

Toward accessible 3*H*-pyrroles

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Abstract

Yet recently difficult-to-access 3*H*-pyrroles, rare nonaromatic pyrrole systems, now have become readily available due to essential modification of their synthesis from aryl isoalkyl ketoximes and acetylene in the KOH/DMSO system allowing to carry out the process under atmospheric pressure. In contrast to the known procedure implemented under pressure, the modified method is expedient, much safer and feasible that makes it friendly for any laboratory.

Keywords: 3*H*-Pyrroles, ketoximes, acetylene, superbase

Introduction

3*H*-Pyrroles still constitute a little-known family of nonaromatic pyrrole compounds. They display a rich chemistry owing to their proneness to diverse rearrangements, addition and cycloaddition reactions.¹⁻⁶ Some 3*H*-pyrroles exhibit antitumor and antimicrobial activities.⁷⁻⁹ The quantum chemical calculations (MP2/6-311++G**//B3LYP/6-31G**) show that the total electronic energy of 3*H*-pyrroles exceeds that of their aromatic 1*H*-isomer by 12-17 kcal/mol.¹⁰ Thus, 3*H*-pyrroles are high energy compounds, and that is the cause of their enhanced and multifaceted (compared to 1*H*-pyrroles) reactivity.

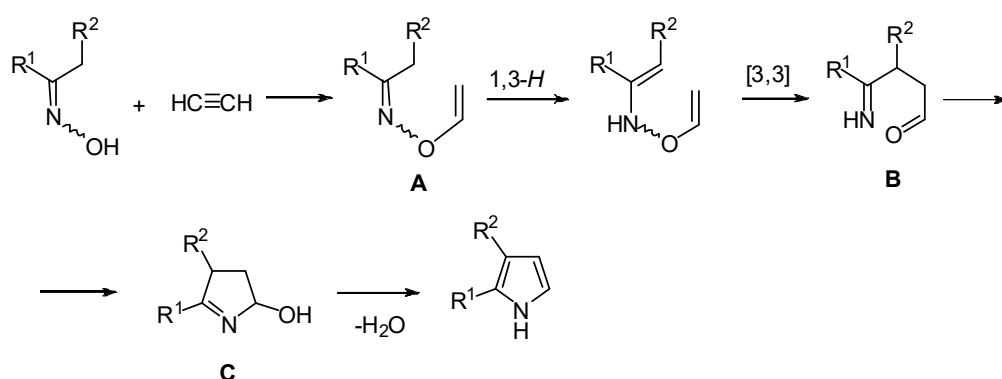
Despite the theoretical interest in these molecules and their attracting potential for organic synthesis as intermediates with unique reactivity, until this work no general approach for their synthesis was known; only some special examples of stable 3*H*-pyrroles synthesis were described.¹¹⁻¹⁴ Just recently, a method, which can be rated as having some generality, has been published.¹⁰ This method is based on the reaction between ketoximes with only one C-H bond neighboring to the oxime function and acetylene in the presence of KOH/DMSO system. Although the advantages of this protocol are obvious, it suffers from using the compressed acetylene (10-13 atm) that requires special facilities, safety precautions and expertise for its implementation. All

this impedes a broader application of such a synthesis and hence 3*H*-pyrroles keep remaining difficult-to-access.

Therefore, the purpose of the present work was to improve the above synthesis using pressurized acetylene to make it safer and more practically feasible so that it could be rendered in any laboratory without special facilities. Generally, it is clear enough that in the acetylene chemistry the transfer from pressure synthesis to that under atmospheric pressure is not always achievable and hence, when done, represents a remarkable novelty since it greatly enhances the safety and feasibility of the method.

Until now the systematic investigations of this reaction in a flow reactor avoiding the use of compressed acetylene were not carried out. Particularly, it was unclear whether this pressure-free procedure could replace the method based on the use of compressed acetylene preserving the same scope of the substituents.

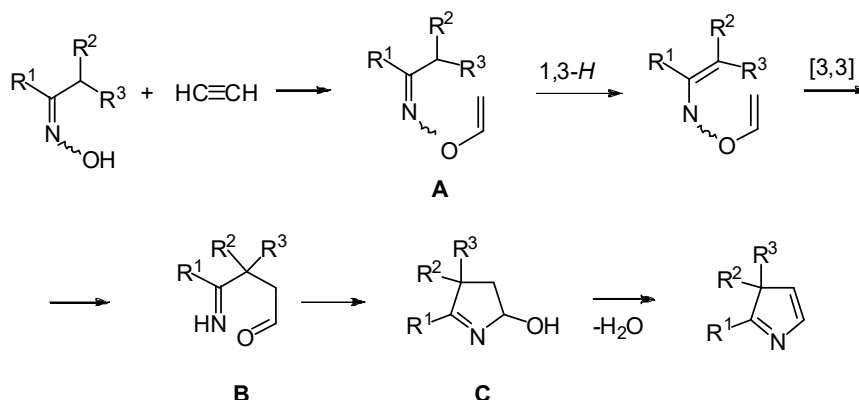
Commonly,¹⁵⁻¹⁷ the synthesis of pyrroles from ketoximes and acetylene is considered as a cascade reaction starting from the formation of *O*-vinyl ketoxime **A**, which undergoes 3,3-sigmatropic shift to iminoaldehyde **B** further cyclizing to hydroxypyrroline **C** and dehydration to the final product (Scheme 1).



