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Graphical Abstract

Synthesis of 5-hydroxy-Δ^1-pyrrolines from *sec*-alkyl aryl ketoximes and acetylene

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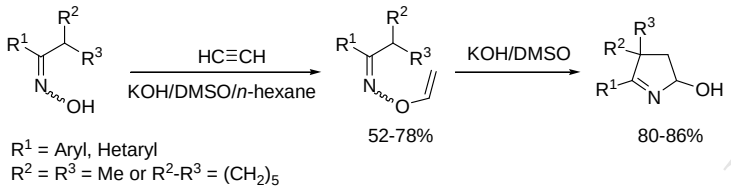

52-78% 80-86%

R^1 = Aryl, Hetaryl
R^2 = R^3 = Me or R^2-R^3 = $(CH_2)_5$

Synthesis of 5-hydroxy-Δ^1-pyrrolines from *sec*-alkyl aryl ketoximes and acetylene

Dmitrii A. Shabalin, Marina Yu. Dvorko, Elena Yu. Schmidt, Igor' A. Ushakov, Boris A. Trofimov*

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Synthesis of 5-hydroxy-Δ^1-pyrrolines conjugated with aryl substituents has been effected via the rearrangement of *O*-vinylketoximes, having only one C-H bond adjacent to the oxime function and readily prepared by addition of *sec*-alkyl aryl ketoximes to acetylene. The target compounds were obtained in 80-86% yields (based on the *O*-vinylketoximes).

Keywords: hydroxypyrroline, 3,4-dihydro-2*H*-pyrrol-2-ol, ketoxime, acetylene, superbase

1. Introduction

The Δ^1-pyrroline core is widespread in natural products[1] and living organisms,[2] mainly in the form of hemes, chlorophylls and alkaloids. It has been shown that Δ^1-pyrrolines could be used as templates for new drugs,[3] and building blocks for constructing light-driven switches[4] and boranil fluorophores,[5] as well as valuable synthons toward biologically active compounds.[6] The syntheses of these important heterocycles include intramolecular cyclizations of bifunctional compounds and multi-component cyclizations,[7] 1,3-dipolar cycloadditions,[8] and photo- and thermo-induced reactions.[9]

In contrast, until now fewer achievements are known in the synthesis of hydroxy-substituted pyrrolines, especially 5-hydroxy-Δ^1-pyrrolines (3,4-dihydro-2*H*-pyrrol-2-ols) conjugated with aromatic and heteroaromatic moieties, although their reactive hydroxyl function makes them much more powerful pyrroline synthons. A method for their synthesis from 1,4-diketones and ammonia was scrupulously studied[10] and further employed in a few recent works.[11] Perhaps, the two issues of this synthesis are the limited availability of starting 1,4-diketones and the reaction selectivity (in some cases, mixtures of isomeric 5-hydroxypyrrolines were obtained). Condensed 5-hydroxypyrrolines were synthesized from tetramic acids and 2*H*-azirines under copper (I)–NHC catalysis.[12] Recently, the reaction between phenacylbromide derivatives, malononitrile and *N*,*N*'-bis(arylmethylidene)-arylmethanediamines leading to 5-

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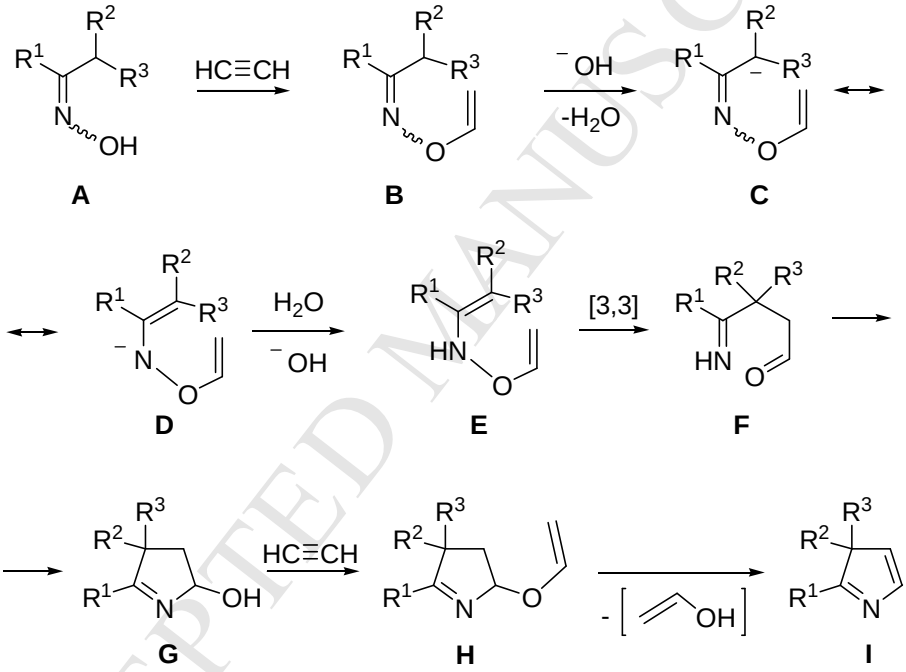
hydroxypyrroline-3,3-dicarbonitriles has been reported.[13] The other known 5-hydroxypyrrolines syntheses are occasional and often characterized by narrow substrate scope.[14] They include the brief notes concerning the identification of the 3,3-dimethyl-2-phenyl-5-hydroxypyrroline as the intermediate in the synthesis of 3*H*-pyrrole from isopropyl phenyl ketoxime and acetylene.[15]

Previously, we have developed an expedient method for 3*H*-pyrroles synthesis from *sec*-alkyl aryl(hetaryl) ketoximes and acetylene.[16] The key step in this assembly of the 3*H*-pyrrole core is the [3,3]-sigmatropic rearrangement of *N*,*O*-dialkenylhydroxylamines **E** (formed by deprotonation of **B** with further proton transfer to the nitrogen atom) to iminoaldehydes **F**, which further ring close to 5-hydroxypyrrolines **G**, and undergo base-catalyzed vinylation/elimination of vinyl alcohol to 3*H*-pyrroles **I** (Scheme 1).[16,17]



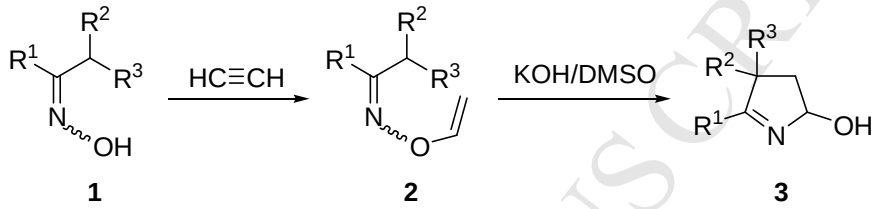
Scheme 1. Tandem reaction sequence for 3*H*-pyrrole synthesis from *sec*-alkyl aryl(hetaryl) ketoximes and acetylene.

[3,3]-Sigmatropic rearrangements that involve heteroatom-heteroatom bonds in the six-atom fragment are now becoming more popular in the synthesis of heterocycles.[18] Noteworthy, for ketoximes, having methylene (R^2 = H) or methyl substituents (R^2 = R^3 = H) at the α-position to the oxime function, the above mentioned reaction sequence can not be stopped at 5-hydroxypyrroline formation due to its easy dehydration and further aromatization to 1*H*-pyrrole.[17]

In the previous works, the 3*H*-pyrroles synthesis from ketoximes and acetylene via 5-hydroxy-Δ^1-pyrrolines was implemented as a one-step procedure both with pressurized

acetylene[16a] and under atmospheric pressure.[16b] Although advantageous as straightforward transition from ketoximes to the 3*H*-pyrrole core, this method did not allow understanding the proper role of the key intermediates, *O*-vinylketoximes and 5-hydroxy-Δ^1-pyrrolines, in the whole process. Therefore, the further study of these syntheses with the emphasis on *O*-vinylketoximes as possible starting materials for the preparation of 5-hydroxy-Δ^1-pyrrolines and 3*H*-pyrroles was necessary.

Consequently, here we report the first general synthesis of 5-hydroxypyrrolines conjugated with aromatic systems via rearrangement of *O*-vinylketoximes (Scheme 2).

