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Synthesis of γ-Spirolactams by Birch Reduction of Arenes

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Dedicated to Professor Siegfried Hünig on the occasion of his 100th birthday.

A convenient method for the synthesis of γ-spirolactams in only three steps is described. Birch reduction of inexpensive and commercially available aromatic carboxylic acids in the presence of chloroacetonitrile affords nitriles in moderate to good yields. Suitable precursors are methyl-substituted benzoic acids, naphthoic, and anthroic acid. Subsequent catalytic hydrogenation proceeds smoothly with PtO_2 or Raney Ni as catalysts and lactams are isolated in excellent yields and stereoselectivities. Thus, up to 3 new stereogenic centers can be constructed as sole diastereomers from achiral benzoic acids. Furthermore, it is possible to control the degree of saturation at different pressures, affording products with 0, 1, or 2 double bonds. Overall, more than 15 new γ-spirolactams have been synthesized in analytically pure form.

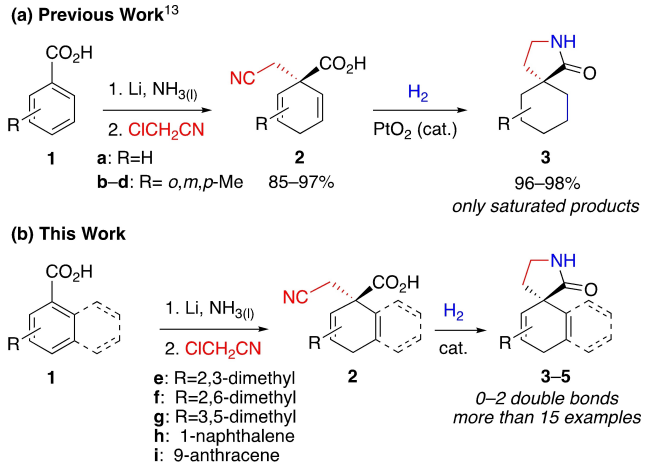
Introduction

The Birch reduction of arenes is an important synthetic transformation in organic chemistry, providing an easy access to 1,4-cyclohexadienes.[1,2] It has been applied for several total syntheses of natural products.[3,4] Aromatic carboxylic acids are especially attractive starting materials, since they afford high yields and regioselectivities, and alkyl substituents can be directly introduced in the reduction step.[5] The most practical method for large-scale reactions is a solution of alkali metals in liquid ammonia.[6] However, electrochemical[7] or very recent photocatalytic reductions[8] have been developed as well.

Our group is working with 1,4-cyclohexadienes, derived from Birch reductions, since more than twenty years. Initially, we investigated their regio- and stereoselective oxidations with singlet oxygen.[9,10] Later on, we developed a two-step substitution of aromatic carboxylic acids,[11] which was extended by Studer for palladium-catalyzed functionalizations.[12] Very recently, we described first Birch reductions in the presence of chloroacetonitrile in a communication (Scheme 1a).[13]

Thus, benzoic or toluic acids (**1 a–d**) reacted smoothly with lithium in liquid ammonia and subsequent alkylation to nitriles **2**, which were directly hydrogenated with PtO_2 as catalyst. Cyclization afforded γ-spirolactams **3** in only few steps and high yields. Lactams are structural motifs of natural products[14] and are potential medicinal agents.[15] Furthermore, their ability to form hydrogen bridges has been applied in enantioselective reactions.[16] On the other hand, the synthesis of spiro compounds requires usually many steps,[17–19] in contrast, our method offered an easy entry by Birch reduction.[13]

However, in our communication we investigated only simple benzoic or toluic acids (**1 a–d**) and obtained completely saturated products **3** (Scheme 1a). Herein, we describe that the sequence Birch reduction of aromatic carboxylic acids – catalytic hydrogenation is a general method for the synthesis of γ-spirolactams **3**–**5** (Scheme 1b). Birch reductions in the presence of chloroacetonitrile proceeded smoothly with various dimethyl substituted benzoic acids (**1 e–g**), naphthoic (**1 h**), and anthracene carboxylic acid (**1 i**) for the first time. Furthermore, now it was possible to obtain unsaturated products with 1 or 2 double bonds by optimization of the catalyst and reaction conditions. Thus, we could synthesize more than 15 new γ-spirolactams in only few steps and good yields.



Scheme 1. Synthesis of γ-spirolactams **3**–**5** by Birch reduction of arenes **1** and subsequent catalytic hydrogenation.

Results and Discussion

Although the Birch reduction is known since more than half a century,[1,2] we published reactions in the presence of chloroacetonitrile, a commercially available and inexpensive reagent,[20] for simple benzoic acids very recently.[13] Herein, we applied such optimized reaction conditions with no co-solvent and high

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concentrations for the regioisomeric dimethyl benzoic acids (**1e–g**) for the first time (Table 1, entries 1–3).

In contrast to benzoic acid (**1a**), such arenes are more electron rich and react more slowly with lithium in ammonia. Furthermore, chloro-acetonitrile is CH acidic, resulting in protonated 1,4-cyclohexadienes **6** as side-products, which is especially a problem for sterically hindered substrates. Thus, 2,3- and 2,6-dimethylbenzoic acids (**1e** and **1f**) afforded the desired nitriles **2e** and **2f** in only 65 and 64% yield (Table 1, entries 1 and 2). However, separation of the side-products **6e** and **6f** was possible by column chromatography, and all compounds could be isolated in analytically pure form. On the other hand, the sterically less hindered 3,5-dimethylbenzoic acid (**1g**) afforded only very small amounts of protonation **6g**, and the main product **2g** was isolated in good yield (entry 3).

After the successful Birch reductions of dimethylbenzoic acids (**1e–g**), we became interested in reactions of bi- and tricyclic aromatic carboxylic acids in the presence of chloroacetonitrile. Thus, 1-naphthoic acid (**1h**) reacted smoothly and afforded nitrile **2h** in excellent yield (Table 1, entry 4). On the other hand, 9-anthracenecarboxylic acid (**1i**) gave a complex mixture under the same reaction conditions (entry 5). Besides protonation **6i** and small amounts of the desired nitrile **2i**, alkylation products at the 10-position were formed as well. Although a reductive alkylation of 9-anthracenecarboxylic acid (**1i**) was hitherto unknown,[2] this behavior is in accordance to Birch reductions of anthracene and its corresponding esters.[21,22] Therefore, we altered the reaction conditions and added tert-butanol prior to chloroacetonitrile to the Birch reduction (Table 1, entry 6). Indeed, now the formation of the 10-alkyl product was suppressed completely. Although this procedure afforded a somehow larger amount of side-product **6i** due to protonation by the alcohol, the desired nitrile **2i** was now easily separated by column chromatography and isolated in analytically pure form.

In summary, we applied the Birch reduction in the presence of chloroacetonitrile to various methyl-substituted benzoic acids, naphthoic and anthroic acid for the first time. For sterically hindered substrates protonation afforded side-products. However, all nitriles could be isolated in analytically pure form and represent suitable precursors for new γ-spirolactams.

To obtain the desired γ-spirolactams **3**, we had to reduce the nitriles **2** and cyclize the corresponding amino acids. In our previous communication with simple benzoic or toluic acids (**1a–d**),[13] we found catalytic hydrogenations in the presence of PtO_2 suitable for the reduction of the nitrile group and all double bonds in one step. Furthermore, cyclization to lactams was achieved by simple heating in pyridine, without isolation of the intermediate amino acids. Thus, we applied such reaction conditions (method A) to the herein newly synthesized nitriles **2e–i** (Table 2).

