Palladium-catalyzed C—O hydrogenolysis in γ-hydroxy γ-lactams as an efficient approach to 5-alkyl(aryl)pyrrolidin-2-ones

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5-R-Pyrrolidin-2-ones were synthesized by Pd/Sibunit-catalyzed C—O hydrogenolysis of 5-R-5-hydroxypyrrolidin-2-ones with molecular hydrogen.

Key words: γ-hydroxy γ-lactams, pyrrolidin-2-ones, C—O hydrogenolysis, hydrogen, palladium catalysts.

Alkyl- and aryl-substituted pyrrolidin-2-ones are the structural fragments of a number of naturally occurring substances (*e.g.*, alkaloids[1,2]), antibiotics,[3,4] muscarinic receptor agonists,[5] Na^+ channel blockers, antimalarial agents, and other biologically active compounds.[5,6] Several approaches have been developed for the synthesis of 5-alkylpyrrolidin-2-ones: reduction of the C—Hal bond of halo-substituted γ-lactams,[1,5,7—9] alkylation of the C—Hal bond with the Grignard reagent,[2] hydrogenation of the C=C bond (either *endo* or *exo*) of unsaturated γ-lactams,[3,6] hydrogenation of γ-keto ester hydrazones,[10,11], cyclization of linear unsaturated and γ-hydroxy-substituted amides,[12,13] ruthenium-catalyzed ring closure of α-diazoacetamides.[14,15] At the same time, all mentioned approaches are of limited value. The key steps of these methods often require stoichiometric amounts of poorly available or unstable reagents, *e.g.*, hydrides or organometallic compounds. Moreover, the reactions are often non-selective.

In the present work, we describe simple and versatile procedure towards 5-alkyl(aryl)pyrrolidin-2-ones *via* Pd-catalyzed hydrogenolysis of γ-hydroxy γ-lactams similar to previously studied[16] hydrogenolysis of substituted 3-hydroxyisoindolin-1-ones.

Results and Discussion

The starting γ-hydroxy γ-lactams **1** were synthesized by amidation of unsaturated lactones **2** and by the reaction of *N*-benzylsuccinimide **3** with either benzylmagnesium chloride or sodium borohydride (Scheme 1). Hydrogenolysis of substrates **1** was carried out over Pd^0 supported on mesoporous carbon Sibunit (Pd/Sibunit) catalyst.[17]

The effect of the solvent on composition of hydrogenolysis products was examined with the model hydroxy lactam **1a** (Table 1). In aprotic media (toluene, THF), the reaction is completed within 2—6 h at 50 °C to give *N*-benzyl-5-methylpyrrolidin-2-one (**4a**) at 100% conversion (see Table 1, entries *1—6*). In protic solvents (MeOH, EtOH, CF_3CH_2OH), hydrogenolysis is accompanied by substitution of the hydroxy group at the quaternary carbon with an alkoxy group to yield alkoxy lactams of type **5**. Depending on the nature of the protic solvent and hydrogenolysis conditions, a **4a** : **5** ratio is widely varied, from 0 : 100 to 98 : 2. For instance, lactam **5** was the major product in the reaction carried out in MeOH at 50 °C for 2 h (entry *8*); in trifluoroethanol, lactam **4a** predominates (entry *12*); while in EtOH lactams **4a** and **5´** are obtained in a 1 : 1 ratio (entry *10*). Taking into account these results, toluene was a solvent of choice for the most syntheses of substituted pyrrolidin-2-ones from other substrates (Table 2). It should be noted that in contrast to substrate **1a**

Table 1. Pd-Catalyzed hydrogenolysis of hydroxy lactam **1a***

Entry	Solvent	*T*/°C	*t*/h	Conversion (%)	Yield (%)	
					4a	**5**
1	Toluene	22	2	18	100	—
2	Toluene	22	65	100	100	—
3	Toluene	50	2	90	100	—
4	Toluene	50	6	100	100	—
5	THF	22	2	53	100	—
6	THF	50	2	100	100	—
7	MeOH	22	2	95	0	100
8	MeOH	50	2	100	4	96
9	MeOH	50	6	100	91	9
10	EtOH	50	2	88	50	50
11	EtOH	50	6	96	85	15
12	CF_3CH_2OH	50	2	100	>95	<5

* Reaction conditions: **1a** (0.23 mmol), solvent (2 mL), 1% Pd/Sibunit, **1a** : Pd = 100, H_2 (20 atm).

