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Allenyloxime—a new source of heterocyclizations to stable cyclic nitrones

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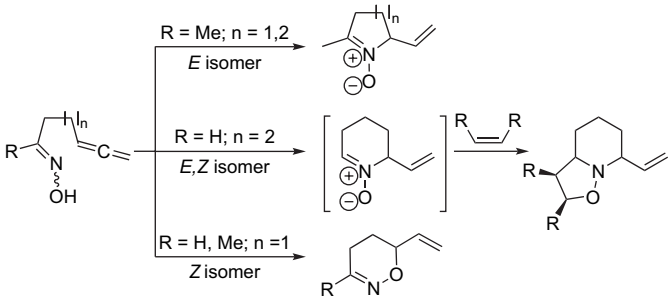
ABSTRACT

A variety of conditions including reductive and/or basic reagents in aqueous or alcoholic solution was applied to 2,2-dimethylpenta-3,4-dienal oxime. Formation of various five-membered heterocycles with excellent chemical selectivity was observed. Most of the reactions yielded cyclic nitrones with stable dipolar structure and unique functionalities present. All products of cyclization were isolated and fully characterized.

1. Introduction

Although there has been remarkable development in the field of allene chemistry,[1] allenyloximes have not attracted a lot of attention among chemists during the last decade. There are only several papers dealing with the allenyloxime cyclizations,[2,3] which were discussed in our previous report.[4] A distinct advance in allenyloxime chemistry was made by Gallagher et al., who for the first time presented an idea of approaching nitrone-type compounds by allenyloxime cyclization using $AgBF_4$ (as electrophilic catalyst) in dichloromethane (Scheme 1).[5]



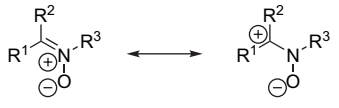
Scheme 1. Cyclization of allenyloximes.

That methodology is based on the cyclization of allenyloximes with minimally substituted alkyl chain leading to five- or six-membered cyclic nitrones bearing vinyl substitution.

However, the dipolar compounds could be effectively isolated only in the case of ketoximes. Due to their lower reactivity in dipolar cycloadditions, they afforded reasonable yields of nitrones. The more reactive aldoximes afforded unstable nitrones, which were trapped in situ by adding a dipolarophile.

This procedure is also complicated by the different reactivity of *E*/*Z* oxime isomers. In particular, *Z*-isomers showed considerable yields of cyclization via oxygen (Scheme 1). Nevertheless this method has got a very good application in preparation of some synthetically interesting targets.[5,6]

On the other hand, nitrones (azomethine oxides) were first prepared in 1890 by Beckman.[7] The application and new methods for the preparation of nitrones, as important building blocks in organic synthesis, still maintain general interest more than a century after their discovery. Most of the studied chemistry is based on their dipolar properties (Scheme 2).



Scheme 2.

This behaviour provides a relatively easy access to different heterocyclic structures via 1,3-dipolar cycloadditions. Depending

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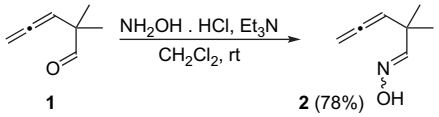
on the type of dipolarophile used, isoxazoles (with alkene, alkyne and allene dipolarophiles) or more complex rings (with isocyanates, nitriles and thiocarbonyles) could be obtained. The efficiency of such reactions is documented by a wide application not only in heterocyclic but also in the natural products chemistry.[8]

Our interest shown in this paper is on the ability of the prepared allenyloximes to undergo heterocyclizations. We present several methods based on simple conditions without any metallic catalyst involved. The procedure provides a suitable way to construct five-membered stable cyclic nitrones together with introduction of various functional groups in one step process.

2. Results and discussion

We have selected 2,2-dimethylpenta-3,4-dienal oxime **2** as a principal building block for our experiments. An unsubstituted allenyl moiety with no additional steric demands and the presence of geminal methyl groups[9] makes this compound ideal for investigation aimed on the allenyloxime cyclization potential. The ready avalibility[10] of allenylaldehyde **1** and its easy transformation to desired oxime **2** (Scheme 3) supported our proposal even more.

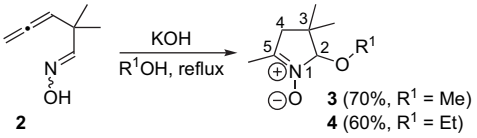


Scheme 3. Preparation of starting material.

This work, for the most part, deals with examination of this particular derivative and through a methodical approach points out possible applications in synthesis.

2.1. Base catalyzed cyclizations

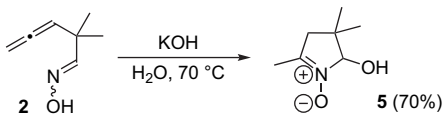
One of the first successful attempt at cyclization was based on application of base catalysis. Oxime **2** undergoes ring closure in an alcoholic solution of potassium hydroxide yielding alkoxy-substituted nitrones **3** and **4** (Scheme 4). The base present in 0.1 equiv relative to starting material seems to be the most efficient choice. At this concentration, the reactions still proceed within 4 h and the separated crude product possesses a high level of purity (suitable for further reactions) and yield (>90% for **3**, >80% for **4**).



Scheme 4. Cyclization of oxime **2** in alcohols.

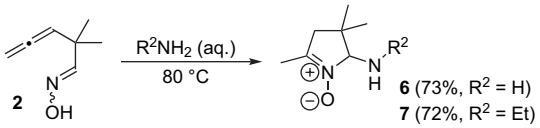
To obtain nitrones as colourless oils, high vacuum distillation was used as the only practical method. However, the limited thermal stability of the concentrated products above 80 °C makes this procedure less efficient and notably lowers the yields (70% and 60%, respectively).

Based on the high stability of oxime **2** in alkaline aqueous solution, we were able to switch from organic solvents to water as a medium and implement the same methodology. Compound **2** showed a rapid cyclization in alkaline water leading to hydroxy-substituted nitrone **5** (Scheme 5). However, the very low solubility of the starting compound in water required a higher concentration of base (2 equiv) to be used to obtain a homogeneous solution and speed up the process. Otherwise, partial decomposition was observed.



Scheme 5. Cyclization of oxime **2** in alkaline aqueous solution.

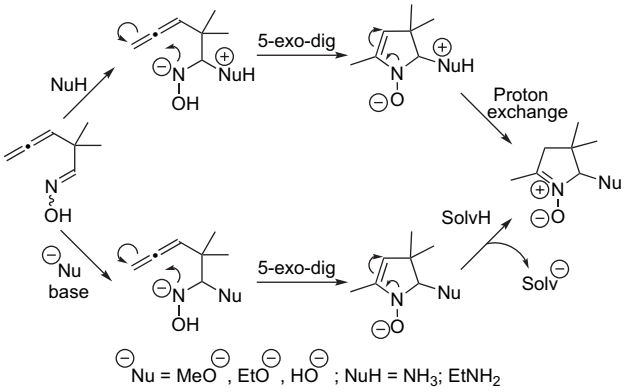
When oxime **2** was heated in concentrated aqueous ammonia or ethylamine (with no other base present), cyclization led exclusively to nitrones **6** and **7**, respectively. Both products, as in the previous cases, involved addition of a nucleophile onto the C=N bond (Scheme 6).



Scheme 6. Cyclization of oxime **2** in aqueous amine solutions.

Nitrones **5**–**7** are characterized by high solubility in water (**6** is strongly hygroscopic), which necessarily makes any extraction into organic solvents difficult. Nitrone **5** is practically insoluble in diethyl ether. But we found extraction into dichloromethane to be the most effective. In the case of compound **5**, acidifying the pH to neutral values was necessary, due to its ability to form salts in the presence both base and acid (for complete procedures see Section 4).