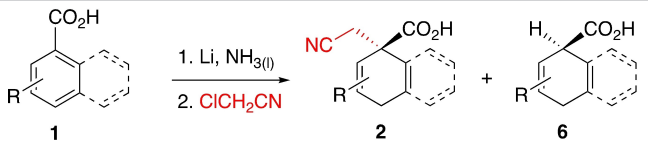
Indeed, regioisomeric dimethyl nitriles **2e–g** afforded completely saturated γ-spirolactams **3e–g** in very good overall yields (Table 2, entries 1–3). Furthermore, two new stereogenic centers were formed during the hydrogenation with excellent selectivity. The isolation of only one diastereomer is in accordance to our previous communication,[13] and can be rationalized by coordination of the nitrile to PtO_2. Thus, hydrogen must attack from the same face, and the methyl groups are oriented *cis* to the carbonyl group (for detailed structures see Figure 1).

The bicyclic nitrile **2h** reacted smoothly as well and afforded γ-spirolactam **3h** in 94% yield (Table 2, entry 4). Only with nitrile **2i**, derived from 9-anthracenecarboxylic acid (**1i**), the corresponding lactam **3i** was isolated in slightly lower yield of 90% (Table 2, entry 5), due to decarboxylation, which was described in similar catalytic hydrogenations as well.[23]

To retain the double bonds for future further functionalizations, we became interested in other reducing procedures and optimized them with nitrile **2b** derived from *o*-toluic acid (Table 3). Catalytic hydrogenation with palladium on charcoal, a common and cheap catalyst,[24] gave full conversion, but only one double bond was reduced (entry 1). On the other hand, rhodium on alumina, which has been applied for the synthesis of lactams from nitriles,[25] gave no conversion (entry 2).

The reason for the slow reduction of the nitrile group might be due to steric hindrance by the adjacent quaternary carbon atom. Lithium aluminum hydride was not a suitable reagent,

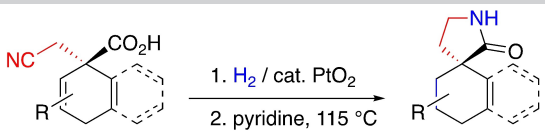
Table 1. Birch reduction of carboxylic acids **1**.[a]



Entry	Acid	R	2 [%][b]	6 [%][b]
1	**1e**	2,3-dimethyl	65	33
2	**1f**	2,6-dimethyl	64	34
3	**1g**	3,5-dimethyl	86	< 5
4	**1h**	1-naphthalene	92	< 5
5	**1i**	9-anthracene	28	45[c]
6	**1i**	9-anthracene[d]	45	45

[a] Reactions were performed on a 20 mmol scale. For procedure and conditions, see the Experimental Section. [b] Yield of analytically pure product, isolated by column chromatography. [c] Alkylation at 10-position as side-product. [d] Addition of tert-butanol (3.0 mL) prior to chloroacetonitrile.

Table 2. Catalytic hydrogenation of nitriles **2** with PtO_2 and subsequent cyclization to γ-spirolactams **3**.[a]



Entry	Nitrile	R	3 [%][b]
1	**2e**	2,3-dimethyl	92
2	**2f**	2,6-dimethyl	92
3	**2g**	3,5-dimethyl	94
4	**2h**	1-naphthalene	94
5	**2i**	9-anthracene	90

[a] Reactions were performed on a 2 mmol scale. For procedure and conditions, see the Experimental Section. For detailed structures see Figure 1. [b] Yield of analytically pure product, isolated by column chromatography.

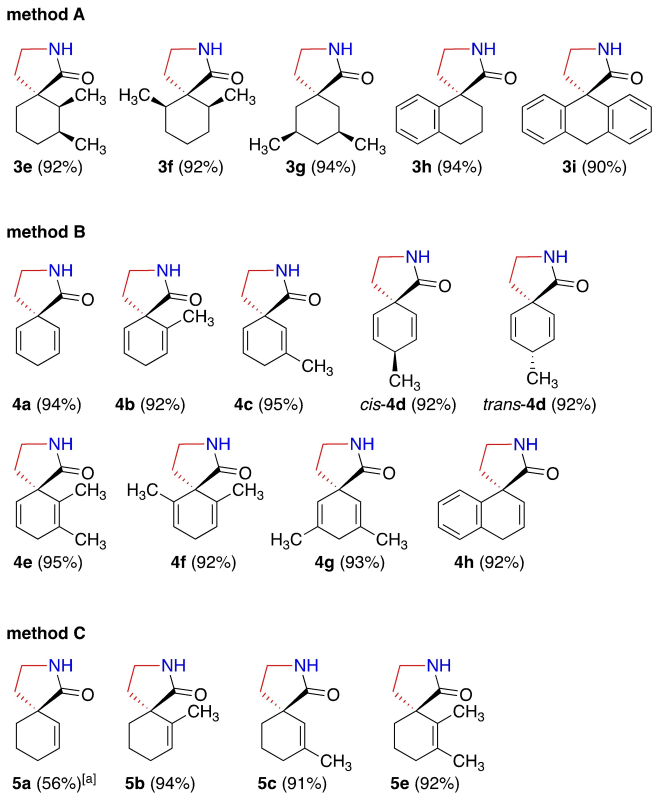
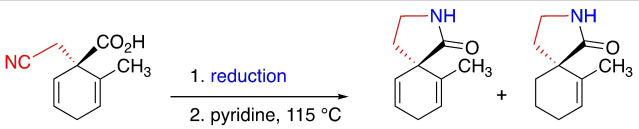


Figure 1. Library of γ-spirolactams **3**–**5**, obtained by catalytic hydrogenations. Reactions were performed on a 2 mmol scale; method A: PtO_2, 1 bar H_2, 3 d; method B: Raney nickel, 1 bar H_2, 4 h; method C: Raney nickel, 50 bar H_2, 3 d. Yield of analytically pure product, isolated by column chromatography. [a] Formation of 34% of diene **4a** as side-product, separated by column chromatography.

Table 3. Optimization of the reduction of nitrile **2b** and subsequent cyclization to γ-spirolactams **4b** or **5**.[a]



2b **4b** **5b**

Entry	Reagent/Catalyst	H_2 (bar)	4b [%][b]	5b [%][b]
1	Pd/C	1	75[c]	–
2	Rh/Al_2O_3	1	–[d]	–
3	$LiAlH_4$	–	70[e]	–
4	$NaBH_4/CoCl_2$	–	28[e]	10
5	Raney Ni	1	92	5
6	Raney Ni	10	83	12
7	Raney Ni	30	38	48
8	Raney Ni	50	3	94

[a] Reactions were performed on a 2 mmol scale. For procedure and conditions, see the Experimental Section. For detailed structures see Figure 1. [b] Yield of analytically pure product, isolated by column chromatography. [c] Only reduction of one double bond. [d] No conversion. [e] Only reduction of the carboxylic acid group. [f] Only 40% conversion.

because the acid was directly reduced to the corresponding alcohol (entry 3). To overcome this problem, we investigated $NaBH_4$ in the presence of $CoCl_2$ next, which has been applied for the synthesis of lactams previously.[26] Indeed, now the unsaturated γ-spirolactam **4b** could be isolated for the first time. However, the yield was only 28%, due to low conversion and formation of side-product **5b** (entry 4).