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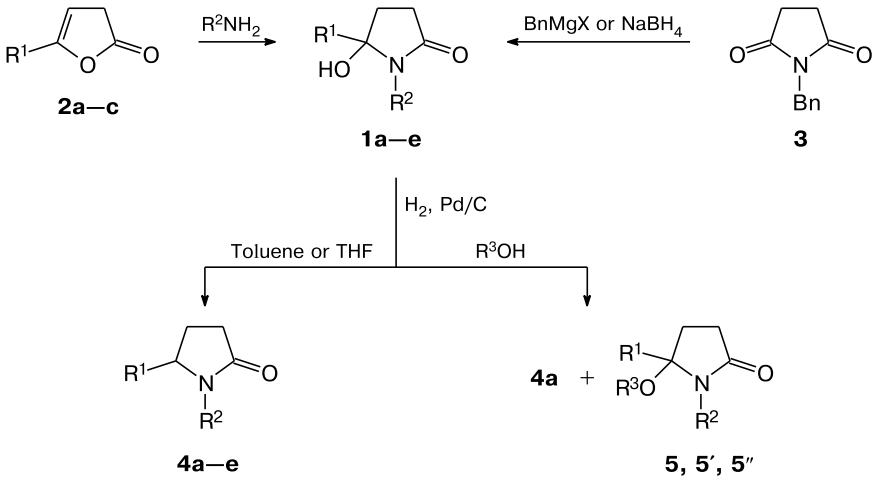
Scheme 1



1, 2, 4: R^1= Me, R^2 = Bn (**a**); R^1 = R^2 = Me (**b**); R^1 = Ph, R^2 = Me (**c**); R^1 = R^2 = Bn (**d**); R^1 = H, R^2 = Bn (**e**)
5, 5′, 5″: R^1 = Me, R^2 = Bn, R^3 = Me (**5**), Et (**5′**), CF_3CH_2 (**5″**)

(see Table 1), dibenzyl-substituted compound **1d** gives only lactam **4d** in both methanol and aprotic solvents (see Table 2, entry *7*). Slow rate of hydrogenolysis of 5-phenyl-substituted hydroxy lactam **1c** is also noteworthy. Complete conversion of **1c** was achieved only within 24 h at 50 °C (entry *4*), which can be due to the presence of the bulky phenyl group in the molecule.

To suggest the plausible mechanism of hydrogenolysis, we performed deuterolysis of substrate **1a** with molecular deuterium and determined the content of deuterium bonded to some carbon atoms for the reaction product D_n-**4a** by ^{1}H NMR. It was found that deuterolysis of hydroxy lactam **1a** leads to an isotopic enrichment (from 30 to 70%) at the C(4), C(5), and C(6) carbon atoms; whereas, no deuteration at the C(3) and benzyl group occurs (Scheme 2). These results suggest the most likely mechanism of the catalytic cycle involving heterolysis of the molecular hydrogen (deuterium) at the Pd^0 atoms to give anionic hydride (deuteride) complex **A** and its subsequent reaction with the starting hydroxy lactam to yield acyliminium intermediate **B**. Complex **B** further decayed to give product D_n-**4a** and the Pd^0 species thus resuming

