Bromocyclization of Unsaturated Oximes. Synthesis of Five-Membered Cyclic Nitrones (Pyrroline *N*-Oxides)* [1]

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Dedicated to Professor Dieter Enders on the occasion of his 60th birthday

The cyclization of a ribose-derived pentenose oxime with various halogen electrophiles showed bromine to be the most effective reagent, leading to 80% of L-*lyxo*/D-*ribo*-pyrroline *N*-oxides in an 84:16 diastereomeric ratio. In order to explore the scope of this facile process, several other γ,δ-unsaturated oximes were submitted to this reaction. Depending on the substitution pattern, 23 – 87%, yields of pyrroline *N*-oxides of were registered. With α-allyl-β-ketoester oximes the alkoxycarbonyl group proved a similar (ethoxy) or even better (*t*-butoxy) trapping nucleophile, leading preferentially to the corresponding bromolactone oxime. – With 2,2-dimethyl-3-butene aldoxime, the corresponding 3-bromopyrroline *N*-oxide was formed, due to a formal, unusual *N-endo* cyclization to the chain terminus. This was exploited for a new access to six-membered nitrones from a γ,δ-pentene aldoxime, with addition of Br/OH to the C=C of the 4-pentenal first, and oximation/cyclization following then.

Key words: Unsaturated Oximes, Bromocyclization, Cyclic Nitrones, *endo*/*exo*-Cyclization, Bromolactonization

Introduction

Natural mono- and bicyclic iminopolyols have been found to display strong and selective inhibition of glycosidases. Well-known examples are represented by deoxynojirimicin, castanospermine, or swainsonine [2]. Related 1,4-iminopolyols can have similar effects, like 1,4-dideoxy-1,4-imino-D-arabinitol (DAB) or D-lyxitol, but with less pronounced activities [2, 3]. Recently, 1-substituted 1,4,5-trideoxy-1,4-imino-L-lyxitols have been reported to be highly active inhibitors of α-L-fucosidases [1, 2, 4 – 6].

We had developed several approaches to such 1,4-iminopolyols earlier [3, 7, 8], and had then devised a variety of non-classical structures, such as *N*-hydroxy-1,4-iminopolyols or related pyrrolidine *N*-oxides [2, 4, 5]. The latter approaches were based on unsaturated oximes and nitrones, respectively. Cyclizations were induced either by electrophilic addition (bromine) to the C=C bond (ene oximes) or by addition of nucleophiles to the C=N bond (ene oximes or nitrones); in the latter case Cope-House cyclization of intermediate ene hydroxylamines had led to *N*-(hydr)oxy-pyrrolidines [2, 5, 8].

In this paper a full account on our results concerning the bromocyclization of unsaturated oximes is given, as communicated earlier. The products – bromomethyl-pyrroline-*N*-oxides, *i. e.* cyclic nitrones – constitute versatile intermediates in organic synthesis, as expected from members of this class. Both additions of *C*-nucleophiles or dipolarophiles occur with ease, and have often been drawn upon to assemble complex structures [9, 10], as had been demonstrated for the case of our first product of ene oxime bromocyclization, the L-*lyxo*-nitrone derived from D-ribose [1, 2, 4, 5].

Cyclic nitrones have been obtained by a variety of procedures involving already cyclic precursors as well as acyclic structures with appropriate functionalities (Scheme 1). Approaches based on cyclic amines (1,n-imino compounds) or hydroxylamines (*N*-hydroxypyrrolidines, f. e.), necessitate ox-

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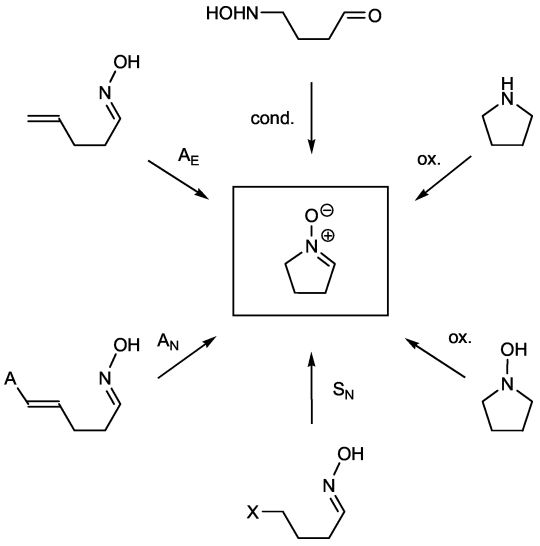
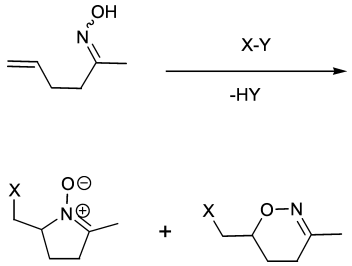


Scheme 1. Principal routes to cyclic nitrones (pyrroline *N*-oxides).

idation [9, 11 – 13]. This, however, often is hampered by insufficient regioselectivity (enantioselectivity with *meso* substrates) and has not been addressed vigorously so far. No problems of this kind are met with intramolecular condensations of hydroxylaminocarbonyl derivatives (N → C=O addition), but access to such precursors is rather limited [1, 14]. Related to this are cyclizations involving intramolecular nucleophilic substitution of a suitable leaving group by the oxime nitrogen atom. Epoxide [15], iodide [16], or mesylate [6, 17] have served to that purpose, and this strategy has seen many applications.

A more promising – and challenging – approach is offered with unsaturated oximes as cyclization substrates. Two modes of *N*-cyclization have been shown to be feasible: *N*-Nucleophilic addition of the oxime part to an acceptor-substituted C=C bond [18] or an olefinic part "activated" by prior addition of an electrophile. Such cyclizations of unsaturated oximes have systematically been studied by Grigg and his group. A range of electrophiles has been employed, notably mercuric acetate [19], phenylselenenyl bromide [18b,20], bis(acetonitrile) palladium(II) chloride [21], *N*-bromo- and –iodosuccinimide [20b, 22], iodine [18b, 22], and iodine chloride [22]. In some cases, the (*Z*)/(*E*) ratio of the starting oximes was reflected in the product distribution, the nitrone forming from the (*E*) isomer and the dihydrooxazine arising from *O*-cyclization of the (*Z*) oxime [20, 22] (Scheme 2).



Scheme 2. Cyclization of alkenyloximes induced by electrophiles X-Y: $Hg(OAc)_2$, PhSeBr, I_2, *N*-bromosuccinimide.

In view of our objective, access to potential inhibitors of α-L-fucosidases [1, 5, 23], we have studied cyclizations of a ribose-derived pentenose oxime, and, when successful with bromocyclization [1, 2, 4, 5], several other substrates were screened to this respect, in order to define the scope of this reaction.

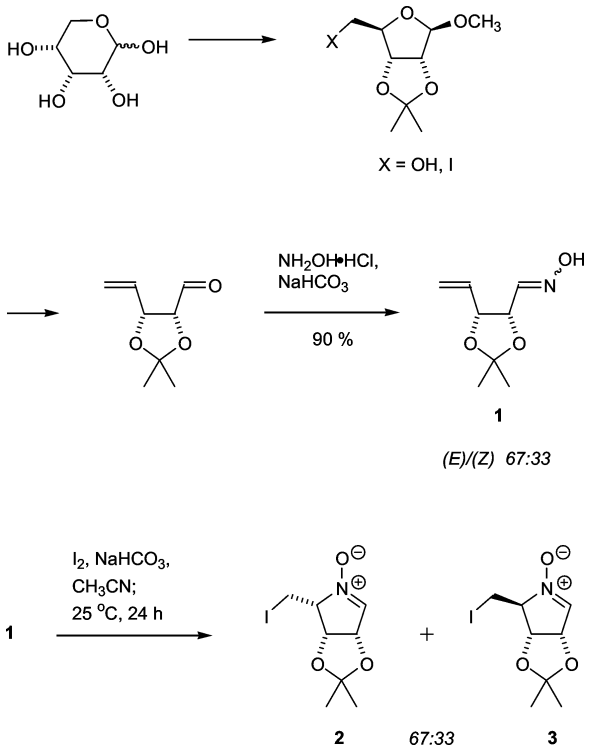
Results and Discussion

Iodo- and bromocyclization of D-erythro-pentenose oxime acetonide

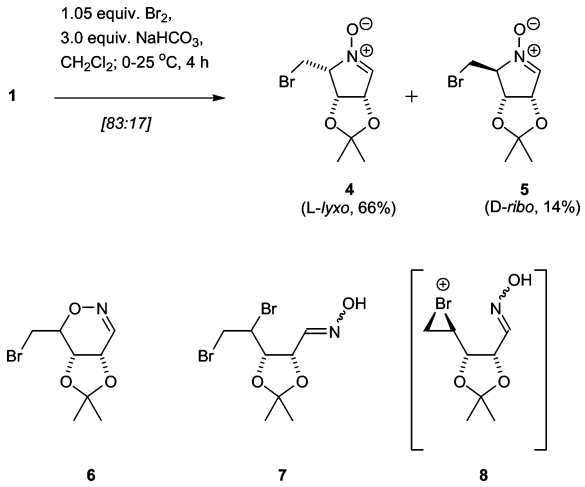
The substrate for cyclization studies, the pentenose oxime **1**, was prepared from D-ribose in four steps, *via* the aldehyde described earlier [8b]. The last step, oximation, furnished a 2 : 1 mixture of (*E*)/(*Z*) oximes **1** which could be separated by MPLC; from the (*Z*) oxime a crystal structure analysis was obtained [24].

Iodocyclization was attempted first, with various reagents (iodine, potassium triiodide, and *N*-iodosuccinimide), bases ($NaHCO_3$, Na_2CO_3, or pyridine), and solvents. The cyclization occurred slowly, at best with excess iodine/sodium bicarbonate at room temperature in acetonitrile. After chromatography the two nitrones **2** and **3** were isolated in 40 and 20% yield, respectively (Scheme 3). Both iodomethylnitrones were solids, but proved unstable on storage even under argon at −20 °C, in line with observations by Grigg *et al.* [22]. Similar cyclization of **1** had been reported meanwhile by Wightman *et al.*, resulting in a 3 : 5 iodomethylnitrone mixture "in poorer combined yield" [18b].

We therefore turned our attention to bromine reagents. The use of bromonium di-*sym*-collidine hexafluorophosphate [25] led to decomposition, while the action of *N*-bromosuccinimide in dichloromethane produced a mixture of two diastereomeric nitrones **4**/**5** and of two dihydrooxazines **6**, *vide supra* [22]. Bromine itself, however, proved more promising and,



Scheme 3. Preparation and iodocyclization of *D* − *erythro*-4-pentenose oxime acetonide **1**.



Scheme 4. Bromocyclization of D-*erythro*-4-pentenose oxime acetonide **1**.

after some optimization, gave a mixture of the nitrones **4** and **5** only, in 66 and 14% yield, respectively (Scheme 4). Both nitrones were crystalline; the configurations were determined as L-*lyxo* for the major nitrone **4** and as D-*ribo* for the minor one **5** by crystal structure analyses [26] and also from NMR data (in particular distinct high-field shifts of ^{13}C NMR signals of C-4, C-5, and C-1' for **4**).