Finally, best conditions were found by catalytic hydrogenation with Raney nickel as catalyst.[27] Thus, reaction of nitrile **2b** under 1 bar hydrogen pressure proceeded smoothly and gave full conversion after 3 d. Subsequent cyclization in the presence of pyridine afforded γ-spirolactam **4b** in 92% yield in analytically pure form (entry 5, method B). Only a small amount of side-product **5b** was formed, which was easily separated by column chromatography. We repeated the hydrogenations at various pressures (entries 6–8), to increase the amount of this γ-spirolactam **5b**. Indeed, at 50 bar this compound with only one double bond was isolated as main product in analytically pure form in 94% yield (entry 8, method C). Thus, we could control the degree of saturation in γ-spirolactams **4b** and **5b** by simple variation of the hydrogen pressure.

To demonstrate the generality of such Raney nickel reductions, we applied methods B and C to various other nitriles **2a**–**h**[13] (Figure 1). Indeed, method B afforded completely unsaturated γ-spirolactams **4a**–**h** in all cases in high yields. Method C gave very good yields with nitriles **2b**, **2c**, and **2e**, because they differ in their substitution pattern. In all cases, the sterically less hindered double bond was reduced selectively. Unsubstituted nitrile **2a** afforded a mixture of lactams, but the partly hydrogenated product **5a** could be isolated by column chromatography in 56% yield. Overall, together with the catalytic hydrogenations in the presence of PtO_2 (method A), we obtained a library of 18 new γ-spirolactams **3**–**5** in high yields (Figure 1).

Conclusion

In summary, we have demonstrated that Birch reduction of aromatic carboxylic acids in the presence of chloroacetonitrile and subsequent catalytic hydrogenation is a general and convenient method for the synthesis of γ-spirolactams. Various regioisomeric dimethyl benzoic, naphthoic, and anthroic acids have been used as starting materials for the first time, and nitrile carboxylic acids were isolated in moderate to good yields. Hydrogenation in the presence of PtO_2 as catalyst (method A) affords completely saturated lactams in high yields in analytically pure form. Furthermore, the reactions proceed with excellent stereoselectivities and up to 3 new stereogenic centers can be constructed. Catalytic hydrogenations with Raney nickel give γ-spirolactams with 2 double bonds at 1 bar (method B) and with 1 double bond at 50 bar (method C). Thus, it is possible to control the degree of saturation by simple variation of the hydrogen pressure. Additionally, the double bonds might be used for further functionalizations. Overall, we synthesized more than 15 new γ-spirolactams from inexpensive aromatic carboxylic acids in only few steps and good yields.

Experimental Section

General Information. Melting points were determined by using a Mel-Temp from Electrothermal. TLC was performed using TLC Silica gel 60 F254 aluminum sheets from Merck. ^{1}H NMR and ^{13}C NMR spectra were measured by using a Bruker NEO 500 (500 MHz, 125 MHz) or a Bruker Avance 600 (600 MHz, 150 MHz) NMR spectrometer. Signals were assigned by two-dimensional methods (HSQC). The IR spectra were recorded in KBr pellets by using a Nicolet Avatar 370 FT-IR spectrometer from Thermo Electron Corporation. Elemental analysis was performed on a Vario EL III elemental analyzer. HRMS spectra were measured at a GC-MS Trace DSX II spectrometer. All starting materials were used as purchased without further purification. Raney nickel was activated according to the procedure of Nishimura.[27]

General Procedure for Birch Reductions. Arene carboxylic acid **1** (20 mmol) was introduced into a three-necked flask (250 mL), equipped with a dry-ice condenser and cooled to – 78 °C by a dry-ice acetone bath. Ammonia (100 mL) was condensed into the three-necked flask, and lithium (275 mg, 40 mmol) was added in small pieces to the solution at – 78 °C, until it remained blue. For anthroic acid **1 i** 200 mL of ammonia was used, due to solubility problems. For this acid, tert.-butanol (3.0 mL) was added after lithium as well, to suppress formation of 10-alkylation. After stirring for 1 h at – 78 °C, chloroacetonitrile (2.5 mL, 40 mmol) was added via syringe within 2 min and the ammonia was allowed to evaporate overnight at RT. The solid residue was dissolved in water (70 mL), cooled to 0 °C, acidified with 6 M HCl to pH 2 and extracted with dichloromethane (3×50 mL). The combined organic layers were dried over sodium sulfate, filtered over a small pad of silica gel, and the solvent was removed in vacuo. The crude products were purified by column chromatography (hexanes/Me–O-^{t}Bu 1:1 +0.5% AcOH) to obtain the nitriles **2** and side-products **6** in analytically pure form. The syntheses and analytical data of nitriles **2 a**–**d** have been reported previously.[13]

1-(Cyanomethyl)-2,3-dimethylcyclohexa-2,5-diene-1-carboxylic acid (2 e). Following the general procedure, the title compound was obtained as a white solid (2.49 g, 65%). R_f = 0.31 (dichloromethane/methanol/AcOH = 9:0.9:0.1). Mp = 147–148 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.67 (s, 3H), 1.76 (s, 3H), 2.67–2.83 (m, 2H), 2.79 (d, J = 17.0 Hz, 1H), 2.84 (d, J = 17.0 Hz, 1H), 5.60 (dt, J = 9.9, 2.1 Hz, 1H), 6.13 (dt, J = 9.9, 3.5 Hz, 1H), 10.65 (br, 1H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 14.4 (q), 19.2 (q), 25.9 (t), 33.0 (t), 51.1 (s), 117.1 (s), 120.3 (s), 124.0 (d), 130.0 (d), 131.3 (s), 178.4 (s). IR (KBr): v = 3135, 2274, 1728, 1220, 729 cm^{-1}. Anal. Calcd for $C_{11}H_{13}NO_2$ (191.23): C, 69.09; H, 6.85; N, 7.33. Found: C, 68.89; H, 6.76; N, 7.21.

2,3-Dimethylcyclohexa-2,5-diene-1-carboxylic acid (6 e). Following the general procedure, the title compound was obtained as a white solid as side-product (1.01 g, 33%). R_f = 0.71 (dichloromethane/methanol/AcOH = 9:0.9:0.1). Mp = 86–87 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.71 (s, 3H), 1.72 (s, 3H), 2.58 (dm, J = 22.2 Hz, 1H), 2.73 (dm, J = 22.2 Hz, 1H), 3.62–3.66 (m, 1H), 5.74 (dm, J = 9.9 Hz, 1H), 5.91 (dm, J = 9.9 Hz, 1H), 11.47 (br, 1H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 17.5 (q), 18.9 (q), 32.8 (t), 49.1 (d), 120.5 (s), 122.2 (d), 127.5 (s), 127.9 (d), 179.9 (s). IR (KBr): v = 2871, 1699, 1288, 1227, 890, 779, 682 cm^{-1}. Anal. Calcd for $C_9H_{12}O_2$ (152.19): C, 71.03; H, 7.95. Found: C, 71.06; H, 8.01.

