 (62) (Found: M^+, 282.1728. $C_{18}H_{22}N_2O$ requires *M*, 282.1732).

trans-3-Butyl-2,5-dimethyl-6-phenyl-1,2,5-oxadiazinane 46b

The nitrone **8** (82 mg, 0.61 mmol) and (*E*)-*N*-methylhex-2-enamine[42] **45b** (69 mg, 0.61 mmol) were refluxed together in toluene (2 ml) for 21 h. Evaporation of the cooled solution and CC (EtOAc–LP, 1:4) gave the *3-butyloxadiazinane* **46b** (68 mg, 45%) as a pale yellow oil; ν_{max}/cm^{-1} 936; δ_H (400) 0.92 (3H, t, *J* 7.0, 4′-Me), 1.25–1.40 (6H, m, 1′-, 2′- and 3′-CH_2), 2.00 (3H, s, 5-Me), 2.40 (1H, dd, *J* 12.8 and 11.3, 4-H^{ax}), 2.69 (3H, s, 2-Me), 2.84 (1H, m, 3-H), 3.09 (1H, dd, *J* 11.3 and 2.6, 4-H^{eq}), 4.76 (1H, s, 6-H), 7.32–7.36 (3H, m, Ph) and 7.44–7.47 (2H, m, Ph); δ_C (100) 13.9 (4′-Me), 23.0, 27.4, 30.1 (all CH_2), 39.3 (5-Me), 43.5 (2-Me), 59.4 (4-CH_2), 64.4 (3-CH), 97.6 (6-CH), 128.0, 128.2, 128.4 (Ph CH) and 137.5 (Ph C); *m*/*z* 248 (M^+, 82%), 120 (21), 119 (47), 118 (100), 105 (19), 91 (29), 77 (28) and 72 (14) (Found: M^+, 248.1877. $C_{15}H_{24}N_2O$ requires *M*, 248.1889).

trans-3-Ethyl-2,5-dimethyl-6-phenyl-1,2,5-oxadiazinane 46c

The nitrone **8** (310 mg, 2.3 mmol) and (*E*)-*N*-methylcrotylamine[42] **45c** (195 mg, 2.30 mmol) were refluxed together in benzene (5 ml) for 120 h. Evaporation of the cooled solution and CC (ether) gave the *3-ethyloxadiazinane* **46c** (480 mg, 95%) as a pale yellow oil, R_f 0.38; ν_{max}/cm^{-1} 933; δ_H (400) 0.96 (3H, t, *J* 7.5, 2′-Me), 1.29–1.40 (1H, m, 1′-H), 1.53–1.63 (1H, m, 1′-H), 2.01 (3H, s, 5-Me), 2.40 (1H, dd, *J* 11.7 and 11.7, 4-H^{ax}), 2.70 (3H, s, 2-Me), 2.75–2.79 (1H, m, 3-H), 3.10 (1H, dd, *J* 11.7 and 2.6, 4-H^{eq}), 4.76 (1H, s, 6-H), 7.33–7.38 (3H, m, Ph) and 7.45–7.49 (2H, m, Ph); δ_C (100) 9.7 (2′-Me), 23.4 (1′-CH_2), 39.4 (5-Me), 43.6 (2-Me), 59.0 (4-CH_2), 65.6 (3-CH), 97.7 (6-CH), 128.0, 128.1, 128.5 (Ph CH) and 138.6 (Ph C); *m*/*z* 220 (M^+, 33%), 133 (40), 132 (100), 120 (10), 119 (20), 118 (48), 105 (16), 91 (13), 77 (17) and 72 (5) (Found: M^+, 220.1579. $C_{13}H_{20}N_2O$ requires *M*, 220.1576).

(3*RS*,4*RS*,6*RS*)-2,3,4,5-Tetramethyl-6-phenyl-1,2,5-oxadiazinane 48a

A solution of the nitrone **8** (263 mg, 1.96 mmol) and *N*-methylbut-3-en-2-amine[42] **47a** (166 mg, 1.96 mmol) in benzene (20 ml) was stirred and refluxed for 20 h, then was cooled and evaporated. CC (ether) separated the *tetramethyloxadiazinane* **48a** (408 mg, 95%) as an oil, R_f 0.34; ν_{max}/cm^{-1} 930; δ_H (400) 1.06 (3H, d, *J* 6.3, 3-Me), 1.20 (3H, d, *J* 6.2, 4-Me), 1.93 (3H, s, 5-Me), 2.53–2.57 (2H, m, 3- and 4-H), 2.68 (3H, s, 2-Me), 5.04 (1H, s, 6-H), 7.32-7.38 (3H, m, Ph) and 7.45–7.49 (2H, m, Ph) δ_C (100) 15.3, 16.5 (3- and 4-Me), 34.8 (5-Me), 44.1 (2-Me), 63.0 (4-CH), 65.1 (3-CH), 97.0 (6-CH), 128.4, 128.7, 129.1 (Ph CH) and 137.7 (Ph C) (Found: M^+, 220.1561. $C_{13}H_{20}N_2O$ requires *M*, 220.1576).

