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Metal-Free Selective Synthesis of 1,4-Dihydropyridazines from Hydroxypyrrolines and Hydrazines

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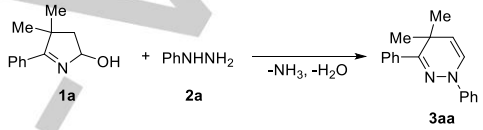
Abstract: An efficient and selective synthesis of 1,4-dihydropyridazines by the acid-catalyzed recyclization of 5-hydroxy-Δ^1-pyrrolines with hydrazines has been developed. The scope of this reaction was thoroughly explored resulting in the generation of a library of title compounds in good to excellent yields (25 examples, 67-100% yields).

Introduction

1,4-Dihydropyridazine structural unit could be referred to a privileged scaffold[1] for the drug discovery because of two main reasons. First, it is the aza-analog of 1,4-dihydropyridine which is generally considered as the motif for important cardiovascular drugs, namely, calcium antagonists including nifedipine, nitrendipine, amlodipine, etc.[1,2] Indeed, some 1,4-dihydropyridazine derivatives have already demonstrated a potential use as antihypertensive, coronary insufficiency therapeutic and spasmolytic agents,[3] and as inhibitors of ocular inflammation induced by lens protein, endotoxin, and interleukin-1.[4] The various routes to 1,4-dihydropyridazines are known.[5] Among them are reaction between 1,2-diaza-1,3-butadienes and activated methine compounds,[6] cycloaddition of 1,2,4,5-tetrazines with different dienophiles,[7] reaction of activated alkenes with hydrazones,[8] and some miscellaneous synthesis.[9] One of the most common approach is the reaction of 1,4-dicarbonyl compounds with hydrazines.[10] However, in reviews concerning dihydropyridazine chemistry[5,11] it has been emphasized that not all reactions of 1,4-dicarbonyl compounds with hydrazines proceed as simply as assumed. Depending on the reaction conditions and structural factors, problems of chemo- and regioselectivity usually emerge. The former relates to the simultaneous formation of the mono- and bishydrazones, N-aminopyrroles, and 1,4-dihydropyridazines, and the latter refers to the different reactivity of carbonyl groups of unsymmetrical 1,4-dicarbonyl compounds.

Recently, we have developed a general method for the synthesis of stable 5-hydroxy-Δ^1-pyrrolines by the reaction of easily accessible aryl isoalkyl ketoximes with acetylene in the presence of inexpensive KOH/DMSO superbase catalytic system.[12] Combination of reactive hydroxyl group and pyrroline moiety in a one molecule makes these compounds perspective building blocks for construction of various pyrroline ensembles. As part of our ongoing research in this direction, we have unexpectedly found regioselective recyclization of 3,3-dimethyl-5-hydroxy-2-phenyl-Δ^1-pyrroline (**1a**) with phenylhydrazine (**2a**) to form pharmaceutically attractive 1,4-dihydropyridazine **3aa** (Scheme 1).



Scheme 1. Unexpected formation of 1,4-dihydropyridazine **3aa** from 5-hydroxy-Δ^1-pyrroline **1a** and phenylhydrazine (**2a**).

Therefore, in the present work we aimed to thoroughly investigate the applicability of the reaction between 5-hydroxy-Δ^1-pyrrolines and hydrazines for the selective synthesis of 1,4-dihydropyridazines.

Results and Discussion

At the outset of our study, we have examined the reaction of 3,3-dimethyl-5-hydroxy-2-phenyl-Δ^1-pyrroline (**1a**) with phenylhydrazine (**2a**) as a model (Scheme 1). As shown in Table 1, the 1,4-dihydropyridazine **3aa** was obtained in 34% yield along with a large number of unidentified products in the presence of trifluoroacetic acid (TFA, 10 mol%) in acetonitrile at room temperature (Entry 3). Without acid catalyst, the recyclization of **1a** with **2a** in acetonitrile at room temperature (Entry 1) as well as under reflux (Entry 2) does not almost occur. Pleasingly, the selectivity of reaction of **1a** with **2a** toward the target product was improved up to 75% yield of **3aa**, when TFA and refluxing were applied together (Entry 4). Stepwise decreasing of the reaction time from 3 h to 1 h allowed to reach 89% yield of **3aa** (Entries 4-7) that indicated the poor stability of 1,4-dihydropyridazines under the studied reaction conditions at prolonged heating. An increase in TFA loading from 10 mol% to 20 mol% resulted in a slightly lower yield of 1,4-dihydropyridazine **3aa** (84%, Entry 9). However, if 5 mol% of TFA (Entry 8) or 10 mol% of stronger Brønsted acids like trifluoromethanesulfonic (Entry 10) and p-toluenesulfonic (Entry 11) acids were used the yield of **3aa** deteriorated significantly (down to 71, 72 and 56%, respectively). Among the solvents tested, acetonitrile provided the best results, while other solvents such as benzene, ethanol, and dimethyl sulfoxide afforded lower

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yields (Entries 12-14). Hence, the arbitrary optimal conditions were determined to perform the reaction of 3,3-dimethyl-5-hydroxy-2-phenyl-Δ^1-pyrroline (**1a**) with phenylhydrazine (**2a**) in acetonitrile with TFA (10 mol%) under reflux for 1 h (Table 1, entry 6).

Table 1. Optimization of the reaction conditions.[a]

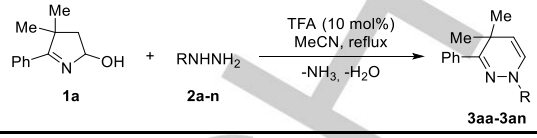
Entry	Catalyst (mol%)	Solvent	T [°C]	t [h]	Yield [%][b]
1	none	MeCN	rt	8	traces
2	none	MeCN	82	3	traces
3	TFA (10)	MeCN	rt	3	34
4	TFA (10)	MeCN	82	3	75
5	TFA (10)	MeCN	82	2	80
6	**TFA (10)**	**MeCN**	**82**	**1**	**89**
7	TFA (10)	MeCN	82	0.5	69
8	TFA (5)	MeCN	82	1	71
9	TFA (20)	MeCN	82	1	84
10	TfOH (10)	MeCN	82	1	72
11	$TsOH \cdot H_2O$ (10)	MeCN	82	1	56
12	TFA (10)	PhH	80	1	43
13	TFA (10)	EtOH	78	1	50
14	TFA (10)	DMSO	80	1	5

[a] Reaction conditions: 5-hydroxy-Δ^1-pyrroline **1a** (0.5 mmol), phenylhydrazine (**2a**, 0.5 mmol), catalyst, solvent (3 mL). [b] Isolated yield.