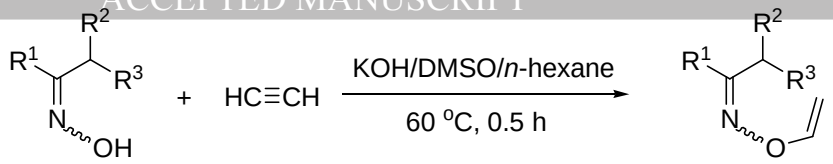


Scheme 2. Synthesis of 5-hydroxy-Δ^1-pyrrolines from *sec*-alkyl aryl(hetaryl) ketoximes and acetylene via *O*-vinylketoximes.

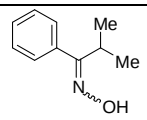
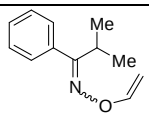
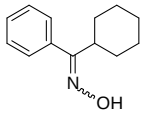
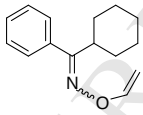
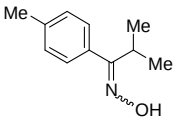
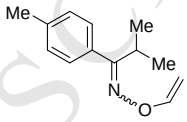
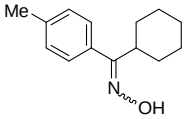
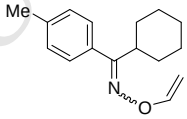
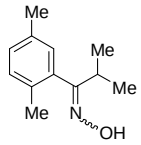
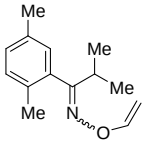
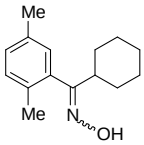
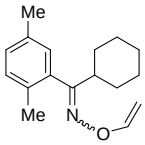
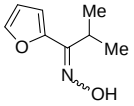
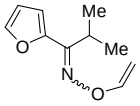
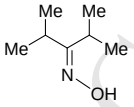
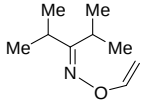
2. Results and discussion

O-Vinylketoximes **2a-h** were synthesized from the corresponding ketoximes **1a-h** and acetylene using a multi-phase superbase system.[19] The brief optimization of their synthesis on the example of the reaction between isopropyl phenyl ketoxime **1a** and acetylene has shown that the appropriate conditions for this process are the following: acetylene under pressure (18-20 atm, an autoclave), KOH/DMSO/*n*-hexane system (equimolar ratio of ketoxime **1a** and KOH), 60 °C, 0.5 h. Under these conditions, the yield of *O*-vinylketoxime **2a** was 28% based on the ketoxime taken and 72% based on the ketoxime consumed (39% conversion). A significant experimental benefit of this protocol is the column chromatography-free isolation of the target compounds: *O*-vinylketoxime **2a** is exhaustively extracted from the reaction mixture with *n*-hexane, and ketoxime **1a** is recovered after pouring the residual DMSO solution into water with further extraction with diethyl ether. Table 1 shows that the procedure, carried out at low conversion of starting ketoxime, allowed us to obtain diversely substituted *O*-vinylketoximes **2b-h**, including alkyl, aryl and hetaryl substituted ones in 24-39% yields (based on the ketoxime taken) or 52-78% yields (based on the ketoxime consumed).

Table 1. Synthesis of *O*-vinylketoximes **2a-h** from ketoximes **1a-h** and acetylene.[a]



1a-h **2a-h**

Ketoxime **1**	Conversion of ketoxime **1** (%)	*O*-Vinylketoxime **2**	Yield of **2** (%)[b]
 **1a**	39	 **2a**	28 (72)
 **1b**	39	 **2b**	29 (74)
 **1c**	52	 **2c**	34 (65)
 **1d**	45	 **2d**	31 (69)
 **1e**	51	 **2e**	30 (59)
 **1f**	50	 **2f**	39 (78)
 **1g**	34	 **2g**	24 (71)
 **1h**	54	 **2h**	28 (52)

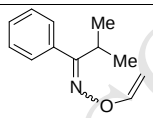
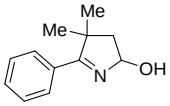
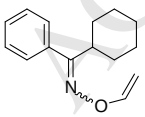
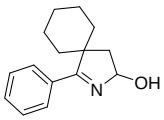
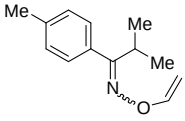
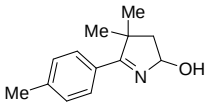
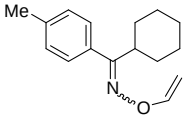
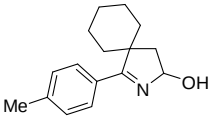
[a] Conditions: ketoxime **1** (12.50 mmol), KOH·0.5H_2O (0.813 g, 12.50 mmol), DMSO (25 mL), *n*-hexane (20 mL), saturation with acetylene at 18-20 atm, 60 °C, 0.5 h.
[b] In the brackets yields calculated by the ketoxime consumed are given.

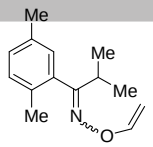
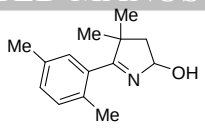
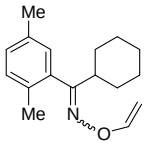
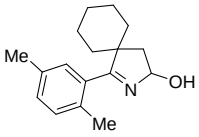
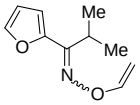
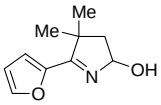
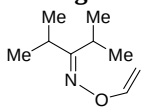
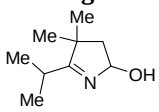
Further, using *O*-vinylketoxime **2a** as an example we have studied the rearrangement of *O*-vinylketoximes to 5-hydroxypyrrolines. Despite the fact that methyl and methylene substituted *O*-vinylketoximes are transformed to 1*H*-pyrroles in DMSO (120 °C) without a special catalyst,[19] isopropyl phenyl *O*-vinylketoxime **2a** failed to undergo the analogous rearrangement (60-120 °C, 1 h) to the expected 5-hydroxypyrroline **3a** (in all cases only the starting **2a**, tar and

no **3a** were observed). The fundamental cause of this is the excessive energy of 3*H*-pyrroles compared to their 1*H*-isomers[16a] that makes dehydration thermodynamically less favorable than in the case of *O*-vinylketoximes with methyl or primary alkyl substituents. Moreover, the rearrangement of 3*H*-pyrroles of the synthesized type is impossible without the methyl group transfer, which is also energy-consuming process. The dehydration can be brought about at a higher basicity. Our attempts to carry out this reaction were briefly described previously.[16a] Here, we have found that addition of equimolar amount of potassium hydroxide to the solution of *O*-vinylketoxime **2a** in DMSO (room temperature, 4 h) gave 5-hydroxypyrroline **3a** in 78% yield. At a higher temperature (50 °C) and a shorter reaction time (1 h, **2a** was consumed entirely according to TLC), the yield of **3a** slightly increased (81%). Cyclization of *O*-vinylketoximes **2b,d,f** with the bulky cyclohexyl substituent was accomplished at 70 °C (Table 2), since at a lower temperature (50 °C), a considerable amount of tar formation was observed due to a longer reaction time (ca. 5 h). Diisopropyl *O*-vinylketoxime **2h**, a representative of aliphatic *O*-vinylketoximes, turned out to be inactive in this reaction at 50 °C: 55% was recovered, with no hydroxypyrroline **3h**. The traces of the expected 5-hydroxypyrroline **3h** were still discernible (^{1}H NMR spectroscopy) in the crude along with large amounts of unidentifiable products, when the reaction was carried out at 70 and 90 °C.

Table 2. Cyclization of *O*-vinylketoximes **2a-h** to 5-hydroxypyrrolines **3a-h**.[a]

2a-h **3a-h**

O-Vinylketoxime **2**	5-Hydroxypyrroline **3**	Conditions	Yield of **3** (%)
 **2a**	 **3a**	50 °C, 1 h	81
 **2b**	 **3b**	70 °C, 0.5 h	85
 **2c**	 **3c**	50 °C, 1 h	86
 **2d**	 **3d**	70 °C, 0.5 h	82

 **2e**	 **3e**	50 °C, 1 h	83
 **2f**	 **3f**	70 °C, 0.5 h	80
 **2g**	 **3g**	70 °C, 0.5 h	81
 **2h**	 **3h**	70 or 90 °C, 1 h	traces

[a] Conditions: *O*-vinylketoxime **2** (1.00 mmol), KOH·0.5H_2O (0.065 g, 1.00 mmol), DMSO (4 mL).