Scheme 2

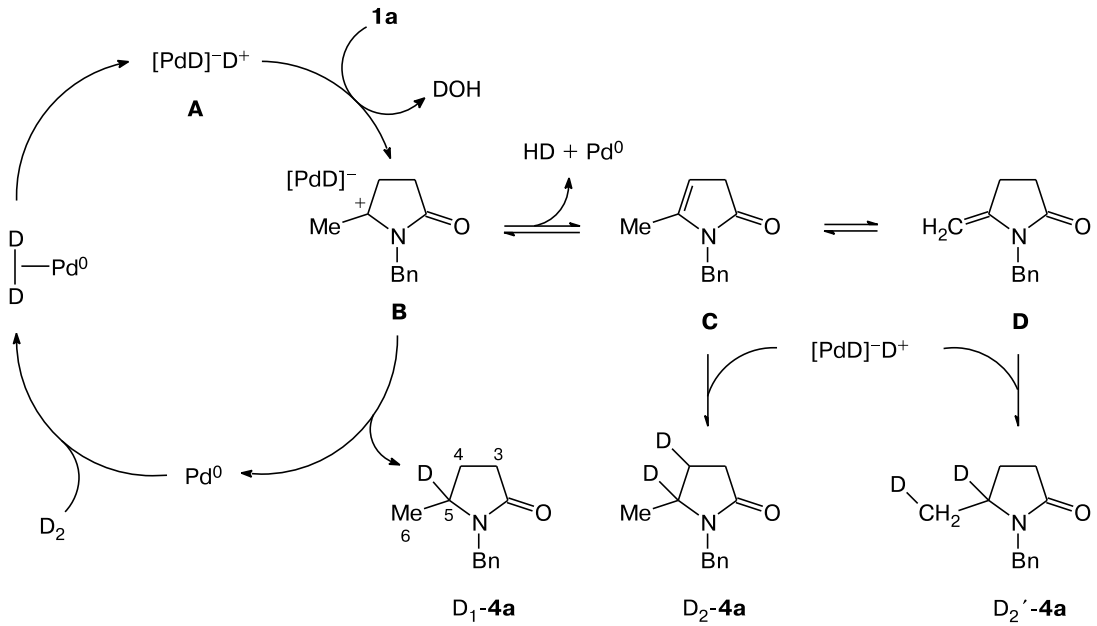


Table 2. Synthesis of substituted pyrrolidin-2-ones **4a—e** by catalytic hydrogenolysis of hydroxy lactams **1***

Entry	Substrate	Solvent	*t*/h	Conversion (%)
1	**1a**	Toluene	6	100
2	**1b**	Toluene	2	100
3	**1c**	Toluene	8	78
4	**1c**	Toluene	24	100
5	**1d**	Toluene	2	100
6	**1d**	THF	2	100
7	**1d**	MeOH	2	100
8	**1e**	Toluene	2	100

* Reaction conditions: **1** (0.23 mmol), solvent (2 mL), 1% Pd/Sibunit, **1** : Pd = 100, H_2 (20 atm), 50 °C. Hydrogenolysis of substrates **1** selectively gives pyrrolidin-2-ones **4** (^{1}H NMR data).

the next catalytic cycle (the left part of Scheme 2). Furthermore, the presence of deuterium at the C(4) and C(6) positions of the target product indicates that acyliminium intermediate **B** undergoes at least partial deprotonation to give unsaturated heterocycles **C** and **D** involved also in hydride reduction (deuteration) with complex **A** (the right part of Scheme 2). These steps have the very high rate, since enamines **C** and **D** were not detected in the reaction mixtures. Apparently, upon decay of complex **B** enamines **C** and **D** retain the bonding with the Pd^0 species due to π coordination with the C=C bond, which have to favor their rapid hydride reduction.

In summary, we developed simple and versatile procedure towards 5-alkyl and 5-arylpyrrolidin-2-ones *via* the Pd-catalyzed hydrogenolysis of the C—O bond of the relatively available γ-hydroxy γ-lactams. This method can be applied for the synthesis of both mono- and disubstituted pyrrolidin-2-ones.