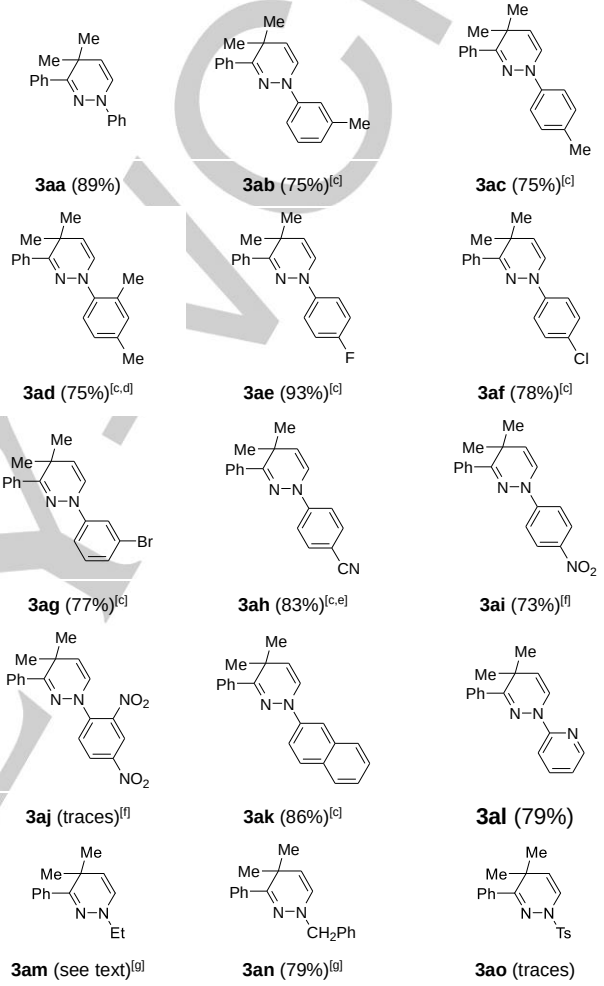
With the conditions established, the scope of the reaction was first explored with respect to the diversely substituted hydrazines (Table 2). It should be noted that if hydrazines were used in the form of hydrochloride salts, the recyclization was successfully performed even without addition of TFA (products **3ab**-**3ah** and **3ak**, Table 2).

As follows from Table 2, hydrazines with alkyl, aryl and hetaryl substituents are amenable for the recyclization of 5-hydroxy-Δ^1-pyrroline **1a** to 1,4-dihydropyridazines in good to excellent yields. The substituent pattern has the expected influence on the studied process. Thus, when using arylhydrazines with electron-donor methyl group in the phenyl ring under chosen arbitrary optimal reaction conditions, the yields of the corresponding 1,4-dihydropyridazines dropped to 75% (**3ab** and **3ac**) in comparison with unsubstituted phenylhydrazine (89% yield for **3aa**). The introduction of second methyl group to the phenyl ring leads to formation of the corresponding product **3ad** in 66% yield. This contradiction between increasing of hydrazine nucleophilicity and decreasing of the product yield could be explained by faster formation of 1,4-dihydropyridazine and its further transformation. Indeed, when the reaction between 5-hydroxy-Δ^1-pyrroline **1a** and 2,4-dimethylphenylhydrazine (**2d**) was carried out for 30 min, the yield of 1,4-dihydropyridazine **3ad** was improved up to 75%.

Table 2. Reaction of 5-hydroxy-Δ^1-pyrroline **1a** with hydrazines **2a-n**.[a,b]



1a **2a-n** **3aa-3an**



3aa (89%) **3ab** (75%)[c] **3ac** (75%)[c]

3ad (75%)[c,d] **3ae** (93%)[c] **3af** (78%)[c]

3ag (77%)[c] **3ah** (83%)[c,e] **3ai** (73%)[f]

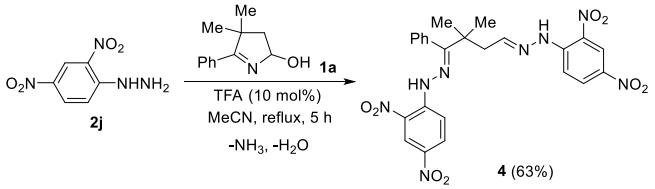
3aj (traces)[f] **3ak** (86%)[c] **3al** (79%)

3am (see text)[g] **3an** (79%)[g] **3ao** (traces)

[a] Reaction conditions: 5-hydroxy-Δ^1-pyrroline **1a** (0.5 mmol), hydrazine or hydrazine hydrochloride **2** (0.5 mmol), with or without TFA (10 mol%), MeCN (3 mL), reflux, 1 h. [b] Isolated yields are given. [c] Hydrazine hydrochloride without addition of TFA was used. [d] Reaction time was 30 min. [e] Reaction time was 3 h. [f] Reaction time was 5 h. [g] Reaction time was 15 min.

On the contrary, the reaction of 5-hydroxy-Δ^1-pyrroline **1a** with arylhydrazines bearing electron-withdrawing substituents in the phenyl ring naturally required a longer time, e.g. 3 h for 4-cyanophenylhydrazine (**2h**) and 5 h for 4-nitrophenylhydrazine (**2i**). The use of 2,4-dinitrophenylhydrazine (**2j**) as a nucleophile shed light on the recyclization mechanism, since only traces of the desired 1,4-dihydropyridazine **3aj** were detected (^{1}H NMR), and the main product was dihydrazone **4** (63%, Scheme 2). Noteworthy, when tosylhydrazine **2o** was introduced in the reaction with 5-hydroxy-Δ^1-pyrroline **1a** for 1 h the latter was fully consumed, although only traces of 1,4-dihydropyridazine **3ao**

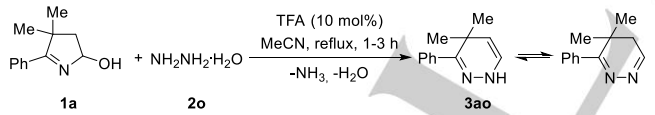
were observed (^{1}H NMR) in complex reaction mixture. Apparently, more electron-withdrawing tosyl substituent (in comparison with 2,4-dinitrophenyl substituent) significantly decrease the nucleophilicity of both amino functions, thus precluding even initial ring opening (no dihydrazone of type **4** was detected).



Scheme 2. Reaction of 5-hydroxy-Δ^1-pyrroline **1a** with 2,4-dinitrophenylhydrazine (**2j**).

The violation of regioselectivity has not been observed for the recyclization of 5-hydroxy-Δ^1-pyrroline **1a** with alkylhydrazines as it could be expected from increasing of nucleophilicity of secondary nitrogen atom (NH), bearing σ-donor alkyl group instead of electron-withdrawing aryl group. Ethylhydrazine (**2m**) and benzylhydrazine (**2n**) were successfully tested in the studied reaction affording the corresponding 1,4-dihydropyridazines in good yields for 15 min (Table 2). Despite the good yield of 1-ethyl-1,4-dihydropyridazine **3am**, observed in ^{1}H NMR spectrum of the reaction mixture, the isolated yield of **3am** was insignificant (ca. 6%) due to its instability upon isolation and storage.