The success of this bromocyclization relies on careful, slow addition of bromine to the solution of the oxime **1** at a concentration of *ca.* 0.1 M. The stereoselectivity of the addition/cyclization did not change notably when carried out at lower temperature (86 : 14 at −80 °C), however, formation of open-chain dibromide **7** (*ca.* 29%) was deduced from the NMR spectra of the crude product [1b].

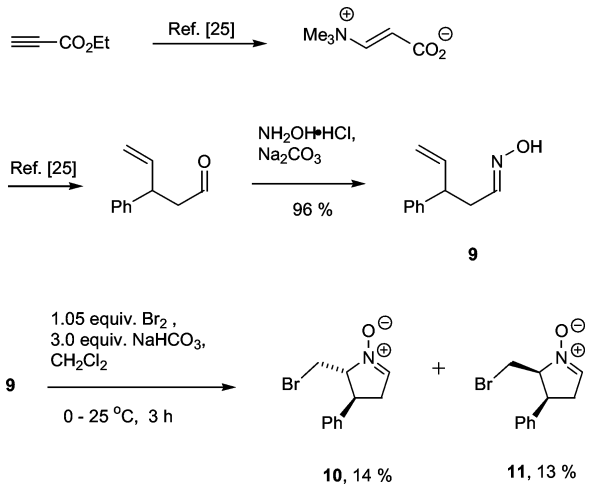
The stereoselectivity of the bromine addition/cyclization of the unsaturated oxime **1** can be rationalized on the basis of the "alkoxy inside/alkyl anti" model proposed by Houk, Jäger *et al.* for electrophilic nitrile oxide cycloadditions to allyl-substituted alkenes [27, 28]. Thus, attack of bromine to the α-oxygenated C=C bond should be slowed down by the inductive, electron-withdrawing effect of the α-alkoxy group of the π-system. This unfavourable interaction would be maximized in the *anti*-OR conformation due to σ^*,π-interaction, similarly as shown with nitrile oxide (electrophile) cycloadditions to allyl-substituted alkenes or with Sharpless' asymmetric epoxidation of allylic alcohols [27]. Bromonium ion formation would then preferably lead to a species with *ribo* (*cis*; "*anti*") configuration, **8**, and the ensuing attack of the oxime nitrogen atom would invert the C-4 stereocentre to yield the *lyxo* (*cis*; "*syn*") product **4**.

After this first successful case, some further substrates were devised, in order to find out about the scope and generality of such bromocyclizations of ene oximes.

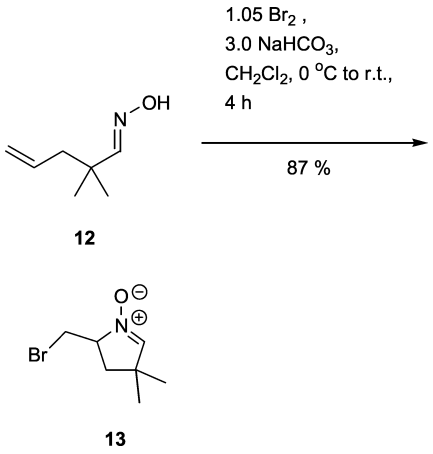
Bromocyclization of 3-phenyl- and 2,2-dimethyl-4-pentene aldoximes

The 3-phenyl-4-pentene aldoxime **9** was chosen as a substrate which would test as to the capability of cyclization without a favouring device such as the dioxolane ring present in **1**. For its preparation we used a sequence described by Dennis and George [29], noteworthy for its use of ethyl propiolate as a vinyl ether equivalent which with trimethylamine and cinnamyl alcohol was converted to the Claisen rearrangement product, the 4-pentenal (Scheme 5).

Treatment with bromine under the conditions as optimized above after 1 h at 0 °C indeed led to complete consumption of the starting oxime **9**, but from TLC analysis it was evident that a mixture of many products had been formed (confirmed also by NMR



Scheme 5. Preparation and bromocyclization of 3-phenyl-4-pentene aldoxime **9**.



Scheme 6. Bromocyclization of 2,2-dimethyl-4-pentene aldoxime **12**.

spectra of the fractions collected after chromatographic separation). Fortunately, TLC analyses also showed that there were two more polar products which then were separated by column chromatography on sili*ca.* The major one (14%) was isolated as an analytically pure, crystalline substance and proved to be the *trans*-5-bromomethyl-3-phenylpyrroline *N*-oxide **10** (crystal structure analysis [1d]). To the minor product (13%), a colorless oil, the structure of the *cis*-nitrone **11** was assigned, based on IR and NMR data.

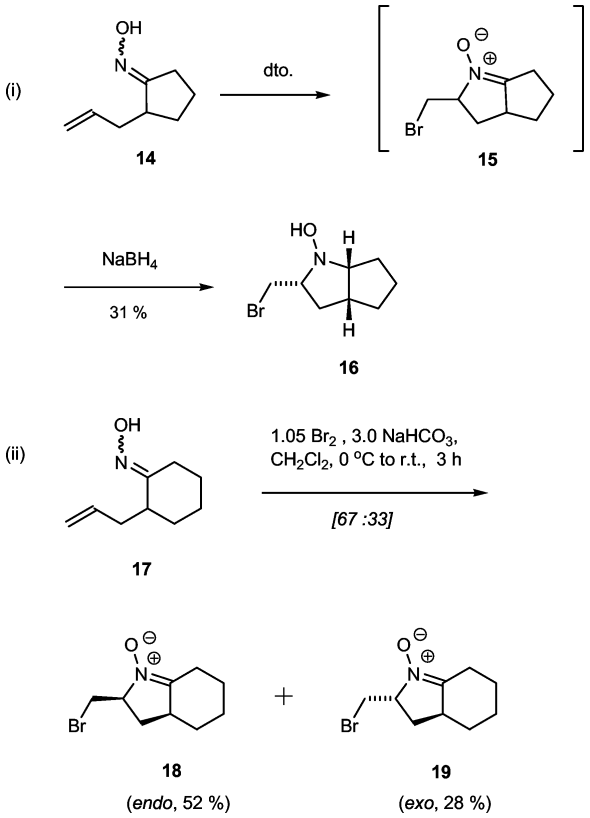
The outcome of this experiment led us to conclude that substrates without an element favouring cyclization would not serve well as precursors for cyclic bromomethyl-nitrones. Recourse to a substrate with a *gem*-dimethyl unit was sought therefore, in order to take advantage of the Thorpe-Ingold effect [30]. A requisite substrate, the 2,2-dimethyl-4-pentene aldoxime **12**, was readily prepared from isobutyraldehyde and allyl alcohol, followed by standard oximation of the intermediate aldehyde formed by Claisen rearrangement. Indeed, bromocyclization of **12** under the usual conditions after 1 h at r. t. gave a single, crystalline product, the nitrone **13** (Scheme 6).

Attempts at bromocyclization of oximes derived from 2-allylcyclopentanone and –cyclohexanone; nitrone vs. lactone formation

Conformational restraint, as successful with the cases of **1** and **12**, respectively, should also foster bromo-cyclization of oximes derived from 2-allylcycloalkanones. With the cyclopentanone derivative **14**, however, the bicyclic nitrone **15** proved unstable and could not be isolated in pure state. Its formation was made evident by reducing the crude product mixture with sodium borohydride in ethanol. From this, the bicyclic bromomethyl-*N*-hydroxypyrrolidine **16** was isolated in 31% yield as a single diastereomer of so far unassigned configuration, see Scheme 7 (i). The configuration of **16** is tentatively assigned as *endo*, based on the crystal structure analysis of a styrene cycloaddition product of the nitrone **15** [1d].

On the other hand, the cyclohexanone derivative **17** reacted readily on action of bromine to furnish the two nitrones **18** and **19** in 80% combined yield, Scheme 7 (ii). The minor isomer was assigned the *exo* configuration, due to a crystal structure analysis [1d]; the small differences of NMR chemical shifts would not have permitted this.

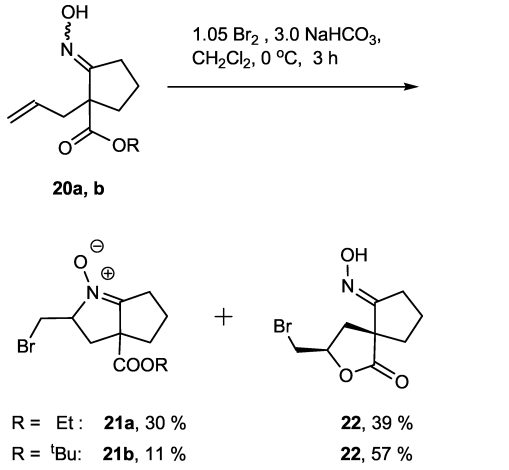
The allylcyclopentanone oxime **14** had been prepared from ethyl 2-cyclopentanonecarboxylate by allylation followed by hydrolysis and decarboxylation of the intermediate β-keto acid. Cyclization of the α-allyl β-oximino ethyl ester **20a** itself was attempted also, since the resulting ester **21a** with a β-nitrone function would represent an immediate precursor of novel β-amino acid structures. In fact, cyclization occurred readily on bromine treatment, but after work-up and chromatographic separation the bicyclic nitrone ethyl ester **21a** was isolated in 30% yield, besides another, less polar product. According to spectral data and, notably, a crystal structure determination [1d], the latter constituted a cyclic bromomethyl-spirolactone **22** with intact oximino group, obtained in 39% yield (Scheme 8). The *oxime nitrogen* thus exhibits some-



Scheme 7. Bromocyclization of 2-allylcycloalkanone oximes.

what less tendency for nucleophilic attack on the (presumed) bromonium ion, as compared to the *ester oxygen atom* which undergoes bromo*lactonization*. Actually, halolactonization of unsaturated esters is well precedented [30c, 31]. The alkoxy group OR of the cyclized product formed first (a dialkoxyoxonium ion) looses R either by substitution on attack of halide, or by splitting off a stabilized carbocation (such as benzyl). Related de-benzylations or de-allylations of respective unsaturated *O*-substituted oximes have been observed on treatment with phenylselenenyl bromide by Grigg *et al.* and have been mentioned as "fragmentation" [32].

Next, the *tert*-butyl ester of the α-allyl-cyclopentanone oxime was tested – the bulkier *tert*-butyl group might change the competing pathways. In fact, the course of cyclization was shifted towards bromolactonization which now amounted to 57% of bromomethyl-lactone **22** and only 11% of the nitrone **23a** (Scheme 8). Obviously, the reaction course now is dominated by the facile loss of the *tert*-butyl cation from the presumed alkoxy-oxonium ion intermediate.

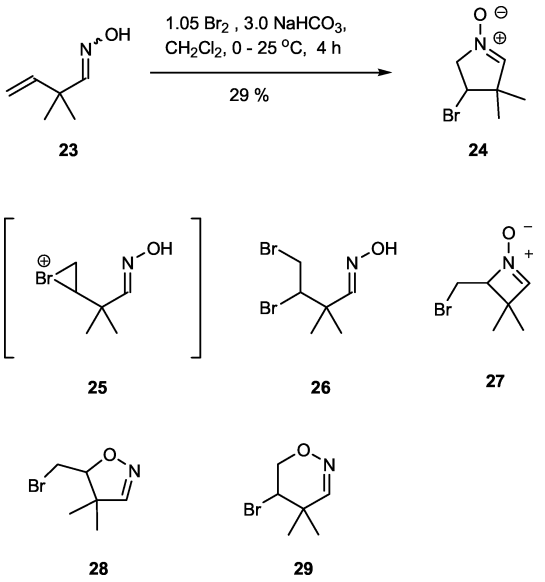


Scheme 8. Nitrone *vs.* lactone formation in the bromocyclization of ethyl and *tert*-butyl 2-allylcyclopentanone-2-carboxylate oximes.