Experimental

Commercially available lactone **2a** (α-angelica lactone), 3-benzoylpropionic acid, succinic and acetic anhydrides, benzoyl chloride, acetyl chloride, benzylamine, aqueous methylamine, anhydrous sodium acetate, magnesium (chips), sodium borohydride, and Pd/Sibunit were used as purchased.

Solvents for catalytic studies and synthesis of the Grignard reagent were dehydrated and distilled under argon prior to use. Methanol was dehydrated by reflux over magnesium; ethanol was refluxed over calcium; benzene, toluene, THF, and diethyl ether were refluxed over sodium in the presence of benzophenone.

Argon was purified by passing through the columns loaded with nickel-chrome catalyst, Kieselgel impregnated with copper (80 °C), and molecular sieves (4 Å). Hydrogen was purified by passing through the columns loaded with nickel-chrome catalyst and molecular sieves (4 Å).

^{1}H and ^{13}C NMR spectra were run on a Bruker AM-300 instrument (working frequencies of 300.13 and 75.47 MHz, respectively). Melting points were measured with a Kofler apparatus. Elemental analyses were carried out with a Perkin—Elmer Series II 2400 analyzer. High resolution electrospray ionization (ESI) mass spectrometry was performed on a Bruker microTOF instrument.

1-Benzyl-5-hydroxy-5-methylpyrrolidin-2-one (1a)[18]. To a solution of unsaturated lactone **2a** (2.2 mL, 25 mmol) in water (3 mL), benzylamine (2.9 mL, 26.5 mmol) was added and the mixture was stirred at room temperature for 1 h. The reaction mixture was extracted with dichloromethane (3×3 mL) and dried with anhydrous $MgSO_4$. Removal of the solvent *in vacuo* to dryness and recrystallization of the residue from diethyl ether afforded product **1a** in the yield of 1.72 g (33%), colorless crystals, m.p. 76—78 °C (*cf.* Ref. 19: m.p. 64—66 °C). ^{1}H NMR ($CDCl_3$), δ: 1.35 (s, 3 H, CH_3); 2.07—2.18 (m, 2 H, $C(O)CH_2$); 2.32—2.43 (m, 1 H, $C(O)CH_2CH_a\underline{H}_b$); 2.53—2.64 (m, 1 H, $C(O)CH_2C\underline{H}_aH_b$); 4.13 (br.s, 1 H, OH); 3.98 (m, 1 H, $C\underline{H}_aH_bPh$, J = 15.4 Hz); 4.98 (m, 1 H, $CH_a\underline{H}_bPh$, J = 15.4 Hz); 7.35—7.20 (m, 5 H, Ph). ^{13}C NMR ($CDCl_3$), δ: 27.03, 29.06, 34.83, 42.22, 90.39, 127.06, 127.65, 128.45, 138.52, 175.41. Found (%): C, 70.09; H, 7.40; N, 6.85. $C_{12}H_{15}NO_2$. Calculated (%): C, 70.22; H, 7.37; N, 6.82. MS (ESI), *m/z*: 206.1185 $[M + H]^+$, 228.1003 $[M + Na]^+$, 244.0738 $[M + K]^+$. Calculated: for $[C_{12}H_{16}NO_2]^+$, 206.1181 $[M + H]^+$; for $[C_{12}H_{15}NNaO_2]^+$, 228.1000 $[M + Na]^+$; for $[C_{12}H_{15}NKO_2]^+$, 244.0740 $[M + K]^+$.

5-Hydroxy-1,5-dimethylpyrrolidin-2-one (1b)[20]. Colorless crystals, m.p. 65—67 °C (*cf.* Ref 21: m.p. 66—68 °C), yield 2.4 g (74%). ^{1}H NMR ($CDCl_3$), δ: 1.40 (s, 3 H, CH_3); 2.02—2.08 (m, 2 H, $C(O)CH_2$); 2.16—2.27 (m, 1 H, $C(O)CH_2CH_a\underline{H}_b$); 2.39—2.50 (m, 1 H, $C(O)CH_2C\underline{H}_aH_b$); 2.69 (s, 3 H, CH_3); 5.16 (br.s, 1 H, OH). ^{13}C NMR ($CDCl_3$), δ: 23.77, 25.53, 29.24, 34.38, 89.61, 174.52.