Scheme 1

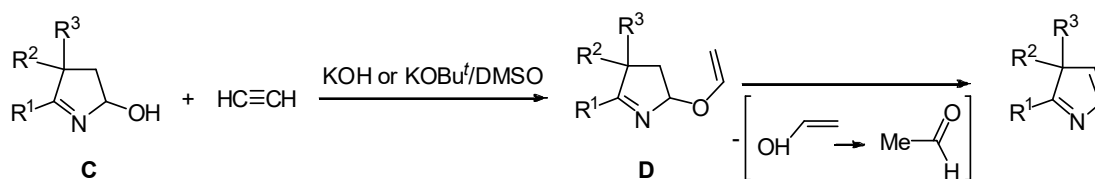
Consequently, the key step of the synthesis is the intramolecular regioselective C-H functionalization of the C-H bond adjacent to the oxime function readily transforming it into an aldehyde group. Here it should be noted that mild and selective C-H functionalizations are justifiably claimed as a mainstream of organic chemistry.¹⁸

In the case of aryl(hetaryl) isoalkyl(cycloalkyl) ketoximes, the pyrrole assembly stops at the stage of formation of 3,3-dialkylsubstituted 3*H*-pyrroles, which cannot isomerize to aromatic 1*H*-pyrroles (Scheme 2).



Scheme 2

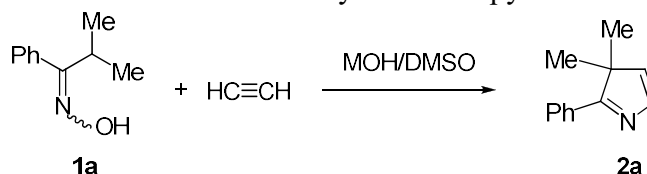
Recently,¹⁰ it was proved that for transformation of hydroxypyrrrolines to 3*H*-pyrroles, vinylation of the former under acetylene pressure was required and the final step of the assembly was superbase-promoted elimination of vinyl alcohol (acetaldehyde) from *O*-vinylloxypyrrrolines **D** (Scheme 3).



Scheme 3

Results and Discussion

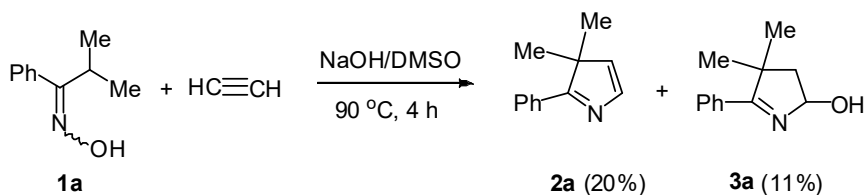
For the optimization of 3*H*-pyrrole synthesis under atmospheric pressure, we have chosen isopropyl phenyl ketoxime **1a**. The reaction was performed under atmospheric pressure (flow reactor) in the MOH (M = Na, K, Cs)/DMSO superbase system. Acetylene was passed through the stirred reaction mixture with a rate of 40-45 mL/min (12.5 mmol of ketoxime **1a**, 25-100 mL of DMSO). The following parameters were varied: type of the superbase system, ketoxime : base molar ratio, co-solvent (*n*-octane), the reactants concentration, temperature and time. 3,3-Dimethyl-2-phenyl-3*H*-pyrrole **2a** was isolated and purified by column chromatography (Table 1).

Table 1. Effect of the reaction conditions on the yield of 3*H*-pyrrole **2a**^a

Entry	MOH, mol per 1 mol of 1a	Time, h	Conversion of ketoxime 1a , %	The content of 3 <i>H</i> -pyrrole 2a in crude product, % ^b	Isolated yield of 3 <i>H</i> -pyrrole 2a , % ^c
1	NaOH, 1.0	4	88	43	20
2	KOH, 1.0	4	90	64	33
3 ^d	KOH, 1.0	4	89	59	31
4	CsOH, 1.0	4	92	53	24
5	KOH, 0.5	4	85	60	32
6	KOH, 1.5	4	88	58	30
7	KOH, 1.0	2	75	50	29
8	KOH, 1.0	6	96	62	28
9 ^e	KOH, 1.0	4	92	58	23
10 ^f	KOH, 1.0	4	90	60	22
11 ^g	KOH, 1.0	4	85	63	29

^a Conditions: ketoxime **1a** (12.5 mmol), DMSO (50 mL), acetylene (atmospheric pressure), 90 °C. ^b According to ¹H NMR data of crude product. ^c The yield was calculated on the reacted ketoxime. ^d The reaction was carried out at 80 °C. ^e 25 mL of DMSO was used. ^f 100 mL of DMSO was used. ^g The additive of *n*-octane (40 mL) was used.