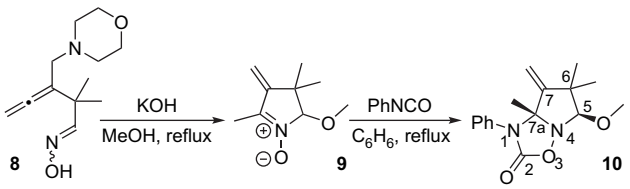
We assume that the mechanism of all the mentioned cyclizations is initiated by the addition of a nucleophile on carbon atom of C=N bond of the oxime moiety. Then after formation of a negatively charged nitrogen atom of the former oxime, its nucleophile addition favours the attack upon central allenylic atom described as 5-*exo*-digonal ring closure.[11] The process ends probably at the more stable tautomer containing endocyclic double bond (Scheme 7). This intermediate, substituted cyclic enamine, could be stabilized by protonation on β-nonsaturated carbon forming observed nitrone product. Such a pathway correlates well with behaviour of alkynylhydroxylamine systems published earlier[12] and differs from electrophile catalyzed procedure discussed above.[5] The nucleophile itself could react as an anion, which we believe occurs in the case of nitrones **3**–**5** formation, where the alkoxide and hydroxide ion, respectively, are present in the reaction mixture (shown as lower path in Scheme 7). That means that the enamine intermediate is protonated probably with participation of the used solvent. This is supported by experiments in dry aprotic solvents where the use of pure alkoxides as nucleophiles did not effect any cyclization. Alternatively, nitrones **6** and **7** are most probably products of ammonia/amine molecule addition, followed by consequent deprotonation of amino moiety in a proton exchange process (shown as higher path in Scheme 7). Moreover, the role of the base



Scheme 7. Proposed mechanism for the formation of nitrones **3**–**7**.

seems to be crucial for all cyclizations. First, in alcohol or water as a medium, the presence of the base determines the concentration of alkoxide and hydroxide ions, respectively, considered as cyclization initiators. It should be mentioned here, that in the absence of base, no cyclic products were detected. Second, base (including ammonia) could take part in acid–base reactions with starting material,[13] which is documented by increased solubility of oxime **2** in water, resulting in a notable influence on reaction times and purity of the isolated products as was mentioned above.

To support the proposed mechanism on a more general basis, we have done several experiments on substituted oxime **8** that showed interesting behaviour under conditions of base catalyzed cyclization. As products of the reaction in methanol, the unusual nitrone **9** containing an exocyclic double bond and morpholine were observed (Scheme 8). Because of the difficulties with purification process, the structure of compound **9** was determined by 1,3-dipolar cycloaddition with phenylisocyanate and subsequent X-ray analysis[14] of cycloadduct **10** (Fig. 1). Interestingly the cycloaddition, according to NMR analysis of the crude reaction mixture, proceeds with complete diastereoselectivity, yielding exclusively one diastereomer **10** (racemate) only.



Scheme 8. Cyclization of oxime **8**.

Nevertheless, the same mechanism as shown in Scheme 7 assuming enamine intermediate as a key step could be fully expected in this case and so perfectly explaining the cleavage of C–N bond in oxime **8** (Scheme 9).

Both solvents (alcohol and water) used in the reactions with starting compound **2** listed above, afforded products with full

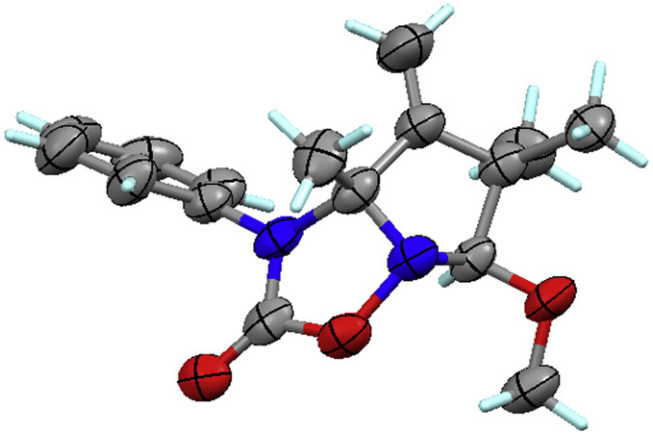
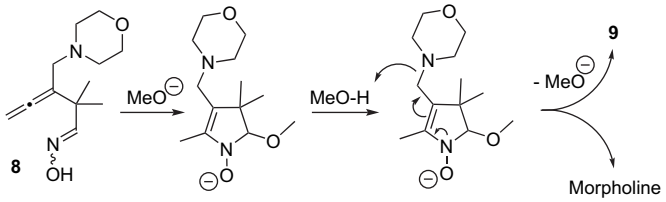


Figure 1. ORTEP structure representation of compound **10**.



Scheme 9. Cyclization mechanism of nitrone **9** formation.

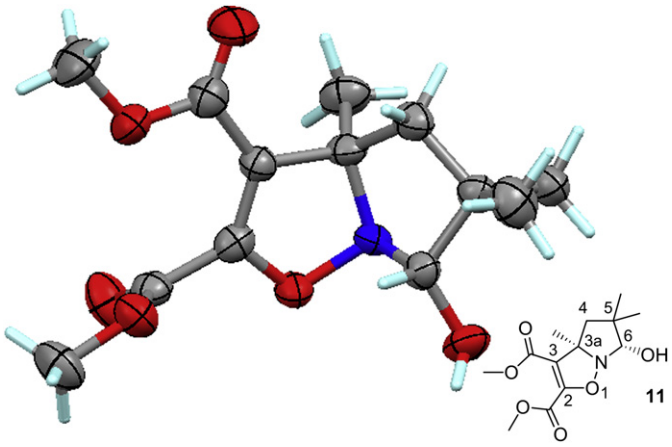


Figure 2. ORTEP structure representation of compound **11**.

characterization and determination of their structure by X-ray diffraction.[14] The structure of nitrone **3** was confirmed by the analysis of its corresponding picrate.[4] Compound **5** containing a hydroxy group was identified indirectly by the structure analysis of its cycloadduct **11** with dimethyl acetylenedikarboxylate (Fig. 2) as a single diastereomer. Cycloaddition had to be used here again for structural elucidation because by the direct X-ray analysis of **5** we were not able to fully assign the structure. Later we found that this matches with already published information[15] where nitrone **5** was prepared by oxidation of **16** by a peracid.

The observed interesting and exceptional properties of atoms in compound **5** that at first caused some problems in the product identification inspired us to perform additional experiments. Figure 3 shows that the differentiation in chemical shifts of the diastereotopic hydrogen atoms of CH_2 (~2.4 ppm) and methyl groups (~1.15 ppm) in ^{1}H NMR of **5** was lost when the sample was measured between 30 °C and 35 °C. Repeated measurements at different temperatures showed that methyl signal coalescence temperature is 30 °C. It could be assumed that it is a consequence of configuration inversion at the stereogenic centre (hydroxy-substituted carbon), which necessarily means that a bond cleavage takes place.

If we exclude the possibility of carbon–carbon or carbon–heteroatom bond breaking under such mild conditions, there is only a carbon–hydrogen atom dissociation left as an option (a simple proton exchange between the two oxygen atoms would not affect chemical shifts that way as it is observed), which may explain the described behaviour. If you take into consideration the neighbouring electron attracting nitrogen atom, such a transformation could be expected.

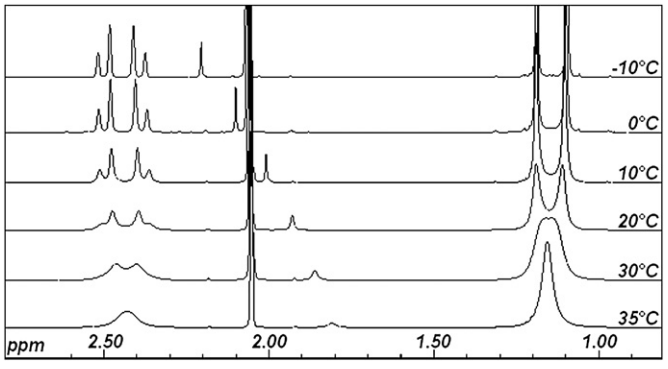


Figure 3. Influence of the temperature upon ^{1}H NMR signals of compound **5** (500 MHz, $CDCl_3$).