5-Hydroxy-1-methyl-5-phenylpyrrolidin-2-one (1c)[22]. *Step 1.* To 3-benzoylpropionic acid (15 g, 0.084 mol), acetyl chloride (150 mL, 2.1 mol) was added and the mixture was stirred at room temperature for 1 h. The acetyl chloride excess was removed *in vacuo*. Recrystallization of the residue from diethyl ether afforded 5-phenylfuran-2(3*H*)-one, light yellow powder, m.p. 86—88 °C (*cf.* Ref. 23: 88—89 °C), yield 11.7 g (87%). ^{1}H NMR ($CDCl_3$), δ: 3.42 (d, 2 H, CH_2, J = 2.3 Hz); 5.79 (m, 1 H, CH); 7.38—7.47 (m, 3 H, *m*-Ph, *p*-Ph); 7.58—7.63 (m, 2 H, *o*-Ph).

Step 2. To 5-phenylfuran-2(3*H*)-one (1 g, 6.24 mmol), 33% aqueous methylamine (8 mL) was added and the mixture was stirred at room temperature for 1 h. Removal of the volatiles *in vacuo* and recrystallization of the residue from water afforded compound **1c**, white powder, m.p. 131—133 °C (*cf.* Ref. 22: m.p. 130—135 °C), yield 0.7 g (59%). ^{1}H NMR ($CDCl_3$), δ: 2.26—2.55 (m, 3 H, $C(O)C\underline{H}_2CH_a\underline{H}_b$); 2.58—2.75 (m, 1 H, $C(O)CH_2C\underline{H}_aH_b$); 2.62 (s, 3 H, CH_3); 5.22 (br.s, 1 H, OH); 7.25—7.45 (m, 5 H, Ph). ^{13}C NMR ($CDCl_3$), δ: 25.19, 29.56, 37.44, 92.96, 125.46, 128.08, 128.65, 142.42, 175.73.

1,5-Dibenzyl-5-hydroxypyrrolidin-2-one (1d)[24]. *Step 1.* To a solution of succinic anhydride (5 g, 0.05 mol) in chloroform (50 mL), a solution of benzylamine (5.7 mL, 0.05 mol) in chloroform (10 mL) was added and the mixture was stirred for 1 h. *N*-Benzylsuccinic acid monoamide was collected by filtration and used on the next step without further purification. White powder, m.p. 130—132 °C (*cf.* Ref. 25: m.p. 144 °C), yield 10.05 g (97%). ^{1}H NMR (DMSO-d_6), δ: 2.35—2.47 (m, 4 H, 2 CH_2); 4.27 (d, 2 H, $PhC\underline{H}_2$, J = 6.0 Hz); 7.19—7.45 (m, 5 H, Ph); 8.35 (t, 1 H, NH, J = 6.0 Hz).

Step 2. To *N*-benzylsuccinic acid monoamide, calcined sodium acetate (1.02 g, 12.15 mmol) and acetic anhydride (50 mL)

were added and the mixture was refluxed for 2 h. Removal of the solvent *in vacuo* and recrystallization of the residue from diethyl ether afforded *N*-benzylsuccinimide (**3**), white crystals, m.p. 96—98 °C (*cf.* Ref. 26: m.p. 102—103 °C), yield 8.7 g (92%). ^{1}H NMR ($CDCl_3$), δ: 2.68 (s, 4 H, 2 CH_2); 4.65 (s, 2 H, PhC$\underline{H}_2$); 7.28—7.39 (m, 5 H, Ph).