As previously shown,[16] the ketoximes with adjacent C-H moiety are convertible directly to the corresponding 3*H*-pyrroles via the subsequent in situ vinylation of the hydroxyl function, i.e. via the vinyloxy derivatives. This elimination becomes possible due to the absence of repulsion between ionized hydroxyl group and the attacking hydroxide anion and also because of easy removal of vinyl alcohol in its stable isomeric form (acetaldehyde).

In fact, as mentioned above, if instead of an aryl substituent was taken *sec*-alkyl (compound **2h**), only traces of the target product were formed (Table 2) and in the case of methyl or primary alkyls, the reaction led to NH-pyrroles,[17] i.e. the methyl or methylene groups were preferably involved into the 1*H*-pyrrole ring formation. Thus, combination of *sec*-alkyl and aryl(hetaryl) substitutents in the starting ketoximes appears to be a crucial structural feature for the transformation of *O*-vinylketoximes to 5-hydroxy-Δ^1-pyrrolines. This is in keeping with destabilization of the initial intermediate carbanion **C**, generated in the first stage of the rearrangement under the action of base (Scheme 1), by the second electron-donating isopropyl substitutent imposing also some steric hindrance for attack of the hydroxide anion (screening of the CH hydrogen by the methyl group). On the contrary, the aryl and hetaryl substituents stabilize intermediates **E** and **F** due to conjugation with emerging double bonds, both in *N*-alkenylhydroxylamine and iminoaldehyde after reprotonation and [3,3]-sigmatropic rearrangement, thereby facilitating the overall reaction. In fact, this phenomenon is synthetically advantageous since it allows us to readily conjugate diverse aromatic or heteroaromatic moieties with the hydroxypyrroline core. As the range of aromatic or heteroaromatic ketoximes with *sec*-alkyl groups is essentially unlimited (due to easy straightforward acylation of aromatics and heteroaromatics) this method may be considered as rather general one.

3. Conclusions

To summarize, rearrangement of accessible *O*-vinylketoximes leading to the formation of 5-hydroxy-Δ^1-pyrrolines in good yields in the presence of a superbase KOH/DMSO system has been elaborated. The developed methodology provides a short-cut route to valuable unsaturated azaheterocycles, having a reactive hydroxyl group, which makes them helpful pyrroline synthons and universal carriers of the Δ^1-pyrroline core.

4. Experimental section

4.1. General

All chemicals and solvents are commercially available from Sigma Aldrich and were used without further purification. Starting ketoximes **1a-g** were prepared by a literature method.[16a] The absolute stereochemistry of *O*-vinylketoximes **2a-g** was determined based on the ^{13}C NMR data.[20]

IR spectra were recorded on a Bruker Vertex-70 spectrophotometer. NMR spectra were measured from solutions in $CDCl_3$ on Bruker DPX-400 and AV-400 spectrometers (400.1 MHz for ^{1}H, 100.6 MHz for ^{13}C, and 40.5 MHz for ^{15}N) using hexamethyldisiloxane (^{1}H, ^{13}C) and nitromethane (^{15}N) as internal references. Melting points (uncorrected) were measured on a Kofler micro hot-stage apparatus. The C, H, N microanalyses were performed on a Flash EA 1112 Series elemental analyzer.

4.2. General procedure for the synthesis of *O*-vinylketoximes 2a-h

A mixture of ketoxime **1a-h** (12.50 mmol) and finely powdered $KOH{\cdot}0.5H_2O$ (0.813 g, 12.50 mmol) in DMSO (25 mL) was heated up to 105-110 °C in order to obtain a homogenous potassium ketoximate solution. The resulting solution and *n*-hexane (20 mL) were placed into a 0.25-L steel rotating autoclave. Then acetylene gas was transferred to the autoclave to remove air and the autoclave was charged with acetylene again from a cylinder at room temperature (initial pressure 18-20 atm). The autoclave was heated (60 °C) upon rotating for 30 min. After cooling to room temperature and discharging, the *n*-hexane layer was separated and the DMSO layer was extracted with *n*-hexane (4×20 mL). The hexane extracts were combined, washed with water (3×20 mL) and dried over K_2CO_3. After evaporation of the *n*-hexane, *O*-vinylketoximes **2a-h** were obtained. The DMSO layer was diluted with cold water (10-12 °C, 100 mL), neutralized with NH_4Cl, and extracted with diethyl ether (3×50 mL). The extract was washed with water (2×50 mL) and dried over K_2CO_3. After desiccant filtering off and solvent evaporation, starting ketoximes **1a-h** were recovered.

*4.2.1. 2-Methyl-1-phenyl-1-propanone O-vinyloxime (**2a**).* Yield: 0.66 g (28%); light yellow liquid (mixture of isomers, *E*/*Z* ≈ 85/15). IR (film): 3060, 3025, 2968, 2935, 2876, 1640, 1605, 1496, 1444, 1385, 1364, 1335, 1180, 1116, 1009, 981 cm^{-1}. ^{1}H NMR: δ = 1.16 (d, ^3J = 6.9 Hz, 6H, Me, *Z*-isomer), 1.24 (d, ^3J = 7.2 Hz, 6H, Me, *E*-isomer), 2.85-2.91 (m, 1H, CH, *Z*-isomer), 3.51-3.61 (m, 1H, CH, *E*-isomer), 4.07 (dd, ^2J = 1.4 Hz, ^3J = 6.6 Hz, 1H, H^a, *Z*-isomer), 4.16 (dd, ^2J = 1.8 Hz, ^3J = 6.6 Hz, 1H, H^a, *E*-isomer), 4.53 (dd, ^2J = 1.4 Hz, ^3J = 14.3 Hz, 1H, H^b, *Z*-isomer), 4.64 (dd, ^2J = 1.8 Hz, ^3J = 14.3 Hz, 1H, H^b, *E*-isomer), 6.84 (dd, ^3J = 6.6 Hz, ^3J = 14.3 Hz, 1H, H^x, *Z*-isomer), 7.01 (dd, ^3J = 6.6 Hz, ^3J = 14.3 Hz, 1H, H^x, *E*-isomer), 7.23-7.25, 7.38-7.45 (m, 10H, Ph, *E*- and *Z*-isomers) ppm. ^{13}C NMR: for *E*-isomer, δ = 19.6 (2Me), 29.2 (CH),

87.9 (OCH=$\underline{C}H_2$), 127.9 (C^o, Ph), 128.3 (C^m, Ph), 129.0 (C^p, Ph), 135.1 (C^i, Ph), 153.0 (O$\underline{C}$H=CH_2), 167.1 (C=N) ppm; for *Z*-isomer, δ = 20.2 (2Me), 34.8 (CH), 87.5 (OCH=$\underline{C}H_2$), 127.5 (C^o, Ph), 128.1 (C^m, Ph), 128.6 (C^p, Ph), 133.8 (C^i, Ph), 152.5 (O$\underline{C}$H=CH_2), 165.7 (C=N) ppm. Anal. Calcd. for $C_{12}H_{15}NO$: C, 76.16; H, 7.99; N, 7.40. Found: C, 75.91; H, 7.78; N, 7.65.