(3*RS*,4*RS*,6*RS*)-5-Butyl-2,3-dimethyl-4,6-diphenyl-1,2,5-oxadiazinane 48b

A solution of the nitrone **8** (0.30 g, 2.20 mmol) and *N*-butyl-1-phenylprop-2-enamine[43] **47b** (0.41 g, 2.20 mmol) in toluene (20 ml) was stirred and refluxed for 17 h, then was cooled and evaporated. CC (EtOAc–LP, 1:2) separated the *4-phenyloxadiazinane* **48b** (0.632 g, 89%) as an oil, R_f 0.30; ν_{max}/cm^{-1} 917; δ_H (400) 0.50 (3H, t, *J* 7.2, 4′-Me), 0.70 (2H, m, 3′-CH_2), 0.81 (3H, d, *J* 6.4, 3-Me), 0.90–0.95 (1H, m, 2′-H^a), 1.00–1.10 (1H, m, 2′-H^b), 2.09 (2H, m, 1′-CH_2), 2.68 (3H, s, 2-Me), 2.84 (1H, dq, *J* 9.0 and 6.4, 3-H), 3.56 (1H, d, *J* 9.0, 4-H), 5.38 (1H, s, 6-H), 7.28–7.40 (6H, m, Ph), 7.43–7.49 (2H, m, Ph) and 7.55–7.63 (2H, m, Ph); δ_C (100) 13.6 (4′-Me), 14.9 (3-Me), 20.3, 25.3 (2′- and 3′-CH_2), 43.9 (2-Me), 48.3 (1′-CH_2), 66.7 (3-H), 70.1 (4-H), 95.1 (6-H), 127.5, 128.2, 128.3, 128.6, 129.1, 129.2 (all Ph CH), 138.3 and 140.7 (Ph C); *m*/*z* 324 (M^+, 35%), 307 (13), 251 (65), 194 (32), 118 (100), 91 (57) and 77 (34) (Found: M^+, 324.2172. $C_{21}H_{28}N_2O$ requires *M*, 324.2202).

NOE data: 3-Me ~ 4-H^{ax} (9%); 4-H^{ax} ~ 1′-CH_2 (5%); 1′-CH_2 ~ 6-H^{ax} (5%); 3-H^{ax} ~ Ph (δ_H 7.43–7.49) (16%).

2,3,3,5-Tetramethyl-6-phenyl-1,2,5-oxadiazinane 50

The nitrone **8** (79 mg, 0.58 mmol) and *N*,2-dimethylprop-2-

enamine[42] **49** (50 mg, 0.58 mmol) were heated together at 60 °C for 16 h in chloroform (2 ml). The cooled solution was evaporated to leave the 3,3-*dimethyloxadiazinane* **50** (120 mg, 93%) as a colourless oil, consisting of a single component according to ^{1}H NMR and TLC analysis [R_f 0.36 (EtOAc–LP, 1:8)], which showed ν_{max}/cm^{-1} 941; δ_H (270) 1.05 (3H, s, 3-Me), 1.40 (3H, s, 3-Me), 1.91 (3H, s, 5-Me), 2.34 (1H, d, *J* 10.9, 4-H^a), 2.54 (3H, s, 2-Me), 2.75 (1H, d, *J* 10.9, 4-H^b), 4.58 (1H, s, 6-H), 7.26–7.37 (3H, m, Ph) and 7.48–7.52 (2H, m, Ph); δ_C (100) 15.7, 25.3 (both 3-Me), 37.7 (5-Me), 40.3 (2-Me), 67.4 (4-CH_2), 99.3 (6-CH), 128.4, 128.5, 129.3 (Ph CH) and 138.0 (Ph C); *m*/*z* 220 (M$^+$, 40%), 174 (6), 133 (57), 119 (48), 118 (100), 91 (16) and 77 (20) (Found: M$^+$, 220.1600. $C_{13}H_{20}N_2O$ requires *M*, 220.1576).