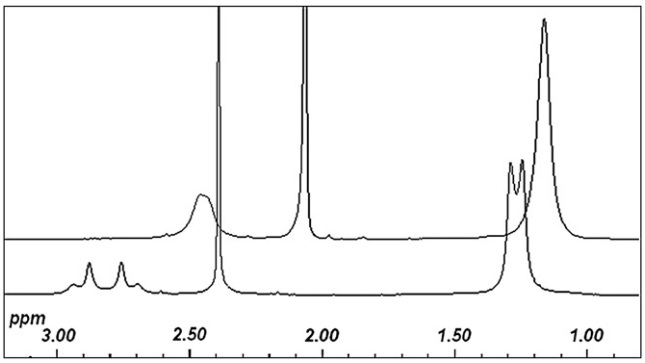


Figure 4. ^{1}H NMR spectra (300 MHz, $CDCl_3$, 30 °C) of compound **5** (upper spectrum) and mixture of compound **5** and 1.5 equiv of picric acid.

Such a process should be strongly influenced by the acidity of the solution. Based on the experimentally proved ability of nitrone **3** to form picrates,[4] we have simulated the same conditions for compound **5** by addition of picric acid to the measured solution. The resulted spectra (Fig. 4) demonstrated a notable suppression of the configuration inversion.

On the other hand, the presence of a base (KOH) in D_2O solution enhanced the process (Fig. 5). However, there is no observable decrease of the intensity of the hydrogen atom signal at C4 (integrals were calculated relative to CH_2 signal). Therefore, C4 carbon–hydrogen bond cleavage cannot be considered.

Bapat et al. presented other possible explanation, in which C4–N cleavage was proposed as a key step.[15a] But because the paper lacks any sufficient experimental evidence, the mechanism won't be presented here.

After solving the composition of compound **5**, including exceptional structural nature, we focused on its chemical reactivity. The most curious transformation of the structure was observed in the presence of amines. The most demonstrative behaviour of compound **5** is a reaction where simple mixing of nitrone **5** at room temperature with a small excess of benzylamine without any solvent leads to the product of substitution **12** (Scheme 10). The exact structure of **12** was confirmed by X-ray structure analysis (Fig. 6).[14]

Analogous conditions, albeit at higher temperatures, were used for the reaction with aliphatic amine. We chose butyl-amine with a higher boiling temperature to avoid problems of pressure increases. The reaction afforded the expected product **13** (Scheme 10) and in combination with method described above (Scheme 6) represent a second route to amino substituted nitrones.

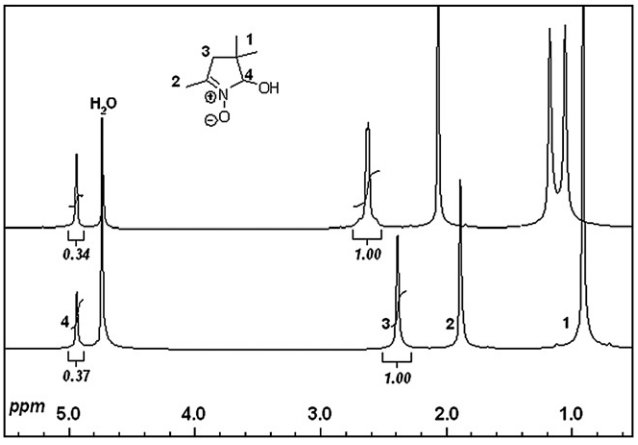
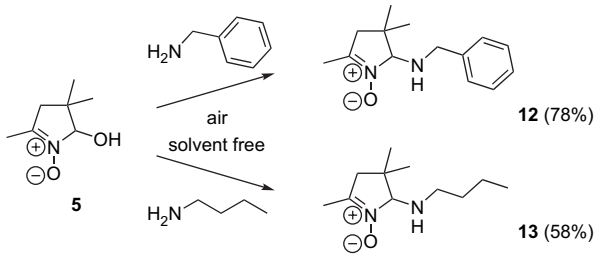


Figure 5. ^{1}H NMR spectra (300 MHz, D_2O, 30 °C) of compound **5** (upper spectrum) and mixture of compound **5** and 1.5 equiv of KOH.



Scheme 10. Reaction of nitrone **5** with amines.

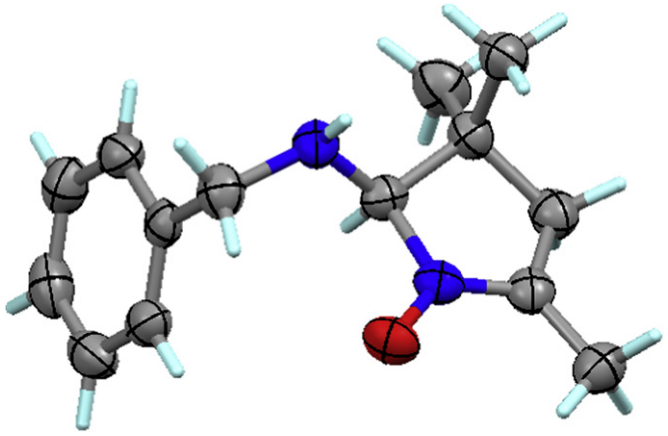
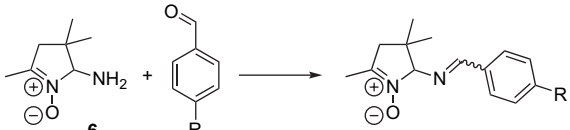


Figure 6. ORTEP representation of compound **12**.

The mechanism, however, simple cannot be considered to be a polar substitution. The most simple and convincing argument is the fact that the reaction is oxygen dependent and under a protective argon atmosphere only traces of product are detectable (this process was studied on the reaction with benzylamine). Secondly, we were neither able to carry out the procedure in solvent nor in a solvent when air was bubbled through the reaction mixture. The oxygen presence requirement could indicate a possible (hidden) oxidation step in the reaction mechanism. Oxidation or any other involvement of oxygen in reaction with a nitrone moiety producing radical species is probably the process trigger. This is supported by the well known ability of these compounds to act as spin traps and afford relatively stable radical adducts, e.g., with singlet oxygen[16] or the superoxide anion radical.[17] Since the absence of solvent makes the study of the mechanism difficult, we have not been able to find any experimentally supported suggestions yet. Despite the unsolved course of the reaction, the method is very simple, effective and offers a new type of stable nitrones in good yields.

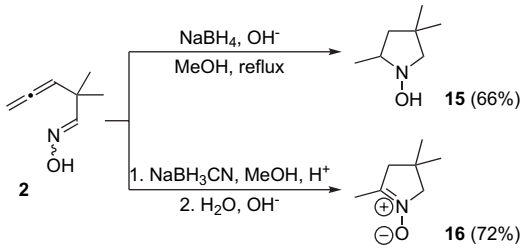
The second object of our further experimental study, nitrone **6**, is constitutionally a completely new compound with an amino functionality located right next to the nitrone moiety.

We were interested in its applications in chemical transformations. As demonstrative experiment, treatment with several *para*-substituted benzaldehydes was chosen. The reactions led clearly to the expected condensation products **14a–c** (Scheme 11).



14a (81%, R = OH)
14b (67%, R = H)
14c (38%, R = CN)

Scheme 11. Condensation of nitrone **6** with benzaldehydes.



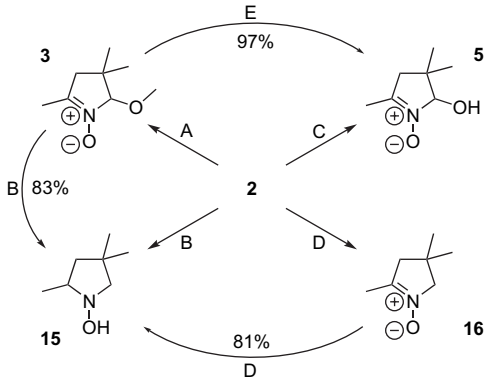
Scheme 12. Cyclization of oxime **2** under reductive conditions.