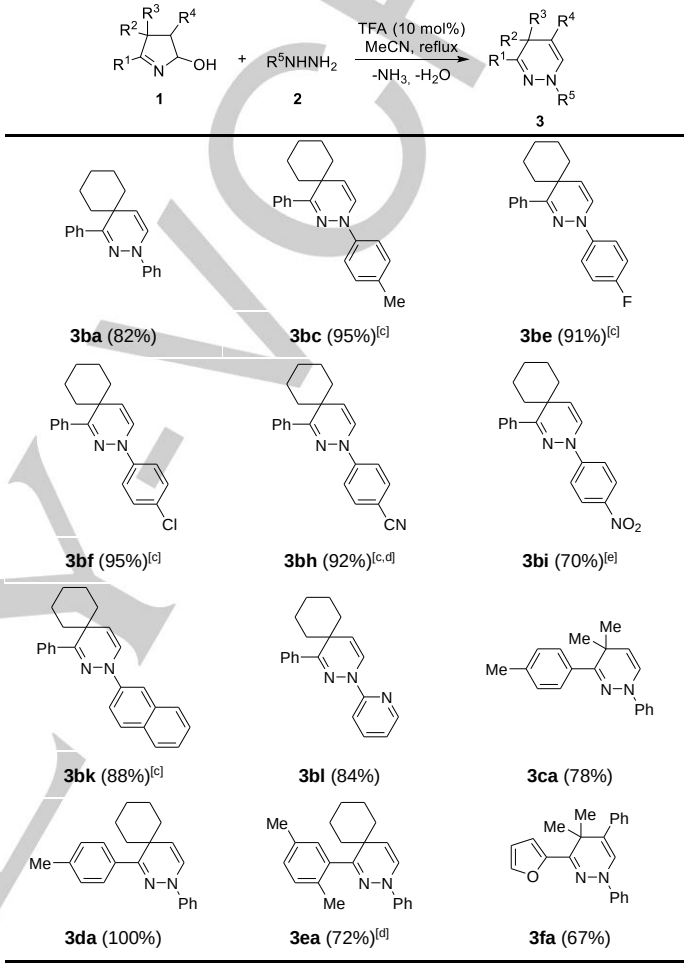
The reaction of 5-hydroxy-Δ^1-pyrroline **1a** with hydrazine hydrate (**2o**) for 1 h led to formation of the corresponding 1,4-dihydropyridazine **3ao** in trace amounts (^{1}H NMR). Increasing the reaction time did not improve the yield of **3ao** apparently due to the known tautomeric equilibrium between 1,4- and 4,5-dihydropyridazines and inclination of the latter to be transformed into dimer, trimer and polymeric products (Scheme 3).[13]



Scheme 3. Reaction of 5-hydroxy-Δ^1-pyrroline **1a** with hydrazine hydrate (**2o**).

Further, we have investigated the reactivity of diversely substituted 5-hydroxy-Δ^1-pyrrolines **1b-f** in the reaction with hydrazines **2** (Table 3). Generally, the yields of spiro-fused 1,4-dihydropyridazines are higher than those of 4,4-dimethyl-1,4-dihydropyridazines that is explicated neither by electronic nor by steric influence of spiro-fused cyclohexyl ring but by easy isolation of the target products after treatment of the reaction mixture with diethyl ether and, therefore, by the absence of column chromatography purification step. In the case of 5-hydroxy-Δ^1-pyrroline **1e**, having 2,5-dimethylphenyl substituent at the carbon-nitrogen double bond, acceptable yield of **3ea** (72%) was obtained only when the reaction time was increased up to 3 h. This is apparently associated with both the electron-donor effect of 2,5-dimethylphenyl substituent reducing electrophilicity of carbon atom of the imine function and the shielding effect of *ortho*-methyl group hindering interaction with acid catalyst and nucleophile.

Table 3. Reaction of 5-hydroxy-Δ^1-pyrrolines **1** with hydrazines **2**.[a,b]

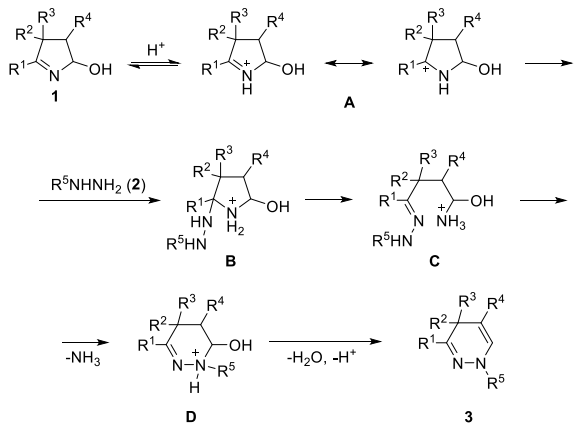


[a] Reaction conditions: 5-hydroxy-Δ^1-pyrroline **1b-f** (0.5 mmol), hydrazine or hydrazine hydrochloride **2** (0.5 mmol), with or without TFA (10 mol%), MeCN (3 mL), reflux, 1 h. [b] Isolated yields are given. [c] Hydrazine hydrochloride without addition of TFA was used. [d] Reaction time was 3 h. [e] Reaction time was 5 h.

The structures of all synthesized compounds **3** were unambiguously proven by ^{1}H, ^{13}C NMR spectroscopy (2D COSY, NOESY, HMBC, HSQC techniques were also employed in some cases) and X-ray diffraction study of their representative, **3ai** (Figure 1) and **3da** (Figure 2).

A tentative mechanism for recyclization of 5-hydroxy-Δ^1-pyrrolines with hydrazines to form 1,4-dihydropyridazines is depicted in Scheme 4. Protonation of the starting 5-hydroxy-Δ^1-pyrroline **1** (with TFA or hydrogen chloride, when hydrazine hydrochloride salts are used) leads to formation of cation **A**, which reacts with hydrazine **2** to afford protonated pyrrolidine **B**. Further ring opening gives linear intermediate **C**, which cyclizes

to 3-hydroxy-2,3,4,5-tetrahydropyridazine **D** via intramolecular nucleophilic substitution of ammonium moiety by the NH-function of hydrazine. Dehydration of intermediate **D** ends the formation of 1,4-dihydropyridazine **3**. This mechanism is in an agreement with the abovementioned reaction between 2,4-dinitrophenylhydrazine (**2j**) and 5-hydroxy-Δ^1-pyrroline **1a** resulting in dihydrazone **4** (Scheme 2), formation of which is explained by decrease of nucleophilicity of the NH-function conjugated with 2,4-dinitrophenyl ring that eventually prevents intramolecular cyclization of intermediate **C** (Scheme 4).



Scheme 4. A tentative mechanism for recyclization of 5-hydroxy-Δ^1-pyrrolines with hydrazines.

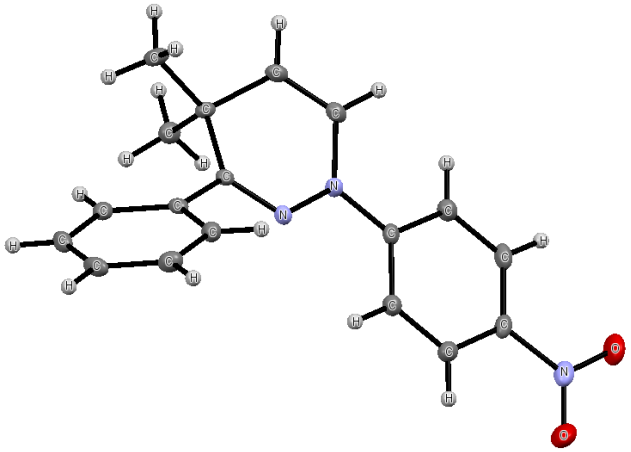


Figure 1. ORTEP diagram of 4,4-dimethyl-1-(4-nitrophenyl)-3-phenyl-1,4-dihydropyridazine (**3ai**) as determined by X-ray analysis. Thermal ellipsoids set at 50% probability.