As follows from Table 1, the conversion of ketoxime **1a** ranged 75-96%, while the yields of pyrrole **2a** spanned 20-33%. The best result (33% isolated yield of **2a** at 90% conversion of **1a**) was attained in superbase system KOH/DMSO (**1a** : KOH molar ratio = 1 : 1, Entry 2, Table 1). In the NaOH/DMSO system, the yield of pyrrole **2a** is much lower (20%, Entry 1). In this case, the reaction mixture contained 31% of hydroxypyrroline **3a**, which was isolated in 11% yield (Scheme 4). At either lower (0.5 equiv.) or higher (1.5 equiv.) content of KOH in the reaction mixture (Entries 5 and 6), the yield of **2a** changed insignificantly (32 and 30%, respectively). However, at the equimolar ratio of **1a** : KOH (Entry 2), the number and quantities of side products decreased that makes easier isolation of pyrrole **2a**. The 75% conversion of the ketoxime **1a** was reached already after 2 h, the yield of pyrrole **2a** being 29% (Entry 7). When the reaction time increased up to 6 h (Entry 8), conversion of **1a** became almost complete (96%), while the yield of pyrrole **2a** slightly dropped (28%). At both lower (25 mL of DMSO, Entry 9) and higher (100 mL of DMSO, Entry 10) dilution vs. optimal one (12.5 mmol of **1a** in 50 mL of DMSO), the yield of **2a** noticeably diminished (23 and 22%, respectively).



Scheme 4

In the synthesis of 3*H*-pyrroles under pressure,¹⁰ the non-polar co-solvent (*n*-hexane) allowed to considerably increase (by about 10%) the yields of the target products. However, in this case, the application of a similar mixed solvent (50 mL of DMSO and 40 mL of *n*-octane) led to the decreased yield of pyrrole **2a** (29%, Entry 11). Thus, this pressure-free protocol happened to be even simpler (with regard to solvent) than the synthesis under pressure.

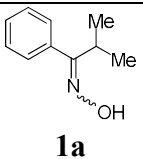
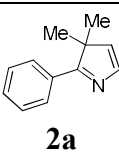
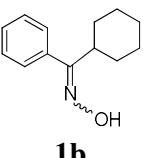
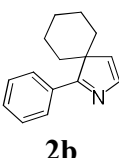
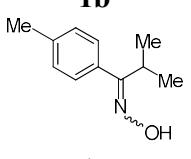
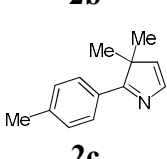
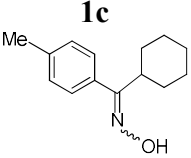
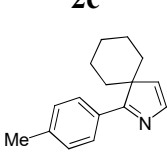
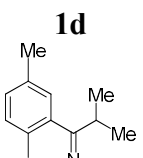
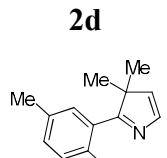
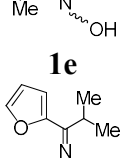
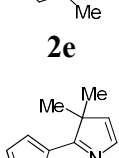
Noteworthy, the isolated yields of 3*H*-pyrroles are about twice as less compared with the content of the target pyrroles in the crude product. It might be due to further transformations of the products on chromatography column, e.g. silica-catalyzed addition of unreacted ketoximes to the double bond of 3*H*-pyrroles. At the same time, partial hydration of 3*H*-pyrrole **2a** early observed¹⁰ when passing through chromatography column on aluminium oxide has not occurred on silica (neat 3*H*-pyrrole **2a** lost just about 2 wt %).

Taking into account such a high sensitivity of 3*H*-pyrroles to the isolation protocols, it might be understandable the failure to reproduce the yield of 3*H*-pyrrole **2a** reported in 1991 (53%)¹⁹ that may be caused by the differences in quality and nature of the sorbents and eluents employed. In fact, the content of this pyrrole in the crude product (Table 1) is 64%.