Step 3. A three-neck flask (205 mL, predried) equipped with two dropping funnels with pressure-equalization arms and a reflux condenser with a drying tube was flushed with argon and charged with magnesium chips (1 g, 0.04 mmol) and anhydrous diethyl ether (20 mL). Then, a solution of BnCl (4.7 mL, 0.04 mmol) in anhydrous diethyl ether (40 mL) was added dropwise. After addition of approximately 1/10 of the BnCl solution, formation of the Grignard reagent began (exothermic reaction, the clear solution became turbid). The rest of the BnCl solution was added dropwise with a rate to maintain a gentle reflux. After cessation of the reaction, the mixture was cooled (ice/NaCl cooling bath) and a solution of *N*-benzylsuccinimide (**3**) (7.5 g, 0.04 mol) in THF (85 mL) was added dropwise with vigorous stirring. The reaction mixture was refluxed for 4 h and cooled to 0 °C. The mixture was washed with saturated aqueous NH_4Cl (~100 mL), the organic phase was separated, the aqueous layer was extracted with diethyl ether (2×70 mL). The combined organic layers were washed with brine and dried with anhydrous $MgSO_4$. Removal of the solvent *in vacuo* afforded the target product **1d**, white powder, m.p. 112—114 °C (*cf.* Ref. 27: m.p. 130—132 °C, yield 4.8 g (52%). ^{1}H NMR ($CDCl_3$), δ: 1.70—1.81 (m, 1 H, C(O)$CH_2CH_a\underline{H}_b$); 1.94—2.06 (m, 1 H, C(O)$CH_2C\underline{H}_aH_b$); 2.27—2.47 (m, 2 H, C(O)CH_2); 2.87 (d, 1 H, C(OH)$C\underline{H}_aH_b$Ph, J = 13.7 Hz); 3.09 (d, 1 H, C(OH)$CH_a\underline{H}_b$Ph, J = 13.7 Hz); 4.54 (d, 1 H, NC$\underline{H}_aH_b$Ph, J = 15.1 Hz); 4.71 (d, 1 H, NC$H_a\underline{H}_b$Ph, J = 15.1 Hz); 7.10—7.44 (m, 10 H, 2 Ph). ^{13}C NMR ($CDCl_3$), δ: 27.78, 32.06, 41.52, 43.66, 91.15, 125.93, 126.07, 126.81, 127.26, 127.38, 128.84, 133.80, 137.40, 173.40. Found (%): C, 76.59; H, 6.54; N, 4.98. $C_{18}H_{19}NO_2$. Calculated (%): C, 76.84; H, 6.81; N, 4.98. MS (ESI), *m/z*: 282.1489 $[M + H]^+$, 304.1308 $[M + Na]^+$, 320.1047 $[M + K]^+$. Calculated: for $[C_{18}H_{20}NO_2]^+$, 282.1494 $[M + H]^+$; for $[C_{18}H_{19}NNaO_2]^+$, 304.1313 $[M + Na]^+$; for $[C_{18}H_{19}NKO_2]^+$, 320.1053 $[M + K]^+$.

1-Benzyl-5-hydroxypyrrolidin-2-one (1e)[26]. To a 0 °C solution of *N*-benzylsuccinimide **3** (3 g, 16 mmol) in CH_2Cl_2—MeOH (80 mL, 1 : 3), $NaBH_4$ (1.5 g, 40 mmol) was added portionwise over a period of 2 h with stirring. Then water (50 mL) was added and the volatiles were removed *in vacuo*. The precipitate formed was collected by filtration, washed with water and air-dried. The filtrate was extracted with dichloromethane, dried with $MgSO_4$, and the solvent was removed *in vacuo* to give the addition crop of the target product. The products were combined and recrystallized from benzene. White powder, m.p. 110—111 °C (*cf.* Ref. 26: m.p. 105—106 °C), yield 1.73 g (57%). ^{1}H NMR ($CDCl_3$), δ: 1.84—1.97 (m, 1 H, C(O)$CH_2CH_a\underline{H}_b$); 2.16—2.39 (m, 2 H, C(O)CH_2); 2.50—2.70 (m, 1 H, C(O)$CH_2C\underline{H}_aH_b$); 4.27 (d, 1 H, OH, J = 7.8 Hz); 4.17 (d, 1 H, NC$\underline{H}_aH_b$Ph, J = 14.8 Hz); 4.85 (d, 1 H, NC$H_a\underline{H}_b$Ph, J = 14.8 Hz); 5.03—5.12 (m, 1 H, CH); 7.22—7.38 (m, 5 H, Ph). ^{13}C NMR ($CDCl_3$), δ: 28.10, 29.00, 43.42, 82.47, 127.67, 128.35, 128.76, 136.55, 174.98.