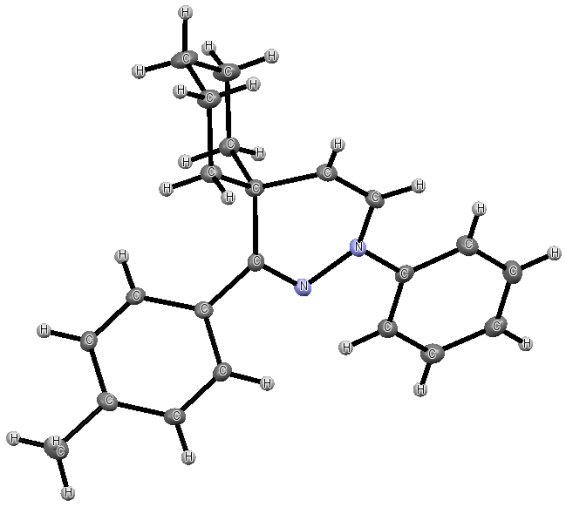


Figure 2. ORTEP diagram of 1-(4-methylphenyl)-3-phenyl-2,3-diazaspiro[5.5]undeca-1,4-diene (**3da**) as determined by X-ray analysis. Thermal ellipsoids set at 50% probability.

Conclusions

In conclusion, we have presented a selective synthesis of pharmaceutically perspective 1,4-dihydropyridazines based on the acid-catalyzed recyclization of available 5-hydroxy-Δ^1-pyrrolines with hydrazines. The reaction is operationally simple and tolerant to a variety of substituted hydrazines and 5-hydroxy-Δ^1-pyrrolines, and provides desired heterocycles in good to excellent preparative yields.

Experimental Section

General information. All chemicals and solvents were purchased from commercial sources and used without further purification. Starting 5-hydroxy-Δ^1-pyrrolines **1a-e** were prepared by literature method,[12] and 5-hydroxy-Δ^1-pyrroline **1f** was synthesized from furyl isopropyl ketoxime and phenylacetylene (for details see SI). Commercial acetonitrile was dried with 4Å MS before use. Thin layer chromatography was carried out on Merck silica gel 60 F_{254} pre-coated aluminium foil sheets (eluent: hexane/diethyl ether 1:1) and were visualized using UV light (254 nm). Flash column chromatography was carried out using slurry packed Sigma Aldrich silica gel (SiO_2), 70-230 mesh, pore size 60 Å, eluting with benzene. IR spectra were recorded on a Bruker Vertex-70 spectrophotometer as thin films dispersed from $CDCl_3$ or KBr pellets. NMR spectra were recorded 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). Chemical shifts (δ) are quoted in parts per million (ppm). The residual solvent peak, δ_H 7.27 and δ_C 77.10 for $CDCl_3$, δ_H 2.50 and δ_C 39.50 for DMSO-d_6, δ_H 1.94 and δ_C 118.26 for CD_3CN, was used as a reference. Coupling constants (J) are reported in Hertz (Hz). The multiplicity abbreviations used are: s singlet, d doublet, t triplet, q quartet, m multiplet, br broad signal. Signal assignment was achieved by analysis of COSY, NOESY, HMBC, and HSQC experiments if required. Melting points (uncorrected) were measured on a Kofler micro hot-stage apparatus. The CHN microanalyses were performed on a Flash EA 1112 Series elemental analyzer.

Atomic coordinates, bond lengths, bond angles and thermal parameters for compounds **3ai** and **3da** have been deposited at the Cambridge Crystallographic Data Centre (CCDC) and allocated the deposition numbers CCDC 1542500, 1542502. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

General procedure for the synthesis of 1,4-dihydropyridazines 3. A mixture of 5-hydroxy-Δ^1-pyrroline **1** (0.5 mmol), hydrazine or hydrazine hydrochloride salt **2** (0.5 mmol), TFA (10 mol%, if needed) and acetonitrile (3 mL) was refluxed for appropriate time (see Table 2 and 3). The residue after solvent evaporation was purified by Method A (flash column chromatography, SiO_2, eluent - benzene) or Method B (treatment with diethyl ether and further evaporation of ether solution).

4,4-Dimethyl-1,3-diphenyl-1,4-dihydropyridazine (3aa): purification by Method A; yield 0.116 g, 89%; an yellow oil; R_f = 0.87 (hexane/diethyl ether 1:1); ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.62-7.60 (m, 2H, Ph), 7.46-7.41 (m, 5H, Ph), 7.35-7.33 (m, 2H, Ph), 7.05-7.02 (m, 1H, Ph), 6.83 (d, J = 7.4 Hz, 1H, H^6), 4.81 (d, J = 7.4 Hz, 1H, H^5), 1.32 (s, 6H, Me) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 150.2, 144.9, 137.8, 129.3, 129.1, 128.2, 127.9, 124.8, 122.1, 115.4, 109.9, 32.7, 28.9 ppm; ^{15}N NMR (40.5 MHz, $CDCl_3$): δ = −215.4, −64.9 ppm; IR (film): ν_{max} = 2963, 2927, 2868, 1650, 1598, 1495, 1328, 1285, 1243, 1107, 1004 cm^{-1}; elemental analysis calcd (%) for $C_{18}H_{18}N_2$: C 82.40, H 6.92, N 10.68; found: C 82.23, H 6.74, N 10.74.

4,4-Dimethyl-1-(3-methylphenyl)-3-phenyl-1,4-dihydropyridazine (3ab): purification by Method A; yield 0.103 g, 75%; an orange oil; R_f = 0.89 (hexane/diethyl ether 1:1); ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.59-7.57 (m, 2H, Ph), 7.40-7.38 (m, 3H, Ph), 7.27-7.26 (m, 1H, Ar), 7.21-7.20 (m, 2H, Ar), 6.84-6.82 (m, 1H, Ar), 6.80 (d, J = 7.2 Hz, 1H, H^6), 4.77 (d, J = 7.2 Hz, 1H, H^5), 2.36 (s, 3H, Me), 1.28 (s, 6H, Me) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 150.0, 144.9, 138.9, 137.8, 129.2, 128.9, 128.2, 127.9, 124.9, 123.0, 116.1, 112.5, 109.6, 32.7, 28.8, 21.7 ppm; IR (film): ν_{max} = 2962, 2924, 2866, 1650, 1598, 1492, 1331, 1289, 1242, 1108, 1004 cm^{-1}; elemental analysis calcd (%) for $C_{19}H_{20}N_2$: C 82.57, H 7.29, N 10.14; found: C 82.69, H 7.30, N 10.08.