*4.2.2. Cyclohexyl(phenyl)methanone O-vinyloxime (**2b**).* Yield: 0.83 g (29%); light yellow liquid (mixture of isomers, *E*/*Z* ≈ 70/30). IR (film): 3058, 2930, 2854, 1639, 1616, 1494, 1449, 1382, 1325, 1179, 1075, 978 cm^{-1}. ^{1}H NMR: δ = 1.13-1.56, 1.66-1.90 (m, 20H, CH_2, *E*- and *Z*-isomers), 2.50-2.56 (m, 1H, CH, *Z*-isomer), 3.24-3.30 (m, 1H, CH, *E*-isomer), 4.06 (dd, ^2J = 1.2 Hz, ^3J = 6.9 Hz, 1H, H^a, *Z*-isomer), 4.16 (dd, ^2J = 1.3 Hz, ^3J = 6.6 Hz, 1H, H^a, *E*-isomer), 4.52 (dd, ^2J = 1.2 Hz, ^3J = 14.4 Hz, 1H, H^b, *Z*-isomer), 4.65 (dd, ^2J = 1.3 Hz, ^3J = 14.1 Hz, 1H, H^b, *E*-isomer), 6.83 (dd, ^3J = 6.9 Hz, ^3J = 14.4 Hz, 1H, H^x, *Z*-isomer), 7.01 (dd, ^3J = 6.6 Hz, ^3J = 14.1 Hz, 1H, H^x, *E*-isomer), 7.22-7.24, 7.35-7.45 (m, 10H, Ph, *E*- and *Z*-isomers) ppm. ^{13}C NMR: for *E*-isomer, δ = 26.0 (C-4), 26.3 (C-3, C-5) 29.4 (C-2, C-6), 39.6 (CH), 87.8 (OCH=$\underline{C}H_2$), 128.1 (C^o, Ph), 128.2 (C^m, Ph), 128.8 (C^p, Ph), 135.4 (C^i, Ph), 152.9 (O$\underline{C}$H=CH_2), 166.5 (C=N) ppm; for *Z*-isomer, δ = 26.0 (C-4), 26.2 (C-3, C-5) 30.5 (C-2, C-6), 44.4 (CH), 87.5 (OCH=$\underline{C}H_2$), 127.3 (C^o, Ph), 128.0 (C^m, Ph), 128.5 (C^p, Ph), 134.0 (C^i, Ph), 152.5 (O$\underline{C}$H=CH_2), 165.2 (C=N) ppm. Anal. Calcd. for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11. Found: C, 78.26; H, 8.45; N, 5.84.

*4.2.3. 2-Methyl-1-(4-methylphenyl)-1-propanone O-vinyloxime (**2c**).* Yield: 0.86 g (34%); light yellow liquid (mixture of isomers, *E*/*Z* ≈ 85/15). IR (film): 3052, 3030, 2967, 2933, 2876, 1639, 1615, 1465, 1384, 1365, 1336, 1180, 1116, 980 cm^{-1}. ^{1}H NMR: for *E*-isomer, δ = 1.24 (d, ^3J = 7.2 Hz, 6H, Me), 2.39 (s, 3H, Me), 3.51-3.58 (m, 1H, CH), 4.15 (dd, ^2J = 1.3 Hz, ^3J = 6.9 Hz, 1H, H^a), 4.64 (dd, ^2J = 1.3 Hz, ^3J = 14.4 Hz, 1H, H^b), 7.01 (dd, ^3J = 6.9 Hz, ^3J = 14.4 Hz, 1H, H^x), 7.20 (d, ^3J = 7.9 Hz, 2H, H^m, Ar), 7.35 (d, ^3J = 7.9 Hz, 2H, H^o, Ar) ppm; for *Z*-isomer, δ = 1.16 (d, ^3J = 6.9 Hz, 6H, Me), 2.40 (s, 3H, Me), 2.86-2.89 (m, 1H, CH), 4.07 (dd, ^2J = 1.0 Hz, ^3J = 6.9 Hz, 1H, H^a), 4.55 (dd, ^2J = 1.0 Hz, ^3J = 14.4 Hz, 1H, H^b), 6.85 (dd, ^3J = 6.9 Hz, ^3J = 14.4 Hz, 1H, H^x), 7.16 (d, ^3J = 7.9 Hz, 2H, H^m, Ar), 7.23 (d, ^3J = 7.9 Hz, 2H, H^o, Ar) ppm. ^{13}C NMR: for *E*-isomer, δ = 19.6 (2Me), 21.3 (Me, Ar), 29.2 (CH), 87.7 (OCH=$\underline{C}H_2$), 127.8 (C^o, Ar), 128.9 (C^m, Ar), 132.2 (C^i, Ar), 138.9 (C^p, Ar), 153.0 (O$\underline{C}$H=CH_2), 167.0 (C=N) ppm; for *Z*-isomer, δ = 20.2 (2Me), 21.4 (Me, Ar) 34.8 (CH), 87.4 (OCH=$\underline{C}H_2$), 127.5 (C^o, Ar), 128.8 (C^m, Ar), 130.8 (C^i, Ar), 138.5 (C^p, Ar), 152.5 (O$\underline{C}$H=CH_2), 165.7 (C=N) ppm. Anal. Calcd. for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89. Found: C, 77.09; H, 8.34; N, 6.68.

*4.2.4. Cyclohexyl(4-methylphenyl)methanone O-vinyloxime (**2d**).* Yield: 0.95 g (31%); light yellow liquid (mixture of isomers, *E*/*Z* ≈ 70/30). IR (film): 3029, 2929, 2854, 1637, 1615, 1512, 1450, 1382, 1328, 1178, 1082, 978 cm^{-1}. ^{1}H NMR: δ = 1.15-1.42, 1.47-1.57, 1.67-1.89 (m, 20H, CH_2, *E*- and *Z*-isomers), 2.38 (s, 3H, Me, *E*-isomer), 2.39 (s, 3H, Me, *Z*-isomer), 2.50-2.55 (m, 1H, CH, *Z*-isomer), 3.23-3.29 (m, 1H, CH, *E*-isomer), 4.07 (dd, ^2J = 1.1 Hz, ^3J = 6.9 Hz, 1H, H^a, *Z*-isomer), 4.15 (dd, ^2J = 1.3 Hz, ^3J = 6.7 Hz, 1H, H^a, *E*-isomer), 4.54 (dd, ^2J = 1.1 Hz, ^3J = 14.3 Hz, 1H, H^b, *Z*-isomer), 4.64 (dd, ^2J = 1.3 Hz, ^3J = 14.4 Hz, 1H, H^b, *E*-isomer), 6.84 (dd, ^3J = 6.9 Hz, ^3J = 14.3 Hz, 1H, H^x, *Z*-isomer), 7.00 (dd, ^3J = 6.7 Hz, ^3J = 14.4 Hz, 1H, H^x, *E*-isomer), 7.15 (d, ^3J = 8.2 Hz, 2H, H^m, Ar, *Z*-isomer), 7.19 (d, ^3J = 8.0 Hz, 2H, H^m, Ar, *E*-isomer), 7.22 (d, ^3J = 8.2 Hz, 2H, H^o, Ar, *Z*-isomer), 7.31 (d, ^3J = 8.0 Hz, 2H, H^o, Ar, *E*-isomer) ppm. ^{13}C NMR: for *E*-isomer, δ = 21.2 (Me), 26.0 (C-4), 26.1 (C-3, C-5) 29.4 (C-2, C-6), 39.6 (CH), 87.6 (OCH=$\underline{C}H_2$), 127.9 (C^o, Ar), 128.8 (C^m, Ar), 132.5 (C^i, Ar), 138.6 (C^p, Ar), 152.9 (O$\underline{C}$H=CH_2), 166.3 (C=N) ppm; for *Z*-isomer, δ = 21.3 (Me), 25.9 (C-4), 26.3 (C-3, C-5) 30.5 (C-2, C-6), 44.4 (CH), 87.3 (OCH=$\underline{C}H_2$), 127.3 (C^o, Ar), 128.7 (C^m, Ar), 131.0 (C^i, Ar),138.3 (C^p, Ar), 152.5 (O$\underline{C}$H=CH_2), 165.1 (C=N) ppm. Anal. Calcd. for $C_{16}H_{21}NO$: C, 78.97; H, 8.70; N, 5.76. Found: C, 78.70; H, 8.61; N, 5.49.