trans-3,5-Dibenzyl-2-methyl-6-phenyl-1,2,5-oxadiazinane 52

The nitrone **8** (0.84 g, 6.25 mmol) and *N*-benzyl-(*E*)-cinnamylamine[41] **51** (1.40 g, 6.25 mmol) were heated together in chloroform (2 ml) in a sealed tube at 110 °C for 120 h. Evaporation of the cooled solution followed by CC (ether–LP, 1:8) separated the *dibenzyloxadiazinane* **52** (0.27 g, 12%) as a yellow oil, R_f 0.19; ν_{max}/cm^{-1} 910; δ_H (400) 2.18 (3H, s, 2-Me), 2.46 (1H, dd, *J* 9.3 and 8.6, 4-H^{eq}), 2.74 (1H, dd, *J* 13.1 and 8.6, 4-H^{ax}), 2.87 (1H, m, 3-H), 2.98 (1H, dd, *J* 9.2 and 4.4, 1′-H^a), 3.01 (1H, dd, *J* 9.2 and 4.4, 1′-H^b), 3.09 (1H, d, *J* 13.5, NCH^a), 3.63 (1H, s, 6-H), 3.69 (1H, d, *J* 13.5, NCH^b), 7.15–7.25 (9H, m, Ph), 7.30–7.40 (4H, m, Ph) and 7.50–7.60 (2H, m, Ph); δ_C (100) 38.2 (2-Me), 41.4 (4-CH_2), 55.9, 56.4 (both Ph*C*H$_2$), 65.5 (3-CH), 91.6 (6-CH), 125.7, 126.6, 128.0, 128.2, 128.5, 129.2, 129.3 (all Ph CH), 139.2, 139.5 and 140.6 (all Ph C); *m*/*z* 341 (M$^+$, 9%), 265 (17), 251 (100) and 91 (98) (Found: M$^+$ − 17, 341.2008. $C_{24}H_{25}N_2$ requires *M*, 341.2018).

1,4-Diaza-9-oxa-2,4,8,8-tetramethylbicyclo[3.3.1]nonane 54

5,5-Dimethyl-Δ′-pyrroline *N*-oxide **53** (75 mg, 0.66 mmol) and *N*-methylallylamine **43a** (47 mg, 0.66 mmol) were heated in deuteriochloroform (1.5 ml) at 60 °C for 72 h. ^{1}H NMR analysis showed a 75% yield of the product **54**, together with decomposition products. Attempted purification by CC resulted in decomposition.

An identical solution was stored in a sealed NMR tube at ambient temperature for approximately 2 months, when ^{1}H NMR analysis showed complete conversion into the *bicyclononane* **54** (≈ 100%), as an oil which showed ν_{max}/cm^{-1} 920; δ_H (400) 1.04 (3H, s, 8-Me^a), 1.17 (3H, d, *J* 6.5, 2-Me), 1.23 (1H, ddd, *J* 8.4, 8.4 and 1.8, 7-H^a), 1.33 (3H, s, 8-Me^b), 1.54 (1H, ddd, *J* 8.4, 8.4 and 1.8, 7-H^b), 1.98–2.03 (2H, m, 6-CH_2), 2.35 (3H, s, 4-Me), 2.41 (1H, dd, *J* 10.7 and 9.2, 3-H^a), 2.68 (1H, dd, *J* 10.7 and 4.9, 3-H^b), 3.33 (1H, m, 2-H) and 4.05 (1H, d, *J* 2.3, 5–H); δ_C (100) 22.3, 24.4, 24.8 (all Me), 26.0, 27.6 (6- and 7-CH_2), 43.3 (4-Me), 51.5 (3-CH_2), 53.1 (2-CH), 56.1 (8-C) and 85.0 (5-CH); *m*/*z* 184 (M$^+$, 18%), 167 (38), 125 (16), 112 (20), 111 (29), 110 (21), 99 (18), 98 (75), 96 (21), 85 (22), 84 (91), 82 (29), 81 (42), 70 (45), 69 (23), 56 (32), 55 (34), 44 (55) and 42 (100) (Found: M$^+$, 184.1568. $C_{10}H_{20}N_2O$ requires *M*, 184.1575).