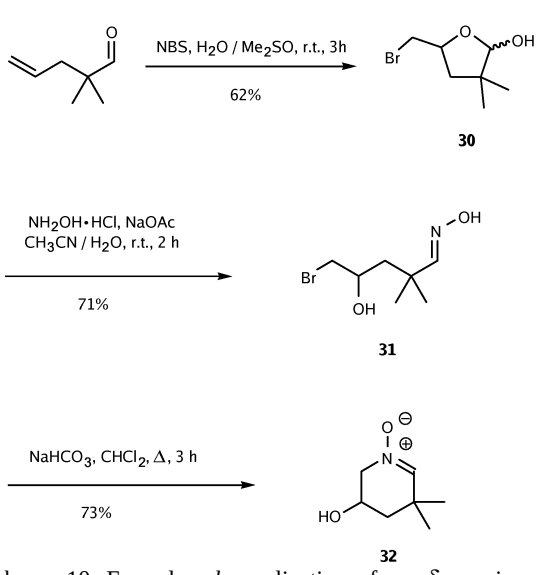
Formal endo cyclization of a β,γ- and γ,δ-enoxime

In the cases detailed above, as well as with the many examples of electrophile-induced cyclizations of γ,δ-alkenyloximes reported by Grigg and his group [15, 19 – 22], only products of *exo-tet* ring closures [33] were observed. A first example of a different mode of cyclization now was found, when the β,γ-enoxime was submitted to the usual conditions of the above bromocyclizations. The polar product (TLC analysis) was separated by chromatography to yield a crystalline compound which, according to elemental and spectroscopic data, constituted the 4-bromopyrroline *N*-oxide **24**, Scheme 9. Besides, several other, less polar products were formed but could not be isolated in pure form.

The formation of **24**, representing the formal product of a 5-*endo-tet* cyclization, shows that the "usual" *N*-cyclization here is disfavoured, since this would lead to a four-membered species **27** with respective ring strain. Nitrones of this type are known; they show a tendency to dimerize easily [34] which releases part of the strain (for cyclobutene and cyclopentene values of 30 and 7 kcal/mol, respectively, are estimated [35]). With **23**, the initially formed bromonium ion **25** could cyclize by *N*-attack at the terminus C-4. Alternatively, from **25** by addition of bromide the open-chain dibromo-oxime **26** could result, and then relatively strain-free *N*-cyclization to the terminal bromomethyl site would lead to the nitrone **24**. Remarkably, none of the respective cyclic oxime ethers **28** and **29**, respectively, was detected.



Scheme 9. Bromocyclization of 2,2-dimethyl-3-butene aldoxime; possible intermediates and products.



Scheme 10. Formal *endo* cyclization of a γ,δ-enoxime to give a piperidine *N*-oxide.

This example shows that *N*-cyclization to the *C*-terminus is possible, at least with the β,γ-enoxime **23**. This mode of cyclization would be desirable also for γ,δ-enoximes. The 4-pentene aldoxime **12** was chosen to explore this. Thus, 2,2-dimethyl-4-pentenal was treated with *N*-bromosuccinimide in dimethyl sulfoxide/water forming the bromohydrin (present as the hemiacetal **30**) as expected [31, 36, 37]. This was transformed into the 5-bromo-oxime **31** with hydroxylamine. The dibromoalkyl-oxime **31** was isolated in 71% yield and then heated to reflux in CH_2Cl_2 with sodium bicarbonate. Indeed, cyclization occurred smoothly, and the 6-membered nitrone **32** was secured in 73% yield in analytically pure form (Scheme 10).

Conclusion

Several structurally different γ,δ-unsaturated oximes have been shown to undergo bromocyclization to yield bromomethyl-nitrones. Although yields so far are variable and await optimization in some cases, these new pyrroline *N*-oxides constitute attractive intermediates for applications in synthesis. With a 3-butene aldoxime the 3-bromopyrroline *N*-oxide was obtained, the formal product of a rare *endo* cyclization. Most likely this is due to a change in mechanism, *i. e.* that the cyclizing step occurs with the dibromide and not with the bromonium ion intermediate. Reversal of the over-all cyclization, to occur at the terminal carbon, has been achieved by switching the reaction sequence: First addition of bromine to the C=C bond of the unsaturated aldehyde, and then oxime formation with subsequent *N*-cyclization.

Continuation of this work has focussed on the use of these new nitrones, in particular of the L-*lyxo*-nitrone **4**, for syntheses of fucosidase inhibitors [1, 4, 5], to be detailed elsewhere. Likewise, application of the enoxime bromocyclization to other carbohydrate precursors seems promising [37]. Further, bicyclic ester nitrones or lactones such as **21a** and **22**, respectively, might become attractive precursors of complex branched amino (imino) acids if the competing cyclization modes could be made more selective.

Experimental Section

For general experimental details see ref. [8b]. Aldehyde starting materials: 4,5-Dideoxy-2,3-*O*-isopropylidene-D-*erythro*-4-pentenose [1a, 8b]; 3-phenyl-4-pentenal [29]; 2,2-dimethyl-4-pentenal oxime [38]; 2-allylcyclopentanone [39]; 2-allylcyclohexanone (Acros); ethyl 2-allylcyclopentanone-2-carboxylate [40]; *tert*-butyl 2-allylcyclopentanone-2-carboxylate [41]; 2,2-dimethyl-3-butenal [42].

4,5-Dideoxy-2,3-O-isopropylidene-D-erythro-4-pentenose oxime (**1**)

a) *4,5-Dideoxy-2,3-O-isopropylidene-D-erythro-4-pentenose*: In a dry flask (heat gun) under nitrogen methyl

5-deoxy-5-iodo-2,3-isopropylidene-β-D-ribofuranoside [1a, 8b] (2.51 g, 8.00 mmol) was dissolved in THF (45 ml, abs.). The solution was cooled to −80 °C, then butyllithium in hexane (1.6 M, 7.5 ml, 12 mmol; E. Merck) was added dropwise within 15 min. The mixture was stirred at −80 °C for 2 h, then solid NH_4Cl (0.8 g) was added. After warming to −40 °C water (20 ml) was added. The aqueous phase was extracted with Et_2O (3 × 25 ml), the organic solutes were combined, dried ($MgSO_4$), and rota-evaporated until most of the solvent was removed. The remaining solution was carefully concentrated for *ca.* 15 min at 30 °C/10 Torr, since the aldehyde proved somewhat volatile. The pentenose (1.24 g, quant.) was obtained as a slightly yellow oil, which was used without further purification.

^{1}H NMR (250.1 MHz, $CDCl_3$): $\delta = 1.45$, 1.63 (2 s, 3 H each, $C(CH_3)_2$), 4.42 (dd, $J_{1,2} = 3.1$, $J_{2,3} = 7.5$ Hz, 1 H, 2-H), 4.86 (dd, $J_{2,3} = 7.5$, $J_{3,4} = 6.8$ Hz, 1 H, 3-H), 5.33 (dm, $J_{4,5E} = 10.3$ Hz, 1 H, 5-H_E), 5.47 (dm, $J_{4,5Z} = 17.0$ Hz, 1 H, 5-Hz), 5.77 (ddd, $J_{3,4} = 6.8$, $J_{4,5E} = 10.3$, $J_{4,5Z} = 17.0$ Hz, 1 H, 4-H), 9.56 (d, $J_{1,2} = 3.1$ Hz, 1 H, 1-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta = 25.3$, 27.4 (2 q, $C(CH_3)_2$), 79.1, 82.3 (2 d, C-2, C-3), 111.3 (s, $C(CH_3)_2$), 119.7 (t, C-5), 131.3 (d, C-4), 200.7 (d, C-1).

b) *Oxime* **1**: Hydroxylammonium chloride (2.28 g, 32.8 mmol) in water (5 ml) was treated with Na_2CO_3 (1.73 g, 16.4 mmol, in 10 ml of water). Then the pentenose (obtained as above; 2.56 g, 16.4 mmol) dissolved in EtOH (15 ml) was added. The mixture was stirred at r.t. overnight, then extracted with CH_2Cl_2 (4 × 30 ml) and dried ($MgSO_4$). After rota-evaporation (30 °C/10 Torr) a yellow oil remained, which was filtered (silica, 27 g, column 3 cm × 10 cm, petrol ether/EtOAc 80 : 20) to afford the oxime **1** (2.53 g, 90%, (*E*)/(*Z*) 80 : 20 according to NMR analyses) as an analytically pure, colorless oil which slowly solidified. – In an analogous experiment with the pentenose (1.00 g, 6.40 mmol) MPLC separation (eluent petrol ether/EtOAc 80 : 20) gave (*Z*)-**1** (307 mg, 31%) and (*E*)-**1** (628 mg, 57%), both as analytically pure, colorless solids; for (*Z*)-**1** a crystal structure analysis was made [24].

(*Z*)-**1**: M. p. 89 – 90 °C. – $[\alpha]_D^{20} = 216$ ($c = 0.545$, CH_2Cl_2). – IR (KBr): $\nu = 3210$ (OH), 3080, 3020, 2970, 2870, 1455, 1380, 1360, 1295, 1245, 1205, 1145, 1040, 975, 935, 905, 890, 870, 845, 780 cm^{-1}. – ^{1}H NMR (250.1 MHz, $CDCl_3$): $\delta = 1.40$, 1.55 (2 s, 3 H each, $(C(CH_3)_2)$, 4.84 ("tt", $J_{2,3} = J_{3,4} = 6.7$, $^4J_{3,5E} = {}^4J_{3,5Z} = 1.2$ Hz, 1 H, 3-H), 5.21 (ddd, $^4J_{3,5E} = 1.2$, $J_{4,5E} = 10.3$, $^2J_{5E,5Z} = 1.8$ Hz, 1 H, 5-H_E), 5.31 (dd, $J_{1,2} = 5.2$, $J_{2,3} = 6.7$ Hz, 1 H, 2-H), 5.36 (ddd, $^4J_{3,5Z} = 1.2$, $J_{4,5Z} = 17.0$, $^2J_{5E,5Z} = 1.8$ Hz, 1 H, 5-Hz), 5.77 (ddd, $J_{3,4} = 6.7$, $J_{4,5E} = 10.3$, $J_{4,5Z} = 17.0$ Hz, 1 H, 4-H), 6.82 (d, $J_{1,2} = 5.2$ Hz, 1 H, 1-H), 8.68 (s, 1 H, OH). – ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta = 25.2$, 27.6 (2 q, $C(CH_3)_2$), 72.8, 78.5 (2 d, C-2, C-3), 109.6 (s, $C(CH_3)_2$), 118.1 (t, C-5), 133.2 (d, C-4), 150.2 (d, C-1).