*4.2.5. 1-(2,5-Dimethylphenyl)-2-methyl-1-propanone O-vinyloxime (**2e**).* Yield: 0.81 g (30%); light yellow liquid (mixture of isomers, *E*/*Z* ≈ 25/75). IR (film): 3043, 3019, 2970, 2930, 2874, 1641, 1619, 1501, 1467, 1384, 1364, 1208, 1174, 1040, 977 cm^{-1}. ^1H NMR: δ = 1.14 (d, ^3J = 6.8 Hz, 3H, Me, *Z*-isomer), 1.16 (d, ^3J = 7.2 Hz, 3H, Me, *Z*-isomer), 1.23 (d, ^3J = 6.8 Hz, 6H, Me, *E*-isomer), 2.17 (s, 3H, 2-Me, Ar, *Z*-isomer), 2.29 (s, 3H, 2-Me, Ar, *E*-isomer), 2.34 (s, 3H, 5-Me, Ar, *Z*-isomer), 2.34 (s, 3H, 5-Me, Ar, *E*-isomer), 2.75-2.82 (m, 1H, CH, *Z*-isomer), 3.51-3.54 (m, 1H, CH, *E*-isomer), 4.06 (dd, ^2J = 1.3 Hz, ^3J = 6.6 Hz, 1H, H^a, *Z*-isomer), 4.13 (dd, ^2J = 1.5 Hz, ^3J = 6.6 Hz, 1H, H^a, *E*-isomer), 4.55 (dd, ^2J = 1.3 Hz, ^3J = 14.3 Hz, 1H, H^b, *Z*-isomer), 4.61 (dd, ^2J = 1.5 Hz, ^3J = 14.3 Hz, 1H, H^b, *E*-isomer), 6.84 (s, 1H, H^o, Ar, *Z*-isomer), 6.85 (dd, ^3J = 6.6 Hz, ^3J = 14.3 Hz, 1H, H^x, *Z*-isomer), 6.96 (s, 1H, H^o, Ar, *E*-isomer), 7.00 (dd, ^3J = 6.6 Hz, ^3J = 14.3 Hz, 1H, H^x, *E*-isomer), 7.07-7.14 (m, 4H, Ar, *E*- and *Z*-isomers) ppm. ^{13}C NMR: for *E*-isomer, δ = 19.4 (2Me), 19.7 (2-Me, Ar), 21.0 (5-Me, Ar), 29.7 (CH), 87.5 (OCH=$\underline{C}H_2$), 129.1 (C-6, Ar), 129.4 (C-4, Ar), 130.5 (C-3, Ar), 133.3 (C-1, Ar), 134.1 (C-5, Ar), 134.9 (C-2, Ar), 153.1 (O$\underline{C}$H=CH_2), 167.9 (C=N) ppm; for *Z*-isomer, δ = 19.5 (2Me), 20.2 (2-Me, Ar), 21.1 (5-Me, Ar), 35.5 (CH), 87.5 (OCH=$\underline{C}H_2$), 126.7 (C-6, Ar), 129.1 (C-4, Ar), 129.8 (C-3, Ar), 132.3 (C-1, Ar), 134.5 (C-5, Ar), 134.8 (C-2, Ar), 152.6 (O$\underline{C}$H=CH_2), 165.8 (C=N) ppm. Anal. Calcd. for $C_{14}H_{19}NO$: C, 77.38; H, 8.81; N, 6.45. Found: C, 77.11; H, 8.52; N, 6.23.

*4.2.6. Cyclohexyl(2,5-dimethylphenyl)methanone O-vinyloxime (**2f**).* Yield: 1.27 g (39%); light yellow liquid (mixture of isomers, *E*/*Z* ≈ 25/75). IR (film): 3042, 3018, 2930, 2854, 1639, 1618, 1500, 1450, 1380, 1204, 1181, 1166, 1151, 1039, 975 cm^{-1}. ^1H NMR: δ = 1.10-1.46, 1.66-1.87, 1.96-2.03 (m, 20H, CH_2, *E*- and *Z*-isomers), 2.16 (s, 3H, 2-Me, Ar, *Z*-isomer), 2.27 (s, 3H, 2-Me, Ar, *E*-isomer), 2.34 (s, 3H, 5-Me, Ar, *Z*-isomer), 2.34 (s, 3H, 5-Me, Ar, *E*-isomer), 2.40-2.45 (m, 1H, CH, *Z*-isomer), 3.23-3.29 (m, 1H, CH, *E*-isomer), 4.04 (dd, ^2J = 1.2 Hz, ^3J = 6.7 Hz, 1H, H^a, *Z*-isomer), 4.12 (dd, ^2J = 1.3 Hz, ^3J = 6.7 Hz, 1H, H^a, *E*-isomer), 4.53 (dd, ^2J = 1.2 Hz, ^3J = 14.4 Hz, 1H, H^b, *Z*-isomer), 4.61 (dd, ^2J = 1.3 Hz, ^3J = 14.3 Hz, 1H, H^b, *E*-isomer), 6.81 (s, 1H, H^o, Ar, *Z*-isomer), 6.82 (dd, ^3J = 6.7 Hz, ^3J = 14.4 Hz, 1H, H^x, *Z*-isomer), 6.94 (s, 1H, H^o, Ar, *E*-isomer), 6.99 (dd, ^3J = 6.7 Hz, ^3J = 14.3 Hz, 1H, H^x, *E*-isomer), 7.06-7.13 (m, 4H, Ar, *E*- and *Z*-isomers) ppm. ^{13}C NMR: δ = 19.4 (2-Me, Ar, *Z*-isomer), 19.7 (2-Me, Ar, *E*-isomer), 21.0 (5-Me, Ar, *E*-isomer), 21.1 (5-Me, Ar, *Z*-isomer), 25.9, 26.1, 26.2, 26.4, 29.3, 29.9, 30.5 (cyclohexyl, *E*- and *Z*-isomers), 39.9 (CH, *E*-isomer), 45.2 (CH, *Z*-isomer), 87.5 (OCH=$\underline{C}H_2$, *E*- and *Z*-isomers), 126.7 (C-6, Ar, *Z*-isomer), 129.0 (C-4, Ar, *Z*-isomer), 129.2 (C-6, C-4, Ar, *E*-isomer), 129.7 (C-3, Ar, *Z*-isomer), 130.4 (C-3, Ar, *E*-isomer), 132.3 (C-1, Ar, *Z*-isomer), 133.3 (C-1, Ar, *E*-isomer), 134.3 (C-5, Ar, *E*-isomer), 134.6 (C-5, Ar, *Z*-isomer), 134.8 (C-2, Ar, *Z*-isomer), 135.0 (C-2, Ar, *E*-isomer),152.6 (O$\underline{C}$H=CH_2, *Z*-isomer), 153.1 (O$\underline{C}$H=CH_2, *E*-isomer), 165.3 (C=N, *Z*-isomer), 167.1 (C=N, *E*-isomer) ppm. Anal. Calcd. for $C_{17}H_{23}NO$: C, 79.33; H, 9.01; N, 5.44. Found: C, 79.17; H, 8.73; N, 5.33.

*4.2.7. 1-(2-Furyl)-2-methyl-1-propanone O-vinyloxime (**2g**).* Yield: 0.54 g (24%); light yellow liquid (mixture of isomers, *E*/*Z* ≈ 30/70). IR (film): 3121, 3075, 2972, 2937, 2877, 1639, 1610, 1482, 1468, 1385, 1366, 1307, 1258, 1192, 1181, 1170, 1149, 1117, 1090 cm^{-1}. ^1H NMR: for *E*-isomer, δ = 1.32 (d, ^3J = 7.2 Hz, 6H, Me), 3.47-3.54 (m, 1H, CH), 4.19 (dd, ^2J = 1.8 Hz, ^3J = 6.7 Hz, 1H, H^a), 4.65 (dd, ^2J = 1.8 Hz, ^3J = 14.1 Hz, 1H, H^b), 6.45 (dd, ^3J = 1.8 Hz, ^3J = 3.5 Hz, 1H, H-4, furyl), 6.73 (dd, ^3J = 3.5 Hz, ^4J = 0.6 Hz, 1H, H-3, furyl), 7.01 (dd, ^3J = 6.7 Hz, ^3J = 14.1 Hz, 1H, H^x), 7.50 (dd, ^3J = 1.8 Hz, ^4J = 0.6 Hz, 1H, H-5, furyl) ppm; for *Z*-isomer, δ = 1.27 (d, ^3J = 6.6 Hz, 6H, Me), 3.24-3.31 (m, 1H, CH), 4.19 (dd, ^2J = 1.6 Hz, ^3J = 6.6 Hz, 1H, H^a), 4.71 (dd, ^2J = 1.6 Hz, ^3J = 14.1 Hz, 1H, H^b), 6.54 (dd, ^3J = 1.8 Hz, ^3J = 3.6 Hz, 1H, H-4, furyl), 7.00 (dd, ^3J = 6.6 Hz, ^3J = 14.1 Hz, 1H, H^x), 7.39 (dd, ^3J = 3.6 Hz, ^4J = 0.8 Hz, 1H, H-3, furyl), 7.48 (dd, ^3J = 1.8 Hz, ^4J = 0.8 Hz, 1H, H-5, furyl) ppm. ^{13}C NMR: for *E*-isomer, δ = 19.4 (2Me), 28.3 (CH), 88.4 (OCH=$\underline{C}H_2$), 111.3 (C-3, C-4, furyl), 143.8 (C-5, furyl), 148.9 (C-2, furyl), 153.2 (O$\underline{C}$H=CH_2), 157.8 (C=N) ppm; for *Z*-isomer, δ = 20.8 (2Me), 31.2 (CH), 88.2 (OCH=$\underline{C}H_2$), 112.1 (C-4, furyl), 119.1 (C-3, furyl), 142.7 (C-5, furyl), 145.0 (C-2, furyl), 153.0 (O$\underline{C}$H=CH_2),