1-(Cyanomethyl)-2,6-dimethylcyclohexa-2,5-diene-1-carboxylic acid (2 f). Following the general procedure, the title compound was obtained as a white solid (2.46 g, 64%). R_f = 0.61 (dichloromethane/methanol/AcOH = 9:0.9:0.1). Mp = 215–216 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.64 (s, 6H), 2.62 (dm, J = 23.1 Hz, 1H), 2.69 (dm, J = 23.1 Hz, 1H), 3.03 (s, 2H), 5.77 (s, 2H), 13.03 (br, 1H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 18.8 (q), 22.3 (t), 26.9 (t), 52.6 (s), 118.0 (s), 124.2 (d), 129.1 (s), 173.0 (s). IR (KBr): v = 3071, 2275, 1733, 1225, 782, 702 cm^{-1}. Anal. Calcd for $C_{11}H_{13}NO_2$ (191.23): C, 69.09; H, 6.85; N, 7.33. Found: C, 69.37; H, 7.19; N, 7.40.

2,6-Dimethylcyclohexa-2,5-diene-1-carboxylic acid (6 f). Following the general procedure, the title compound was obtained as a white solid as side-product (1.03 g, 34%). R_f = 0.75 (dichloromethane/methanol/AcOH = 9:0.9:0.1). Mp = 105–106 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.77 (s, 6H), 2.64 (dm, J = 22.6 Hz, 1H), 2.78 (dm, J = 22.6 Hz, 1H), 3.46 (tm, J = 6.2 Hz 1H), 5.67–5.68 (m, 2H), 11.72 (br, 1H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 21.9 (q), 27.6 (t), 52.2 (d), 122.5 (d), 128.4 (s), 179.5 (s). IR (KBr): v = 2879, 1706, 1294, 964, 777 cm^{-1}. Anal. Calcd for $C_9H_{12}O_2$ (152.19): C, 71.03; H, 7.95. Found: C, 71.00; H, 7.94.

1-(Cyanomethyl)-3,5-dimethylcyclohexa-2,5-diene-1-carboxylic acid (2 g). Following the general procedure, the title compound was obtained as a white solid (3.30 g, 86%). R_f = 0.40 (dichloromethane/methanol/AcOH = 9:0.9:0.1). Mp = 115–116 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.80 (s, 6H), 2.54 (dm, J = 22.4 Hz, 1H), 2.59 (dm, J = 22.4 Hz, 1H), 2.68 (s, 2H), 5.40 (d, J = 0.5 Hz, 2H), 10.58 (br, 1H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 22.9 (q), 28.3 (t), 35.9 (t), 48.4 (s), 117.1 (s), 117.9 (d), 137.5 (s), 178.7 (s). IR (KBr): v = 3184, 2268, 1723, 1205, 926, 815, 687 cm^{-1}. Anal. Calcd for $C_{11}H_{13}NO_2$ (191.23): C, 69.09; H, 6.85; N, 7.33. Found: C, 68.85; H, 6.93; N, 7.39.

1-(Cyanomethyl)-1,4-dihydronaphthalene-1-carboxylic acid (2 h). Following the general procedure, the title compound was obtained as a white solid (3.92 g, 92%). R_f = 0.60 (dichloromethane/methanol/AcOH = 9:0.9:0.1). Mp = 117–118 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.01 (d, J = 16.7 Hz, 1H), 3.09 (d, J = 16.7 Hz, 1H), 3.54 (ddd, J = 22.2, 3.6, 2.2 Hz, 1H), 3.61 (ddd, J = 22.2, 3.6, 2.2 Hz, 1H), 5.91 (dt, J = 10.1, 2.2 Hz, 1H), 6.38 (dt, J = 10.1, 3.6 Hz, 1H), 7.25–7.35 (m, 4H), 11.00 (br, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 29.2 (t), 29.6 (t), 48.8 (s), 117.0 (s), 124.0 (d), 126.1 (d), 127.3 (d), 128.5 (d), 129.4 (d), 129.8 (d), 131.8 (s), 133.9 (s), 178.1 (s). IR (KBr): v = 3133, 3075, 2278, 1733, 1227, 741 cm^{-1}. Anal. Calcd for $C_{13}H_{11}NO_2$ (213.24): C, 73.22; H, 5.20; N, 6.57. Found: C, 73.15; H, 5.49; N, 6.59.

9-(Cyanomethyl)-9,10-dihydroanthracene-9-carboxylic acid (2 i). Following the general procedure, the title compound was obtained as a white solid (2.35 g, 45%). R_f = 0.15 (MeOtBu/hexane/AcOH = 4.9:4.9:0.2). Mp = 203–204 °C. ^{1}H NMR (500 MHz, DMSO): δ = 3.38 (s, 2H), 4.13 (d, J = 20.1 Hz, 1H), 4.25 (d, J = 20.1 Hz, 1H), 7.32–7.42 (m, 8H), 13.29 (br, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO): δ = 28.9 (t), 33.4 (t), 53.0 (s), 118.4 (s), 126.7 (d), 126.8 (d), 127.7 (d), 128.3 (d), 134.7 (s), 134.9 (s), 173.9 (s). IR (KBr): v = 3667, 2982, 2903, 2279, 1727, 1401, 1232, 1049, 714 cm^{-1}. Anal. Calcd for $C_{17}H_{13}NO_2$ (263.29): C, 77.55; H, 4.98; N, 5.32. Found: C, 77.46; H, 4.94; N, 5.25.

10-(Cyanomethyl)-9,10-dihydroanthracene-9-carboxylic acid (10-2 i). Following the general procedure, the title compound was obtained as a white solid as side-product (2.35 g, 45%). R_f = 0.45 (MeOtBu/hexane/AcOH = 4.9:4.9:0.2). Mp = 190–191 °C. ^{1}H NMR (500 MHz, DMSO): δ = 2.98 (d, J = 7.9 Hz, 2H), 4.43 (t, J = 7.9 Hz, 1H), 5.11 (s, 1H), 7.34 (ddd, J = 7.3, 7.1, 1.4 Hz, 2H), 7.36 (ddd, J = 7.3, 7.1, 1.5 Hz, 2H), 7.46 (dd, J = 7.1, 1.5 Hz, 2H), 7.51 (dd, J = 7.1, 1.4 Hz, 2H), 12.93 (br, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO): δ = 27.6 (t), 40.9 (d), 51.0 (d), 119.2 (s), 127.3 (d), 127.5 (d), 128.8 (d), 129.1 (d), 133.9 (s), 136.5 (s), 173.8 (s). IR (KBr): v = 3249, 2988, 2901, 1694, 1486, 1450, 1194, 765, 654 cm^{-1}. Anal. Calcd for $C_{17}H_{13}NO_2$ (263.29): C, 77.55; H, 4.98; N, 5.32. Found: C, 77.40; H, 4.90; N, 5.30.

9,10-Dihydroanthracene-9-carboxylic acid (4 i). Following the general procedure with addition of tert.-butanol, the title compound was obtained as a white solid as side-product (2.02 g, 45%). R_f = 0.51 0.15 (MeOtBu/hexane/AcOH = 4.9:4.9:0.2). Mp = 207–208 °C. ^{1}H NMR (500 MHz, DMSO): δ = 3.92 (d, J = 18.1 Hz, 1H), 4.13 (d, J = 18.1 Hz, 1H), 5.00 (s, 1H), 7.25 (dd, J = 7.4, 6.8 Hz, 2H), 7.29

(ddd, J = 7.4, 6.8, 1.7 Hz, 2H), 7.37 (d, J = 6.8 Hz, 2H), 7.42 (dd, J = 6.8, 1.7 Hz, 2H), 12.54 (br, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, DMSO): δ = 35.0 (t), 52.3 (d), 126.2 (d), 127.1 (d), 127.8 (d), 128.3 (d), 134.6 (s), 136.5 (s), 172.7 (s). IR (KBr): v = 3031, 2901, 1698, 1216, 713 cm^{-1}. Anal. Calcd for $C_{15}H_{12}O_2$ (224.26): C, 80.34; H, 5.39. Found: C, 80.15; H, 5.23.