(*E*)-**1**: M. p. 48 – 52 °C. – $[\alpha]_D^{20} = -49$ ($c = 0.51$, CH_2Cl_2). – IR (film): $\nu = 3375$ (OH), 2989, 1376, 1246, 1218, 1165, 1053, 934, 867 cm^{-1}. – ^{1}H NMR (250.1 MHz, $CDCl_3$): $\delta = 1.35$, 1.47 (2 s, 3 H each, $C(CH_3)_2$), 4.62 (dd, $J_{1,2} = 7.7$, $J_{2,3} = 6.6$ Hz, 1 H, 2-H), 4.68 ("tt", $J_{2,3} = J_{3,4} = 6.6$, $^4J_{3,5E} = {}^4J_{3,5Z} = 1.0$ Hz, 1 H, 3-H), 5.24 (ddd, $^4J_{3,5E} = 1.0$, $J_{4,5E} = 10.4$, $^2J_{5E,5Z} = 1.6$ Hz, 1 H, 5-H_E), 5.34 (ddd, $^4J_{3,5Z} = 1.0$, $J_{4,5Z} = 17.1$, $^2J_{5E,5Z} = 1.6$ Hz, 1 H, 5-Hz), 5.69 (ddd, $J_{3,4} = 6.6$, $J_{4,5E} = 10.4$, $J_{4,5Z} = 17.1$ Hz, 1 H, 4-H), 7.24 (d, $J_{1,2} = 7.7$ Hz, 1 H, 1-H), 8.27 (s, 1 H, OH). – ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta = 25.4$, 27.9 (2 q, $C(CH_3)_2$), 75.9, 79.1 (2 d, C-2, C-3), 110.1 (s, $C(CH_3)_2$), 119.4 (t, C-5), 132.2 (d, C-4), 148.9 (s, C-1). – $C_8H_{13}NO_3$ (171.2): calcd. C 56.13, H 7.65, N 8.18; found for (*Z*)-**1**: C 55.86, H 7.59, N 7.97; found for (*E*)-**1**: C 55.89, H 7.66, N 8.02.

(3S,4R,5R)-5-Iodomethyl-3,4-isopropylidenedioxy-3,4-dihydro-5H-pyrrole 1-oxide **2** *(L-lyxo) and (3S,4R,5S)-diastereomer* (**3**)

In a dry flask the oxime **1** (514 mg, 3.00 mmol, (*E*)/(*Z*) = 2 : 1) was dissolved in acetonitrile (25 ml). $NaHCO_3$ (757 mg, 9.00 mmol) and iodine (2.29 g, 9.00 mmol) were then added sequentially in portions at 0 °C in the dark. The mixture was allowed to warm to r.t. and stirred for 24 h. Ethyl acetate (30 ml) was added and the mixture was treated with saturated $Na_2S_2O_3$ solution (30 ml). The aqueous phase was extracted with ethyl acetate (3 × 30 ml) and the combined organic solutes were dried ($MgSO_4$). The solvent was removed *in vacuo* (20 °C/10 Torr) to leave a brown oil (1.40 g, d.r. **2** : **3** = 67 : 33). Chromatography on silica (70 g, column 3 cm × 25 cm; petrol ether/EtOAc 30 : 70) afforded the D-*ribo*-nitrone **3** (182 mg, 20%) as a spectroscopically pure yellowish solid. Further elution (petrol ether/EtOAc 10 : 90) gave the L-*lyxo*-nitrone **2** (356 mg, 40%) as a brownish solid, again spectroscopically pure, with slightly deviating elemental analysis.

L-*lyxo* isomer **2**: M. p. 107 – 109 °C. – $[\alpha]_D^{20} = 117$ ($c = 0.605$, CH_2Cl_2). – MS (FAB pos., mNBA, 345 K): $m/z(\%) = 595$ (10) $[2M+H]^+$, 298 (100 $[M+H]^+$. – HRMS (FAB pos., mNBA): $[M+H]^+$ $C_8H_{13}INO_3$, calcd. 297.9940, found 297.9914. – IR (KBr): $\nu = 1570$ (C=N), 1370, 1360, 1250, 1210, 1200, 1110, 1050, 1030, 880, 840 cm^{-1}. – ^{1}H NMR (300.1 MHz, $CDCl_3$): $\delta = 1.36$, 1.38 (2 s, 3 H each, $C(CH_3)_2$), 3.28 (dd, $J_{5,1A} = 11.9$, $^2J_{1'A,1'B} = 9.4$ Hz, 1 H, 1'-H_A), 3.84 (dd, $J_{5,1'B} = 3.5$, $^2J_{1'A,1'B} = 9.4$ Hz, 1 H, 1'-H_B), 4.22 (m, 1 H, 5-H), 4.99 (dd, $J_{3,4} = 6.1$, $J_{4,5} = 4.8$ Hz, 1 H, 4-H), 5.20 (dd, $J_{2,3} = 1.8$, $J_{3,4} = 6.1$ Hz, 1 H, 3-H), 6.91 (d, $J_{2,3} = 1.8$ Hz, 1 H, 2-H). – ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = -5.9$ (t, C-1'), 26.1, 27.2 (2 q, $C(CH_3)_2$), 74.7, 76.5, 76.8 (3 d, C-3, C-4, C-5), 112.5 (s, $C(CH_3)_2$), 131.9 (d, C-2).

D-*Ribo* isomer **3**: M. p. 200 - 205 °C (dec.). – $[\alpha]_D^{20} = 43$ ($c = 0.63$, CH_2Cl_2). – MS (FAB pos., mNBA, 345 K): $m/z(\%) = 595$ (12) $[2M+H]^+$, 298 (100) $[M+H]^+$. – HRMS (FAB pos., mNBA): $[M+H]^+$ $C_8H_{13}INO_3$, calcd. 297.9940, found 297.9912. – IR (KBr): $\nu = 1570$ (C=N), 1375, 1365, 1270, 1250, 1220, 1190, 1175, 1135, 1025, 1010, 830 cm^{-1}. – ^1H NMR (300.1 MHz, $CDCl_3$): $\delta = 1.32$, 1.39 (2 s, 3 H each, $C(CH_3)_2$), 3.53 (dd, $J_{5,1'A} = 3.1$, $^2J_{1'A,1'B} = 11.0$ Hz, 1 H, 1'-H_A), 3.75 (dd, $J_{5,1'B} = 4.5$, $^2J_{1'A,1'B} = 11.0$ Hz, 1 H, 1'-H_B), 4.04 (ddd, $J_{4,5} = 1.3$, $J_{5,1'A} = 3.1$, $J_{5,1'B} = 4.5$ Hz, 1 H, 5-H), 4.59 (dd, $J_{3,4} = 6.5$, $J_{4,5} = 1.3$ Hz, 1 H, 4-H), 5.26 (dd, $J_{2,3} = 1.7$, $J_{3,4} = 6.5$ Hz, 1 H, 3-H), 6.98 (d, $J_{2,3} = 1.7$ Hz, 1 H, 2-H). – ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 3.5$ (t, C-1'), 25.6, 27.0 (2 q, $C(CH_3)_2$), 78.1, 78.3, 79.4 (3 d, C-3, C-4, C-5), 112.3 (s, $C(CH_3)_2$), 133.0 (d, C-2). – $C_8H_{12}INO_3$ (297.1): calcd. C 32.34, H 4.07, N 4.71; found for **2** (L-*lyxo*) C 33.13, H 4.23, N 4.62; found for **3** (D-*ribo*) C 33.05, H 4.12, N 4.77.

(3S,4R,5R)-5-Bromomethyl-3,4-isopropylidenedioxy-3,4-dihydro-5H-pyrrole 1-oxide **4** *and (3S,4R,5S)-diastereomer* **5***; typical procedure A for bromocyclization*

To the oxime **1** (171 mg, 1.00 mmol), dissolved in abs. CH_2Cl_2 (6 ml), was added $NaHCO_3$ (252 mg, 3.00 mmol). With vigorous stirring then a solution of bromine (168 mg, 1.05 mmol) in CH_2Cl_2 (abs., 4 ml) was added by means of a precision funnel at 0 °C within 3 h. The mixture was allowed to warm to r. t. and was stirred for another hour. The slightly yellow solution was decanted and washed with dilute $Na_2S_2O_3$, saturated $NaHCO_3$, and saturated NH_4Cl solution (3 ml each). The aqueous phases were reextracted with CH_2Cl_2 (2×5 ml). The organic solutes were combined, dried ($MgSO_4$), and rota-evaporated (30 °C/10 Torr). This left a colorless solid (255 mg, d. r. **4** : **5** = 83 : 17 according to HPLC and ^{13}C NMR analyses) which was chromatographically separated on silica (16 g, column 2 cm ×17 cm; petrol ether/EtOAc 30 : 70) and first afforded the D-*ribo*-nitrone **5** (35 mg, 14%; purity > 99 : 1 according to HPLC and NMR analyses), then the L-*lyxo*-nitrone **4** (elution with EtOAc; 165 mg, 66%; purity > 99 : 1 as above), both as analytically pure samples. – In other experiments with up to 25 mmol of **1** yields ranged from 65 to 80%, with like d. r. – The bromocyclization was carried out at various lower temperatures, down to −80 °C. While the d. r. **4**/**5** did not change notably (to 86 : 14), the chromatographic separation done as above gave an additional fraction containing a mixture of three isomeric dibromo-oximes **7** as a colorless oil.

L-*lyxo*-nitrone **4**: colorless solid, m. p. 130 – 135 °C (dec.). – $[\alpha]_D^{20} = 104$ ($c = 0.715$, CH_2Cl_2). – IR (KBr): $\nu = 1570$ (C=N), 1340, 1200, 1110, 1050, 1030 cm^{-1}. – ^1H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.43$, 1.46 (2 s, 3 H each, $C(CH_3)_2$), 3.65 (dd, $J_{5,1'A} = 11.3$, $^2J_{1'A,1'B} = 9.7$ Hz, 1 H, 1'-H_A), 4.08 (dd, $J_{5,1'B} = 3.6$, $^2J_{1'A,1'B} = 9.7$ Hz, 1 H, 1'-H_B), 4.34 (m, 1 H, 5-H), 5.04 (dd, $J_{3,4} = 6.1$, $J_{4,5} = 4.8$ Hz, 1 H, 4-H), 5.30 (dd, $J_{2,3} = 2.0$, $J_{3,4} = 6.1$ Hz, 1 H, 3-H), 6.94 (d, $J_{2,3} = 2.0$ Hz, 1 H, 2-H). – ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 23.9$ (t, C-1'), 26.1, 27.2 (2 q, $C(CH_3)_2$), 74.3 (d, C-4), 75.4 (d, C-5), 77.2 (d, C-3), 112.6 (2 s, $C(CH_3)_2$), 132.3 (d, C-2).

D-*Ribo*-nitrone **5**: colorless solid, m. p. 103 – 106 °C. – $[\alpha]_D^{20} = 26$ ($c = 0.50$, CH_2Cl_2). – IR (KBr): $\nu = 1560$ (C=N), 1370, 1360, 1270, 1250, 1200, 1150, 1140, 1070, 1050, 1030, 850, 840 cm^{-1}. – ^1H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.39$, 1.47 (2 s, 3 H each, $C(CH_3)_2$), 3.75 (dd, $J_{5,1'A} = 2.9$, $^2J_{1'A,1'B} = 11.3$ Hz, 1 H, 1'-H_A), 4.09 (dd, $J_{5,1'B} = 3.6$, $^2J_{1'A,1'B} = 11.3$ Hz, 1 H, 1'-H_B), 4.38 (m, 1 H, 5-H), 4.81 (dd, $J_{3,4} = 6.4$, $J_{4,5} = 1.4$ Hz, 1 H, 4-H), 5.29 (dd, $J_{2,3} = 1.7$, $J_{3,4} = 6.4$ Hz, 1 H, 3-H), 7.02 (d, $J_{2,3} = 1.7$ Hz, 1 H, 2-H). – ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 25.6$, 27.1 (2 q, $C(CH_3)_2$), 30.0 (t, C-1'), 77.9 (d, C-4), 78.5 (d, C-3), 78.7 (d, C-5), 112.3 (s, $C(CH_3)_2$), 133.5 (d, C-2). – $C_8H_{12}BrNO_3$ (250.1): calcd. C 38.42, H 4.84, N 5.60, Br 31.95; found for **4** (L-*lyxo*) C 38.45, H 4.85, N 5.47, Br 31.84; found for **5** (D-*ribo*) C 38.56, H 4.91, N 5.57, Br 31.81. – NMR peak assignments were done by means of C,H COSY. Structures and configurations of **4** and **5** were ascertained by crystal structure analyses [26].