153.2 (C=N) ppm. Anal. Calcd. for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82. Found: C, 66.83; H, 7.05; N, 7.94.

*4.2.8. 2,4-Dimethyl-3-pentanone O-vinyloxime (**2h**).* Yield: 0.55 g (28%); light yellow liquid. Physical-chemical characteristics were identical to those reported in the literature.[19a]

4.3. General procedure for the synthesis of 5-hydroxypyrrolines 3a-g

O-Vinylketoxime **2a-g** (1.00 mmol) was dissolved in DMSO (4 mL) and finely powdered $KOH{\cdot}0.5H_2O$ (0.065 g, 1.00 mmol) was added. The suspension obtained was heated for appropriate time (see Table 2). After cooling to room temperature reaction mixture was poured into cold water (10-12 °C, 20 mL), neutralized with NH_4Cl, and extracted with diethyl ether (3×15 mL). The extract was washed with water (2×10 mL) and dried over K_2CO_3. The residue obtained after filtering off the desiccant and solvent evaporation was mixed with cold *n*-hexane (5-7 °C, 2 mL). The powdered 5-hydroxypyrrolines **3a-g** were filtered off, their yields as well as physical-chemical characteristics are given below.

*4.3.1. 4,4-Dimethyl-5-phenyl-3,4-dihydro-2H-pyrrol-2-ol (**3a**).* Yield: 0.153 g (81%); beige powder; mp 104-106 °C (hexane). Physical-chemical characteristics were identical to those reported in the literature.[15a,c]

*4.3.2. 1-Phenyl-2-azaspiro[4.5]dec-1-en-3-ol (**3b**).* Yield: 0.195 g (85%); beige powder; mp 123-125 °C (hexane). IR (KBr): 3140, 2993, 2935, 2851, 1602, 1571, 1447, 1334, 1142, 1116, 1042 cm^{-1}. ^1H NMR: δ = 1.13-1.23 (m, 1H, cyclohexyl), 1.29-1.39 (m, 1H, cyclohexyl), 1.44-1.50 (m, 2H, cyclohexyl), 1.60-1.86 (m, 6H, cyclohexyl, 1H, CH_2), 2.47 (dd, ^2J = 13.2 Hz, ^3J = 6.5 Hz, 1H, CH_2), 5.75 (dd, ^3J = 6.5 Hz, 1H, CH), 6.08 (br. s, 1H, OH), 7.40-7.43 (m, 3H, H^m, H^p, Ph), 7.61-7.63 (m, 2H, H^o, Ph) ppm. ^{13}C NMR: δ = 23.2 (C-7), 23.5 (C-9), 25.6 (C-8), 33.2 (C-6), 35.5 (C-10), 42.7 (C-4), 56.2 (C-5), 92.1 (C-3), 128.2 (C^o, Ph), 128.3 (C^m, Ph), 129.6 (C^p, Ph), 134.8 (C^i, Ph), 181.9 (C-1) ppm. ^{15}N NMR: δ = −60.5 ppm. Anal. Calcd. for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11. Found: C, 78.50; H, 8.10; N, 6.26.

*4.3.3. 4,4-Dimethyl-5-(4-methylphenyl)-3,4-dihydro-2H-pyrrol-2-ol (**3c**).* Yield: 0.174 g (86%); beige powder; mp 115-117 °C (hexane). IR (KBr): 3180, 2963, 2927, 2868, 1615, 1566, 1511, 1463, 1339, 1314, 1172, 1133, 1110, 1041, 1016 cm^{-1}. ^1H NMR: δ = 1.40 (s, 3H, Me), 1.43 (s, 3H, Me), 1.85 (dd, ^2J = 12.8 Hz, ^3J = 6.4 Hz, 1H, CH_2), 2.27 (dd, ^2J = 12.8 Hz, ^3J = 5.9 Hz, 1H, CH_2), 2.39 (s, 3H, Me, Ar), 5.49 (br. s, 1H, OH), 5.75 (dd, ^3J = 5.9 Hz, ^3J = 6.4 Hz, 1H, CH), 7.22 (d, ^3J = 8.2 Hz, 2H, H^m, Ar), 7.68 (d, ^3J = 8.2 Hz, 2H, H^o, Ar) ppm. ^{13}C NMR: δ = 21.4 (Me, Ar), 27.0 (Me), 27.5 (Me), 49.6 (C-3), 49.9 (C-4), 91.2 (C-2), 128.2 (C^o, Ar), 129.2 (C^m, Ar), 130.8 (C^i, Ar), 140.4 (C^p, Ar), 180.6 (C-5) ppm. ^{15}N NMR: δ = −63.3 ppm. Anal. Calcd. for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89. Found: C, 76.92; H, 8.16; N, 6.78.

*4.3.4. 1-(4-Methylphenyl)-2-azaspiro[4.5]dec-1-en-3-ol (**3d**).* Yield: 0.200 g (82%); beige powder; mp 159-161 °C (hexane). IR (KBr): 3170, 2991, 2933, 2850, 1609, 1564, 1447, 1335, 1184, 1112, 1041 cm^{-1}. ^1H NMR: δ = 1.15-1.25 (m, 1H, cyclohexyl), 1.29-1.39 (m, 1H, cyclohexyl), 1.46-1.49 (m, 2H, cyclohexyl), 1.60-1.79 (m, 5H, cyclohexyl), 1.69 (dd, ^2J = 13.3 Hz, ^3J = 6.2 Hz, 1H, CH_2), 1.84-1.91 (m, 1H, cyclohexyl), 2.38 (s, 3H, Me, Ar), 2.47 (dd, ^2J = 13.3 Hz, ^3J = 6.4 Hz, 1H, CH_2), 5.63 (br. s, 1H, OH), 5.73 (dd, ^3J = 6.2 Hz, ^3J = 6.4 Hz, 1H, CH), 7.21 (d, ^3J = 7.9 Hz, 2H, H^m, Ar), 7.57 (d, ^3J = 7.9 Hz, 2H, H^o, Ar) ppm. ^{13}C NMR: δ = 21.4 (Me, Ar), 23.2 (C-7), 23.5 (C-9), 25.6 (C-8), 33.3 (C-6), 35.5 (C-10), 42.8 (C-4), 56.0 (C-5), 91.9 (C-3), 128.2 (C^o, Ar), 129.0 (C^m, Ar), 131.8 (C^i, Ar), 139.8 (C^p, Ar), 181.7 (C-1) ppm. ^{15}N NMR: δ = −62.0 ppm. Anal. Calcd. for $C_{16}H_{21}NO$: C, 78.97; H, 8.70; N, 5.76. Found: C, 78.73; H, 8.44; N, 5.99.