4,4-Dimethyl-1-(4-methylphenyl)-3-phenyl-1,4-dihydropyridazine (3ac): purification by Method A; yield 0.103 g, 75%; an orange oil; R_f = 0.86 (hexane/diethyl ether 1:1); ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.59-7.57 (m, 2H, Ph) 7.40-7.38 (m, 3H, Ph), 7.31 (d, J = 8.3 Hz, 2H, Ar), 7.13 (d, J = 8.3 Hz, 2H, Ar), 6.77 (d, J = 7.3 Hz, 1H, H^6), 4.75 (d, J = 7.3 Hz, 1H, H^5), 2.32 (s, 3H, Me), 1.29 (s, 6H, Me) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 149.6, 142.8, 137.9, 131.5, 129.6, 129.2, 128.1, 127.9, 125.1, 115.5, 109.3, 32.6, 28.9, 20.7 ppm; IR (film): ν_{max} = 2961, 2924, 2863, 1648, 1612, 1512, 1360, 1283, 1241, 1107, 1005 cm^{-1}; elemental analysis calcd (%) for $C_{19}H_{20}N_2$: C 82.57, H 7.29, N 10.14; found: C 82.43, H 7.08, N 10.23.

1-(2,4-Dimethylphenyl)-4,4-dimethyl-3-phenyl-1,4-dihydropyridazine (3ad): purification by Method A; yield 0.109 g, 75%; an orange oil; R_f = 0.87 (hexane/diethyl ether 1:1); ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.54-7.52 (m, 2H, Ph), 7.35-7.33 (m, 3H, Ph), 7.30-7.27 (m, 1H, Ar), 7.03-7.01 (m, 2H, Ar), 6.37 (d, J = 7.2 Hz, 1H, H^6), 4.62 (d, J = 7.2 Hz, 1H, H^5), 2.31 (s, 6H, Me), 1.29 (s, 6H, Me) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 148.3, 143.2, 137.8, 135.4, 132.4, 131.7, 129.2, 129.7, 127.9, 127.8, 127.2, 124.2, 106.4, 32.1, 28.2, 20.9, 18.3 ppm; IR (film): ν_{max} = 2959, 2924, 2865, 1647, 1503, 1458, 1094, 1006 cm^{-1}; elemental analysis calcd (%) for $C_{20}H_{22}N_2$: C 82.72, H 7.64, N 9.65; found: C 82.61, H 7.87, N 9.44.

1-(4-Fluorophenyl)-4,4-dimethyl-3-phenyl-1,4-dihydropyridazine (3ae): purification by Method B; yield 0.130 g, 93%; an orange oil; ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.57-7.55 (m, 2H, Ph), 7.40-7.34 (m, 5H, Ar, Ph), 7.04-7.00 (m, 2H, Ar), 6.72 (d, J = 7.3 Hz, 1H, H^6), 4.78 (d, J = 7.3 Hz, 1H, H^5), 1.29 (s, 6H, Me) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 158.7 (d, J = 240.5 Hz), 150.2, 141.5 (d, J = 2.3 Hz), 137.7, 129.2, 128.3, 127.9, 125.1, 116.9 (d, J = 7.7 Hz), 115.6 (d, J = 22.5 Hz), 109.7, 32.6, 28.8 ppm; IR (film): ν_{max} = 2963, 2928, 2867, 1648, 1505, 1327, 1288, 1219, 1104, 1005 cm^{-1}; elemental analysis calcd (%) for $C_{18}H_{17}FN_2$: C 77.12, H 6.11, F 6.78, N 9.99; found: C 76.92, H 5.87, F 7.03, N 9.74.

1-(4-Chlorophenyl)-4,4-dimethyl-3-phenyl-1,4-dihydropyridazine (3af): purification by Method A; yield 0.116 g, 78%; an orange oil; R_f = 0.87 (hexane/diethyl ether 1:1); ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.56-7.55 (m, 2H, Ph), 7.41-7.39 (m, 3H, Ph), 7.34 (d, J = 8.9 Hz, 2H, Ar), 7.27 (d, J = 8.9 Hz, 2H, Ar), 6.75 (d, J = 7.4 Hz, 1H, H^6), 4.82 (d, J = 7.4 Hz, 1H, H^5), 1.29 (s, 6H, Me) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 150.9, 143.4, 137.5, 129.2, 129.0, 128.4, 128.0, 127.0, 124.4, 116.4, 110.5, 32.8, 28.8 ppm; IR (film): ν_{max} = 2962, 2925, 2861, 1650, 1595, 1491, 1360, 1286, 1103, 1004 cm^{-1}; elemental analysis calcd (%) for $C_{18}H_{17}ClN_2$: C 72.84, H 5.77, Cl 11.95, N 9.44; found: C 73.01, H 5.89, Cl 11.78, N 9.23.

1-(3-Bromophenyl)-4,4-dimethyl-3-phenyl-1,4-dihydropyridazine (3ag): purification by Method A; yield 0.132 g, 77%; an orange oil; R_f = 0.86 (hexane/diethyl ether 1:1); ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.61-7.59 (m, 1H, Ar), 7.56-7.54 (m, 2H, Ph), 7.41-7.40 (m, 3H, Ph), 7.31-7.29 (m, 1H, Ar), 7.19-7.15 (m, 1H, Ar), 7.12-7.10 (m, 1H, Ar), 6.76 (d, J = 7.4 Hz, 1H, H^6), 4.84 (d, J = 7.4 Hz, 1H, H^5), 1.29 (s, 6H, Me) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 151.4, 145.9, 137.4, 130.3, 129.2, 128.4, 128.0, 124.7, 124.1, 123.1, 118.2, 113.5, 110.9, 32.8, 28.8 ppm; IR (film): ν_{max} = 2963, 2927, 2866, 1653, 1589, 1478, 1331, 1288, 1237, 1102, 1013, 1001 cm^{-1}; elemental analysis calcd (%) for $C_{18}H_{17}BrN_2$: C 63.35, H 5.02, Br 23.42, N 8.21; found: C 63.12, H 5.14, Br 23.68, N 8.20.

1-(4-Cyanophenyl)-4,4-dimethyl-3-phenyl-1,4-dihydropyridazine (3ah): purification by Method A; yield 0.119 g, 83%; an yellow oil; R_f = 0.63 (hexane/diethyl ether 1:1); ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.58 (d, J = 9.0 Hz, 2H, Ar), 7.55-7.53 (m, 2H, Ph), 7.45 (d, J = 9.0 Hz, 2H, Ar), 7.42-7.41 (m, 3H, Ph), 6.82 (d, J = 7.5 Hz, 1H, H^6), 4.97 (d, J = 7.5 Hz, 1H, H^5), 1.31 (s, 6H, Me) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 153.5, 147.2, 137.0, 133.3, 129.0, 128.7, 128.0, 122.8, 119.6, 114.4, 113.0, 103.9, 33.0, 28.8 ppm; IR (film): ν_{max} = 2966, 2928, 2870, 2219, 1602, 1509, 1393, 1337, 1292, 1174, 1106, 1002 cm^{-1}; elemental analysis calcd (%) for $C_{19}H_{17}N_3$: C 79.41, H 5.96, N 14.62; found: C 79.51, H 5.67, N 14.92.