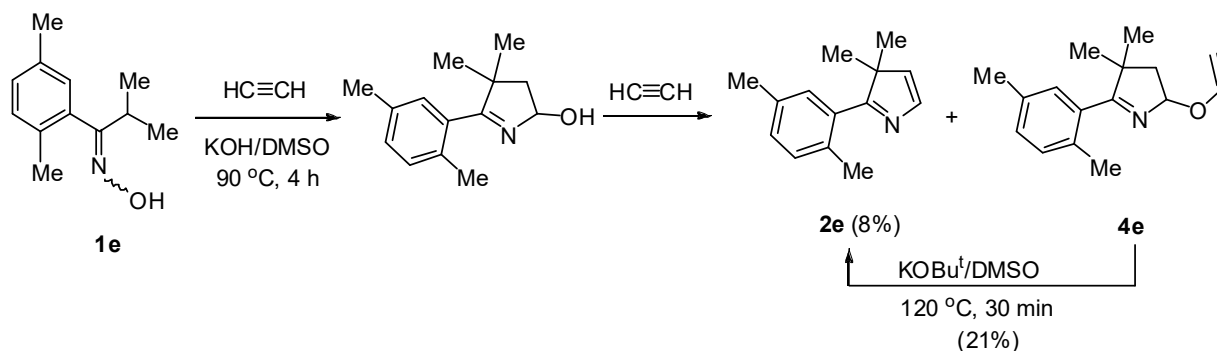
The best conditions here elaborated (equimolar ratio of ketoxime/KOH in DMSO, 90 °C, 4 h) were applied to other aryl(hetaryl) isopropyl or cyclohexyl ketoximes **1a-f** and the corresponding 3*H*-pyrroles were synthesized in 16-38% yields (Table 2).

The only exception was 2-(2,5-dimethylphenyl)-3,3-dimethyl-3*H*-pyrrole **2e** formed under the above conditions just in 8% yield (Scheme 5), while the major product was 5-vinyloxypyrroline **4e**, which was identified in the reaction mixture by its ¹H NMR spectrum. As mentioned above (Scheme 3), this compound is formed by vinylation of the corresponding intermediate hydroxypyrroline. 3*H*-Pyrrole **2e** was obtained (21% yield) by additional treatment of the reaction mixture with 3 equiv. of KOBu^t at 120 °C for 30 min, during which the intermediate 5-vinyloxypyrroline **4e** was transformed into the target product (Scheme 5).

Table 2. Synthesis of 3*H*-pyrroles **2a-f** from ketoximes **1a-f** and acetylene^a

$ \begin{array}{c} \text{R}^1 \quad \text{R}^2 \\ \diagdown \quad \diagup \\ \text{C} \\ \diagup \quad \diagdown \\ \text{N} \quad \text{R}^3 \\ \text{OH} \end{array} + \text{HC}\equiv\text{CH} \xrightarrow[\text{DMSO, 90 }^\circ\text{C, 4 h}]{\text{KOH (1.0 equiv.)}} \begin{array}{c} \text{R}^3 \\ \diagdown \quad \diagup \\ \text{C} \\ \diagup \quad \diagdown \\ \text{N} \\ \text{R}^1 \quad \text{R}^2 \end{array} $					
<div style="display: flex; justify-content: space-around; align-items: center;"> <div> 1a-f </div> <div> 2a-f </div> </div>					
Entry	Ketoxime 1	Conversion of ketoxime 1 , %	3 <i>H</i> -Pyrrole 2	Content of 2 in crude product, % ^b	Isolated yield of 2 , % ^c
1		90		64	33
2		85		58	38
3		82		58	38
4		87		55	34
5 ^d		100		45	21
6 ^e		85		Indefinable	16
	1f		2f		

^a Conditions: oxime **1** (12.5 mmol), KOH (12.5 mmol), DMSO (50 mL), acetylene (atmospheric pressure), 90 °C. ^b According to ¹H NMR data of the crude product. ^c The yield was calculated on the reacted ketoxime. ^d The initial reaction mixture was additionally treated with KOBu^t (3.0 equiv.) at 120 °C for 30 min, see text below. ^e Too complex ¹H NMR spectrum of the crude product.



Scheme 5

Conclusions

An expedient, pressure-free, safe and feasible synthesis of 3*H*-pyrroles, until now difficult-to-access, has been developed improving the cascade reaction of ketoximes, having only one C-H bond adjacent to the oxime function, with acetylene. The synthesis does not require transition metal catalysts, utilizes inexpensive starting materials and can be implemented using ordinary laboratory facilities. Consequently, 3*H*-pyrroles have been rendered from yet recently exotic compounds to readily available family of promising potent synthetic intermediates for the preparation of biologically active compounds and reactive building blocks for organic synthesis.