The nitrone group seems to be unaffected by this procedure or by the purification process. Furthermore no side products were detected, indicating that any involvement of other molecular parts in the reaction does not occur. Such knowledge greatly increases the synthetic potential of compound **6** and indicates a lot of other possible transformations based on amino group.

2.2. Cyclizations under reductive conditions

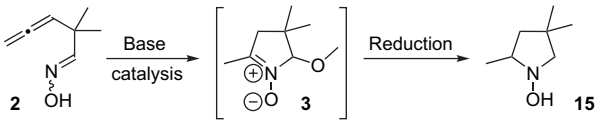
The presence of reducing reagents could also initiate the ring closure of allenyloxime **2**. We have observed a great difference in the product character depending on the property of the reduction reagent used. Treatment with sodium borohydride under basic conditions leads to substituted pyrrolidine-1-ol **15**, as we have already reported earlier.[4] On the other hand, cyanoborohydride reduction affords cyclic nitrone **16** exclusively (Scheme 12). Surprisingly, no acyclic product of oxime reduction (amine or hydroxylamine) was detected.

In order to derive a reaction mechanism proposal, we have done several experiments to search for reaction intermediates, selected results are shown in Scheme 13.



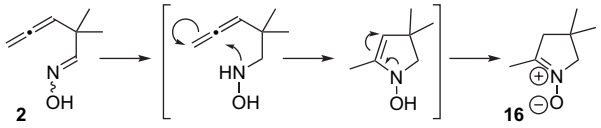
Scheme 13. Interconversion of cyclization products **3**, **5**, **15** and **16**; A: KOH, MeOH, Δ; B: $NaBH_4$, OH^-, MeOH, Δ; C: KOH, H_2O, 70 °C; D: $NaBH_3CN$, H^+, MeOH and then OH^-/H_2O; E: H_2SO_4 (1.5 equiv), H_2O. Yields represent isolated crude products.

First, the mechanism of pyrrolidine **15** formation was considered. Based on the experimental proof that conversion of **3** to **15** is possible under the same conditions as of **2** to **15** (Scheme 13), we assumed that mechanism of reductive cyclization with sodium borohydride is stepwise including the base catalyzed cyclization to nitrone **3** as the first step, followed by the reduction of nitrone moiety together with C–O bond cleavage (Scheme 14).



Scheme 14. Proposed mechanism of compound **15** formation.

Nitrone **16** formation[18] is probably the result of oxime reduction to hydroxylamine, followed by cyclization to the observed product (Scheme 15). This proposal is based on a published procedure,[19] where a set of oxime derivatives transformed to corresponding hydroxylamines under similar conditions. Moreover, we have experimentally proved the instability of the isolated nitrone **16** under the same reductive conditions (Scheme 13, conversion of **16** to **15**). Thus, we can anticipate that the cyclization takes place during the separation process probably caused by concentration of hydroxylamine in aqueous solution in the presence of the base and brief heating. Similar observations were made by House et al. on alkene analogues.[20]



Scheme 15. Proposed mechanism of nitrone **16** formation.

Another interesting transformation was observed when nitrone **3** was acidified by treatment with hydrochloric acid in water. Instead of expected chloride, immediate conversion to hydroxy-substituted nitrone **5** proceeded (Scheme 13, condition E).

Products **15** and **16** were determined by X-ray analysis.[14] Compound **15** was analyzed as a corresponding picrate.[4] Structure of nitrone **16** (a liquid) was confirmed in the form of the cycloaddition product with phenylisocyanate (Fig. 7, structure **17**).

3. Summary and conclusion

We have established an effective method to obtain functionalized stable five-membered cyclic nitrones synthesis by a tandem addition–cyclization one step process (Scheme 16). This way allenyloxime **2** was transformed into 12 cyclic products (11 classified as nitrones, Table 1) differing in functionality and/or reaction pathway used. All cyclizations were performed in alcoholic or aqueous solutions. Those reactions offered exclusive products with no side reactions involved. Additionally, the chemistry of selected products in relation to their reaction mechanism and possible synthetic applications were studied. Some of the new unusual reactions were described and qualified as potentially very helpful in possible consequent research.

In conclusion, our study demonstrated that chosen allenyloxime **2** is a suitable substrate for heterocyclizations. The presented work highlights the chemistry of allenyloximes and shows that just one simple starting compound may be a source of plenty of different products as presented in Table 1.

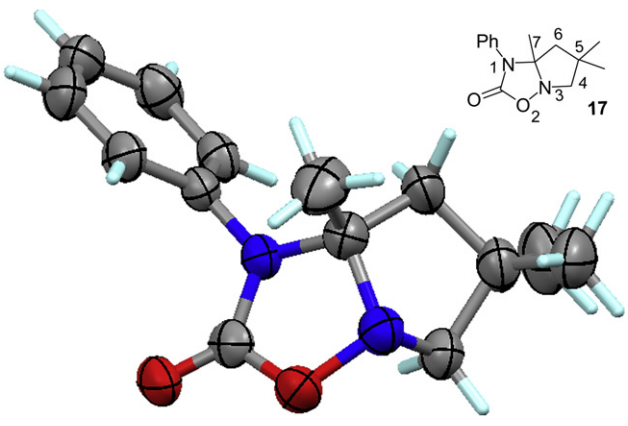
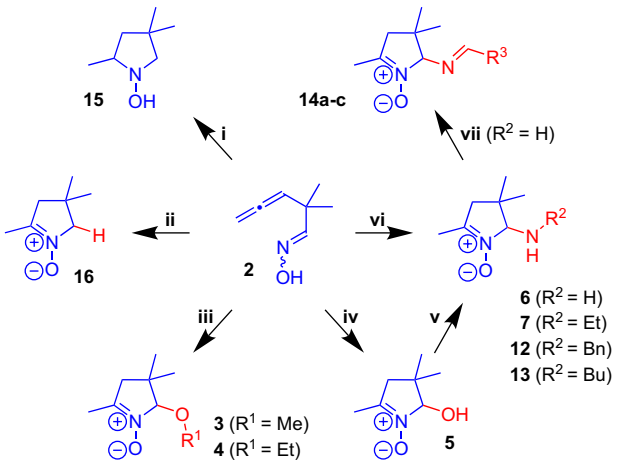


Figure 7. ORTEP representation of compound **17**.



Scheme 16. Heterocyclizations of allenyloxime **2** and transformations of products; (i) $NaBH_4$, OH^-, MeOH, Δ; (ii) $NaBH_3CN$, H^+, MeOH and then OH^-/H_2O; (iii) KOH, R^1OH, Δ; (iv) KOH, H_2O, 70 °C; (v) R^2NH_2, no solvent, air; (vi) R^2NH_2, H_2O, 80 °C; (vii) aldehyde, C_6H_6 or Et_2O, Δ.

4. Experimental section

4.1. Instrumentation and materials

All chemicals were used as purchased. Solvents (benzene, diethyl ether) were dried over sodium/benzophenone and distilled before use. Column chromatography was performed on Horizon HPFC System (Biotage), with FLASH Si 25+M cartridge. All distillations were carried out using BÜCHI Glass Oven B-580 'Kugelrohr' apparatus. Melting points are uncorrected. FTIR spectra were recorded with Genesis ATI (Unicam) apparatus. NMR spectra were collected on a Bruker AC-300 (all experimental section data) and Bruker AC-500 (low temperature measurements, see Fig. 3). TMS (δ=0.00 ppm) and $CHCl_3$ (δ=7.27 ppm) for ^1H and $CDCl_3$ (δ=77.23) for ^{13}C NMR were used as internal standards, interaction constants are in hertz. MS data were obtained with MS TRIO 1000 (Fisons) apparatus at 30 eV in the EI mode. Elemental CHN analyses were performed at Analytical laboratory of Department of Organic Chemistry, Faculty of Chemical Technology, University of Pardubice. Diffraction data were collected on a Kuma KM-4 four-circle CCD diffractometer and corrected for Lorentz and polarization effects. The structures were solved by direct methods and refined using the *SHELXTL* program package.[21] The hydrogen atoms were placed in calculated idealized positions and refined as riding.