trans-5-Benzyl-3-deuteriomethyl-2-methyl-6-phenyl-1,2,5-oxadiazinane 56

N-Benzylallylamine **43c** (2.00 g, 13.6 mmol) was stirred in deuterium oxide (50 ml) for 12 h, and then the solution was extracted with ether (3 × 50 ml). The combined organic extracts were dried and evaporated and the residue distilled to give the *N*-deuterio derivative **55** (1.70 g, 85%); δ_H (250) 3.16 (2H, dt, *J* 7 and 1, C*H*$_2$CH=), 3.56 (2H, s, PhC*H*$_2$), 5.07 (1H, ddd, *J* 10, 2 and 1, =CH^c), 5.14 (1H, ddd, *J* 17, 2 and 1, =CH^t), 5.87 (1H, ddd, *J* 17, 10 and 7, C*H*=CH$_2$) and 7.12–7.28 (5H, m, Ph); *m*/*z* 148 (M$^+$, 5%), 91 (100) and 77 (11). The ^{1}H NMR data showed deuterium incorporation of 83%.

A solution of the foregoing *N*-deuterioamine **55** (276 mg, 1.86 mmol) and the nitrone **8** (252 mg, 1.86 mmol) in deuteriochloroform (2 ml) was kept at 60 °C for 48 h, then was cooled and evaporated. ^{1}H NMR analysis showed complete and clean conversion into the expected deuteriated and non-deuteriated oxadiazinanes **56** and **44c**. The signals due to the minor, non-deuteriated product **44c** were identical to those displayed by the previously characterized material (see above). The *major*, *deuteriated product* **56** showed data which were also identical to those of the foregoing sample, except ν_{max}/cm^{-1} 2196; δ_H (400) 0.95 (2H, d, *J* 6.3, 3-CH_2D) and 2.87–2.93 (1H, m, 3-H); δ_D (250; $CDCl_3$ as solvent and standard) 0.95 (br s, 3-CH_2D); δ_C (100) 15.7 (t, *J* 19.2, 3-CH_2D), 43.3 (2-Me), 54.1 (1′-CH_2), 57.1 (4-CH_2), 58.6 (3-CH), 96.0 (6-CH), 126.7, 127.8, 128.0, 128.2, 128.3, 128.6 (all Ph CH), 137.7 and 138.4 (both Ph C); *m*/*z* 283 (M$^+$, 12%), 266 (14), 209 (11), 190 (33), 118 (59), 105 (16), 91 (100) and 77 (15) (Found: M$^+$, 283.1800. $C_{18}H_{21}DN_2O$ requires *M*, 283.1795).

The ^{1}H and ^{13}C NMR data showed no evidence of deuterium incorporation at any other site in the product.

trans-5-(4-Methoxybenzyl)-2,3-dimethyl-6-phenyl-1,2,5-oxadiazinane 58a

A solution of the nitrone **8** (1.41 g, 10.5 mmol) and (4-methoxybenzyl)allylamine[41] **57a** (1.86 g, 10.5 mmol) in toluene (50 ml) was stirred and refluxed for 53 h, then was cooled and evaporated. Crystallization of the product from MeOH–CH_2Cl_2–LP, (2:1:1) gave the *oxadiazinane* **58a** (2.84 g, 87%) as a colourless solid, mp 139–141 °C (Found: C, 72.9; H, 7.8; N, 8.9. $C_{19}H_{24}N_2O_2$ requires 73.0; H, 7.8; N, 9.0%); ν_{max}/cm^{-1} 905; δ_H (400) 0.95 (3H, d, *J* 6.2, 3-Me), 2.28 (1H, dd, *J* 12.2 and 11.0, 4-H^{ax}), 2.69 (3H, s, 2-Me), 2.84 (1H, dd, *J* 11.0 and 2.7, 4-H^{eq}), 2.86 (1H, dqd, *J* 12.2, 6.2 and 2.7, 3-H), 2.98 (1H, d, *J* 13.2, 1′-H^a), 3.53 (1H, d, *J* 13.2, 1′-H^b), 3.76 (3H, s, OMe), 5.16 (1H, s, 6-H), 6.81 (2H, d, *J* 8.6, 2 × ArH), 7.16 (2H, d, *J* 8.6, 2 × ArH), 7.30–7.39 (3H, m, Ph) and 7.58–7.60 (2H, m, Ph); δ_C (100) 16.4 (3-Me), 43.6 (2-Me), 53.9 (1′-CH_2), 55.3 (OMe), 57.4 (4-CH_2), 59.2 (3-CH), 96.5 (6-CH), 113.7, 128.1, 128.6, 129.0, 129.8 (all Ar CH), 130.6, 137.9 and 158.7 (all Ar C); *m*/*z* 312 (M$^+$, 100%), 122 (63), 121 (9), 105 (14) and 91 (35) (Found: M$^+$, 312.1802. $C_{19}H_{24}N_2O_2$ requires *M*, 312.1838).