Reduction with Pd/C. Nitrile **2b** (355 mg, 2.0 mmol) was dissolved in methanol (30 mL) at RT and palladium on charcoal (25 mg, 1 mol%) was added. The solution was purged with hydrogen gas for 5 min, equipped with a balloon filled with hydrogen gas and hydrogenated under stirring at 1 bar for 2 h. The solution was filtered through a pad of Celite, washed with methanol (2×30 mL) and the solvent was removed in vacuo. The crude product showed in the NMR that the nitrile was intact but the unsubstituted double bond was hydrogenated besides small amount of hydrogenation of both double bonds. Purification by column chromatography (hexanes/Me–O-^{t}Bu 1:1 + 0.5% AcOH) afforded the partly hydrogenated product as colorless oil (270 mg, 75%).

1-(Cyanomethyl)-2-methylcyclohex-2-ene-1-carboxylic acid. R_f = 0.45 (dichloromethane/methanol/AcOH = 9:0.9:0.1). ^1H NMR (500 MHz, $CDCl_3$): δ = 1.60–1.73 (m, 1H), 1.72 (td, J = 1.9, 1.5 Hz, 3H), 1.84 (ddtd, J = 13.9, 9.6, 6.6, 3.1 Hz, 1H), 1.69 (ddd, J = 13.6, 9.6, 3.1 Hz, 1H), 2.08–2.03 (m, 2H), 2.19 (ddd, J = 13.6, 8.0, 3.1 Hz, 1H), 2.71(d, J = 16.9 Hz,1H), 2.86 (d, J = 16.9 Hz,1H), 5.81 (dqd, J = 4.0, 1.5, 0.7 Hz, 1H), 10.18 (br, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 18.5 (q), 19.8 (t), 24.9 (t), 25.1 (t), 32.4 (t), 48.2 (s), 117.6 (s), 129.5 (d), 129.7 (s), 178.9 (s). IR (film): v = 3207, 2932, 2867, 1698, 1446, 1219, 1174, 934, 807, 712 cm^{-1}. HRMS (ESI-TOF) m/z: $[M]^+$ Calcd for $C_{10}H_{13}NO_2$ 179.0946; Found: 179.0935.

Reduction with $LiAlH_4$. Nitrile **2b** (355 mg, 2.0 mmol) was dissolved in dry diethyl ether (20 mL) and lithium aluminum hydride (38 mg, 1.0 mmol) was added slowly. The mixture was stirred for 16 h under nitrogen atmosphere, filtered through a pad of Celite, washed with methanol (3×50 mL) and the solvent was removed in vacuo. The crude product showed in the NMR that the nitrile was intact but the acid group was reduced to the alcohol. Purification by column chromatography (dichloromethane/EtOAc = 5:1) afforded the alcohol as colorless oil (230 mg, 70%).

1-(Cyanomethyl)-1-(hydroxymethyl)-2-methylcyclohex-2,5 diene. R_f = 0.41 (dichloromethane/EtOAc = 5:1). ^1H NMR (500 MHz, $CDCl_3$): δ = 1.73 (q, J = 1.7 Hz, 3H), 2.14 (br, 1H), 2.39 (d, J = 16.7 Hz,1H), 2.49 (d, J = 16.7 Hz,1H), 2.65 (ddqd, J = 23.2, 3.4, 2.1, 1.7, 1.6 Hz,1H), 2.75 (ddqd, J = 23.2, 3.4, 2.1, 1.7, 1.6 Hz,1H), 3.41 (d, J = 10.7 Hz,1H), 3.58 (d, J = 10.7 Hz,1H), 5.48 (dt, J = 10.0, 2.1 Hz, 1H), 5.79 (qq, J = 1.7, 1.6 Hz,1H), 6.08 (dtd, J = 10.0, 3.4, 1.6 Hz, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 18.4 (q), 24.8 (t), 27.3 (t), 43.8 (s), 67.1 (t), 117.6 (s), 126.4 (d), 127.2 (d), 129.8 (d), 130.3 (s). IR (film): v = 3423, 2922, 2875, 2250, 1714, 1421, 1016, 739 cm^{-1}. 182.1545. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{10}H_{14}NO$ 164.1075; Found: 164.1075.

General Procedure for the Catalytic Hydrogenation with PtO_2 (method A). Nitrile **2** (2.0 mmol) was dissolved in methanol (30 mL) at RT and platinum(IV) oxide (5.0 mg, 1 mol%) and 37% HCl (0.2 mL) was added. The solution was purged with hydrogen gas for 5 min, equipped with a balloon filled with hydrogen gas and hydrogenated under stirring at 1 bar for 3d. The solution was filtered through a pad of Celite, washed with methanol (2×30 mL) and the solvent was removed in vacuo. Diastereoselectivities were determined from the NMR of the crude products. The residue was dissolved in pyridine (50 mL) and heated for 8 h under reflux. The pyridine was removed in vacuo and the residue was dissolved in dichloromethane (50 mL), extracted with 1 N HCl (30 mL), the organic phase was dried over sodium sulfate, and concentrated in vacuo. The crude products were purified by column chromatography (EtOAc) to obtain the γ-spirolactams **3** in analytically pure form.

***cis*-6,7-Dimethyl-2-azaspiro[4.5]decan-1-one (3e)**. Following the general procedure, the title compound was obtained as a white solid (335 mg, 92%). R_f = 0.31 (EtOAc). Mp = 129–130 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.83 (d, J = 6.9 Hz, 3H), 0.89 (d, J = 7.1 Hz, 3H), 1.10–1.30 (m, 4H), 1.55–1.64 (m, 2H), 1.73–1.80 (m, 1H), 1.81–1.88 (m, 2H), 2.24 (ddd, J = 12.7, 6.7, 1.7 Hz, 1H), 3.19 (tm, J = 9.7 Hz, 1H), 3.27 (td, J = 9.7, 6.7 Hz, 1H), 7.27 (br, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 8.4 (q), 20.2 (q), 22.6 (t), 27.6 (t), 27.9 (t), 31.7 (d), 34.0 (t), 36.5 (d), 38.8 (t), 47.9 (s), 182.6 (s). IR (KBr): v = 3667, 3193, 2982, 2917, 1684, 1075, 789 cm^{-1}. Anal. Calcd for $C_{11}H_{19}NO$ (181.28): C, 72.88; H, 10.56; N, 7.73. Found: C, 73.51; H, 10.56; N, 7.61.

***cis*-6,10-Dimethyl-2-azaspiro[4.5]decan-1-one (3f)**. Following the general procedure, but the pressure was adjusted to 50 bar, the title compound was obtained as a white solid (333 mg, 92%). R_f = 0.27 (EtOAc). Mp = 163–164 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.90 (d, J = 6.7 Hz, 6H), 1.23 (qt, J = 13.2, 3.5 Hz, 1H), 1.30–1.38 (m, 4H), 1.67 (dm, J = 13.2 Hz, 1H), 1.78 (qd, J = 13.2, 3.5 Hz, 2H), 1.98 (t, J = 7.7 Hz, 2H), 3.20 (t, J = 7.7 Hz, 2H), 6.77 (br, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 17.2 (q), 26.1 (t), 30.9 (t), 33.2 (t), 40.1 (t), 41.2 (d), 50.2 (s), 179.6 (s). IR (KBr): v = 3667, 2968, 2906, 1672, 1387, 1278, 1057, 794 cm^{-1}. Anal. Calcd for $C_{11}H_{19}NO$ (181.28): C, 72.88; H, 10.56; N, 7.73. Found: C, 72.94; H, 10.58; N, 7.70.