Table 1
Summarized yields of cyclic nitrones

Starting compound	Nitrone	Substitution in position 2	Number of steps	Overall yield (%)
2	**16**	–H	**1**	**72**
2	**5**	–OH	**1**	**70**
2	**3**	–O–	**1**	**70**
2	**4**	–O–	**1**	**60**
2	**6**	$–NH_2$	**1**	**73**
2	**7**	–NH–	**1**	**72**
2	**13**	–NH–	**2**	**42**
2	**12**	–NH–	**2**	**57**
2	**14a–c**	–N=	**2**	**28–59**

4.2. 2,2-Dimethylpenta-3,4-dienal oxime (2)

Improved reported[4] procedure. A solution of hydroxylamine hydrochloride (13.9 g, 0.200 mol), triethylamine (20.6 g, 0.204 mol) and 3 Å molecular sieves (6 g) in dichloromethane (150 mL) were cooled down to 0 °C and then allenylaldehyde[10] **1** (20.0 g, 0.182 mol) was added slowly. The mixture was stirred at room temperature for 5 h. After filtration (to remove molecular sieves), the solution was washed with water (3×100 mL) and brine (1×100 mL) and dried over $MgSO_4$. Residual solvent was removed under reduced pressure and subsequent oil was purified by distillation in a Kugelrohr apparatus (121 °C, 8 mbar) to give **2** (colourless oil, 17.73 g, 78%). For spectral data see Ref. 4.

4.3. 2-Methoxy-3,3,5-trimethyl-3,4-dihydro-2*H*-pyrrole 1-oxide (3)

Improved reported[4] procedure. Potassium hydroxide (645 mg, 11.5 mmol) was dissolved in methanol (100 mL) and then oxime 2 (14.4 g, 0.115 mol) was added. The mixture was heated to reflux for 4 h under an argon atmosphere. Afterwards, the solution was concentrated under reduced pressure to remove most of the solvent. Then, 30 mL of water was added, followed by extraction with dichloromethane (5×30 mL). Combined extracts were dried over $MgSO_4$ and evaporated. Obtained oil was purified by distillation using a Kugelrohr apparatus (65 °C, 2.5×10^{-2} mbar) to give nitrone **3** as colourless oil (12.66 g, 70%). For spectral data see Ref. 4. Calcd for $C_8H_{15}NO_2$ (157.21): C, 61.12; H, 9.62; N, 8.91. Found: C, 60.86; H, 9.62; N, 8.97.

4.4. 2-Ethoxy-3,3,5-trimethyl-3,4-dihydro-2*H*-pyrrole 1-oxide (4)

Same procedure as for **3**, 6.00 g (47.9 mmol) of oxime **2**, KOH (269 mg, 4.79 mmol), EtOH (60 mL), water (10 mL) and extraction with dichloromethane (5×15 mL) was used to get nitrone **7** (4.92 g, 60%) as colourless oil after same distillation method (70 °C, 2.0×10^{-2} mbar). δ_H ($CDCl_3$): 1.08 (s, 3H, H_3C–C–CH_3), 1.17 (s, 3H, H_3C–C–CH_3), 1.24 (t, $^3J_{H,H}$ 6.9, 3H, O–CH_2–CH_3), 2.03 (s, 3H, N=C–CH_3), 2.31 (d, $^2J_{H,H}$ 17.5, 1H, N=C–CH_2), 2.54 (d, $^2J_{H,H}$ 17.5, 1H, N=C–CH_2), 3.83–3.94 (m, 1H, O–CH_2), 4.35–4.45 (m, 1H, O–CH_2), 4.55 (s, 1H, CH); δ_C ($CDCl_3$): 12.9 (N=C–CH_3), 15.3 (O–CH_2–CH_3), 22.1 (H_3C–C–CH_3), 27.4 (H_3C–C–CH_3), 36.5 (H_3C–C–CH_3), 45.6 (N=C–CH_2), 68.9 (O–CH_2), 106.2 (CH), 143.8 (C=N); IR (film): 1038, 1111, 1178, 1243,1344, 1387, 1446, 1468, 1610, 2872, 2929, 2972; MS *m*/*z* (%): 172 (M^+, 33), 127 (65), 112 (100), 100 (20), 72 (39), 56 (50), 41 (65). Anal. Calcd for $C_9H_{17}NO_2$ (171.24): C, 63.13; H, 10.01; N, 8.18. Found: C, 62.92; H, 10.10; N, 7.93.

4.5. 2-Hydroxy-3,3,5-trimethyl-3,4-dihydro-2*H*-pyrrole 1-oxide (5)

Potassium hydroxide (269 mg, 4.79 mmol) was dissolved in water (2.5 mL) and then oxime **2** (300 mg, 2.40 mmol) was added. The mixture was then heated to 70 °C under argon atmosphere for 3 h. After cooling to room temperature, the solution was neutralized to pH=7–8 (lacmus) and 0.5 g of NaCl was added to saturate

the solution. Then, the mixture was extracted with dichloromethane (7×5 mL). Combined extracts were dried over $MgSO_4$ and evaporated. Crude solid product was crystallized from Et_2O/CH_2Cl_2=5:1 to give nitrone **5** as white solid (240 mg, 70%), mp 142–144 °C. δ_H ($CDCl_3$): 1.16 (br, 6H, H_3C–C–CH_3), 2.06 (s, 3H, H_3C–C=N), 2.45 (br, 2H, CH_2), 5.08 (s, 1H, CH); δ_C ($CDCl_3$): 13.4 (N=C–CH_3), 22.2[22] (br, H_3C–C–CH_3), 27.1[22] (br, H_3C–C–CH_3), 36.9 (H_3C–C–CH_3), 45.7 (CH_2), 99.7 (CH), 145.6 (C=N); IR (KBr): 821, 1120, 1153, 1174, 1190, 1228, 1330, 1386, 1450, 1468, 1633, 2744, 2844, 2933, 2964; MS *m*/*z* (%): 144 (M^+, 68), 97 (40), 82 (40), 73 (100), 56 (60), 41 (90). Calcd for $C_7H_{13}NO_2$ (143.18): C, 58.72; H, 9.15; N, 9.78. Found: C, 58.98; H, 9.27; N, 9.65.

4.6. 2-Amino-3,3,5-trimethyl-3,4-dihydro-2*H*-pyrrole 1-oxide (6)

Oxime **2** (0.500 g, 3.99 mmol) was mixed with concentrated (8 mL, 26%) aqueous ammonia solution in a closed apparatus fitted with a balloon to avoid over pressuring. After 24 h of vigorous stirring at 80 °C, the homogenous pale yellow solution was concentrated under reduced pressure to remove the rest of ammonia, followed by the addition of NaCl (1.5 g) and extraction with dichloromethane (8×10 mL). The combined extracts were dried over $MgSO_4$ and evaporated. The resulting oil was purified by column chromatography (EtOAc/MeOH=1:1, R_f 0.26) to give white solid (403 mg, 71%), mp (unstable). δ_H ($CDCl_3$): 1.00 (s, 3H, H_3C–C–CH_3), 1.26 (s, 3H, H_3C–C–CH_3), 2.03 (s, 3H, N=C–CH_3), 2.07 (br, 2H, NH_2), 2.31 (dm, $^2J_{H,H}$ 17.5, 1H, CH_2), 2.47 (dm, $^2J_{H,H}$ 17.5, 1H, CH_2), 4.27 (t, $^3J_{H,H}$ 8.4, 1H, CH); δ_C ($CDCl_3$): 13.2 (N=C–CH_3), 21.7 (H_3C–C–CH_3), 26.8 (H_3C–C–CH_3), 36.5 (H_3C–C–CH_3), 45.2 (CH_2), 87.6 (CH), 140.6 (C=N); IR (KBr): 924, 1188, 1217, 1387, 1470, 1631, 2872, 2937, 2958; MS *m*/*z* (%): 143 (M^+, 40), 110 (20), 71 (50), 56 (100), 41 (35). Calcd for $C_7H_{14}N_2O$: 142.20.