trans-2,3-Dimethyl-5-(4-nitrobenzyl)-6-phenyl-1,2,5-oxadiazinane 58b

A solution of the nitrone **8** (2.00 g, 14.8 mmol) and (4-nitrobenzyl)allylamine[41] **57b** (2.85 g, 14.8 mmol) in toluene (50 ml) was stirred and refluxed for 230 h, then was cooled and evaporated to leave the *oxadiazinane* **58b** (4.75 g, 98%) as a brown oil; ν_{max}/cm^{-1} 917; δ_H (400) 0.96 (3H, d, *J* 6.2, 3-Me), 2.44 (1H, dd, *J* 11.9 and 10.5, 4-H^{ax}), 2.71 (3H, s, 2-Me), 2.78 (1H, dd, *J* 11.9 and 2.7, 4-H^{eq}), 2.91 (1H, dqd, *J* 10.5, 6.2 and 2.7, 3-H), 3.23 (1H, d, *J* 14.9, 1′-H^a), 3.66 (1H, d, *J* 14.9, 1′-H^b), 5.29 (1H, s, 6-H), 7.11–7.61 (7H, m, ArH) and 8.10–8.23 (2H, m, ArH); δ_C (100) 15.9 (3-Me), 43.3 (2-Me), 53.3 (1′-CH_2), 57.4 (4-CH_2), 58.4 (3-CH), 95.6 (6-CH), 123.2, 127.6, 128.4, 128.7 (all Ar CH), 137.1 and 146.7 (both Ar C); *m*/*z* 327 (M$^+$, 100%), 254 (37), 91 (68) and 77 (29) (Found: M$^+$, 327.1587. $C_{18}H_{21}N_3O_3$ requires *M*, 327.1583).

trans-6-(4-Methoxyphenyl)-2,3-dimethyl-1,2,5-oxadiazinane 60a

A solution of the *C*-4-methoxyphenyl nitrone **59a**[11,40] (182 mg, 1.10 mmol) and allylamine **II** (83 μl, 1.10 mmol) in deuteriochloroform (1 ml) was sealed in an NMR tube and kept at 60 °C for 12 h. The cooled solution was evaporated to leave the *oxadiazinane* **60a** (240 mg, 99%) as a light yellow oil; ν_{max}/cm^{-1} 3362 and 952; δ_H (400) 1.00 (3H, d, *J* 6.3, 3-Me), 2.49 (1H, dqd, *J* 10.3, 6.3 and 3.2, 3-H), 2.70 (3H, s, 2-Me), 2.86 (1H, dd, *J* 13.7 and 10.3, 4-H^{ax}), 3.04 (1H, dd, *J* 13.7 and 3.2, 4-H^{eq}), 3.78 (3H,

s, OMe), 5.48 (1H, s, 6-H), 6.85–6.95 (2H, m, ArH) and 7.36–7.44 (2H, m, ArH); δ_C (67.8) 15.7 (3-Me), 43.8 (2-Me), 51.3 (4-CH_2), 55.2 (OMe), 61.8 (3-CH), 89.3 (6-CH), 113.6, 127.1 (both Ar CH), 136.1 and 159.3 (both Ar C); *m/z* 222 (M^+, 26%), 135 (100), 121 (31) and 74 (46) (Found: M^+, 222.1393. $C_{12}H_{18}N_2O_2$ requires *M*, 222.1368).