NMR and MS data of 4,5-dibromopentanal oximes **7**: – ^1H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.43$, 1.65 (2 s, 6 H, $C(CH_3)_2$), 3.75 (dd, 1 H, $^3J_{4,5} = 5.1$, $^2J_{5a,5b} = 10.2$ Hz, 5-H_a), 3.80 (m, 1 H, 4-H), 4.13 (dd, 1 H, $^3J_{4,5} = 5.7$, $^2J_{5a,5b} = 10.2$ Hz, 5-H_b), 5.09 (d, 1 H, $^3J_{2,3} = 7.9$ Hz, 3-H), 5.32 (dd, 1 H, $^3J_{1,2} = 3.6$, $^3J_{2,3} = 7.9$ Hz, 2-H), 7.30 (d, 1 H, $^3J_{1,2} = 3.6$ Hz, 1-H), 8.77 (sb, 1 H, N-OH). – ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 24.5$, 26.8 (2 s, $C(CH_3)_2$), 32.3 (t, C-5), 50.5 (d, C-4), 73.1, 75.6 (2 d, C-2, C-3), 109.9 ($C(CH_3)_2$), 150.8 (d, C-1). – $C_8H_{13}Br_2NO_3$ (331.0). – MS (EI, 70 eV, 340 K): $m/z(\%) = 331$ (5) $[M]^+$, 316 (45) $[M-CH_3]^+$, 144 (5), 115 (10), 98 (15), 59 (20), 43 (100).

3-Phenyl-4-pentenal oxime (**9**)*; typical procedure B for oxime formation*

3-Phenyl-4-pentenal (2.11 g, 13.2 mmol) in ethanol (12 ml) was added to a solution of hydroxylamine hydrochloride (1.83 g, 26.3 mmol) in water (4 ml) and Na_2CO_3(1.44 g, 13.2 mmol) in water (10 ml). The mixture was heated to reflux overnight with vigorous stirring. After cooling the reaction mixture was extracted with CH_2Cl_2 (4×30 ml) and dried ($MgSO_4$). The organic solvents were concentrated *in vacuo*. The crude product (2.29 g, 99%) was chromatographed to give the (*E*)-oxime **9** exclusively as a colorless oil (1.97 g, 86%). – IR (film): $\nu = 3241$, 1491, 1451, 991, 917, 753, 699 cm^{-1}. – ^1H NMR (250.1 MHz, $CDCl_3$): $\delta = 2.59 - 2.69$ (m, 1 H, 3-H_A), 2.76 – 2.83 (m, 1 H, 3-H_B),

3.46 – 3.59 (m, 1 H, 4-H), 5.03 – 5.14 (m, 2 H, 5-H), 5.89 – 6.03 (m, 1 H, 5-H), 6.68 (t, $J = 10.4$, 1 H, 2-H), 7.17 – 7.3 (m, 5 H, C_6H_5), 8.7 – 9.23 (sb, 1 H, OH). – ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta = 46.3$ (t, C-2), 47.4 (d, C-3), 115.3 (t, C-5), 126.7, 127.5, 128.6, 140.5, 142.4, 142.6 (6 d, C-4, C_6H_5), 150.6 (d, C-1). – $C_{11}H_{13}NO$ (175.2): calcd. C 75.40, H 7.48, N 7.99, found C 75.00, H 7.42, N 7.93.

trans-5-Bromomethyl-4-phenyl-3,4-dihydro-5H-pyrrole 1-oxide (**10**) *and* cis*-isomer* **11**

In the dark, to the oxime **9** (526 mg, 3.00 mmol) in methylene chloride (40 ml) was added $NaHCO_3$ (757 mg, 9.00 mmol); the mixture was cooled to 0 °C and bromine (503 mg, 3.15 mmol) in methylene chloride (12 ml, abs.) was slowly added within 3 h at the same temperature. The reaction mixture was successively washed with saturated $Na_2S_2O_3$solution (10 ml), saturated $NaHCO_3$ (10 ml), and saturated NH_4Cl (10 ml). The aqueous portions were extracted with CH_2Cl_2 (2×50 ml). The organic solutes were dried ($MgSO_4$) and concentrated *in vacuo*. The residue was subjected to flash chromatography (silica, column 3 cm ×30 cm, EtOAc/MeOH 9 : 1) to yield spectroscopically pure *trans*-nitrone **10** (110 mg, 14%) as a colorless solid and *cis*-nitrone **11** (100 mg, 13%) as a colorless oil with somewhat deviating analysis. The crystals of **10** proved suitable for crystal structure analysis [1d].

trans-Nitrone **10**: M. p. 125 – 127 °C. – IR (film): $\nu = 1638$, 1589, 1497, 1435, 1399, 1252, 1244, 1220, 1025 cm^{-1}. – ^{1}H NMR (500.1 MHz, $CDCl_3$): $\delta = 2.74$ – 2.80 (dddd, $J = 1.7$, $J_{2,3A} = 3.1$, $J_{3A,3B} = 19.1$, $J_{3A,4} = 6.05$ Hz, 1 H, 3-H_A), 3.13 – 3.20 (ddt, $J_{2,3B} = 2.4$, $J_{3A,3B} = 19.1$, $J_{3B,4} = 9.5$ Hz, 1 H, 3-H_B), 3.58 – 3.62 (m, 1 H, 1'-H_A), 3.76 – 3.81 (m, 1 H, 1'-H_B), 4.23 – 4.27 (m, 2 H, 4-H, 5-H), 7.08 (s, 1 H, 2-H), 7.26 – 7.39 (m, 5 H, C_6H_5). – ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 32.4$ (t, C-1'), 36.1 (t, C-3), 43.1 (d, C-4), 78.9 (d, C-5), 127.5, 128.2, 129.7 (d, C_6H_5), 134.9 (s, C_6H_5), 141.5 (d, C-2).

cis-Nitrone **11**: IR (film): $\nu = 1603$, 1203, 698 cm^{-1}. – ^{1}H NMR (500.1 MHz, $CDCl_3$): $\delta = 3.01$ – 3.07 (ddd, $J_{2,3A} = 4.1$, $J_{3A,3B} = 18.3$, $J_{3A,4} = 8.17$ Hz, 1 H, 3-H_A), 3.07 – 3.13 (ddd, $J_{2,3B} = 2.3$, $J_{3A,3B} = 18.3$, $J_{3B,4} = 6.1$ Hz, 1 H, 3-H_B), 3.34 – 3.38 (dd, $J_{1'A,1'B} = 10.8$, $J_{1'A,5} = 7.6$ Hz, 1 H, 1'-H_A), 3.59 – 3.62 (dd, $J_{1'A,1'B} = 10.8$, $J_{1'B,5} = 7.6$ Hz, 1 H, 1'-H_B), 4.05 – 4.1 (td, $J_{3,4} = 8.5$, $J_{4,5} = 6.1$, 1 H, 4-H), 4.53 – 4.58 (m,1 H, 5-H), 7.18 – 7.19 (dd, $J_{2,3A} = 4.1$, $J_{2,3B} = 2.3$ Hz, 2-H), 7.26 – 7.38 (m, 5 H, C_6H_5). – ^{13}C NMR (125.7 MHz $CDCl_3$): $\delta = 27.9$ (t, C-1'), 33.1 (t, C-3), 42.1 (d, C-4), 75.44 (d, C-5), 127.9, 128.42, 128.8 (d,C_6H_5), 134.7 (s, C_6H_5), 136.2 (d, C-2). – $C_{11}H_{12}BrNO$ (254.1): calcd. C 51.99, H 4.76, N 5.51, Br 31.44; found for **10** (*trans*): C 51.95, H 4.81, N 5.52, Br 31.83; found for **11** (*cis*): C 51.95, H 4.78, N 5.39, Br 34.80.

2-Bromomethyl-4,4-dimethyl-3,4-dihydro-2H-pyrrole 1-oxide (**13**)

Prepared according to the Typical Procedure A given for **4**/**5**; from oxime **12** (1.0 g, 7.8 mmol) in CH_2Cl_2 (20 ml, abs.) with $NaHCO_3$ (1.96 g, 23.4 mmol), addition of bromine (1.31 g, 8.19 mmol) in CH_2Cl_2 at 0 °C within 3 h, then 1 h at r. t. Work-up by washing the reaction mixture successively with saturated solutions of $Na_2S_2O_3$ (10 ml), $NaHCO_3$ (10 ml), and NH_4Cl (10 ml), drying ($MgSO_4$), and rotaevaporation. The crude product (1.65 g) was purified by flash chromatography on silica (column 6 cm ×15 cm, EtOAc/MeOH = 9 : 1) to yield analytically pure nitrone **13** (1.42 g, 87%) as a colorless, crystalline solid.

M. p. 53 – 54 °C. – IR (film): $\nu = 3043$, 1595 (C=N), 1245, 1166, 1120 cm^{-1}. – ^{1}H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.25$, 1.30 (2 s, 3 H each, $C(CH_3)_2$), 2.08 (dd, $J_{4A,4B} = 13.2$, $J_{4A,5} = 8.15$ Hz, 1 H, 4-H_A), 2.21 (dd, $J_{4A,4B} = 13.2$, $J_{4B,5} = 8.45$ Hz, 1 H, 4-H_B), 3.67 (dd, $J_{5,1'A} = 2.8$, $J_{1'A,1'B} = 13.2$ Hz, 1 H, 1'-H_A), 4.05 (dd, $J_{5,1'B} = 5.3$, $J_{1'A,1'B} = 10.8$ Hz, 1 H, 1'-H_B), 4.40 (m, 1 H, 5-H), 6.83 (d, $J = 1.6$ Hz, 1 H, 2-H). – ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 27.3$, 27.4 (2 q, $C(CH_3)_2$), 38.9 (t, C-4), 39.7 (s, C-3), 71.2 (d, C-5), 143.5 (d, C-2). – $C_7H_{14}BrNO$ (206.1): calcd. C 40.80, H 5.87, N 6.80, Br 38.77; found C 40.71, H 5.86, N 6.74, Br 38.35.