***cis*-7,9-Dimethyl-2-azaspiro[4.5]decan-1-one (3g)**. Following the general procedure, the title compound was obtained as a white solid (340 mg, 94%). R_f = 0.20 (EtOAc). Mp = 140–141 °C. ^1H NMR (600 MHz, $CDCl_3$): δ = 0.59 (dt, J = 12.8, 11.9 Hz, 1H), 0.87 (d, J = 6.7 Hz, 6H), 1.18 (dd, J = 13.2, 12.4 Hz, 2H), 1.40 (dtd, J = 13.2, 3.0, 2.0 Hz, 2H), 1.47 (ddqdd, J = 12.4, 11.9, 6.7, 3.6, 3.0 Hz, 1H), 1.62 (dtt, J = 12.8, 3.6, 2.0 Hz, 1H), 1.95 (t, J = 7.0 Hz, 2H), 3.27 (t, J = 7.0 Hz, 2H), 7.26 (br, 1H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ = 22.6 (q), 28.8 (d), 32.3 (t), 39.3 (t), 40.3 (t), 43.3 (t), 45.3 (s), 183.6 (s). IR (KBr): v = 3195, 2948, 2907, 1698, 1304, 809, 583 cm^{-1}. Anal. Calcd for $C_{11}H_{19}NO$ (181.28): C, 72.88; H, 10.56; N, 7.73. Found: C, 72.87; H, 10.68; N, 7.72.

3,4-Dihydro-2*H*-spiro[naphthalene-1,3′-pyrrolidin]-2′-one (3h). Following the general procedure, the title compound was obtained as a white solid (380 mg, 94%). R_f = 0.24 (EtOAc). Mp = 172–173 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.76 (dddddd, J = 21.0, 13.3, 5.5, 4.1, 2.3 Hz, 1H), 1.87–1.91 (m, 1H), 2.01–2.08 (m, 2H), 2.25–2.34 (m, 2H), 2.81 (d, J = 16.6, 4.1 Hz, 1H), 2.89 (ddd, J = 16.6, 11.4, 5.5 Hz, 1H), 3.37–3.44 (m, 2H), 7.07–7.20 (m, 4H), 8.04 (br, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 19.8 (t), 29.5 (t), 31.4 (t), 38.7 (t), 39.4 (t), 48.9 (s), 126.5 (d), 126.6 (d), 127.7 (d), 129.2 (d), 137.2 (s), 138.8 (s), 183.2 (s). IR (KBr): v = 3204, 3086, 2863, 1680, 1284, 732 cm^{-1}. Anal. Calcd for $C_{13}H_{15}NO$ (201.27): C, 77.58; H, 7.51; N, 6.96. Found: C, 77.69; H, 7.76; N, 6.95.

10*H*-spiro[anthracene-9,3′-pyrrolidin]-2′-one (3i). Following the general procedure, the title compound was obtained as a white solid (450 mg, 90%). R_f = 0.37 (EtOAc). Mp = 255–256 °C. ^1H NMR (500 MHz, DMSO): δ = 2.29 (t, J = 6.6 Hz, 2H), 3.29 (t, J = 6.6 Hz, 2H), 4.04 (s, 2H), 7.22–7.26 (m, 6H), 7.35–7.37 (m, 2H), 8.44 (br, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, DMSO): δ = 35.2 (t), 38.6 (t), 38.7 (t), 54.1 (s), 126.2 (d), 126.8 (d), 126.9 (d), 128.1 (d), 136.4 (s), 139.6 (s), 178.1 (s). IR (KBr): v = 3218, 3061, 2859, 1655, 1485, 1277, 746 cm^{-1}. Anal. Calcd for $C_{17}H_{15}NO$ (249.31): C, 81.90; H, 6.06; N, 5.62. Found: C, 81.83; H, 6.01; N, 5.67.

General Procedure for the Catalytic Hydrogenation with Raney Nickel (method B and C). Nitrile **2** (2.0 mmol) was dissolved in methanol/water 1:1 (30 mL) at RT and activated Raney nickel (6.0 mg, 10 mol%)[27] was added. The solution was purged with hydrogen gas for 5 min, equipped with a balloon filled with

hydrogen gas and hydrogenated under stirring at 1 bar for 4 h (method B). To obtain partly unsaturated γ-spirolactams **5**, hydrogenation was performed in an autoclave at 50 bar for 3 d (method C). The solution was filtered through a pad of Celite, washed with methanol (2×30 mL) (caution! The Raney nickel should not become completely dry, because it might catch fire) and the solvent was removed in vacuo. The residue was dissolved in pyridine (50 mL) and heated for 8 h under reflux. The pyridine was removed in vacuo and the residue was dissolved in dichloromethane (50 mL), extracted with 1 N HCl (30 mL), the organic phase was dried over sodium sulfate, and concentrated in vacuo. The crude products were purified by column chromatography (EtOAc) to obtain the γ-spirolactams **4** and **5** in analytically pure form.

Products from method B

Azaspiro[4.5]deca-6,9-dien-1-one (4a). Following the general procedure (method B), the title compound was obtained as white solid (280 mg, 94%). R_f = 0.13 (EtOAc). Mp = 144–145 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.09 (t, *J* = 6.8 Hz, 2H), 2.65 (dtt, *J* = 23.2, 3.3, 2.0 Hz, 1H), 2.80 (dtt, *J* = 23.2, 3.3, 2.0 Hz, 1H), 3.36 (td, *J* = 6.8, 0.8 Hz, 2H), 5.57 (dt, *J* = 10.3, 2.0 Hz, 2H), 5.94 (dt, *J* = 10.3, 3.3 Hz, 2H), 7.84 (br, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 26.1 (t), 37.0 (t), 39.2 (t), 46.8 (s), 126.3 (d), 126.6 (d), 180.1 (s). IR (KBr): *v* = 3177, 2887, 1678, 1270, 810, 708, 674 cm^{-1}. Anal. Calcd for $C_9H_{11}NO$ (149.19): C, 72.45; H, 7.43; N, 9.39. Found: C, 72.41; H, 7.40; N, 9.35.