*4.3.5. 5-(2,5-Dimethylphenyl)-4,4-dimethyl-3,4-dihydro-2H-pyrrol-2-ol (**3e**).* Yield: 0.181 g (83%); beige powder; mp 180-182 °C (hexane). IR (KBr): 3173, 2967, 2925, 2871, 1626, 1609, 1500, 1466, 1341, 1311, 1165, 1125, 1114, 1033 cm^{-1}. ^1H NMR: δ = 1.20 (s, 3H, Me), 1.21 (s, 3H, Me), 1.80 (dd, ^2J = 13.1 Hz, ^3J = 6.1 Hz, 1H, CH_2), 2.24 (dd, ^2J = 13.1 Hz, ^3J = 6.2 Hz, 1H, CH_2), 2.28 (s, 3H, 2-Me, Ar), 2.32 (s, 3H, 5-Me, Ar), 5.53 (br. s, 1H, OH), 5.75 (dd, ^3J = 6.1 Hz, ^3J = 6.2 Hz, 1H, CH), 6.96 (s, 1H, H^o, Ar), 7.07 (d, ^3J = 7.7 Hz, 2H, H^p, Ar), 7.13 (d, ^3J = 7.7 Hz, 2H, H^m, Ar) ppm. ^{13}C NMR: δ = 19.5 (2-Me, Ar), 21.1 (5-Me, Ar), 26.3 (Me), 26.8 (Me), 47.3 (C-3), 52.0 (C-4), 92.4 (C-2), 127.7 (C-6, Ar), 129.2 (C-4, Ar), 130.6 (C-3, Ar), 132.9 (C-1, Ar), 134.0 (C-5, Ar), 134.3 (C-2, Ar), 182.8 (C-5) ppm. ^{15}N NMR: δ = −54.2 ppm. Anal. Calcd. for $C_{14}H_{19}NO$: C, 77.38; H, 8.81; N, 6.45. Found: C, 77.63; H, 8.52; N, 6.32.

*4.3.6. 1-(2,5-Dimethylphenyl)-2-azaspiro[4.5]dec-1-en-3-ol (**3f**).* Yield: 0.205 g (80%); beige powder; mp 200-202 °C (hexane). IR (KBr): 3158, 2966, 2927, 2852, 1637, 1608, 1441, 1335, 1168, 1143, 1097, 1041, 1026 cm^{-1}. ^1H NMR: δ = 0.99-1.09 (m, 1H, cyclohexyl), 1.25-1.47 (m, 5H, cyclohexyl), 1.61-1.67 (m, 4H, cyclohexyl), 1.72 (dd, ^2J = 13.3 Hz, ^3J = 5.6 Hz, 1H, CH_2), 2.24 (s, 3H, 2-Me, Ar), 2.32 (s, 3H, 5-Me, Ar), 2.37 (dd, ^2J = 13.3 Hz, ^3J = 6.7 Hz, 1H, CH_2), 5.73 (dd, ^3J = 5.6 Hz, ^3J = 6.7 Hz, 1H, CH), 6.24 (br. s, 1H, OH), 6.89 (s, 1H, H^o, Ar), 7.07 (d, ^3J = 7.8 Hz, 1H, H^p, Ar), 7.12 (d, ^3J = 7.8 Hz, 1H, H^m, Ar) ppm. ^{13}C NMR: δ = 19.5 (2-Me, Ar), 21.1 (5-Me, Ar), 23.0 (C-7), 23.4 (C-9), 25.3 (C-8), 33.1 (C-6), 35.0 (C-10), 41.4 (C-4), 57.6 (C-5), 92.9 (C-3), 128.1 (C-6, Ar), 129.1 (C-4, Ar), 130.4 (C-3, Ar), 132.9 (C-1, Ar), 134.1 (C-5, Ar), 134.5 (C-2, Ar), 183.1 (C-1) ppm. ^{15}N NMR: δ = −55.4 ppm. Anal. Calcd. for $C_{17}H_{23}NO$: C, 79.33; H, 9.01; N, 5.44. Found: C, 79.57; H, 8.82; N, 5.59.

*4.3.7. 5-(2-Furyl)-4,4-dimethyl-3,4-dihydro-2H-pyrrol-2-ol (**3g**).* Yield: 0.145 g (81%); beige powder; mp 71-73 °C (hexane). IR (KBr): 3185, 2962, 2931, 2872, 1605, 1482, 1461, 1334, 1153, 1107, 1082, 1044 cm^{-1}. ^1H NMR: δ = 1.37 (s, 3H, Me), 1.50 (s, 3H, Me), 1.86 (dd, ^2J = 13.0 Hz, ^3J = 5.9 Hz, 1H, CH_2), 2.27 (dd, ^2J = 13.0 Hz, ^3J = 6.4 Hz, 1H, CH_2), 5.82 (dd, ^3J = 5.9 Hz, ^3J = 6.4 Hz, 1H, CH), 6.34 (br. s, 1H, OH), 6.49 (dd, ^3J = 1.0 Hz, ^3J = 3.6 Hz, 1H, H-4, furyl), 7.07 (d, ^3J = 3.6 Hz, 1H, H-3, furyl), 7.56 (d, ^3J = 1.0 Hz, 1H, H-5, furyl) ppm. ^{13}C NMR: δ = 26.7 (Me), 27.5 (Me), 48.2 (C-3), 49.6 (C-4), 92.5 (C-2), 111.8 (C-4, furyl), 114.7 (C-3, furyl), 144.8 (C-5, furyl), 148.8 (C-2, furyl), 171.0 (C-5) ppm. Anal. Calcd. for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82. Found: C, 67.25; H, 7.16; N, 7.92.

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Supplementary data

Copies of ^1H and ^{13}C NMR spectra of all new products. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.XXXX.XX.XXX.

References and notes

1. (a) Tsukamoto, D.; Shibano, M.; Okamoto, R.; Kusanot, G. *Chem. Pharm. Bull.* **2001**, *49*, 492-496; (b) Kleinsasser, N. H.; Wallner, B. C.; Harréus, U. A.; Zwickenpflug, W.; Richter,

E. *Toxicology* **2003**, *192*, 171-177; (c) Adams, A.; De Kimpe, N. *Chem. Rev.* **2006**, *106*, 2299-2319; (d) Huang, T.-C.; Teng, C.-S.; Chang, J.-L.; Chuang, H.-S.; Ho, C.-T.; Wu, M.-L. *J. Agric. Food Chem.* **2008**, *56*, 7399-7404.