trans-2,3,5-Trimethyl-6-styryl-1,2,5-oxadiazinane 62

(*E*)-*N*-Methyl-*C*-styrylnitrone[11,40] **61** (3.00 g, 18.6 mmol) and *N*-methylallylamine **43a** (1.32 g, 18.6 mmol) were refluxed together in toluene (5 ml) for 24 h, then the solution was cooled and evaporated. ^{1}H NMR analysis of the residue showed no starting materials to be present and the presence of ≈80% of the oxadiazinane **62**, together with unidentified decomposition and other products. Attempted purification by CC led to decomposition. The major product was identified as the *oxadiazinane* **62** on the basis of ν_{max}/cm^{-1} 1658 and 910; δ_H (250) 0.97 (3H, d, *J* 6.1, 3-Me), 2.24 (3H, s, 5-Me), 2.25 (1H, dd, *J* 10.2 and 10.2, 4-H^{ax}), 2.67 (3H, s, 2-Me), 2.85 (1H, dd, *J* 10.2 and 2.8, 4-H^{eq}), 2.83–2.87 (1H, m, 3-H), 4.50 (1H, dd, *J* 7.0 and 0.4, 6-H), 6.11 (1H, dd, *J* 16.1 and 7.0, 1′-H), 6.76 (1H, d, *J* 16.1, 2′-H) and 7.13–7.47 (5H, m, Ph); δ_C (67.8) 15.6 (3-Me), 37.9 (5-Me), 42.8 (2-Me), 58.2 (3-CH), 60.3 (4-CH_2), 95.0 (6-CH), 125.0 (1′-CH), 126.1, 127.6, 127.9 (all Ph CH), 134.7 (2′-CH) and 135.5 (Ph C); *m/z* 232 (M^+, 36%), 215 (15), 172 (9), 158 (84), 144 (100), 103 (18), 91 (23) and 77 (27) (Found: M^+, 232.1543. $C_{14}H_{20}N_2O$ requires *M*, 232.1576).

trans-6-Cyclopropyl-2,3,5-trimethyl-1,2,5-oxadiazinane 67

C-Cyclopropyl-*N*-methylnitrone[44] **66** (0.59 g, 5.90 mmol) and *N*-methylallylamine **43a** (0.42 g, 5.90 mmol) were stirred together in chloroform (2 ml) at ambient temperature for 24 h. Evaporation of the solvent left the *cyclopropyloxadiazinane* **67** (1.00 g, 99%) as a colourless oil; ν_{max}/cm^{-1} 912; δ_H (250) 0.38–0.45 (2H, m, 2 × cyclopropyl H), 0.58–0.65 (3H, m, 3 × cyclopropyl H), 0.96 (3H, d, *J* 6.2, 3-Me), 2.31 (1H, dd, *J* 12.6 and 11.0, 4-H^{ax}), 2.41 (3H, s, 5-Me), 2.66 (3H, s, 2-Me), 2.76 (1H, dqd, *J* 11.0, 6.2 and 2.7, 3-H), 2.80 (1H, dd, *J* 12.6 and 2.7, 4-H^{eq}) and 3.25 (1H, d, *J* 8.1, 6-H); δ_C (67.8) 1.8, 3.7 (both cyclopropyl CH_2), 12.4 (cyclopropyl CH), 15.9 (3-Me), 38.0 (5-Me), 43.1 (2-Me), 58.3 (3-CH), 61.1 (4-CH_2) and 99.1 (6-CH); *m/z* 170 (M^+, 8%), 131 (6), 124 (9), 122 (9), 113 (33), 96 (18), 84 (100), 82 (25), 70 (11), 68 (15), 58 (15) and 41 (27) (Found: M^+, 170.1420. $C_9H_{18}N_2O$ requires *M*, 170.1419).

N^1-Allyl-N^2-hydroxy-N^2-methylpropane-1,2-diamine 69a

The 5-allyl-1,2,5-oxadiazinane **44b** (3.00 g, 12.9 mmol) was added to 2 M hydrochloric acid (86 ml) and the resulting mixture was stirred vigorously for 5 min at ambient temperature, then diluted with dichloromethane (80 ml). After mixing, the aqueous layer was separated, and treated with 2 M aq. sodium hydroxide (130 ml) followed by dichloromethane (200 ml). After mixing, the organic layer was separated, dried and evaporated to leave the *N-hydroxydiamine* **69a** (1.33 g, 72%) as a colourless oil; ν_{max}/cm^{-1} 3500–3150; δ_H (400) 1.03 (3H, d, *J* 6.2, 3-Me), 2.55 (3H, s, NMe), 2.58–2.64 (1H, m, 1-H^a), 2.79–2.85 (2H, m, 1-H^b and 2-H), 3.23–2.27 (2H, m, 1′-CH_2), 5.10 (1H, dd, *J* 10.3 and 1.3, 3′-H^c), 5.18 (1H, dd, *J* 17.1 and 1.6, 3′-H^t) and 5.90 (1H, ddd, *J* 17.1, 10.3 and 6.1, 2′-H); δ_C (67.8) 12.4 (3-Me), 44.5 (NMe), 52.2 (1′-CH_2), 53.0 (1-CH_2), 61.7 (2-CH), 116.3 (3′-CH_2=) and 136.3 (2′-CH=); *m/z* 144 (M^+, 5%), 128 (5), 109 (6), 96 (5), 91 (4), 86 (9), 83 (28), 74 (88), 70 (67), 58 (85), 56 (45), 42 (100) and 41 (74) (Found: M^+, 144.1301. $C_7H_{16}N_2O$ requires *M*, 144.1263).