Experimental Section

General. The NMR spectra were measured from solutions in CDCl_3 on Bruker DPX-400 and AV-400 spectrometers (400.1 MHz for ^1H , 100.6 MHz for ^{13}C , and 40.5 MHz for ^{15}N) using hexamethyldisiloxane (^1H , ^{13}C) and nitromethane (^{15}N) as internal references. The IR spectra were recorded on a Bruker Vertex-70 spectrophotometer. Microanalyses were performed on a Flash 2000 elemental analyzer. Silica gel and benzene : diethyl ether = 7 : 1 or petroleum ether (40-70 °C) : diethyl ether = 3 : 1 as eluents were used for column chromatography and Silufol plates for TLC (50% $\text{Et}_2\text{O}/n$ -hexane). Visualization was with iodine vapor. Ketoximes **1a-f** were prepared by literature method.¹⁰

Typical procedure for the synthesis of 3*H*-pyrroles (2a-f). A potassium oximate solution was prepared by heating of a mixture of ketoxime **1a-f** (12.5 mmol) and KOH·0.5H₂O (0.81 g, 12.5 mmol) in DMSO (50 mL) at 110 °C for 0.5 h. Acetylene was bubbled (40-45 mL/min) through this solution of oximate at 90 °C for 4 h. In the case of **2e** the reaction mixture was additionally treated with KOBu^t (4.21 g, 37.5 mmol) at 120 °C for 30 min. Then the mixture was cooled, poured

into ice water (150 mL), neutralized with NH_4Cl and extracted with diethyl ether (5×50 mL). The extract was washed with water (2×30 mL) and dried over K_2CO_3 . After distilling off the extractant, the residue was chromatographed on the column (1.5×20 cm) to afford unreacted oxime **1a-f** and 3*H*-pyrrole **2a-f** (Table 2). Analytical and spectroscopic characteristics of compounds **2a-f** and **4e** were identical to recently reported data.¹⁰

3,3-Dimethyl-2-phenyl-3*H*-pyrrole (2a). Yellow oil, yield 33% (at 90% ketoxime conversion), 0.64 g, R_f 0.49; IR (ν_{max} , cm^{-1} , film): 3058, 2967, 2871, 1567, 1495, 1461, 1331, 1040, 778, 697. ^1H NMR (400.1 MHz, CDCl_3): δ_{H} 1.43 (6H, s, Me), 6.23 (1H, d, J 3.4 Hz, H-4), 7.07 (1H, d, J 3.6 Hz, H-5), 7.43–7.45 (3H, m, $H_{m,p}$ -Ph), 8.00–8.02 (2H, m, H_o , Ph). ^{13}C NMR (100.6 MHz, CDCl_3): δ_{C} 22.4 (2Me), 55.6 (C-3), 127.7 (C_o -Ph), 128.5 (C_m -Ph), 129.9 (C_p -Ph), 133.1 (C_i -Ph), 138.7 (C-4), 140.0 (C-5), 183.4 (C-2). ^{15}N NMR (40.5 MHz, CDCl_3): δ_{N} –66.4. Anal. Calcd for $\text{C}_{12}\text{H}_{13}\text{N}$ (171.24): C, 84.17; H, 7.65; N, 8.18%. Found: C, 84.29; H, 7.72; N, 8.01%.

1-Phenyl-2-azaspiro[4.5]deca-1,3-diene (2b). Yellow oil, yield 38% (at 85% ketoxime conversion), 0.85 g, R_f 0.54; IR (ν_{max} , cm^{-1} , film): 3071, 2932, 2857, 1564, 1493, 1450, 1336, 1144, 1047, 915, 846, 770, 752, 695. ^1H NMR (400.1 MHz, CDCl_3): δ_{H} 1.35–1.64, 1.89–1.94, 2.10–2.17 (10H, m, CH_2), 6.82 (1H, d, J 3.6 Hz, H-4), 7.16 (1H, d, J 3.6 Hz, H-3), 7.43–7.46 (3H, m, $H_{m,p}$ -Ph), 8.02–8.04 (2H, m, H_o -Ph). ^{13}C NMR (100.6 MHz, CDCl_3): δ_{C} 25.1 (C-7, C-9), 25.9 (C-8), 32.1 (C-6, C-10), 61.9 (C-5), 127.9 (C_o -Ph), 128.5 (C_m -Ph), 129.9 (C_p -Ph), 133.7 (C_i -Ph), 134.4 (C-4), 141.4 (C-3), 183.6 (C-1). ^{15}N NMR (40.5 MHz, CDCl_3): δ_{N} –62.7. Anal. Calcd for $\text{C}_{15}\text{H}_{17}\text{N}$ (211.30): C, 85.26; H, 8.11; N, 6.63%. Found: C, 85.41; H, 8.19; N, 6.47%.