2. (a) Rinehart, Jr., K. L.; Kobayashi, J.; Harbour, G. C.; Gilmore, J.; Mascal, M.; Holt, T. G.; Shield, L. S.; Lafargue, F. *J. Am. Chem. Soc.* **1987**, *109*, 3378-3387; (b) Kadish, K. M.; Smith, K. M.; Guilard, R. In *The Porphyrin Handbook, vols. 11-20*; Academic Press: San Diego, 2003; (c) Jones, T. H.; Zottig, V. E.; Robertson, H. G.; Snelling, R. R. *J. Chem. Ecol.* **2003**, *29*, 2721-2727; (d) Clark, V. C.; Raxworthy, C. J.; Rakotomalala, V.; Sierwald, P.; Fisher, B. L. *Proc. Natl. Acad. Sci. U.S.A.* **2005**, *102*, 11617-11622.
3. Dannhardt, G.; Kiefer, W. *Arch. Pharm. Pharm. Med. Chem.* **2001**, *334*, 183-188.
4. Sampedro, D.; Migani, A.; Pepi, A.; Busi, E.; Basosi, R.; Latterini, L.; Elisei, F.; Fusi, S.; Ponticelli, F.; Zanirato, V.; Olivucci, M. *J. Am. Chem. Soc.* **2004**, *126*, 9349-9359.
5. Cardona, F.; Rocha, J.; Silva, A. M. S.; Guieu, S. *Dyes and Pigments* **2014**, *111*, 16-20.
6. (a) Snider, B. B.; Neubert, B. J. *Org. Lett.* **2005**, *7*, 2715-2718; (b) Alibés, R.; Blanco, P.; Casas, E.; Closa, M.; De March, P.; Figueredo, M.; Font, J.; Sanfeliu, E.; Álvarez-Larena, Á. *J. Org. Chem.* **2005**, *70*, 3157-3167; (c) Lygo, B.; Kirton, E. H. M.; Lumley, C. *Org. Biomol. Chem.* **2008**, *6*, 3085-3090; (d) Iska, V. B. R.; Verdolino, V.; Wiest, O.; Helquist, P. *J. Org. Chem.* **2010**, *75*, 1325-1328; (e) Davis, F. A.; Theddu, N.; Edupuganti, R. *Org. Lett.* **2010**, *12*, 4118-4121.
7. (a) Shvekhgeimer, M.-G. A. *Chem. Heterocycl. Compds.* **2003**, *39*, 405-448; (b) Singh, P. N. D.; Klima, R. F.; Muthukrishnan, S.; Murthy, R. S.; Sankaranarayanan, J.; Stahlecker, H. M.; Patel, B.; Gudmundsdóttir, A. D. *Tetrahedron Lett.* **2005**, *46*, 4213-4217; (c) Liang, Y.; Dong, D.; Lu, Y.; Wang, Y.; Pan, W.; Chai, Y.; Liu, Q. *Synthesis* **2006**, 3301-3304; (d) Asghari, S.; Qandalee, M. *Synth. Commun.* **2010**, *40*, 2172-2177; (e) Elamparuthi, E.; Sarathkumar, S.; Girija, S.; Anbazhagan, V. *Tetrahedron Lett.* **2014**, *55*, 3992-3995.
8. (a) Mangelinckx, S.; Giubellina, N.; De Kimpe, N. *Chem. Rev.* **2004**, *104*, 2353-2399; (b) Peddibhotla, S.; Tepe, J. J. *J. Am. Chem. Soc.* **2004**, *126*, 12776-12777; (c) Pandit, P.; Chatterjee, N.; Maiti, D. K.; *Chem. Commun.* **2011**, *47*, 1285-1287; (d) Sathishkannan, G.; Srinivasan, K. *Org. Lett.* **2011**, *13*, 6002-6005; (e) Cui, B.; Ren, J.; Wang, Z. *J. Org. Chem.* **2014**, *79*, 790-796.
9. (a) Campos, P. J.; Soldevilla, A.; Sampedro, D.; Rodríguez, M. A. *Tetrahedron Lett.* **2002**, *43*, 8811-8813; (b) Soldevilla, A.; Sampedro, D.; Campos, P. J.; Rodríguez, M. A. *J. Org. Chem.* **2005**, *70*, 6976-6979.

10. (a) Chiu, P.-K.; Lui, K.-H.; Maini, P. N.; Sammes, M. P. *J. Chem. Soc., Chem. Commun.* **1987**, 109-110; (b) Chiu, P.-K.; Sammes, M. P. *Tetrahedron* **1988**, *44*, 3531-3538; (c) Lui, K.-H.; Sammes, M. P. *J. Chem. Soc. Perkin Trans. 1* **1990**, 457-468.

11. (a) Christoffers, J.; Werner, T.; Rössle, M. *Catal. Today* **2007**, *121*, 22-26; (b) Pflantz, R.; Tielmann, P.; Rössle, M.; Hoenke, C.; Christoffers, J. *Eur. J. Org. Chem.* **2007**, 3227-3238; (c) Zhang, L.; Ang, G. Y.; Chiba, S. *Org. Lett.* **2011**, *13*, 1622-1625.

12. Rostovskii, N. V.; Sakharov, P. A.; Novikov, M. S.; Khlebnikov, A. F.; Starova, G. L. *Org. Lett.* **2015**, *17*, 4148-4151.

13. Alizadeh, A.; Moafi, L. *Helv. Chim. Acta* **2016**, 99,306-309.

14. (a) Saiki, H.; Mukai, T. *Chem. Lett.* **1981**, *10*, 1561-1564; (b) Andersen, S. H.; Sharma, K. K.; Torssell, K. B. G. *Tetrahedron* **1983**, *39*, 2241-2245; (c) Schmitt, G.; Nasser, B.; An, N. D.; Laude, B.; Roche, M. *Can. J. Chem.* **1990**, *68*, 863-868; (d) Shimizu, H.; Hamada, K.; Ozawa, M.; Kataoka, T.; Hori, M.; Kobayashi, K.; Tada, Y.; *Tetrahedron Lett.* **1991**, *32*, 4359-4362; (e) Zimmer, R.; Hoffmann, M.; Reissig, H.-U. *Chem. Ber.* **1992**, *125*, 2243-2248; (f) Depature, M.; Grimaldi, J.; Hatem, J. *Eur. J. Org. Chem.* **2001**, 941-946; (g) Murphy, J. A.; Mahesh, M.; McPheators, G.; Anand, R. V.; McGuire, T. M.; Carling, R.; Kennedy, A. R. *Org. Lett.* **2007**, *9*, 3233-3236; (h) Cai, X.-C.; Snider, B. B. *J. Org. Chem.* **2013**, *78*, 12161-12175.

15. (a) Trofimov, B. A.; Korostova, S. E.; Mikhaleva, A. I.; Sobenina, L. N.; Shcherbakov, V. V.; Sigalov, M. V. *Chem. Heterocycl. Compds.* **1983**, *19*, 231-231; (b) Korostova, S. E.; Shevchenko, S. G.; Sigalov, M. V. *Chem. Heterocycl. Compd.* **1991**, *27*, 1101-1104; (c) Shabalin, D. A.; Glotova, T. E.; Schmidt, E. Yu.; Ushakov, I. A.; Mikhaleva, A. I.; Trofimov, B. A. *Mendeleev Commun.* **2014**, *24*, 100-101.

16. (a) Shabalin, D. A.; Dvorko, M. Yu.; Schmidt, E. Yu.; Ushakov, I. A.; Protsuk, N. I.; Kobychev, V. B.; Soshnikov, D. Yu.; Trofimov, A. B.; Vitkovskaya, N. M.; Mikhaleva, A. I.; Trofimov, B. A. *Tetrahedron* **2015**, *71*, 3273-3281; (b) Trofimov, B. A.; Dvorko, M. Yu.; Shabalin, D. A.; Schmidt, E. Yu. *Arkivoc* **2016**, *iv*, 161-171.

17. (a) Trofimov, B. A.; Mikhaleva, A. I.; Schmidt, E. Yu.; Sobenina, L. N. *Adv. Heterocycl. Chem.* **2010**, *99*, 209-254; (b) Trofimov, B. A.; Mikhaleva, A. I.; Schmidt, E. Yu.; Sobenina, L. N. In *Chemistry of Pyrroles*; CRC Press: Florida, 2014.

18. Anderson, L. L.; Rojas, C. M. *[3,3]-Sigmatropic Rearrangements with Heteroatom-Heteroatom Bonds*, In *Molecular Rearrangements in Organic Synthesis*; J. Wiley & Sons: Hoboken, 2015.

19. (a) Trofimov, B. A.; Mikhaleva, A. I.; Vasil'tsov, A. M.; Schmidt, E. Yu.; Tarasova, O. A.; Morozova, L. V.; Sobenina, L. N.; Preiss, T.; Henkelmann, J. *Synthesis* **2000**, 1125-1132; (b) Trofimov, B. A.; Schmidt, E. Yu.; Zorina, N. V.; Senotrusova, E. Yu.; Protsuk, N. I.; Ushakov, I. A.; Mikhaleva, A. I.; Méallet-Renault, R.; Clavier, G. *Tetrahedron Lett.* **2008**, *49*, 4362-4365; (c) Schmidt, E. Yu.; Zorina, N. V.; Dvorko, M. Yu.; Protsuk, N. I.; Belyaeva, K. V.; Clavier, G.; Méallet-Renault, R.; Vu, T. T.; Mikhaleva, A. I.; Trofimov, B. A. *Chem. Eur. J.* **2011**, *17*, 3069-3073.

20. (a) Afonin, A. V.; Pavlov, D. V.; Ushakov, I. A.; Schmidt, E. Yu.; Mikhaleva, A. I. *Magn. Reson. Chem.* **2009**, *47*, 879–884; (b) Afonin, A. V.; Ushakov, I. A.; Pavlov, D. V.; Ivanov, A. V.; Mikhaleva, A. I. *Magn. Reson. Chem.* **2010**, *48*, 685–692.