N^1-Benzyl-N^2-hydroxy-N^2-methylpropane-1,2-diamine 69b

By the foregoing procedure, hydrolysis of the 5-benzyloxadiazinane **44c** (1.00 g, 3.60 mmol) gave the *N-hydroxydiamine* **69b** (0.59 g, 85%) as a colourless oil; ν_{max}/cm^{-1} 3500–3200; δ_H (250) 1.01 (3H, d, *J* 6.4, 3-Me), 2.54 (3H, s, NMe), 2.59–2.63 (1H, m, 1-H), 2.73–2.77 (1H, m, 1-H), 2.82–2.86 (1H, m, 2-H), 3.75 (1H, d, *J* 14.2, 1′-H^a), 3.79 (1H, d, *J* 14.2, 1′-H^b), 5.55–5.75 (2H, br, NH and OH) and 7.20–7.35 (5H, m, Ph); *m/z* 133 (15%), 106 (6), 91 (100) and 74 (5).

N^2-Hydroxy-N^1-(4-methoxybenzyl)-N^2-methylpropane-1,2-diamine 69c

By the foregoing procedure, hydrolysis of the 5-(methoxybenzyl)oxadiazinane **58a** (0.924 g, 2.96 mmol) gave the *N-hydroxydiamine* **69c** (0.67 g, 99%) as a colourless oil; ν_{max}/cm^{-1} 3500–3100; δ_H (250) 0.99 (3H, d, *J* 6.3, 3-Me), 2.55 (3H, s, NMe), 2.57–2.63 (1H, m, 1-H), 2.73–2.77 (1H, m, 1-H), 2.76–2.83 (1H, m, 2-H), 3.66 (1H, d, *J* 12.9, 1′-H^a), 3.68 (1H, d, *J* 12.9, 1′-H^b), 3.76 (3H, s, OMe), 5.20–5.40 (2H, br, NH and OH), 6.82 (2H, d, *J* 8.6, 2 × ArH) and 7.18 (2H, d, *J* 8.6, 2 × ArH).

N^2-Hydroxy-N^2-methyl-N^1-(4-methylbenzoyl)propane-1,2-diamine 69d

By the foregoing procedure, hydrolysis of the 5-(4-methylbenzoyl)oxadiazinane **68** (3.80 g, 12.2 mmol), prepared by N-acylation of the oxadiazinane **24** derived from allylamine with 4-methylbenzoyl chloride as described above for the preparation of the corresponding 4-nitrobenzoyl derivative **30**, gave the *N^1-acyl-N^2-hydroxydiamine* **69d** (2.23 g, 82%) as a colourless solid, mp 122–124 °C (from ether–LP) (Found: C, 64.8; H, 8.2; N, 12.5. $C_{12}H_{18}N_2O_2$ requires C, 64.8; H, 8.2; N, 12.6%); ν_{max}/cm^{-1} (Nujol) 3301, 3300–3100 and 1634; δ_H (400) 1.04 (3H, d, *J* 6.5, 3-Me), 2.33 (3H, s, Ar*Me*), 2.60 (3H, s, NMe), 2.80 (1H, dqd, *J* 6.8, 6.5 and 3.7, 2-H), 3.42 (1H, ddd, *J* 14.0, 7.2 and 6.8, 1-H^a), 3.58–3.63 (1H, m, 1-H^b), 7.10 (2H, d, *J* 8.1, 2 × ArH), 7.34 (1H, br t, *J* ≈7.2, NH) and 7.65 (2H, d, *J* 8.1, 2 × ArH); δ_C (100) 12.0 (3-Me), 21.3 (Ar*Me*), 43.0 (1-CH_2), 44.5 (NMe), 62.3 (2-CH), 127.1, 129.0 (both 2 × Ar CH), 131.5, 141.7 (both Ar C) and 168.3 (CO); *m/z* 222 (M^+, 6%), 204 (13), 192 (7), 148 (14), 131 (7), 120 (25), 91 (87) and 74 (100) (Found: M^+, 222.1383. $C_{12}H_{18}N_2O_2$ requires *M*, 222.1368).