4,4-Dimethyl-1-(4-nitrophenyl)-3-phenyl-1,4-dihydropyridazine (3ai): purification by Method A; yield 0.112 g, 73%; an yellow powder; m.p. 121-123 °C; R_f = 0.68 (hexane/diethyl ether 1:1); ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 8.20 (d, J = 9.3 Hz, 2H, Ar), 7.56-7.54 (m, 2H, Ph), 7.45 (d, J = 9.3 Hz, 2H, Ar), 7.45-7.43 (m, 3H, Ph), 6.88 (d, J = 7.5 Hz, 1H, H^6), 5.04 (d, J = 7.5 Hz, 1H, H^5), 1.32 (s, 6H, Me) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 154.7, 148.7, 141.6, 136.9, 129.0, 128.9, 128.1, 125.6, 122.6, 114.0, 113.6, 33.2, 28.8 ppm; IR (film): ν_{max} = 2975, 2952, 2934, 1649, 1592, 1501, 1315, 1289, 1106, 1007 cm^{-1}; elemental analysis calcd (%) for $C_{18}H_{17}N_3O_2$: C 70.34, H 5.58, N 13.67; found: C 70.53, H 5.49, N 13.39.

4,4-Dimethyl-1-(2-naphtyl)-3-phenyl-1,4-dihydropyridazine (3ak): purification by Method A; yield 0.134 g, 86%; a beige powder; m.p. 92-94 °C; R_f = 0.83 (hexane/diethyl ether 1:1); ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.81-7.78 (m, 4H, Naphtyl), 7.71-7.69 (m, 1H, Naphtyl), 7.66-7.64 (m, 2H, Ph), 7.47-7.43 (m, 4H, Naphtyl, Ph), 7.38-7.34 (m, 1H, Naphtyl), 6.97

(d, J = 7.4 Hz, 1H, H^6), 4.88 (d, J = 7.4 Hz, 1H, H^5), 1.35 (s, 6H, Me) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 150.7, 142.6, 137.8, 134.3, 129.9, 129.3 (2C), 129.0, 128.3, 128.0, 127.7, 127.3, 126.5, 124.8, 124.0, 117.0, 110.6, 32.9, 29.0 ppm; IR (film): ν_{max} = 3056, 2962, 2931, 2870, 1629, 1594, 1510, 1471, 1361, 1327, 1288, 1102, 1008 cm^{-1}; elemental analysis calcd (%) for $C_{22}H_{20}N_2$: C 84.58, H 6.45, N 8.97; found: C 84.35, H 6.38, N 8.81.

4,4-Dimethyl-3-phenyl-1-(2-pyridinyl)-1,4-dihydropyridazine (3al): purification by Method A; yield 0.104 g, 79%; a pale yellow powder; m.p. 61-63 °C; R_f = 0.78 (hexane/diethyl ether 1:1); ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 8.27-8.24 (m, 1H, Py), 7.73 (d, J = 7.7 Hz, 1H, H^6), 7.59-7.56 (m, 4H, Ph, Py), 7.41-7.39 (m, 3H, Ph), 6.88-6.84 (m, 1H, Py), 4.89 (d, J = 7.7 Hz, 1H, H^5), 1.32 (s, 6H, Me) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 154.8, 152.3, 147.2, 137.8 (2C), 129.1, 128.3, 127.9, 121.4, 117.0, 110.7, 109.4, 32.9, 29.3 ppm; IR (film): ν_{max} = 2963, 2924, 2866, 1661, 1589, 1466, 1441, 1327, 1294, 1101, 1000 cm^{-1}; elemental analysis calcd (%) for $C_{17}H_{17}N_3$: C 77.54, H 6.51, N 15.96; found: C 77.54, H 6.36, N 15.91.

1-Ethyl-4,4-dimethyl-3-phenyl-1,4-dihydropyridazine (3am): ^{1}H NMR (400.1 MHz, CD_3CN): δ = 7.45-7.43 (m, 2H, Ph), 7.36-7.33 (m, 3H, Ph), 6.32 (d, J = 7.2 Hz, 1H, H^6), 4.50 (d, J = 7.2 Hz, 1H, H^5), 3.47 (q, J = 7.1 Hz, 2H, Et), 1.20 (t, J = 7.1 Hz, 3H, Et), 1.13 (s, 6H, Me) ppm; ^{13}C NMR (100.6 MHz, CD_3CN): δ = 148.1, 139.4, 130.3, 130.0, 128.7, 106.8, 51.5, 32.4, 28.3, 14.3 ppm.

1-Benzyl-4,4-dimethyl-3-phenyl-1,4-dihydropyridazine (3an): purification by Method A; yield 0.109 g, 79%; an yellow oil; R_f = 0.85 (hexane/diethyl ether 1:1); ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.49-7.46 (m, 2H, Ph), 7.37-7.29 (m, 8H, Benzyl, Ph), 6.25 (d, J = 7.3 Hz, 1H, H^6), 4.72 (s, 2H, CH_2), 4.50 (d, J = 7.3 Hz, 1H, H^5), 1.21 (s, 6H, Me) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 147.9, 138.7, 138.1, 129.3, 129.2, 128.5, 127.9 (2C), 127.8, 127.3, 106.5, 60.1, 32.0, 28.3 ppm; IR (film): ν_{max} = 2960, 2925, 2860, 1645, 1545, 1454, 1441, 1355, 1309, 1184, 1091, 1007 cm^{-1}; elemental analysis calcd (%) for $C_{19}H_{20}N_2$: C 82.57, H 7.29, N 10.14; found: C 82.68, H 7.31, N 10.38.

1,3-Diphenyl-2,3-diazaspiro[5.5]undeca-1,4-diene (3ba): purification by Method A; yield 0.124 g, 82%; a beige powder; m.p. 78-80 °C; R_f = 0.89 (hexane/diethyl ether 1:1); ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.48-7.46 (m, 2H, Ph), 7.44-7.39 (m, 5H, Ph), 7.34-7.30 (m, 2H, Ph), 7.03-6.99 (m, 1H, Ph), 6.87 (d, J = 7.3 Hz, 1H, H^4), 5.19 (d, J = 7.3 Hz, 1H, H^5), 1.71-1.52 (m, 9H, Cy), 1.20-1.17 (m, 1H, Cy) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 151.1, 145.0, 137.7, 129.5, 129.1, 128.0, 127.8, 125.6, 122.1, 115.4, 105.5, 37.9, 34.8, 25.9, 21.1 ppm; IR (film): ν_{max} = 2928, 2855, 1642, 1598, 1498, 1328, 1288, 1255 cm^{-1}; elemental analysis calcd (%) for $C_{21}H_{22}N_2$: C 83.40, H 7.33, N 9.27; found: C 83.64, H 7.31, N 9.03.