4.7. 2-(Ethylamino)-3,3,5-trimethyl-3,4-dihydro-2*H*-pyrrole 1-oxide (7)

Oxime **2** (0.350 g, 2.80 mmol) was added into aqueous ethylamine (4 mL, 70%) in a closed apparatus fitted with a balloon to avoid over pressuring. After 11 h heating at 80 °C, the reaction mixture was concentrated under reduced pressure to remove the unreacted amine and then 350 mg of NaCl was added and the mixture was extracted with dichloromethane (7×5 mL). Combined extracts were dried over $MgSO_4$ and evaporated. Resulting oil was purified by column chromatography (Et_2O/MeOH=6:1, R_f 0.20) to give yellowish oil (343 mg, 72%). δ_H ($CDCl_3$): 1.01 (s, 3H, H_3C–C–CH_3), 1.12 (t, $^3J_{H,H}$ 7.1, 3H, N–CH_2–CH_3), 1.18 (s, 3H, H_3C–C–CH_3), 1.18 (s, 3H, H_3C–C–CH_3), 1.84 (br, 1H, NH), 2.03 (dd, $^4J_{H,H}$ 3.1, $^4J_{H,H}$ 1.5, 3H, N=C–CH_3), 2.35 (dm, $^2J_{H,H}$ 17.5, 1H, N=C–CH_2), 2.42 (dm, $^2J_{H,H}$ 17.5, 1H, N=C–CH_2), 2.73–2.86 (m, 1H, N–CH_2–CH_3), 3.16–3.28 (m, 1H, N–CH_2–CH_3), 4.28 (d, $^3J_{H,H}$ 8.3, 1H, CH); δ_C ($CDCl_3$): 12.8 (N=C–CH_3), 15.6 (N–CH_2–CH_3), 22.0 (H_3C–C–CH_3), 27.6 (H_3C–C–CH_3), 36.4 (H_3C–C–CH_3), 41.7 (N–CH_2–CH_3), 45.5 (N=C–CH_2), 92.9 (CH), 141.1 (C=N); IR (film): 1142, 1178, 1207, 1240, 1369, 1389, 1470, 1614, 1666, 2871, 2927, 2964; MS *m*/*z* (%): 171 (M^+, 50), 153 (95), 110 (80), 98 (70), 84 (100), 56 (85), 41 (95). Calcd for $C_9H_{18}N_2O$: 170.25.

4.8. 2,2-Dimethyl-3-(morpholinomethyl)penta-3,4-dienal oxime (8)

2,2-Dimethyl-3-(morholinomethyl)penta-3,4-dienal (4.15 g, 19.8 mmol), prepared according to the published method,[10] was slowly added to a mixture of hydroxylamine hydrochloride (1.52 g, 21,9 mmol) and 3 Å molecular sieves (3 g) in 40 mL of dichloromethane and then stirred under argon atmosphere for 4 h. Afterwards, sodium hydroxide (1.5 g in 20 mL of water) was added to the mixture. After dissolving the solid, the molecular sieves were filtered off. The organic phase was separated and residual water phase was extracted with diethylether (6×25 mL). The combined extracts were dried over $MgSO_4$ and concentrated under reduced pressure to give **8** (3.56 g, 80%) as white solid, mp 77–79 °C. δ_H ($CDCl_3$): 1.27 (s, 6H, H_3C–C–CH_3), 2.44 (t, $^3J_{H,H}$ 4.6, 2H, O–CH_2–CH_2–N), 2.93 (t, $^5J_{H,H}$ 2.4, 2H, N–CH_2–C=), 3.69 (t, $^3J_{H,H}$ 4.6, 4H, O–CH_2–CH_2–N), 4.83 (t, $^5J_{H,H}$ 2.4, 2H, H_2C=C), 7.43 (s, 1H, CH), 7.67 (br, 1H, OH); δ_C ($CDCl_3$): 25.3 (H_3C–C–CH_3), 38.6 (H_3C–C–CH_3), 53.7, 58.5, 67.2, 77.6 (C=C=CH_2), 105.3 (C=C=CH_2), 157.5 (N=C), 207.2 (C=C=CH_2); IR (KBr): 875, 945, 1007, 1117, 1303, 1454, 1954 (=C=), 2858, 2966, 3074, 3163; MS *m*/*z* (%): 225 (M^+, 10), 207 (90), 122 (30), 100 (100), 56 (25). Calcd for $C_{12}H_{20}N_2O_2$ (224.30): C, 64.26; H, 8.99; N, 12.49. Found: C, 64.04; H, 8.87; N, 12.38.

4.9. 2-Methoxy-3,3,5-trimethyl-4-methylene-3,4-dihydro-2*H*-pyrrole 1-oxide (9)

Potassium hydroxide (75 mg, 1.34 mmol) was dissolved in methanol (30 mL) and then allenyloxime 8 (3.00 g, 13.4 mmol) was added. The mixture was heated to reflux for 11 h. After cooling to room temperature, the solution was concentrated under vacuum. Then, water (10 mL) was added and mixture extracted with dichloromethane (4×15 mL). The combined extracts were then washed with water (2×20 mL) and brine (1×20 mL), dried over $MgSO_4$ and evaporated. The obtained oil was purified by column chromatography (EtAc/MeOH=18:1, R_f 0.22) to give 65% of yellow-brown oil. δ_H ($CDCl_3$): 1.15 (s, 3H, H_3C–C–CH_3), 1.26 (s, 3H, H_3C–C–CH_3), 2.06 (s, 3H, H_3C–C=N), 3.90 (s, 3H, O–CH_3), 4.57 (s, 1H, CH), 4.99 (s, 1H, CH_2), 5.13 (s, 1H, CH_2); δ_C ($CDCl_3$): 8.9 (N=C–CH_3), 22.0 (H_3C–C–CH_3), 27.7 (H_3C–C–CH_3), 41.1 (H_3C–C–CH_3), 61.6 (O–CH_3), 105.3 (CH_2), 106.4 (CH), 143.3, 151.7.

4.10. (5*R*,7a*S*)-5-Methoxy-6,6,7a-trimethyl-7-methylene-1-phenyltetrahydropyrrolo[1,2-*b*][1,2,4]oxadiazol-2(1*H*)-one (10)

Phenylisocyanate (289 mg, 2.42 mmol) was added to a solution of nitrone **9** (410 mg, 2.42 mmol) in dry benzene (8 mL) and heated to reflux for 4 h. The solvent was removed under vacuum and the crude product was crystallized from Et_2O to give 356 mg (51%) of white solid, mp 120–122 °C. δ_H ($CDCl_3$): 1.10 (s, 3H, H_3C–C–CH_3), 1.32 (s, 3H, H_3C–C–CH_3), 1.62 (s, 3H, N–C–CH_3), 3.67 (s, 3H, O–CH_3), 4.43 (s, 1H), 4.63 (s, 1H), 5.14 (s, 1H), 7.15–7.42 (m, 5H, CH_{Ar}); δ_C ($CDCl_3$): 24.7 (CH_3), 25.3 (CH_3), 26.2 (CH_3), 42.9 (H_3C–C–CH_3), 59.0 (O–CH_3), 86.1 (N–C–CH_3), 106.2 (O–CH), 112.7 (C=CH_2), 129.1 (CH_{Ar}), 129.5 (CH_{Ar}), 129.9 (CH_{Ar}), 133.8 (C_{Ar}), 153.8 (C=CH_2), 156.1 (C=O); IR (KBr): 704, 746, 910, 1041, 1101, 1124, 1161, 1209, 1365, 1496, 1763, 2939, 2983; MS *m*/*z* (%): 169 (45), 139 (80), 119 (100), 91 (80), 67 (35), 64 (35). Calcd for $C_{16}H_{20}N_2O_3$: 288.34 (MS spectrum does not show M^+). Compound was subjected to X-ray diffraction.