Hydrogenolysis (general procedure). A glass ampule for hydrogenolysis (preliminary evacuated and refilled with argon) was charged with a 1% Pd/Sibunit (25 mg, $2.35 \cdot 10^{-3}$ mg-atom of Pd) and substrate **1** (0.23 mmol). The ampule was again evacuated and refilled with argon. After adding the solvent (2 mL), the ampule was transferred into filled with argon stainless steel autoclave (50 cm^3). The autoclave was flushed with purified hydrogen and the hydrogen pressure was adjusted to 20 atm. Then, the reaction mixture was magnetically stirred at temperature indicated in Table 1. After completion of the experiment, the reaction mixture was filtered through a silica gel pad (1.5 cm thick) to remove the catalyst, the products were eluted with ethyl acetate. After removal of the solvent *in vacuo*, the residue was subjected to NMR spectroscopy, mass spectrometry, and elemental analyses.

1-Benzyl-5-methylpyrrolidin-2-one (4a)[28]. Colorless oil. ^{1}H NMR ($CDCl_3$), δ: 1.05 (d, 3 H, CH_3, J = 6.4 Hz); 1.41—1.55 (m, 1 H, C(O)$CH_2CH_a\underline{H}_b$); 1.97—2.12 (m, 1 H, C(O)$CH_2C\underline{H}_aH_b$); 2.20—2.46 (m, 2 H, C(O)CH_2); 3.35—3.49 (sext, 1 H, CH, J = 6.4 Hz); 4.00 (d, 1 H, C$\underline{H}_aH_b$Ph, J = 14.7 Hz); 4.98 (d, 1 H, $CH_a\underline{H}_b$Ph, J = 14.7 Hz); 7.10—7.25 (m, 5 H, Ph). ^{13}C NMR ($CDCl_3$), δ: 19.30, 26.35, 29.95, 43.55, 52.50, 127.04, 127.61, 128.27, 136.61, 174.52. Found (%): C, 76.30; H, 7.75; N, 7.66. $C_{12}H_{15}NO$. Calculated (%): C, 76.16; H, 7.99; N, 7.40. MS (ESI), *m/z*: 190.2222 $[M + H]^+$, 212.1038 $[M + Na]^+$, 228.0839 $[M + K]^+$. Calculated: for $[C_{12}H_{16}NO]^+$, 190.1232 $[M + H]^+$; for $[C_{12}H_{15}NNaO]^+$, 212.1051 $[M + Na]^+$; for $[C_{12}H_{15}NKO]^+$, 228.0791 $[M + K]^+$.

1,5-Dimethylpyrrolidin-2-one (4b)[29]. Colorless oil. ^{1}H NMR ($CDCl_3$), δ: 1.17 (d, 3 H, C$\underline{H}_3$CH, J = 6.3 Hz); 1.47—1.59 (m, 1 H, C(O)$CH_2CH_a\underline{H}_b$); 2.10—2.43 (m, 3 H, C(O)C$\underline{H}_2C\underline{H}_aH_b$); 2.74 (s, 3 H, C$\underline{H}_3$N); 3.50—3.57 (m, 1 H, CH). ^{13}C NMR ($CDCl_3$), δ: 19.72, 26.61, 27.26, 30.19, 55.63, 174.94.