3-(4-Methylphenyl)-1-phenyl-2,3-diazaspiro[5.5]undeca-1,4-diene (3bc): purification by Method B; yield 0.150 g, 95%; a pale yellow powder; m.p. 102-104 °C; ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.48-7.47 (m, 2H, Ph), 7.40-7.39 (m, 3H, Ph), 7.32 (d, J = 8.4 Hz, 2H, Ar), 7.13 (d, J = 8.4 Hz, 2H, Ar), 6.83 (d, J = 7.3 Hz, 1H, H^4), 5.14 (d, J = 7.3 Hz, 1H, H^5), 2.32 (s, 3H, Me), 1.70-1.51 (m, 9H, Cy), 1.20-1.17 (m, 1H, Cy) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 150.4, 142.9, 137.7, 131.4, 129.5 (2C), 127.9, 127.8, 125.8, 115.4, 104.7, 37.7, 34.7, 25.9, 21.1, 20.6 ppm; IR (film): ν_{max} = 2927, 2856, 1641, 1612, 1512, 1446, 1327, 1286, 1247 cm^{-1}; elemental analysis calcd (%) for $C_{22}H_{24}N_2$: C 83.50, H 7.65, N 8.85; found: C 83.30, H 7.76, N 8.63.

3-(4-Fluorophenyl)-1-phenyl-2,3-diazaspiro[5.5]undeca-1,4-diene (3be): purification by Method B; yield 0.146 g, 91%; a beige powder; m.p. 67-69 °C; ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.47-7.44 (m, 2H, Ph), 7.40-7.34 (m, 5H, Ar, Ph), 7.03-6.99 (m, 2H, Ar), 6.78 (d, J = 7.3 Hz, 1H, H^4), 5.16 (d, J = 7.3 Hz, 1H, H^5),1.67-1.52 (m, 9H, Cy), 1.22-1.16 (m, 1H, Cy) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 158.6 (d, J = 240.4 Hz), 151.0, 141.6 (d, J = 2.3 Hz), 137.5, 129.4, 128.0, 127.8, 125.9, 116.8 (d, J = 7.7 Hz), 115.6 (d, J = 22.5 Hz), 105.3, 37.8, 34.6, 25.9, 21.1 ppm; IR (film): ν_{max} = 2929, 2856, 1640, 1608, 1506, 1446, 1330, 1288, 1221 cm^{-1}; elemental analysis calcd (%) for $C_{21}H_{21}FN_2$: C 78.72, H 6.61, F 5.93, N 8.74; found: C 78.50, H 6.61, F 6.00, N 8.71.

3-(4-Chlorophenyl)-1-phenyl-2,3-diazaspiro[5.5]undeca-1,4-diene (3bf): purification by Method B; yield 0.160 g, 95%; a pale yellow powder; m.p. 108-110 °C; ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.46-7.44 (m, 2H, Ph), 7.40-7.39 (m, 3H, Ph), 7.34 (d, J = 9.0 Hz, 2H, Ar), 7.26 (d, J = 9.0 Hz, 2H, Ar), 6.80 (d, J = 7.3 Hz, 1H, H^4), 5.21 (d, J = 7.3 Hz, 1H, H^5), 1.71-1.52 (m, 9H, Cy), 1.22-1.16 (m, 1H, Cy) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 151.6, 143.4, 137.2, 129.2, 128.8, 127.9, 127.7, 126.8, 125.0, 116.2, 105.9, 37.7, 34.5, 25.7, 20.9 ppm; IR (film): ν_{max} = 2929, 2856, 1643, 1595, 1492, 1447, 1331, 1288, 1249, 1091 cm^{-1}; elemental analysis calcd (%) for $C_{21}H_{21}ClN_2$: C 74.88, H 6.28, Cl 10.52, N 8.32; found: C 74.86, H 6.45, Cl 10.58, N 8.52.

3-(4-Cyanophenyl)-1-phenyl-2,3-diazaspiro[5.5]undeca-1,4-diene (3bh): purification by Method B; yield 0.150 g, 92%; a pale yellow powder; m.p. 128-130 °C; ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.57 (d, J = 8.9 Hz, 2H, Ar), 7.44 (d, J = 8.9 Hz, 2H, Ar), 7.43-7.38 (m, 5H, Ph), 6.87 (d, J = 7.4 Hz, 1H, H^4), 5.38 (d, J = 7.4 Hz, 1H, H^5), 1.72-1.57 (m, 9H, Cy), 1.23-1.12 (m, 1H, Cy) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 154.4, 147.2, 136.8, 133.3, 129.1, 128.3, 127.9, 123.7, 119.7, 114.4, 108.7, 103.8, 38.2, 34.7, 25.6, 21.0 ppm; IR (film): ν_{max} = 2928, 2856, 2219, 1601, 1508, 1340, 1290 cm^{-1}; elemental analysis calcd (%) for $C_{22}H_{21}N_3$: C 80.70, H 6.47, N 12.83; found: C 80.47, H 6.41, N 12.54.

3-(4-Nitrophenyl)-1-phenyl-2,3-diazaspiro[5.5]undeca-1,4-diene (3bi): purification by Method A; yield 0.121 g, 70%; an yellow powder; m.p. 146-148 °C; R_f = 0.66 (hexane/diethyl ether 1:1); ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 8.19 (d, J = 9.3 Hz, 2H, Ar), 7.45 (d, J = 9.3 Hz, 2H, Ar), 7.44-7.40 (m, 5H, Ph), 6.93 (d, J = 7.4 Hz, 1H, H^4), 5.45 (d, J = 7.4 Hz, 1H, H^5), 1.73-1.56 (m, 9H, Cy), 1.24-1.12 (m, 1H, Cy) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 155.6, 148.7, 141.5, 136.6, 129.1, 128.5, 128.0, 125.5, 123.5, 113.6, 109.9, 38.4, 34.8, 25.6, 21.0 ppm; IR (film): ν_{max} = 2928, 2856, 1592, 1502, 1325, 1296, 1113 cm^{-1}; elemental analysis calcd (%) for $C_{21}H_{21}N_3O_2$: C 72.60, H 6.09, N 12.10; found: C 72.38, H 6.26, N 11.98.

3-(2-Naphtyl)-1-phenyl-2,3-diazaspiro[5.5]undeca-1,4-diene (3bk): purification by Method A; yield 0.154 g, 88%; a pale peach powder; m.p. 99-101 °C; R_f = 0.84 (hexane/diethyl ether 1:1); ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.80-7.75 (m, 4H, Naphtyl), 7.69-7.67 (m, 1H, Naphtyl), 7.51-7.50 (m, 2H, Ph), 7.43-7.41 (m, 4H, Naphtyl, Ph), 7.35-7.31 (m, 1H, Naphtyl), 7.00 (d, J = 7.3 Hz, 1H, H^4), 5.26 (d, J = 7.3 Hz, 1H, H^5), 1.73-1.53 (m, 9H, Cy), 1.24-1.15 (m, 1H, Cy) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 151.4, 142.6, 137.6, 134.3, 129.8, 129.5, 128.9, 128.1, 127.9, 127.7, 127.3, 126.4, 125.7, 123.9, 116.9, 110.5, 106.0, 38.0, 34.8, 25.9, 21.1 ppm; IR (film): ν_{max} = 2929, 2855, 1628, 1599, 1510, 1471, 1449, 1327, 1288, 1227 cm^{-1}; elemental analysis calcd (%) for $C_{25}H_{24}N_2$: C 85.19, H 6.86, N 7.95; found: C 85.41, H 6.93, N 7.73.