4.11. (3a*R*,6*S*)-Dimethyl-6-hydroxy-3a,5,5-trimethyl-3a,4,5,6-tetrahydropyrrolo[1,2-*b*]isoxazole-2,3-dicarboxylate (11)

Nitrone **5** (200 mg, 1.40 mmol) was suspended in dry benzene (5 mL) and dimethyl acetylenedicarboxylate (218 mg, 1.54 mmol) was added. The mixture was stirred at room temperature for 5 h. Then, the solvent was removed under vacuum and the solid product was crystallized from Et_2O to give **11** (white solid, 303 mg, 76%), mp 149–151 °C. δ_H ($CDCl_3$): 1.07 (s, 3H, H_3C–C–CH_3), 1.11 (s, 3H, H_3C–C–CH_3), 1.51 (s, 3H, N–C–CH_3), 1.96 (d, $^2J_{H,H}$ 13.9, 1H, CH_2), 2.28 (d, $^2J_{H,H}$ 13.9, 1H, CH_2), 2.50 (d, $^3J_{H,H}$ 8.1, 1H, OH), 3.75 (s, 3H, O–CH_3), 3.89 (s, 3H, O–CH_3), 4.44 (d, $^3J_{H,H}$ 8.1, 1H, CH); δ_C ($CDCl_3$): 21.6 (CH_3), 26.5 (CH_3), 28.1 (CH_3), 37.6 (H_3C–C–CH_3), 49.0 (CH_2), 52.0 (O–CH_3), 53.4 (O–CH_3), 70.0 (N–C–CH_3), 99.3 (CH), 115.0 (O–

C=*C*), 151.2, 159.9, 162.7; IR (KBr): 1072, 1109, 1167, 1306, 1350, 1433, 1456, 1649, 1720, 1741, 2968, 2983, 3228 (br, OH); MS *m*/*z* (%): 286 (M^+, 30), 268 (20), 238 (20), 200 (100), 168 (35), 71 (55), 42 (50); Calcd for $C_{13}H_{21}NO_6$: 287.31. Compound was subjected to X-ray diffraction.

4.12. 2-(Benzylamino)-3,3,5-trimethyl-3,4-dihydro-2*H*-pyrrole 1-oxide (12)

Nitrone **5** (200 mg, 1.40 mmol) was triturated with benzylamine (154 mg, 1.44 mmol) and left standing at room temperature in the presence of air for 9 h. The obtained solid product was then crystallized from Et_2O to give **12** (white solid, 253 mg, 78%), mp 91–93 °C. δ_H ($CDCl_3$): 1.04 (s, 3H, H_3C–C–CH_3), 1.15 (s, 3H, H_3C–C–CH_3), 2.02 (dd, $^4J_{H,H}$ 3.0, $^4J_{H,H}$ 1.5, 3H, N=C–CH_3), 2.08–2.19 (m, 1H, NH), 2.32 (dm, $^2J_{H,H}$ 17.4, 1H, N=C–CH_2), 2.40 (dm, $^2J_{H,H}$ 17.4, 1H, N=C–CH_2), 4.21 (dd, $^2J_{H,H}$ 13.5, $^3J_{H,H}$ 6.3, 1H, N–CH_2), 4.33 (dm, $^3J_{H,H}$ 10.9, 1H, CH), 4.48 (dd, $^2J_{H,H}$ 13.5, $^3J_{H,H}$ 5.0, 1H, N–CH_2), 7.21–7.43 (m, 5H, CH_{Ar}); δ_C ($CDCl_3$): 13.1 (N=C–CH_3), 22.3 (H_3C–C–CH_3), 27.2 (H_3C–C–CH_3), 37.0 (H_3C–*C*–CH_3), 45.3 (N=C–CH_2), 51.7 (N–CH_2), 92.1 (CH), 127.1 (CH_{Ar}), 128.4 (CH_{Ar}), 140.6, 140.9; IR (KBr): 706, 758, 1174, 1188, 1389, 1450, 1468, 1493, 1514, 1604, 2867, 2922, 2960, 3253; MS *m*/*z* (%): 233 (M^+, 5), 215 (50), 91 (100), 65 (30), 56 (30), 41 (70). Calcd for $C_{14}H_{20}N_2O$ (232.32): C, 72.38; H, 8.68; N, 12.06. Found: C, 72.60; H, 8.47; N, 12.11.

4.13. 2-(Butylamino)-3,3,5-trimethyl-3,4-dihydro-2*H*-pyrrole 1-oxide (13)

Nitrone **5** (200 mg, 1.40 mmol) was mixed with butylamine (1.00 g, 13.7 mmol) and heated at 80 °C for 7 h in the presence of air. Then, the remaining amine was removed under vacuum. The crude product was purified by column chromatography (Et_2O/MeOH=9:1, R_f 0.28) to give colourless oil (161 mg, 58%). δ_H ($CDCl_3$): 0.91 (t, $^3J_{H,H}$ 7.2, 3H, CH_2–CH_3), 1.00 (s, 3H, H_3C–C–CH_3), 1.17 (s, 3H, H_3C–C–CH_3), 1.31–1.51 (m, 4H, CH_2–CH_2–CH_3), 1.81 (br, 1H, NH), 2.01 (dd, $^4J_{H,H}$ 3.1, $^4J_{H,H}$ 1.5, 3H, N=C–CH_3), 2.32 (dm, $^2J_{H,H}$ 17.4, 1H, N=C–CH_2), 2.39 (dm, $^2J_{H,H}$ 17.4, 1H, N=C–CH_2), 2.70–2.78 (m, 1H, N–CH_2), 3.14–3.22 (m, 1H, N–CH_2), 4.25 (s, 1H, CH); δ_C ($CDCl_3$): 12.9 (N=C–*C*H_3), 14.1 (CH_2–*C*H_3), 20.3 (*C*H_2–CH_3), 22.2 (H_3C–C–CH_3), 27.7 (H_3C–C–*C*H_3), 33.0 (N–CH_2–*C*H_2), 36.6 (H_3C–*C*–CH_3), 45.5 (N=C–*C*H_2), 47.2 (N–CH_2), 93.3 (CH), 141.0 (N=*C*–CH_3); IR (KBr): 788, 1141, 1192, 1228, 1367, 1389, 1468, 1612, 1668, 2869, 2927, 2956, 3284; MS *m*/*z* (%): 199 (M^+, 100), 181 (30), 110 (55), 84 (55), 57 (35), 42 (40). Calcd for $C_{11}H_{22}N_2O$ (198.31): C, 66.62; H, 11.18; N, 14.13. Found: C, 66.60; H, 11.27; N, 13.94.

4.14. General procedure for nitrones 14a,b preparation

Nitrone **6** (150 mg, 1.05 mmol) was dissolved in dry Et_2O (10 mL) and then aldehyde (1.07 mmol) was added. The mixture was heated at reflux for 5 h (**14a**) or 7 h (**14b**). After solvent evaporation, crude nitrones were purified by column chromatography (Et_2O/MeOH).

*4.14.1. 2-(4-Hydroxybenzylideneamino)-3,3,5-trimethyl-3,4-dihydro-2H-pyrrole 1-oxide (**14a**)*

Et_2O/MeOH=4:1, R_f 0.23, white solid (210 mg, 81%), mp 174–176 °C. δ_H ($CDCl_3$): 1.00 (s, 3H, H_3C–C–CH_3), 1.20 (s, 3H, H_3C–C–CH_3), 2.18 (s, 3H, N=C–CH_3), 2.47 (d, $^2J_{H,H}$ 18.0, 1H, N=C–CH_2), 2.83 (d, $^2J_{H,H}$ 18.0, 1H, N=C–CH_2), 4.59 (s, 1H, N–CH), 6.66 (d, $^3J_{H,H}$ 8.6, 1H, CH_{Ar}), 7.17 (d, $^3J_{H,H}$ 8.6, 1H, CH_{Ar}), 7.97 (s, 1H, N=CH), 10.62 (s, 1H, OH); δ_C ($CDCl_3$): 13.6 (N=C–*C*H_3), 23.0 (H_3C–C–CH_3), 28.5 (H_3C–C–*C*H_3), 38.1 (H_3C–*C*–CH_3), 47.0 (CH_2), 103.3 (N–CH), 116.5 (CH_{Ar}), 126.1 (C_{Ar}–C=N), 130.8 (CH_{Ar}), 149.2 (N=*C*–CH_3), 161.3 (C–OH), 166.1 (N=CH); IR (KBr): 837, 1076, 1163, 1172, 1238, 1286, 1518, 1583, 1606, 1641, 2478, 2569, 2671, 2798, 2873, 2929, 2962; MS *m*/*z* (%): 247 (M^+, 5), 127 (80), 120 (30), 112 (100), 41 (55). Calcd for $C_{14}H_{18}N_2O_2$ (246.30): C, 68.27; H, 7.37; N, 11.37. Found: C, 68.12; H, 7.37; N, 11.26.