2-Allylcyclopentanone oxime (**14**)

Prepared following Typical Procedure B; 2-allylcyclopentanone [39] (1.28 g, 10.3 mmol), $NH_2OH{\cdot}HCl$ (0.86 g, 12.4 mmol), NaOAc (1.28 g, 15.5 mmol), dissolved in acetonitrile/water (100 ml, 3:1), 3 h stirring at r. t. Work-up as above gave crude product **14** (850 mg, 59%) which was separated by flash chromatography (silica, column 3 cm ×15 cm, hexane/EtOAc 4 : 1) to yield analytically pure oxime (*E*)-**14** (680 mg, 47.5%) as a colorless oil and analytically pure oxime (*Z*)-**14** (113 mg, 8%) as a colorless oil. – Major isomer (*E*)-**14**: IR (film): $\nu = 3274$ (OH), 1672, 1640, 1437, 1202, 910, 692 cm^{-1}. – ^{1}H NMR (300.1 MHz, $CDCl_3$): $\delta = 1.36$ – 1.69 (m, 1 H), 1.54 – 1.69 (m, 1 H), 1.78 – 1.98 (m, 2 H), 2.0 – 2.2 (m, 1 H), 2.35 – 2.64 (m, 4 H), 4.95 – 5.1 (m, 2 H, 3'-H), 5.74 – 5.87 (m, 1 H, 2'-H), 9.2 (sb, 1 H, OH). – ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 22.8$, 27.8, 31.6, 36.8 (t, C-3, C-4, C-5, C-1'), 43.1 (d, C-2), 116.6 (t, C-3'), 136.8 (d, C-2'), 168.7 (s, C-1). – Minor isomer (*Z*)-**14**: IR (film): $\nu = 3273$ (OH), 2957, 1674, 1639, 1438, 1203, 967, 910 cm^{-1}. – ^{1}H NMR (300.1 MHz, $CDCl_3$): $\delta = 1.50$ – 2.70 (m, 8 H), 3.00 – 3.06 (m, 1 H, 2-H), 4.94 – 5.09 (m, 2 H, 3'-H), 5.71 – 5.89 (m, 2'-H), 8.8 (db, $J = 6.3$ Hz, 1 H, OH). – ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 23.1$, 30.0, 31.2, 34.6 (t, C-3, C-4, C-5, C-1'), 39.1 (d, C-2), 116.3, (t, C-3'), 136.5 (d, C-2'), 168.4 (s, C-1). – $C_8H_{13}NO$ (139.2): calcd. C 69.03, H 9.41, N 10.06, found for (*E*)-**14** C 68.82, H 9.39, N 9.80; found for (*Z*)-**14** C 68.98, H 9.52, N 9.83.

Bromocyclization of 2-allylcyclopentanone oxime (**14**) *and reduction of intermediate nitrone* **15***; 2-bromomethyl-1-hydroxyperhydrocyclopenta[b]pyrrole* (**16**)

To 2-allylcyclopentanone oxime **14** (139 mg, 1.00 mmol) and $NaHCO_3$ (252 mg, 3.00 mmol) in CH_2Cl_2 (20 ml, abs.) at 0 °C bromine (167 mg, 1.05 mmol) in CH_2Cl_2 (10 ml) was added slowly within 2 h. The progress of the reaction was monitored by TLC. $NaHCO_3$was filtered off and the solvents were removed (30 °C/12 mbar). The resulting residue containing the nitrone was dissolved in EtOH (10 ml), cooled to 0 °C and treated with $NaBH_4$(114 mg, 3.00 mmol). The reaction mixture was stirred at the same temp. for 1 h, then citric acid solution (5%) was added. After 10 min the reaction mixture was extracted with CH_2Cl_2 (4×10 ml). The combined organic phases were washed with saturated $NaHCO_3$ (10 ml), the aqueous layer was again extracted with CH_2Cl_2 (2×10 ml). The organic solutes were dried ($MgSO_4$) and solvents were removed *in vacuo*. The residue was chromatographed (silica, column 1.5 cm ×20 cm, hexane/EtOAc 8 : 2), to afford spectroscopically pure 2-bromomethyl-hexahydro-1-hydroxycyclopenta[b]pyrrole **16** (68 mg, 31%) as a volatile, colorless oil, consisting of a single isomer. – IR (film): $\nu = 3350$ (OH), 2940, 2863, 1436, 1216, 914, 710, 654 cm^{-1}. – ^{1}H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.16$ (ddd, $J_{2,3A} = 11.5$, $J_{3A,3B} = 12.8$, $J_{3A,4} = 8.3$ Hz, 1 H, 3-H_A), 1.42 (m, 2 H, CH_2), 1.56 (m, 3 H, CH and CH_2), 1.93 (m, 1 H, CH_2), 2.26 (ddd, $J_{2,3B} = 6.1$, $J_{3A,3B} = 12.8$, $J_{3B,4} = 9.9$ Hz, 1 H, 3-H_B), 2.57 (m, 1 H), 3.08 (dddd, $J_{2,3A} = 11.5$, $J_{2,3B} = 6.1$, $J_{2,1'A} = 7.5$, $J_{2,1'B} = 3.3$ Hz, 1 H, 2-H), 3.39 (dd, $J_{2,1'A} = 7.5$, $J_{1'A,1'B} = 10.0$ Hz, 1 H, 1'-H_A), 3.47 (m, 1 H, 8-H), 3.60 (dd, $J_{2,1'B} = 3.3$, $J_{1'A,1'B} = 10.0$ Hz, 1 H, 1'-H_B). – ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 24.1$, 32.0, 33.1, 34.2, 34.4 (t, 5 CH_2, C-3, C-5, C-6, C-7, C-1'), 37.1 (d, C-4), 68.5 (d, C-2), 74.5 (d, C-8).

2-Allylcyclohexanone oxime (**17**)

In analogy to a literature procedure [38b], $NH_2OH \cdot HCl$ (2.40 g, 3.56 mmol) and NaOAc (3.54 g, 43.6 mmol) were added to a stirred solution of 2-allylcyclohexanone (3.80 g, 27.5 mmol) in CH_3CN/H_2O (200 ml, 3:1) at r. t. Stirring was continued for 3 h, then most of the acetonitrile was removed under reduced pressure and the remaining aqueous solution was extracted with CH_2Cl_2 (3×75 ml). The organic solutes were dried over $mgSO_4$ and concentrated *in vacuo* to afford the crude product of **17** [4.21 g, quant. (*E*)/(*Z*)-mixture 84 : 16 from NMR)]. This was subjected to flash chromatography on silica (column 6 cm ×20 cm, hexane/EtOAc 9 : 1) to yield analytically pure oxime (*E*)-**17** (3.328 g, 79.5%) as a colorless solid and analytically pure oxime (*Z*)-**17** (660 mg, 16%) as a colorless, low-melting solid. – Major isomer (*E*)-**17**: M. p. 70 – 71 °C. – IR (film): $\nu = 3226$ (OH), 3170, 2924, 2862, 2850, 1432, 938, 906, 769 cm^{-1}. – ^{1}H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.30$ (m, 1 H), 1.49 (m, 2 H), 1.72 (m, 2 H), 1.86 – 1.91 (m, 2 H), 2.09 – 2.19 (m, 2 H), 2.26 – 2.31 (m, 1 H), 2.46 – 2.52 (m, 1 H), 2.83 – 2.88 (m, 1 H), 5.02 – 5.05 (m, 2 H, H_2C=), 5.73 – 5.81 (m, 1 H, =CH–), 9.2 (sb, 1 H, OH). – ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 23.4$, 23.9, 26.1, 33.3, 35.2 (t each, C-3, C-4, C-5, C-6, C-1'), 41.9 (d, C-2), 116.2 (t, H_2C=CH), 131.1 (d, H_2C=*C*H), 162.2 (s, C-1). – Minor isomer (*Z*)-**17**: M. p. 38 – 39 °C. – IR (film): $\nu = 3258$ (OH), 2925, 1440, 929, 743 cm^{-1}. – ^{1}H NMR (300.1 MHz, $CDCl_3$): $\delta = 1.37$ – 2.52 (m, 11 H), 4.99 – 5.03 (m, 2 H, H_2C=), 5.69 – 5.80 (m, 1 H, =CH–), 8.15 (db, $J = 3.4$ Hz, 1 H, OH). – ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 20.8$, 27.1, 29.0, 29.1, 32.3 (t each, C-3, C-4, C-5, C-6, C-1'), 35.1 (d, C-2), 116.5 (t, H_2C=CH), 136.6 (d, H_2C=*C*H), 163.2 (s, C-1). – $C_9H_{15}NO$ (153.2): calcd. C 70.55, H 9.87, N 9.14; found for (*E*)-**17** C 70.57, H 9.56, N 9.14; found for (*Z*)-**17** C 70.44, H 9.86, N 9.25.

endo-2-Bromomethyl-3,3a,4,5,6,7-hexahydro-2H-indole 1-oxide (**18**) *and exo isomer* (**19**)

Typical Procedure A was followed: Oxime (*E*)-**17** (500 mg, 3.2 mmol) in CH_2Cl_2 (20 ml, abs.) with $NaHCO_3$ (822 mg, 9.7 mmol); addition of bromine (536 mg) in CH_2Cl_2 (12 ml, abs.) at 0 °C within 3 h, stirring at r. t. for 10 min. Work-up: washing with saturated solutions of $Na_2S_2O_3$, $NaHCO_3$, and NH_4Cl (10 ml each), extraction of aqueous portions with CH_2Cl_2 (2×25 ml); drying ($MgSO_4$), concentration *in vacuo*. The crude product (742 mg, 84%, d. r. **18**/**19** 67 : 33 from NMR) was subjected to flash chromatography on silica (column, 3 cm ×30 cm, EtOAc/MeOH 7 : 3) to yield analytically pure *exo*-nitrone **19** (210 mg, 28%) as a brown solid and *endo*-nitrone **18** (386 mg, 52%) as a brown oil. The crystals of **19** proved suitable for crystal structure analysis [43].

endo-Nitrone **18**: IR (film): $\nu = 2936$, 2856, 1625, 1448, 1378, 1211, 1143 (s) cm^{-1}. – ^{1}H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.24 – 1.26$ (m, 3 H), 1.68 (m, 1 H), 1.86 (d, $J = 10.3$ Hz, 1 H), 1.97 – 2.04 (m, 2 H), 2.09 – 2.12 (m, 1 H), 2.48 (m, 1 H), 2.73 – 2.80 (bm, 1 H), 3.16 (d, $J = 14.7$ Hz, 1 H), 3.69 (dd, $J_{2,1'A} = 2.7$, $J_{1'A,1'B} = 10.7$ Hz, 1 H, 1'-H_A), 4.12 (dd, $J_{2,1'B} = 5.1$, $J_{1'A,1'B} = 10.7$ Hz, 1 H, 1'-H_B), 4.29 (m, 1 H, 2-H). – ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 24.4$, 24.7, 25.0, 29.5, 33.8, 34.2 (t each, C-3, C-5, C-6, C-7, C-8, C-1'), 40.0 (d, C-4), 71.3 (d, C-2), 150.4 (s, C-9).

exo-Nitrone **19**: M. p. 102 – 103 °C. – IR (film): $\nu =$ 2934, 1608, 1209 cm^{-1}. – ^{1}H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.15$ (m, 1 H), 1.36 – 1.43 (m, 2 H), 1.83 – 1.90 (m, 2 H), 1.95 – 1.98 (m, 1 H), 2.01 – 2.12 (m, 2 H), 2.28 – 2.33 (m, 1 H), 2.86 – 2.93 (m, 1 H, 3-H_A), 3.17 (dd, $J_{2,3B} =$ 3.45, $J_{3A,3B} = 15.4$ Hz,1 H, 3-H_B), 3.64 (dd, $J_{2,1'A} = 2.8$, $J_{1'A,1'B} = 10.8$, Hz, 1 H, 1'-H_A), 4.11 (dd, $J_{2,1'B} = 4.4$, $J_{1'A,1'B} = 10.8$ Hz, 1 H, 1'-H_B), 4.33 – 4.34 (m, 1 H, 2-H). –

^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 24.1$, 24.7, 25.1, 29.6, 34.70, 34.74 (t each, C-3, C-5, C-6, C-7, C-8, C-1'), 41.5 (d, C-4), 72.6 (d, C-2), 150.4 (s, C-9). – $C_9H_{14}BrNO$ (232.1): calcd. C 46.56, H 6.08, N 6.03, Br 34.42; found for **19** (*exo*) C 46.26, H 6.11, N 5.95, Br 34.22.