6-Methyl-2-azaspiro[4.5]deca-6,9-dien-1-one (4b). Following the general procedure (method B), the title compound was obtained as white solid (300 mg, 92%). R_f = 0.15 (EtOAc). Mp = 121–122 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.65 (q, *J* = 1.8 Hz, 3H), 1.90 (ddd, *J* = 13.3, 8.5, 4.8 Hz, 1H), 2.28 (ddd, *J* = 13.3, 8.9, 6.3 Hz, 1H), 3.27 (dddd, *J* = 9.9, 8.9, 4.8, 0.9 Hz, 1H), 3.35 (dddd, *J* = 9.9, 8.5, 6.3, 0.7 Hz, 1H), 2.58 (dttq, *J* = 23.1, 3.4, 2.0, 1.8 Hz, 1H), 2.71 (dttq, *J* = 23.1, 3.4, 2.0, 1.8 Hz, 1H), 5.51 (dt, *J* = 9.9, 2.0 Hz, 1H), 5.61 (ddq, *J* = 3.4, 2.0, 1.8 Hz, 1H), 5.82 (dddd, *J* = 9.9, 3.4, 2.0, 1.5 Hz, 1H), 8.31 (br, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 19.2 (q), 26.7 (t), 33.8 (t), 39.8 (t), 49.7 (s), 123.0 (d), 125.3 (d), 127.0 (d), 131.3 (s), 179.9 (s). IR (KBr): *v* = 3198, 2958, 2873, 1685, 1276, 801, 713 cm^{-1}. Anal. Calcd for $C_{10}H_{13}NO$ (163.22): C, 73.59; H, 8.03; N, 8.58. Found: C, 73.35; H, 8.22; N, 8.45.

7-Methyl-2-azaspiro[4.5]deca-6,9-dien-1-one (4c). Following the general procedure (method B), the title compound was obtained as white solid (310 mg, 95%). R_f = 0.16 (EtOAc). Mp = 98–99 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.69 (d, *J* = 1.7 Hz, 3H), 2.01 (ddd, *J* = 7.0, 6.6, 1.5 Hz, 2H), 2.49 (dddd, *J* = 24.6, 3.4, 2.1, 1.5 Hz, 1H), 2.68 (dddd, *J* = 24.6, 4.2, 3.4, 1.5 Hz, 1H), 3.31 (ddd, *J* = 7.0, 6.6, 1.8 Hz, 2H), 5.25 (qt, *J* = 1.7, 1.5 Hz, 1H), 5.52 (ddd, *J* = 9.9, 4.2, 2.1 Hz, 1H), 5.89 (dt, *J* = 9.9, 3.4 Hz, 1H), 8.12 (br, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 23.2 (q), 30.8 (t), 36.8 (t), 39.2 (t), 47.9 (s), 120.8 (d), 126.0 (d), 126.4 (d), 133.9 (s), 180.6 (s). IR (KBr): *v* = 3204, 2959, 2864, 1686, 1273, 712, 692 cm^{-1}. Anal. Calcd for $C_{10}H_{13}NO$ (163.22): C, 73.59; H, 8.03; N, 8.58. Found: C, 73.58; H, 8.31; N, 8.29.

***cis*-8-Methyl-2-azaspiro[4.5]deca-6,9-dien-1-one (*cis*-4d)**. Following the general procedure (method B), the title compound was obtained as white solid (300 mg, 92%). R_f = 0.25 (EtOAc). Mp = 127–128 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.17 (d, *J* = 7.3 Hz, 3H), 2.11 (t, *J* = 6.8 Hz, 2H), 2.75 (qtt, *J* = 7.3, 3.4, 1.9 Hz, 1H), 3.39 (t, *J* = 6.8 Hz, 2H), 5.55 (dd, *J* = 10.1, 1.9 Hz, 2H), 5.89 (dd, *J* = 10.1, 3.4 Hz, 2H), 7.18 (br, 1H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 22.6 (q), 30.8 (d), 37.0 (t), 39.1 (t), 47.0 (s), 125.2 (d), 132.9 (d), 179.5 (s). IR (KBr): *v* = 3667, 3188, 2959, 2893, 1677, 1271, 1069, 1036, 797, 732, 684 cm^{-1}. Anal. Calcd for $C_{10}H_{13}NO$ (163.22): C, 73.59; H, 8.03; N, 8.58. Found: C, 73.38; H, 8.15; N, 8.42.

***trans*-8-Methyl-2-azaspiro[4.5]deca-6,9-dien-1-one (*trans*-4d)**. Following the general procedure (method B), the title compound was obtained as white solid (300 mg, 92%). R_f = 0.24 (EtOAc). Mp = 159–160 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.06 (d, *J* = 7.3 Hz, 3H), 2.06 (t, *J* = 6.8 Hz, 2H), 2.85–2.90 (m, 1H), 3.35 (t, *J* = 6.8 Hz, 2H), 5.52 (dd, *J* = 10.1, 1.9 Hz, 2H), 5.83 (dd, *J* = 10.1, 3.1 Hz, 2H), 7.95 (br, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 21.7 (q), 30.3 (d), 36.9 (t), 39.2 (t), 47.0 (s), 125.1 (d), 132.9 (d), 179.9 (s). IR (KBr): *v* = 3666, 3188, 2961, 2893, 1676, 1271, 798, 735, 680 cm^{-1}. Anal. Calcd for $C_{10}H_{13}NO$ (163.22): C, 73.59; H, 8.03; N, 8.58. Found: C, 73.49; H, 8.06; N, 8.56.

6,7-Dimethyl-2-azaspiro[4.5]deca-6,9-dien-1-one (4e). Following the general procedure (method B), the title compound was obtained as white solid (335 mg, 95%). R_f = 0.31 (EtOAc). Mp = 78–79 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.64 (s, 3H), 1.67 (s, 3H), 1.91 (ddd, *J* = 13.3, 8.2, 3.7 Hz, 2H), 2.32 (ddd, *J* = 13.3, 9.3, 7.7 Hz, 2H), 2.58 (ddd, *J* = 22.7, 3.4, 0.7 Hz, 1H), 2.70 (ddd, *J* = 22.7, 3.4, 0.7 Hz, 1H), 3.31 (ddd, *J* = 9.8, 9.3, 3.7 Hz, 1H), 3.38 (ddd, *J* = 9.8, 8.2, 7.6 Hz, 1H), 5.58 (dt, *J* = 10.0, 0.7 Hz, 1H), 5.82 (dt, *J* = 10.0, 3.4 Hz, 1H), 7.92 (br, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 14.4 (q), 19.2 (q), 32.9 (t), 34.2 (t), 39.7 (t), 51.3 (s), 123.8 (s), 125.4 (d), 127.2 (d), 128.0 (s), 180.7 (s). IR (KBr): *v* = 3667, 2980, 2902, 1678, 1385, 1257, 1057, 890, 695 cm^{-1}. Anal. Calcd for $C_{11}H_{15}NO$ (177.25): C, 74.54; H, 8.53; N, 7.90. Found: C, 74.33; H, 8.72; N, 7.91.

6,10-Dimethyl-2-azaspiro[4.5]deca-6,9-dien-1-one (4f). Following the general procedure (method B), the title compound was obtained as white solid (325 mg, 92%). R_f = 0.24 (EtOAc). Mp = 149–150 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.66 (s, 6H), 2.13 (t, *J* = 7.3 Hz, 2H), 2.56 (d, *J* = 23.0 Hz, 1H), 2.66 (d, *J* = 23.0 Hz, 1H), 3.32 (t, *J* = 7.3 Hz, 2H), 5.55 (s, 2H), 8.26 (br, 1H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 19.1 (q), 27.1 (t), 31.5 (t), 40.6 (t), 52.7 (s), 122.0 (d), 132.1 (s), 179.6 (s). IR (KBr): *v* = 3193, 3087, 2978, 2880, 1690, 1289, 781, 625 cm^{-1}. Anal. Calcd for $C_{11}H_{15}NO$ (177.25): C, 74.54; H, 8.53; N, 7.90. Found: C, 74.49; H, 8.55; N, 7.89.