3,3-Dimethyl-2-(4-methylphenyl)-3*H*-pyrrole (2c). Light orange oil, yield 38% (at 82% ketoxime conversion), 0.72 g, R_f 0.52; IR (ν_{max} , cm^{-1} , film): 3074, 2969, 2928, 2871, 1679, 1609, 1567, 1503, 1459, 1327, 1179, 1099, 1041, 822, 760, 726, 685. ^1H NMR (400.1 MHz, CDCl_3): δ_{H} 1.43 (6H, s, Me), 2.41 (3H, s, Me, Ar), 6.21 (1H, d, J 3.4 Hz, H-4), 7.05 (1H, d, J 3.4 Hz, H-5), 7.26 (2H, d, J 8.2 Hz, H_m -Ph), 7.91 (2H, d, J 8.2 Hz, H_o -Ph). ^{13}C NMR (100.6 MHz, CDCl_3): δ_{C} 21.5 (Me, Ar), 22.6 (2Me), 55.5 (C-3), 127.7 (C_o -Ph), 129.3 (C_m -Ph), 130.5 (C_i -Ph), 138.3 (C-4), 140.0 (C-5), 140.3 (C_p -Ph), 183.4 (C-2). ^{15}N NMR (40.5 MHz, CDCl_3): δ_{N} –68.6. Anal. Calcd for $\text{C}_{13}\text{H}_{15}\text{N}$ (185.27): C, 84.28; H, 8.16; N, 7.56%. Found: C, 84.49; H, 8.28; N, 7.31%.

1-(4-Methylphenyl)-2-azaspiro[4.5]deca-1,3-diene (2d). Orange oil, yield 34% (at 87% ketoxime conversion), 0.83 g, R_f 0.49; IR (ν_{max} , cm^{-1} , film): 3076, 2935, 2859, 1612, 1497, 1451, 1336, 1184, 1050, 908, 820, 733, 650. ^1H NMR (400.1 MHz, CDCl_3): δ_{H} 1.34–1.65, 1.88–1.95, 2.09–2.17 (10H, m, CH_2), 2.40 (3H, s, Me), 6.80 (1H, d, J 3.6 Hz, H-4), 7.14 (1H, d, J 3.6 Hz, H-3), 7.25 (2H, d, J 8.2 Hz, H_m -Ph), 7.95 (2H, d, J 8.2 Hz, H_o -Ph). ^{13}C NMR (100.6 MHz, CDCl_3): δ_{C} 21.5 (Me), 25.1 (C-7, C-9), 25.9 (C-8), 32.2 (C-6, C-10), 61.7 (C-5), 127.9 (C_o -Ph), 129.2 (C_m -Ph), 131.0 (C_i -Ph), 134.0 (C-4), 140.1 (C_p -Ph), 141.4 (C-3), 183.5 (C-1). ^{15}N NMR (40.5 MHz, CDCl_3): δ_{N} –67.9. Anal. Calcd for $\text{C}_{16}\text{H}_{19}\text{N}$ (225.33): C, 85.28; H, 8.50; N, 6.22%. Found: C, 85.39; H, 8.36; N, 6.08%.

2-(2,5-Dimethylphenyl)-3,3-dimethyl-3*H*-pyrrole (2e). Yellow oil, yield 21% (at 100% ketoxime conversion), 0.53 g, R_f 0.47; IR (ν_{max} , cm^{-1} , film): 3075, 3019, 2966, 2927, 2869, 1710,

1633, 1576, 1500, 1464, 1379, 1327, 1096, 1026, 813, 768. ^1H NMR (400.1 MHz, CDCl_3): δ_{H} 1.27 (6H, s, Me), 2.23 (3H, s, 2-Me, Ar), 2.33 (3H, s, 5-Me, Ar), 6.24 (1H, d, J 3.4 Hz, H-4), 7.04 (1H, s, H_o -Ph), 7.07 (1H, d, J 3.4 Hz, H-5), 7.10 (1H, d, J 7.8 Hz, H_p -Ph), 7.17 (1H, d, J 7.8 Hz, H_m -Ph). ^{13}C NMR (100.6 MHz, CDCl_3): δ_{C} 19.7 (2-Me, Ar), 21.1 (5-Me, Ar), 21.2 (2Me), 58.3 (C-3), 128.4 (C-6, Ar), 129.3 (C-4, Ar), 130.7 (C-3, Ar), 133.8 (C-1, Ar), 134.5 (C-5, Ar), 134.6 (C-2, Ar), 136.2 (C-4), 140.4 (C-5), 187.7 (C-2). ^{15}N NMR (40.5 MHz, CDCl_3): δ_{N} -57.2. Anal. Calcd for $\text{C}_{14}\text{H}_{17}\text{N}$ (199.29): C, 84.37; H, 8.60; N, 7.03%. Found: C, 84.19; H, 8.49; N, 6.89%.