Ethyl 1-allyl-2-oximinocyclopentanonecarboxylate (**20a**)

Prepared following Typical Procedure B: Ethyl 1-allyl-2-cyclopentanone-1-carboxylate [40b] (3.00 g, 15.2 mmol), ethanol (18 ml), hydroxylamine hydrochloride (2.12 g, 30.6 mmol) in water (6 ml), Na_2CO_3 (1.61 g, 15.2 mmol) in water (15 ml), reflux overnight; extraction with CH_2Cl_2 (3×50 ml), drying ($MgSO_4$), concentration *in vacuo*; crude product [oxime **20a**, 3.19 g, 99%, (*E*)/(*Z*) mixture 78 : 22 from NMR] subjected to flash chromatography (silica, column 3 cm ×30 cm, hexane/EtOAc 4 : 1) to give analytically pure oxime (*E*)-**20a** (2.46 g, 76%) and analytically pure oxime (*Z*)-**20a** (560 mg, 17%) both as colorless solids. – Major isomer (*E*)-**20a**: M. p. 70 – 71 °C. – IR (film): $\nu =$ 3241 (OH), 2975, 1715, 1440, 1420, 1271, 1217, 1144, 1044, 1025, 983, 938, 915, 866, 724 cm^{-1}. – ^{1}H NMR (250.1 MHz, $CDCl_3$): $\delta = 1.25$ (t, $J = 7.1$ Hz, 3 H, OCH_2CH_3), 1.75 – 1.86 (m, 2 H), 2.3 – 2.47 (m, 2 H), 2.51 – 2.62 (m, 2 H), 2.76 (m, 2 H), 4.1 – 4.23 (m, 2 H, OCH_2CH_3), 5.05 – 5.13 (m, 2 H, 3'-H), 5.77 (dd, $J = 10.2$, 17.0 Hz, 1 H, 2'-H), 9.3 (sb, 1-H, OH). – ^{13}C NMR (62.8 MHz, $CDCl_3$): $\delta = 14.1$ (q, OCH_2CH_3), 21.5, 27.4, 34.1, 40.7 (t each, C-3, C-4, C-5, C-1'), 55.9 (s, C-2), 61.4 (t, OCH_2CH_3), 118.5 (t, C-2'), 133.7 (d, C-3'), 165.6 (s, C-1), 172.8 (s, CO_2Et). – Minor isomer (*Z*)-**20a**: M. p. 38 – 39 °C. – IR (film): $\nu = 1730$, 1220, 746, 666 cm^{-1}. – ^{1}H NMR (250.1 MHz, $CDCl_3$): $\delta = 1.23$ (t, $J = 7.1$ Hz, 3 H, OCH_2CH_3), 1.78 – 2.90 (m, 8 H, 4 CH_2), 4.12 – 4.21 (q, $J = 7.1$ Hz, 2 H, OCH_2CH_3), 5.07 – 5.13 (m, 2 H, 3'-H), 5.60 – 5.83 (m, 1 H, 2'-H), 8.82 (sb, 1 H, OH). – ^{13}C NMR (62.8 MHz, $CDCl_3$): $\delta = 14.1$ (q, OCH_2CH_3), 23.3, 32.0, 36.3, 36.7 (t each, C-3, C-4, C-5, C-1'), 54.0 (s, C-2), 60.8 (t, OCH_2CH_3), 118.6 (t, C-2'), 134.3 (d, C-3'), 165.2 (s, C-1), 174.2 (s, CO_2Et). – $C_{11}H_{17}NO_3$ (232.1): calcd. C 62.54, H 8.11, N 6.63, found for (*E*)-**20a** C 62.28, H 8.08, N 6.53; found for minor isomer (*Z*)-**20a** C 62.51, H 8.11, N 6.53.

Ethyl 2-bromomethyl-2,4,5,6-tetrahydro-3H-cyclopenta[b] pyrrole-3a-carboxylate 1-oxide (**21a**) *and 3-bromomethyl-6-oximino-2-oxa-spiro[4.4]nonane-1,6-dione* (**22**)

Typical Procedure A was used: Oxime (*E*)-**20a** (633 mg, 3.0 mmol) in CH_2Cl_2 (16 ml, abs.), $NaHCO_3$ (755 mg, 9.0 mmol), addition of bromine (503 mg, 3.15 mmol) in CH_2Cl_2 (12 ml, abs.) at 0 °C within 3 h and usual work-up. The crude product was subjected to flash chromatography (silica, column 3 cm ×30 cm, hexane/EtOAc 6 : 4 to EtOAc/MeOH 9 : 1) to afford spectroscopically pure nitrone **21a** (260 mg, 30%) as a pale-yellow oil and the spirolactone **22** (305 mg, 39%) as colorless solid crystals suitable for structure analysis [1d]. – Nitrone **21a**: IR (film): $\nu =$ 1721, 1637, 1187 cm^{-1}. – ^{1}H NMR (300.1 MHz, $CDCl_3$): $\delta = 1.28$ (t, $J = 7.1$ Hz, 3 H, OCH_2CH_3), 1.5 – 2.51 (m, 6 H, 3 CH_2), 2.64 – 2.76 (m) and 2.7 – 2.8 (dd, $J_{2,3} = 6.6$, $J_{3A,3B} = 13.2$ Hz, 1 H, together 2 H, 3-H_A, 3-H_B), 3.64 – 3.68 (dd, $J_{2,1'A} = 2.9$, $J_{1'A,1'B} = 11$ Hz, 1 H, 1'-H_A), 4.06 – 4.12 (dd, $J_{2,1'B} = 5.1$, $J_{1'A,1'B} = 11.0$ Hz, 1 H, 1'-H_B), 4.17 – 4.24 (q, $J = 7.1$ Hz, 2 H, OCH_2CH_3), 4.85 – 4.86 (m, 2-H). – ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 14.2$ (q, OCH_2CH_3), 22.3, 25.9, 32.7, 34.4, 36.1 (t each, C-3, C-6, C-7, C-8, C-1'), 58.9 (s, C-4), 62.1 (t, OCH_2CH_3), 76.4 (d, C-2), 144.2 (s, C-5), 172.0 (s, CO_2Et). – Spirolactone **22**: M. p. 127 – 129 °C. – IR (film): $\nu = 3319$ (OH), 1736, 1202, 1017, 954, 919 cm^{-1}. – ^{1}H NMR (300.1 MHz, $CDCl_3$): $\delta = 1.79 – 2.69$ (m, 8 H, 4 CH_2), 3.50 – 3.56 (dd, $J_{3,1'A} = 6.14$, $J_{1'A,1'B} = 10.8$ Hz, 1 H, 1'-H_A), 3.57 – 3.62 (dd, $J_{3,1'B} = 4.7$, $J_{1'A,1'B} = 10.8$ Hz, 1 H, 1'-H_B), 4.85 – 4.93 (m, 1 H, 3-H), 7.52 (sb, NOH). – ^{13}C NMR (75.5 MHz, $CDCl_3$,): $\delta = 22.1$, 26.9, 33.3, 36.1, 39.6 (t each, C-4, C-7, C-8, C-9, C-1'), 53.5 (s, C-5), 75.8 (d, C-3), 167.3 (s, C-6), 176.6 (s, C-1).

tert-Butyl 1-allyl-2-oximino-cyclopentanecarboxylate (**20b**)

Following Typical Procedure B, from *tert*-butyl 1-allyl-2-cyclopentanonecarboxylate [40] (2.24 g, 10.0 mmol), hydroxylamine hydrochloride (1.39 g, 20.0 mmol) in water (6 ml), with Na_2CO_3 (1.06 g, 10.0 mmol) in water (10 ml), reflux overnight. After the usual work-up the crude product of **20b** [2.30 g, 96%, (*E*)/(*Z*) 90 : 10 from NMR] was subjected to flash chromatography (silica, column 3 cm ×30 cm, hexane/EtOAc 4 : 1) to give analytically pure oxime (*E*)-**20b** (1.85 g, 77%) and analytically pure oxime (*Z*)-**20b** (230 mg, 10%) both as a colorless oil. – Major isomer (*E*)-**20b**: IR (film): $\nu = 3302$ (OH), 1721, 1142, 983, 917, 866 cm^{-1}. – ^{1}H NMR (300.1 MHz, $CDCl_3$): $\delta = 1.43$ (s, 9 H, $C(CH_3)_3$), 1.64 – 1.91 (m, 3 H, CH_2, and H of CH_2), 2.04 – 2.74 (m, 5 H, 2 CH_2, and H of CH_2), 5.05 – 5.11 (m, 2 H, 3'-H), 5.68 – 5.82 (m, 1 H, 2'-H), 9.03 (sb, 1-H, OH). – ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 21.8$, 27.5 (t, C-4, C-3), 27.9 (q, $C(CH_3)_3$), 34.5, 40.5 (t, C-5, C-1'), 56.5 (s, C-2), 81.4 (s, $C(CH_3)_3$), 118.3 (t, C-3'), 134.1 (d, C-2'), 166.0 (s, C-1), 171.2 (s, CO_2CMe_3). – $C_{13}H_{21}NO_3$ (239.3): calcd. C 65.25, H 8.84, N 5.84, found C 65.07, H 8.75, N 5.80. – Minor isomer (*Z*)-**20b**: IR (film): $\nu = 3242$ (OH), 1728, 1367, 1251, 1145, 1059, 915, 847, 734, 649 cm^{-1}. – ^{1}H NMR (300.1 MHz, $CDCl_3$): $\delta = 1.43$ (s, 9 H, $C(CH_3)_3$), 1.77 – 2.0 (m, 4 H, 2 CH_2), 2.27 – 2.52 (m, 2 H, CH_2), 2.53 (dd, $J_{2,1'A} = 8.3$, $J_{1'A,1'B} = 13.8$ Hz, 1 H, 1'-H_A), 2.92 (dd, $J_{2,1'B} = 6.7$, $J_{1'A,1'B} = 13.8$, Hz, 1 H, 1'-H_B), 5.01 – 5.08 (m, 2 H, 3'-H), 5.72 – 5.75 (m, 1 H, 2'-H), 9.03 (sb, 1-H, OH). – ^{13}C NMR

(75.5 MHz, $CDCl_3$): $\delta = 23.4$ (t, C-4), 27.8 (q, C(CH_3)$_3$), 32.2 (t, C-3), 36.4, 36.7 (t, C-5, C-1'), 57.6 (s, C-2), 80.6 (s, C(CH_3)$_3$), 118.3 (t, C-3'), 134.5 (d, C-2'), 165.6 (s, C-1), 173.1 (s, CO_2CMe_3).