7,9-Dimethyl-2-azaspiro[4.5]deca-6,9-dien-1-one (4g). Following the general procedure (method B), the title compound was obtained as white solid (330 mg, 93%). R_f = 0.19 (EtOAc). Mp = 132–133 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.73 (s, 6H), 2.02 (t, *J* = 6.8 Hz, 2H), 2.43 (dm, *J* = 22.1 Hz, 1H), 2.61 (dm, *J* = 22.1 Hz, 1H), 3.32 (dd, *J* = 7.2, 6.8 Hz, 2H), 5.28 (s, 2H), 7.78 (br, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 23.1 (q), 35.9 (t), 37.1 (t), 39.3 (t), 49.1 (s), 120.8 (d), 134.1 (s), 181.0 (s). IR (KBr): *v* = 3197, 3086, 2863, 1685, 1275, 927, 785, 592 cm^{-1}. Anal. Calcd for $C_{11}H_{15}NO$ (177.25): C, 74.54; H, 8.53; N, 7.90. Found: C, 74.42; H, 8.49; N, 7.82.

4*H*-Spiro[naphthalene-1,3′-pyrrolidin]-2′-one (4h). Following the general procedure (method B), the title compound was obtained as white solid (365 mg, 92%). R_f = 0.40 (EtOAc). Mp = 154–155 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.34 (ddd, *J* = 13.3, 7.3, 5.7 Hz, 1H), 2.50 (ddd, *J* = 13.3, 8.0, 6.7 Hz, 1H), 3.44 (ddd, *J* = 21.9, 3.6, 2.2 Hz, 1H), 3.47–3.52 (m, 2H), 3.55 (ddd, *J* = 21.9, 3.6, 2.2 Hz, 1H), 5.82 (dt, *J* = 10.0, 2.2 Hz, 1H), 6.14 (dt, *J* = 10.0, 3.6 Hz, 1H), 7.16–7.26 (m, 4H), 7.89 (br, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 29.8 (t), 38.9 (t), 39.8 (t), 49.6 (s), 126.3 (d), 126.5 (d), 126.9 (d), 127.0 (d), 127.7 (d), 128.7 (d), 134.3 (s), 136.9 (s), 180.8 (s). IR (KBr): *v* = 3191, 3078, 2873, 1679, 1278, 736 cm^{-1}. Anal. Calcd for $C_{13}H_{13}NO$ (199.25): C, 78.36; H, 6.58; N, 7.03. Found: C, 78.40; H, 6.45; N, 6.90.

Products from method C

2-Azaspiro[4.5]dec-6-en-1-one (5a). Following the general procedure (method C), the title compound was obtained as white solid (170 mg, 56%). R_f = 0.27 (EtOAc). Mp = 93–94 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.49–1.56 (m, 1H), 1.60 (ddd, *J* = 13.1, 6.7, 3.1 Hz, 1H), 1.82–2.12 (m, 6H), 3.31 (ddd, *J* = 8.0, 5.5, 1.0 Hz, 2H), 5.48 (ddt, *J* = 10.0, 2.2, 1.0 Hz, 1H), 5.92 (ddd, *J* = 10.0, 4.3, 3.2 Hz, 1H), 7.41 (br,

1H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ = 19.3 (t), 24.7 (t), 30.3 (t), 35.7 (t), 39.2 (t), 45.1 (s), 128.6 (d), 130.4 (d), 182.7 (s). IR (KBr): *v* = 3195, 2902, 1675, 1284, 798, 710, 671 cm^{-1}. Anal. Calcd for $C_9H_{13}NO$ (151.21): C, 71.49; H, 8.67; N, 9.26. Found: C, 71.52; H, 8.48; N, 9.34.

6-Methyl-2-azaspiro[4.5]dec-6-en-1-one (5 b). Following the general procedure (method C), the title compound was obtained as white solid (310 mg, 94 %). R_f = 0.21 (EtOAc). Mp = 92–93 °C. ^1H NMR (600 MHz, $CDCl_3$): δ = 1.40–1.48 (m, 1H), 1.64 (s, 3H), 1.64–1.68 (m, 1H), 1.74–1.80 (m, 2H), 1.89–1.96 (m, 2H), 2.03–2.09 (m, 1H), 2.17–2.26 (m, 1H), 3.28–3.335 (m, 2H), 5.61 (s, 1H), 7.52 (br, 1H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ = 19.0 (t), 19.3 (q), 25.2 (t), 31.6 (t), 32.6 (t), 39.5 (t), 48.6 (s), 126.6 (d), 133.3 (s), 182.4 (s). IR (KBr): *v* = 3206, 2923, 1683, 1285, 802, 641 cm^{-1}. Anal. Calcd for $C_{10}H_{15}NO$ (165.23): C, 72.69; H, 9.15; N, 8.48. Found: C, 72.50; H, 9.27; N, 8.42.

7-Methyl-2-azaspiro[4.5]dec-6-en-1-one (5 c). Following the general procedure (method C), the title compound was obtained as white solid (300 mg, 91 %). R_f = 0.22 (EtOAc). Mp = 106–107 °C. ^1H NMR (600 MHz, $CDCl_3$): δ = 1.52–1.58 (m, 2H), 1.69 (dt, *J* = 1.5, 0.7 Hz, 3H), 1.78 (ddt, *J* = 13.0, 9.8, 0.7 Hz, 1H), 1.85–1.93 (m, 2H), 1.97 (ddd, *J* = 12.7, 6.7, 4.5 Hz, 1H), 1.96–2.05 (m, 1H), 2.04 (dt, *J* = 12.7, 7.8 Hz, 1H), 3.30 (dddd, *J* = 7.8, 6.7, 3.3, 1.1 Hz, 2H), 5.22 (ddq, *J* = 2.7, 1.7, 1.5 Hz, 1H), 6.98 (br, 1H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 19.8 (t), 24.2 (q), 29.7 (t), 30.0 (t), 35.9 (t), 39.2 (t), 45.4 (s), 122.9 (d), 137.8 (s), 183.0 (s). IR (KBr): *v* = 3267, 2962, 2926, 2903, 1659, 1275, 1066, 728 cm^{-1}. Anal. Calcd for $C_{10}H_{15}NO$ (165.23): C, 72.69; H, 9.15; N, 8.48. Found: C, 72.87; H, 9.29; N, 8.48.

6,7-Dimethyl-2-azaspiro[4.5]dec-6-en-1-one (5 e). Following the general procedure (method C), the title compound was obtained as white solid (330 mg, 92 %). R_f = 0.27 (EtOAc). Mp = 99–100 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.43–1.52 (m, 1H), 1.59 (s, 3H), 1.62 (s, 3H), 1.63–1.70 (m, 3H), 1.83–1.93 (m, 2H), 2.01–2.19 (m, 2H), 3.31 (dd, *J* = 9.0, 5.0 Hz, 2H), 7.28 (br, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 14.9 (q), 19.6 (t), 20.0 (q), 31.4 (t), 31.7 (t), 32.4 (t), 39.5 (t), 49.9 (s), 125.4 (s), 131.3 (s), 183.2 (s). IR (KBr): *v* = 3204, 2904, 2826, 1674, 1445, 1381, 1282, 1065, 793 cm^{-1}. Anal. Calcd for $C_{11}H_{17}NO$ (179.26): C, 73.70; H, 9.56; N, 7.81. Found: C, 73.49; H, 9.46; N, 7.55.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords: Arenes · Birch reduction · Hydrogenation · Lactams · Synthetic methods

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