2-(2-Furyl)-3,3-dimethyl-3H-pyrrole (2f). Yellow oil, yield 16% (at 85% ketoxime conversion), 0.28 g, R_f 0.31; IR (ν_{max} , cm^{-1} , film): 3077, 2969, 2932, 2870, 1584, 1564, 1511, 1465, 1327, 1155, 1101, 1083, 1040, 1000, 883, 754. ^1H NMR (400.1 MHz, CDCl_3): δ_{H} 1.38 (6H, s, Me), 6.18 (1H, d, J 3.3 Hz, H-4), 6.54 (1H, dd, J 1.8 Hz, J 3.6 Hz, H-4, furyl), 6.93 (1H, dd, J 3.6 Hz, J 0.6 Hz, H-3, furyl), 7.02 (1H, d, J 3.3 Hz, H-5), 7.58 (1H, dd, J 1.8 Hz, J 0.6 Hz, H-5, furyl). ^{13}C NMR (100.6 MHz, CDCl_3): δ_{C} 22.4 (2Me), 55.6 (C-3), 111.9 (C-4, furyl), 112.4 (C-3, furyl), 136.5 (C-4), 140.9 (C-5), 144.5 (C-5, furyl), 149.6 (C-2, furyl), 175.5 (C-2). ^{15}N NMR (40.5 MHz, CDCl_3): δ_{N} -73.7. Anal. Calcd. for $\text{C}_{10}\text{H}_{11}\text{NO}$: C, 74.51; H, 6.88; N, 8.69%. Found: C, 74.30; H, 6.76; N, 8.85%.

5-(2,5-Dimethylphenyl)-4,4-dimethyl-2-(vinylloxy)-3,4-dihydro-2H-pyrrole (4e). Compound was not isolated in a pure state. Its structure was determined using mixture with 3H-pyrrole **2e** (**2e** : **4e** \approx 1 : 2) obtained after column chromatography. ^1H NMR (400.1 MHz, CDCl_3): δ_{H} 1.23 (3H, s, Me), 1.24 (3H, s, Me), 1.97 (1H, dd, J 13.2 Hz, J 5.6 Hz, H-3), 2.26 (3H, s, 2-Me, Ar), 2.30 (1H, dd, J 13.2 Hz, J 6.6 Hz, H-3), 2.31 (3H, s, 5-Me, Ar), 4.15 (1H, dd, J 1.4 Hz, J 6.6 Hz, H_a), 4.52 (1H, dd, J 1.4 Hz, J 13.9 Hz, H_b), 5.77 (1H, dd, J 5.6 Hz, J 6.6 Hz, H-2), 6.68 (1H, dd, J 6.6 Hz, J 13.9 Hz, H_x), 6.96 (1H, s, H_o -Ph), 7.06 (1H, d, J 8.0 Hz, H_p -Ph), 7.12 (1H, d, J 8.0 Hz, H_m -Ph). ^{13}C NMR (100.6 MHz, CDCl_3): δ_{C} 19.5 (2-Me, Ar), 26.4 (5-Me, Ar), 26.7 (2Me), 45.5 (C-3), 52.1 (C-4), 90.2 ($\text{OCH}=\text{CH}_2$), 98.8 (C-2), 127.8 (C-6, Ar), 129.3 (C-4, Ar), 130.5 (C-3, Ar), 133.0 (C-1, Ar), 134.2 (C-5, Ar), 134.4 (C-2, Ar), 150.3 ($\text{OCH}=\text{CH}_2$), 185.4 (C-5). ^{15}N NMR (40.5 MHz, CDCl_3): δ_{N} -54.8.

4,4-Dimethyl-5-phenyl-3,4-dihydro-2H-pyrrol-2-ol (3a). White powder, yield 11% (at 88% ketoxime conversion), 0.23 g, mp 104-106 $^{\circ}\text{C}$; IR (ν_{max} , cm^{-1} , KBr): 3169, 2972, 2959, 2932, 2844, 1613, 1572, 1447, 1332, 1104, 1043. ^1H NMR (400.1 MHz, CDCl_3): δ_{H} 1.36 (3H, s, Me), 1.37 (3H, s, Me), 1.82 (1H, dd, J 6.7 Hz, J 12.8 Hz, CH_2), 2.24 (1H, dd, J 6.2 Hz, J 12.8 Hz, CH_2), 5.74 (1H, dd, J 6.2 Hz, J 6.7 Hz, CH), 6.35 (1H, br. s, OH), 7.36 (1H, m, H_p -Ph), 7.38 (2H, m, H_m -Ph), 7.71 (2H, m, H_o -Ph). ^{13}C NMR (100.6 MHz, CDCl_3): δ_{C} 26.9 (Me), 27.4 (Me), 49.4 (C-3), 50.1 (C-4), 91.4 (C-2), 128.2, 128.4, 130.2, 133.5 (Ph), 180.8 (C-5). ^{15}N NMR (40.5 MHz, CDCl_3): δ_{N} -60.7. Anal. Calcd for $\text{C}_{12}\text{H}_{15}\text{NO}$ (189.25): C, 76.16; H, 7.99; N, 7.40%. Found: C, 76.31; H, 8.13; N, 7.29%.