1-Phenyl-3-(2-pyridinyl)-2,3-diazaspiro[5.5]undeca-1,4-diene (3bl): purification by Method A; yield 0.127 g, 84%; a pale yellow powder; m.p. 135-137 °C; R_f = 0.76 (hexane/diethyl ether 1:1); ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 8.28-8.26 (m, 1H, Py), 7.74 (d, J = 7.6 Hz, 1H, H^4), 7.58-7.56 (m, 2H, Py), 7.48-7.44 (m, 2H, Ph), 7.41-7.39 (m, 3H, Ph), 6.89-6.84 (m, 1H, Py), 5.33 (d, J = 7.6 Hz, 1H, H^5), 1.72-1.50 (m, 9H, Cy), 1.20-1.11 (m,

1H, Cy) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 155.0, 153.4, 147.3, 137.7, 137.5, 129.3, 128.0, 127.8, 122.6, 117.0, 109.5, 106.0, 37.8, 35.0, 25.7, 20.8 ppm; IR (film): ν_{max} = 2928, 2856, 1647, 1587, 1457, 1440, 1335, 1292 cm^{-1}; elemental analysis calcd (%) for $C_{20}H_{21}N_3$: C 79.17, H 6.98, N 13.85; found: C 79.45, H 6.95, N 13.72.

4,4-Dimethyl-3-(4-methylphenyl)-1-phenyl-1,4-dihydropyridazine (3ca): purification by Method A; yield 0.108 g, 78%; an yellow oil; R_f = 0.89 (hexane/diethyl ether 1:1); ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.48 (d, J = 7.8 Hz, 2H, Ar), 7.43-7.41 (m, 2H, Ph), 7.34-7.30 (m, 2H, Ph), 7.20 (d, J = 7.8 Hz, 2H, Ar), 7.02-6.98 (m, 1H, Ph), 6.80 (d, J = 7.2 Hz, 1H, H^6), 4.77 (d, J = 7.2 Hz, 1H, H^5), 2.40 (s, 3H, Me), 1.29 (s, 6H, Me) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 150.1, 144.9, 138.1, 134.9, 129.1 (2C), 128.6, 124.7, 122.0, 115.2, 109.9, 32.7, 28.9, 21.3 ppm; IR (film): ν_{max} = 2959, 2923, 2859, 1649, 1597, 1496, 1461, 1329, 1285, 1242, 1106, 1006 cm^{-1}; elemental analysis calcd (%) for $C_{19}H_{20}N_2$: C 82.57, H 7.29, N 10.14; found: C 82.73, H 7.16, N, 9.93.

1-(4-Methylphenyl)-3-phenyl-2,3-diazaspiro[5.5]undeca-1,4-diene (3da): purification by Method B; yield 0.158 g, 100%; a beige powder; m.p. 109-111 °C; ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.42 (d, J = 8.4 Hz, 2H, Ar), 7.37 (d, J = 8.4 Hz, 2H, Ar), 7.33-7.29 (m, 2H, Ph), 7.21-7.19 (m, 2H, Ph), 7.01-6.99 (m, 1H, Ph), 6.86 (d, J = 7.3 Hz, 1H, H^4), 5.17 (d, J = 7.3 Hz, 1H, H^5), 2.40 (s, 3H, Me), 1.71-1.52 (m, 9H, Cy), 1.24-1.14 (m, 1H, Cy) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 151.1, 145.0, 137.8, 134.8, 129.4, 129.1, 128.5, 125.5, 122.0, 115.3, 105.4, 37.9, 34.8, 25.9, 21.3, 21.2 ppm; IR (film): ν_{max} = 2927, 2856, 1643, 1597, 1495, 1448, 1329, 1286, 1250 cm^{-1}; elemental analysis calcd (%) for $C_{22}H_{24}N_2$: C 83.50, H 7.65, N 8.85; found: C 83.71, H 7.44, N 8.62.

1-(2,5-Dimethylphenyl)-3-phenyl-2,3-diazaspiro[5.5]undeca-1,4-diene (3ea): purification by Method A; yield 0.119 g, 72%; an orange oil; R_f = 0.89 (hexane/diethyl ether 1:1); ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.42-7.38 (m, 2H, Ph), 7.33-7.29 (m, 2H, Ph), 7.17-7.09 (m, 3H, Ar), 7.01-6.98 (m, 1H, Ph), 6.89 (d, J = 7.2 Hz, 1H, H^4), 5.16 (d, J = 7.2 Hz, 1H, H^5), 2.37 (s, 3H, Me), 2.24 (s, 3H, Me), 1.68-1.48 (m, 7H, Cy), 1.39-1.33 (m, 2H, Cy), 1.19-1.10 (m, 1H, Cy) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 150.8, 145.2, 136.8, 134.5, 133.6, 130.2, 130.1, 129.1, 128.6, 126.0, 121.9, 115.3, 105.0, 38.7, 34.0, 25.9, 21.2, 21.1, 20.3 ppm; IR (film): ν_{max} = 2928, 2856, 1597, 1496, 1451, 1326, 1291 cm^{-1}; elemental analysis calcd (%) for $C_{23}H_{26}N_2$: C 83.59, H 7.93, N 8.48; found: C 83.71, H 7.68, N 8.28.

3-(2-Furyl)-4,4-dimethyl-1,5-diphenyl-1,4-dihydropyridazine (3fa): purification by Method A; yield 0.110 g, 67%; an orange oil; R_f = 0.87 (hexane/diethyl ether 1:1); ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.85 (d, J = 1.8 Hz, 1H, H^5, Furyl), 7.49-7.47 (m, 2H, Ph), 7.40-7.35 (m, 7H, Ph), 7.08-7.05 (m, 1H, Ph),6.83-6.82 (m, 2H, H^6, H^3, Furyl), 6.49 (dd, J = 3.3, 1.8 Hz, 1H, H^4, Furyl), 1.55 (s, 6H, Me) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 152.8, 144.3, 142.4, 141.0, 138.3, 130.3, 129.2, 128.0, 127.1, 123.0, 122.5, 121.3, 115.5, 111.0, 110.5, 35.4, 26.8 ppm; IR (film): ν_{max} = 2969, 2923, 2873, 1645, 1596, 1552, 1496, 1331, 1258, 1224, 1172, 1037, 1010 cm^{-1}; elemental analysis calcd (%) for $C_{22}H_{20}N_2O$: C 80.46, H 6.14, N 8.53; found: C 80.34, H 6.25, N 8.62.

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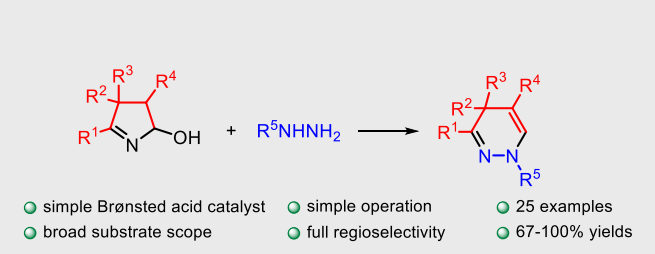

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Metal-Free Selective Synthesis of 1,4-Dihydropyridazines from Hydroxypyrrolines and Hydrazines