*4.14.2. 2-(Benzylideneamino)-3,3,5-trimethyl-3,4-dihydro-2H-pyrrole 1-oxide (**14b**)*

Et_2O/MeOH=3:1, R_f 0.24, white solid (162 mg, 67%), mp 88–90 °C. δ_H ($CDCl_3$): 1.09 (s, 3H, H_3C–C–CH_3), 1.24 (s, 3H, H_3C–C–CH_3), 2.11 (s, 3H, N=C–CH_3), 2.44 (d, $^2J_{H,H}$ 17.5, 1H, N=C–CH_2), 2.79 (d, $^2J_{H,H}$ 17.5, 1H, N=C–CH_2), 4.63 (s, 1H, N–CH), 7.37–7.47 (m, 3H, CH_{Ar}), 7.80–7.84 (m, 2H, CH_{Ar}), 8.42 (s, 1H, N=CH); δ_C ($CDCl_3$): 13.2 (N=C–*C*H_3), 23.1 (H_3C–C–CH_3), 28.5 (H_3C–C–*C*H_3), 38.0 (H_3C–*C*–CH_3), 46.7 (CH_2), 102.1 (N–CH), 128.6 (CH_{Ar}), 129.2 (CH_{Ar}), 131.6 (CH_{Ar}), 135.3 (C_{Ar}–C=N), 144.9 (N=*C*–CH_3), 165.0 (N=CH); IR (KBr): 1178, 1240, 1450, 1610, 1643, 2958; MS *m*/*z* (%): 231 (M^+, 5), 127 (85), 112 (100), 41 (50). Calcd for $C_{14}H_{18}N_2O$: 230.31.

*4.14.3. 2-(4-Cyanobenzylideneamino)-3,3,5-trimethyl-3,4-dihydro-2H-pyrrole 1-oxide (**14c**)*

Nitrone **6** (150 mg, 1.05 mmol) was dissolved in dry benzene (10 mL) and then 3 Å molecular sieves (1.5 g) and cyanobenzaldehyde (159 mg, 1.21 mmol) were added. The mixture was heated to reflux for 9 h and then solvent evaporated. The crude product was purified by column chromatography (Et_2O/MeOH=4:1, R_f 0.21) to give **14c** (yellowish oil, 102 mg, 38%). δ_H ($CDCl_3$): 1.10 (s, 3H, H_3C–C–CH_3), 1.27 (s, 3H, H_3C–C–CH_3), 2.12 (s, 3H, N=C–CH_3), 2.50 (d, $^2J_{H,H}$ 17.7, 1H, N=C–CH_2), 2.80 (d, $^2J_{H,H}$ 17.7, 1H, N=C–CH_2), 4.70 (s, 1H, N–CH), 7.71 (d, $^3J_{H,H}$ 8.1, 1H, CH_{Ar}), 7.94 (d, $^3J_{H,H}$ 8.1, 1H, CH_{Ar}), 8.49 (s, 1H, N=CH); δ_C ($CDCl_3$): 13.1 (N=C–*C*H_3), 23.0 (H_3C–C–CH_3), 28.4 (H_3C–C–*C*H_3), 37.9 (H_3C–*C*–CH_3), 46.5 (CH_2), 101.3 (N–CH), 114.7 (*C*–CN), 118.3 (C–*C*N), 129.3 (CH_{Ar}), 132.3 (CH_{Ar}), 138.9 (C_{Ar}–C=N), 145.5 (N=*C*–CH_3), 163.1 (N=CH); IR (KBr): 1178, 1176, 1244, 1385, 1465, 1610, 1643, 2227, 2872, 2906, 2927, 2962; MS *m*/*z* (%): decomposition.

4.15. 2,4,4-Trimethylpyrrolidin-1-ol (15)

For preparation and spectral data see Ref. 4.

4.16. 3,3,5-Trimethyl-3,4-dihydro-2*H*-pyrrole 1-oxide (16)

Allenyloxime **2** (2.00 g, 16.0 mmol) was added to a solution of $NaBH_3CN$ (1 g, 16.0 mmol) in methanol (30 g). Solution was cooled down to 0 °C and concentrated HCl was dropwise added to set the pH ≈ 3 (lacmus). The mixture was then stirred at room temperature for 3 h (pH was checked every 30 min and kept acidic). The solvent was removed under vacuum and then water (8 mL) was added and finally NaOH pellets were added to make the mixture alkaline. Then, solution was stirred for 5 min. After extraction with dichloromethane (5×10 mL), combined extracts were dried over $MgSO_4$ and evaporated. The crude product was distilled in a Kugelrohr apparatus (70 °C, 3×10^{-2} mbar) to give **16** (colourless oil, 1.46 g, 72%). δ_H ($CDCl_3$): 1.14 (s, 6H, H_3C–C–CH_3), 1.96 (s, 3H, N=C–*C*H_3), 2.45 (s, 2H, N=C–CH_2), 3.68 (s, 2H, N–CH_2); δ_C ($CDCl_3$): 12.7 (N=C–*C*H_3), 28.3 (H_3C–C–*C*H_3), 32.3 (H_3C–*C*–CH_3), 48.2 (N=C–*C*H_2), 74.5 (N–CH_2), 144.5 (N=*C*–CH_3); IR (film): 1171, 1240, 1254, 1389, 1458, 1622, 2872, 2958; MS *m*/*z* (%): 255 (50), 128 (M^+, 100). Calcd for $C_7H_{13}NO$ (127.18): C, 66.10; H, 10.30; N, 11.01. Found: C, 66.16; H, 10.30; N, 10.83.

4.17. 6,6,7a-Trimethyl-1-phenyltetrahydropyrrolo[1,2-*b*][1,2,4]oxadiazol-2(1*H*)-one (17)

Phenylisocyanate (187 mg, 1.57 mmol) was added to a solution of nitrone **16** (200 mg, 1.57 mmol) in dry benzene (4 mL) and stirred at room temperature under argon atmosphere for 5 h. The

solvent was removed under vacuum and the crude product was crystallized from Et_2O to give **17** (white solid, 309 mg, 80%), mp 111–113 °C. δ_H ($CDCl_3$): 1.17 (s, 3H, H_3C–C–CH_3), 1.21 (s, 3H, H_3C–C–CH_3), 1.71 (s, 3H, N=C–CH_3), 1.75 (d, $^2J_{H,H}$ 14.2, 1H, N–C–CH_2), 2.24 (d, $^2J_{H,H}$ 14.2, 1H, N–C–CH_2), 3.08 (d, $^2J_{H,H}$ 9.4, 1H, N–CH_2), 3.48 (d, $^2J_{H,H}$ 9.4, 1H, N–CH_2), 7.30–7.47 (m, 5H, CH_{Ar}); δ_H ($CDCl_3$): 27.3 (CH_3), 28.2 (CH_3), 28.9 (CH_3), 35.8 (H_3C–*C*–CH_3), 49.1 (N–C–CH_2), 69.1 (N–CH_2), 88.9 (N–*C*–CH_2), 125.5 (CH_{Ar}), 127.3 (CH_{Ar}), 129.7 (CH_{Ar}), 135.4 (C_{Ar}), 155.9 (C=O); IR (KBr): 705, 1092, 1211, 1244, 1377, 1495, 1753, 2868, 2958, 2970; MS *m*/*z* (%): 248 (M^+, 20), 127 (100). Calcd for $C_{14}H_{18}N_2O_2$ (246.30): C, 68.27; H, 7.37; N, 11.37. Found: C, 68.37; H, 7.32; N, 11.10.

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