N^1-Benzyl-N^2-methylpropane-1,2-diamine 70a

The 5-benzyloxadiazinane **44c** (4.82 g, 17.1 mmol) and zinc (5.60 g, 85.5 mmol) were added to 2 M hydrochloric acid (170 ml) and the resulting mixture was stirred and heated at 80 °C for 1 h.[45] After cooling of the mixture, dichloromethane (100 ml) was added and, after mixing, the aqueous layer was separated and added to 2 M aq. sodium hydroxide (250 ml). The resulting mixture was extracted with dichloromethane (3 × 100 ml) and the combined extracts were dried and evaporated. Distillation of the residue gave the *diamine* **70a** (2.58 g, 85%) as a yellow oil, bp 140 °C at 1.5 mmHg; ν_{max}/cm^{-1} 3163; δ_H (250) 1.01 (3H, d, *J* 5.9, 3-Me), 2.58 (3H, s, NMe), 2.72–2.78 (1H, m, 2-H), 2.78 (1H, dd, *J* 8.6 and 8.6, 1-H^a), 2.76–2.81 (1H, m, 1-H^b), 3.75 (1H, d, *J* 13.2, 1′-H^a), 3.80 (1H, d, *J* 13.2, 1′-H^b) and 7.19–7.35 (5H, m, Ph); δ_C (100) 12.0 (br, 3-Me), 44.1 (NMe), 52.6 (1-CH_2), 53.6 (1′-CH_2), 61.6 (2-CH), 126.8, 128.0, 128.1 (all Ph CH) and 139.4 (Ph C); *m/z* 119 (12%), 91 (100), 58 (36) and 42 (24).

N^2-Methyl-N^1-(4-methylbenzoyl)propane-1,2-diamine 70b

By the foregoing procedure, reduction of the 5-(4-methylbenzoyl)oxadiazinane **68** (335 mg, 1.50 mmol) using zinc (500 mg, 7.50 mmol) gave the *N-acyldiamine* **70b** as a highly hygroscopic oil which showed ν_{max}/cm^{-1} 3319 and 1643; δ_H (250) 1.10 (3H, d, *J* 6.4, 3-Me), 2.15 (1H, br, NH), 2.37 (3H, s, Ar*Me*), 2.41 (3H, s, NMe), 2.84 (1H, qdd, *J* 6.4, 6.2 and 4.5, 2-H), 3.32 (1H, ddd, *J* 13.7, 6.2 and 5.8, 1-H^a), 3.46 (1H, ddd, *J* 13.7, 4.5 and 4.5, 1-H^b), 7.12 (1H, app. br t, *J* ≈ 5.8, CONH), 7.19 (2H, d,

J 8.0, 2 × ArH) and 7.71 (2H, d, *J* 8.0, 2 × ArH); δ_C (100) 18.0 (3-Me), 21.4 (Ar*Me*), 33.5 (NMe), 44.0 (1-CH_2), 54.1 (2-CH), 127.0, 129.1 (both 2 × Ar CH), 131.3, 141.6 (both Ar C) and 167.7 (CO); *m*/*z* 91 (41%), 72 (7) and 58 (100).

X-ray crystallography for 13a†

Single crystals of the oxadiazinane **13a** were obtained by recrystallization from ethyl acetate–LP. X-ray data were collected on a CAD4 diffractometer using monochromatized Mo-K_a radiation ($\lambda = 0.710\ 73$ Å) and ω-scans.

Crystal data. $C_{16}H_{28}N_2O_6$, M = 344.40, orthorhombic, a = 9.311(2), b = 11.104(2), c = 17.245(2) Å, V = 1782.9(6) Å^3, T = 293 K, space group $P2_12_12_1$ (no. 19), Z = 4, μ(Mo-Kα) = 0.098 mm^{-1}. Total 3676 reflections ($3.22 \geqslant \theta \geqslant 25.2°$) were measured, of which 3202 were unique (R_{int} = 0.0552) and used in the calculations. The structure was solved by direct methods (SHELXS-86)[46] and refined on F^2 (SHELXL-96)[47] to final wR_2 (on F^2) = 0.1329 (all data) and R_1 (on F) = 0.0541 (1873 data with $F^2 > 2\sigma(F^2)$). The non-hydrogen atoms were anisotropic, the hydrogen atom on N(2) was located from a difference map and freely refined; other hydrogen atoms were included in calculated positions (riding model). The absolute structure could not be determined reliably from these crystal data, due to the absence of any significant anomalous scatter in the molecule.

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