tert-Butyl 2-bromomethyl-2,4,5,6-tetrahydro-3H-cyclopenta[b]pyrrole-3a-carboxylate 1-oxide (**21b**) *and 3-bromomethyl-2-oxa-6-oximino-spiro[4.4]nonane-1,6-dione 6-oxime* (**22**)

According to Typical Procedure A: Oxime (*E*)-**20b** (479 mg, 2.00 mmol), CH_2Cl_2 (16 ml), $NaHCO_3$ (512 mg, 6.00 mmol); addition of bromine (335 mg, 2.1 mmol) in CH_2Cl_2 (12 ml, abs.) at 0 °C with 3 h. Work-up as above and flash chromatography (silica, column 3 cm ×15 cm, hexane/EtOAc 6 : 4 to EtOAc/MeOH 9 : 1) afforded spectroscopically pure nitrone **21b** (70 mg, 11%) as a pale-yellow oil and spiro-lactone **22** (300 mg, 57%) as a colorless solid. The configuration of the spiro-lactone was proven by crystal structure analysis [1d]. – Nitrone **21b**: IR (film): $\nu = 1721$, 1637, 1187 (s) cm^{-1}. – ^1H NMR (300.1 MHz, $CDCl_3$): $\delta = 1.46$ (s, 9 H, C(CH_3)$_3$), 1.53 – 1.64 (m, 1 H of CH_2), 2.12 – 2.27 (m, 3 H, CH_2, 1 H of CH_2), 2.37 – 2.49 (m, 2 H, CH_2), 2.62 – 2.82 (m, 1 H, 7-H), 3.66 (dd, $J_{2,1'A} = 2.8$, $J_{1'A,1'B} = 11.0$ Hz, 1 H, 1'-H_A), 4.11 (dd, $J_{2,1'B} = 5.16$, $J_{1'A,1'B} = 11.0$ Hz, 1 H, 1'-H_B), 4.81 (m, 2-H). – ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 27.9$ (q, C(CH_3)$_3$), 22.2, 25.9, 32.9, 34.4, 36.0 (t, C-3, C-5, C-6, C-7, C-1'), 53.4 (s, C-4), 65.5 (q, C(CH_3)$_3$), 76.3 (d, C-2), 141.0 (s, C-5), 167.4 (s, CO_2CMe_3). – Spiro-lactone **22**: IR (film): $\nu = 3319$ (OH), 1736, 1202, 1017, 954, 919 cm^{-1}. – ^1H NMR (300.1 MHz, $CDCl_3$): $\delta = 1.79 – 2.69$ (m, 8 H, 4 CH_2), 3.50 – 3.56 (dd, $J_{3,1'A} = 6.14$, $J_{1'A,1'B} = 10.8$ Hz, 1 H, 1'-H_A), 3.57 – 3.62 (dd, $J_{3,1'B} = 4.7$, $J_{1'A,1'B} = 10.8$ Hz, 1 H, 1'-H_B), 4.85 – 4.93 (m, 1 H, 3-H), 7.52 (sb, NOH). – ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 22.1$, 26.9, 33.3, 36.1, 39.6 (t, C-4, C-7, C-8, C-9, C-1'), 53.5 (s, C-5), 75.8 (d, C-3), 167.3 (s, C-6), 176.6 (s, C-1).

3-Bromo-4,4-dimethyl-3,4-dihydro-2H-pyrrole 1-oxide (**24**)

Following the Typical Procedure A, the oxime **23** (226 mg, 2.00 mmol) was cyclized: CH_2Cl_2 (20 ml, abs.), $NaHCO_3$ (512 mg, 6 mmol), Br_2 (336 mg, 2.1 mmol) in CH_2Cl_2 (12 ml, abs.), addition within 3 h and further stirring for 1 h; washing with $Na_2S_2O_3$, $NaHCO_3$, and NH_4Cl (saturated solutions of 8 ml each), extraction with CH_2Cl_2 (2 × 25 ml), drying ($MgSO_4$), concentration *in vacuo*. The residue was purified by flash chromatography (silica, column 3 cm ×15 cm, EtOAc/MeOH 9 : 1) to yield analytically pure nitrone **24** (110 mg, 0.57 mmol, 29%) as a colorless, crystalline solid. – M. p. 84 – 86 °C. – IR (film): $\nu = 1588$, 1460, 1276, 1171 cm^{-1}. – ^1H NMR (300.1 MHz, $CDCl_3$): $\delta = 1.28$, 1.31 (2 s, 6 H, 2 CH_3), 4.18 – 4.34 (m, 3 H, 4-H, 5-H), 6.76 (s, 1 H, 2-H). – ^{13}C NMR (75.5 MHz, $CDCl_3$,): $\delta = 23.6$, 24.6 (q each, 2 CH_3), 46.4 (s, C-3), 49.2 (d, C-4), 68.7 (t, C-5), 141.5 (d, C-2). – HRMS (FAB, positive ion): exact mass calcd. for $C_6H_{10}BrNO$ 190.9946; found 190.9945. – $C_6H_{10}BrNO$ (192.05): calcd. C 37.52, H 5.25, N 7.29, Br 41.61; found C 37.89, H 5.29, N 7.20, Br 39.92.

5-Bromomethyl-3,3-dimethyltetrahydrofuran-2-ol (**30**)

In analogy to a literature procedure [43], 2,2-dimethyl-4-pentenal (4.48 g, 40 mmol) was dissolved in DMSO (10 ml) at ambient temperature under nitrogen, then water (3.6 ml) was added, followed by *N*-bromosuccinimide (7.46 g, 42 mmol). The mixture was stirred at r. t. for 3 h and then was diluted with EtOAc (50 ml). The organic phase was separated and the aqueous phase was extracted with EtOAc (2 × 50 ml). The combined organic phases were washed with water (10 ml) and brine (10 ml), then dried ($MgSO_4$) for 10 min, and concentrated *in vacuo*. The residue (6.48 g) was subjected to flash chromatography (silica, column 3 cm ×15 cm hexane/EtOAc 9 : 1) to afford analytically pure bromomethyl-tetrahydrofuranol **30** (5.2 g, 62%) as a colorless oil, anomeric ratio 75 : 25 (from NMR). – IR (film): $\nu = 3419$ (OH), 909 cm^{-1}. – ^1H NMR (300.1 MHz, $CDCl_3$): $\delta = 1.04$, 1.14 (2 s, 6 H, C(CH_3)$_2$), 1.75 (dd, $J_{3A,3B} = 12.3$, $J_{3A,4} = 9.2$ Hz, 1 H, 3-H_A), 1.88 (dd, $J_{3A,3B} = 12.3$, $J_{3B,4} = 6.65$ Hz, 1 H, 3-H_B), 3.41 (dd, $J_{4,1'A} = 6.2$, $J_{1'A,1'B} = 10.2$ Hz, 1 H, 1'-H_A), 3.52 (dd, $J_{4,1'B} = 6.0$, $J_{1'A,1'B} = 10.2$ Hz, 1 H, 1'-H_B), 4.3 – 4.51 (m, 1 H, 4-H), 4.95 (d, $J_{1,OH} = 2.4$ Hz, 1 H, 1-H). – ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 22.3$, 25.3 (2 q, C(CH_3)$_2$), 37.7 (t, C-1') 42.5 (t, C-3) 44.6 (s, C-2), 79.0 (d, C-4), 104.8 (d, C-1). – $C_7H_{13}BrO_2$ (209.1): calcd. C 40.21, H 6.27, Br 38.22, found C 40.26, H 6.16, Br 38.17.

5-Bromo-4-hydroxy-2,2-dimethylpentanal oxime (**31**)

Following Typical Procedure B: $NH_2OH{\cdot}HCl$ (1.32 g, 19.1 mmol), NaOAc (2.59 g, 31.6 mmol), (bromomethyl)tetrahydrofuranol **30** (3.32 g, 15.8 mmol) in CH_3CN/H_2O (3 : 1, 200 ml), stirring at r. t. for 2 h. Most of acetonitrile was removed under reduced pressure and the remaining aqueous solution was extracted with CH_2Cl_2 (3 × 50 ml). The organic solutes were dried ($MgSO_4$) and concentrated *in vacuo* to afford a crude product (3.32 g, 94%) which was subjected to flash chromatography (silica, column 3 cm ×22 cm, hexane/EtOAc 9 : 1) to yield analytically pure (*E*)-oxime **31** (2.54 g, 71%) as a colorless oil.

IR (film): $\nu = 3308$ (OH), 2963, 934 (s) cm^{-1}. – ^1H NMR (300.1 MHz, $CDCl_3$): $\delta = 1.15$, 1.16 (2 s, 6 H, 2 CH_3), 1.66 (d, $J_{3A,3B} = 14.8$ Hz, 1 H, 3-H_A), 1.86 (dd, $J_{3A,3B} = 14.8$, $J_{3B,4} = 8.9$ Hz, 1 H, 3-H_B), 3.40 (d, $J_{4A,5} = 5.5$ Hz, 2 H, 5-H), 3.97 (m, 1 H, 4-H), 6.52 (sb, 2 H, 2 OH), 7.38 (s, 1 H, 1-H). – ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 25.6$, 28.9 (2 q,

C(CH_3)$_2$), 36.8 (s, C-2), 39.9 (t, C-5), 45.9 (t, C-3), 68.5 (d, C-4), 159.1 (d, C-1). – $C_7H_{14}BrNO_2$ (224.1): calcd. C 37.52, H 6.30, N 6.25, Br 35.66, found C 37.74, H 6.33, N 5.98, Br 35.71.

3,3-Dimethyl-5-hydroxy-2,3,4,5-tetrahydropyridine 1-oxide (**32**)

The oxime **31** (224 mg, 1.00 mmol) was dissolved in CH_2Cl_2 (10 ml), then $NaHCO_3$ (168 mg, 2.00 mmol) was added and the mixture was heated to reflux for 3 h. Once the entire starting material was consumed (TLC), the solids were filtered off and the filtrate was concentrated *in vacuo* to leave 160 mg of a crude product, which was chromatographed (silica, column 1.5 cm ×15 cm, EtOAc/MeOH 7 : 3) to yield analytically pure nitrone **32** (104 mg, 73%) as a colorless solid. – M. p. 132 – 133 °C. – IR (film): $\nu = 3320$ (OH), 1024, 1001 cm^{-1}. – ^{1}H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.16$, 1.26 (2 s, 6 H, 2 CH_3), 1.66 (dd, $J_{4A,4B} = 13.4$, $J_{4A,5} = 9.0$ Hz, 1 H, 4-H_A), 1.80 (dd, $J_{4A,4B} = 13.4$, $J_{4B,5} = 3.3$ Hz, 1 H, 4-H_B), 3.67 (dd, $J_{5,6A} = 6.9$, $J_{6A,6B} = 15.3$ Hz, 1 H, 6-H_A), 3.91 (dd, $J_{5,6B} = 4.6$, $J_{6A,6B} = 15.3$ Hz, 1 H, 6-H_B), 4.22 – 4.27 (m, 1 H, 5-H), 5.36 (sb, 1 H, OH), 6.95 (s, 1 H, 2-H). – ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 28.4$, 28.7 (2 q, C(CH_3)$_2$), 34.1 (t, C-4), 40.2 (s, C-3), 62.6 (t, C-6), 63.5 (d, C-5), 145.5 (d, C-2). – $C_7H_{13}NO_2$ (143.2): calcd. C 58.72, H 9.15, N 9.78; found C 58.58, H 9.02, N 9.40.

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