Supporting Information

Supporting information (Experimental details, ^1H and ^{13}C NMR spectra for the compounds **2a-f**, **3a** and **4e**), associated with this article can be found, in the online version.

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References

1. Sammes, M. P.; Katritzky, A. R. in *Adv. Heterocycl. Chem.*, Vol. 32; Academic Press: New York, **1982**, 243.
2. Sammes, M. P. in *Pyrroles, Part I*; J. Wiley & Sons: New York, **1990**, 549.
3. Trofimov, B. A.; Shevchenko, S. G.; Korostova, S. E.; Mikhaleva, A. I.; Sigalov, M. V.; Krivdin, L. B. *Chem. Heterocycl. Compd.* **1989**, 25, 1314.
<http://dx.doi.org/10.1007/BF00481535>
4. Perrin, S.; Monnier, K.; Laude, B. *J. Chem. Res. (S)* **1997**, 104.
5. Welch, K. D.; Smith, P. L.; Keller, A. P.; Myers, W. H.; Sabat, M.; Harman, W. D. *Organometallics* **2006**, 25, 5067.
<http://dx.doi.org/10.1021/om060586j>
6. Shimkin, A. A.; Shirinian, V. Z.; Nikalin, D. M.; Krayushkin, M. M.; Pivina, T. S.; Troitsky, N. A.; Vorontsova, L. G.; Starikova, Z. A. *Eur. J. Org. Chem.* **2006**, 2087.
<http://dx.doi.org/10.1002/ejoc.200500912>
7. Cirrincione, G.; Almerico, A. M.; Dattolo, G.; Aiello, E.; Grimaudo, S.; Diana, P.; Misuraca, F. *Farmaco* **1992**, 47, 1555.
8. Cirrincione, G.; Almerico, A. M.; Grimaudo, S.; Diana, P.; Mingoia, F.; Barraja, P.; Misuraca, F. *Farmaco* **1996**, 51, 49.
9. Padmavathi, V.; Radha Lakshmi, T.; Mahesh, K.; Padmaja, A. *Chem. Pharm. Bull.* **2009**, 57, 1200.
<http://dx.doi.org/10.1248/cpb.57.1200>
10. Shabalin, D. A.; Dvorko, M. Yu.; Schmidt, E. Yu.; Ushakov, I. A.; Protsuk, N. I.; Kobychyev, V. B.; Soshnikov, D. Yu.; Trofimov, A. B.; Vitkovskaya, N. M.; Mikhaleva, A. I.; Trofimov, B. A. *Tetrahedron* **2015**, 71, 3273.
<http://dx.doi.org/10.1016/j.tet.2015.03.111>

11. Chiu, P.-K.; Lui, K.-H.; Maini, P. N.; Sammes, M. P. *J. Chem. Soc., Chem. Commun.* **1987**, 109.
<http://dx.doi.org/10.1039/C39870000109>
12. Das, P.; Ray, S.; Mukhopadhyay, C. *Org. Lett.* **2013**, *15*, 5622.
<http://dx.doi.org/10.1021/ol402950a>
13. Yavari, I.; Ghanbari, E.; Hosseinpour, R. *Helv. Chim. Acta* **2014**, *97*, 1004.
<http://dx.doi.org/10.1002/hlca.201300400>
14. Liao, J.-Y.; Shao, P.-L.; Zhao, Y. *J. Am. Chem. Soc.* **2015**, *137*, 628.
<http://dx.doi.org/10.1021/ja511895q>
15. Trofimov, B. A.; Mikhaleva, A. I.; Schmidt, E. Yu.; Sobenina, L. N. *Adv. Heterocycl. Chem.* **2010**, *99*, 209.
[http://dx.doi.org/10.1016/S0065-2725\(10\)09907-1](http://dx.doi.org/10.1016/S0065-2725(10)09907-1)
16. Schmidt, E. Yu.; Zorina, N. V.; Dvorko, M. Yu.; Protsuk, N. I.; Belyaeva, K. V.; Clavier, G.; Meallet-Renault, R.; Vu, T. T.; Mikhaleva, A. I.; Trofimov, B. A. *Chem. Eur. J.* **2011**, *17*, 3069.
<http://dx.doi.org/10.1002/chem.201003242>
17. Trofimov, B. A.; Mikhaleva, A. I.; Schmidt, E. Yu.; Sobenina, L. N. in *Chemistry of Pyrroles*; CRC Press: Florida, **2014**, 398.
18. Davies, H. M. L.; Morton, D. *Angew. Chem., Int. Ed.* **2014**, *53*, 10256.
<http://dx.doi.org/10.1002/anie.201406633>
19. Korostova, S. E.; Shevchenko, S. G.; Sigalov, M. V. *Chem. Heterocycl. Compd.* **1991**, *27*, 1101.
<http://dx.doi.org/10.1007/BF00486806>