1-Methyl-5-phenylpyrrolidin-2-one (4c)[30]. Colorless oil. ^{1}H NMR ($CDCl_3$), δ: 1.84—1.94 (m, 1 H, C(O)$CH_2CH_a\underline{H}_b$); 2.38—2.60 (m, 3 H, C(O)C$\underline{H}_2C\underline{H}_aH_b$); 2.66 (s, 3 H, CH_3); 4.45—4.54 (m, 1 H, CH); 7.18 (d, 2 H, *o*-Ph, J = 7.3 Hz); 7.27—7.41 (m, 3 H, *m*-Ph, *p*-Ph).

1,5-Dibenzylpyrrolidin-2-one (4d)[31]. Colorless oil. ^{1}H NMR ($CDCl_3$), δ: 1.68—1.81 (m, 1 H, C(O)$CH_2CH_a\underline{H}_b$); 1.83—1.98 (m, 1 H, C(O)$CH_2C\underline{H}_aH_b$); 2.23—2.32 (m, 2 H, C(O)CH_2); 2.57 (dd, 1 H, $CHCH_a\underline{H}_b$Ph, J_1 = 13.7 Hz, J_2 = 8.5 Hz); 3.02 (dd, 1 H, $CHC\underline{H}_aH_b$Ph, J_1 = 13.3 Hz, J_2 = 4.3 Hz); 3.62—3.75 (m, 1 H, CH); 4.01 (d, 1 H, NC$\underline{H}_aH_b$Ph, J = 14.9 Hz); 5.10 (d, 1 H, NC$H_a\underline{H}_b$Ph, J = 14.9 Hz); 7.03—7.40 (m, 10 H, 2 Ph). ^{13}C NMR ($CDCl_3$), δ: 23.63, 29.73, 39.08, 44.33, 57.89, 126.63, 127.47, 127.98, 128.51, 128.61, 129.11, 136.65, 136.94, 175.06. Found (%): C, 80.46; H, 7.32; N, 5.29. $C_{18}H_{19}NO$. Calculated (%): C, 81.47; H, 7.22; N, 5.28. MS (ESI), *m/z*: 266.1543 $[M + H]^+$, 288.1362 $[M + Na]^+$, 304.1111 $[M + K]^+$. Calculated for $[C_{18}H_{20}NO]^+$, 266.1545 $[M + H]^+$; for $[C_{18}H_{19}NNaO]^+$, 288.1364 $[M + Na]^+$; for $[C_{18}H_{19}NKO]^+$, 304.1104 $[M + K]^+$.

1-Benzylpyrrolidin-2-one (4e)[32]. Colorless oil. ^{1}H NMR ($CDCl_3$), δ: 1.99 (pent, 2 H, $CH_2C\underline{H}_2CH_2CO$, J = 7.6); 2.45 (t, 2 H, $CH_2CH_2C\underline{H}_2CO$, J = 8.1 Hz); 3.27 (t, 2 H, NC$\underline{H}_2CH_2CH_2CO$, J = 7.0 Hz); 4.46 (s, 2 H, C$\underline{H}_2$Ph); 7.21—7.38 (m, 5 H, Ph).

1-Benzyl-5-methyl-5-methoxypyrrolidin-2-one (5). ^{1}H NMR ($CDCl_3$), δ: 1.35 (s, 3 H, CH_3); 1.95—2.06 (m, 1 H, C(O)$CH_2C\underline{H}_aH_b$); 2.15—2.25 (m, 1 H, C(O)$CH_2CH_a\underline{H}_b$); 2.48—2.57 (m, 2 H, C(O)C$\underline{H}_2CH_aH_b$); 2.96 (s, 3 H, OCH_3); 4.12 (d, 1 H, C$\underline{H}_aH_b$Ph, J = 15.2 Hz); 4.70 (d, 1 H, $CH_a\underline{H}_b$Ph, J = 15.2 Hz); 7.20—7.33 (m, 5 H, Ph).

1-Benzyl-5-ethoxy-5-methylpyrrolidin-2-one (5′). ^{1}H NMR ($CDCl_3$), δ: 1.03 (t, 3 H, $OCH_2C\underline{H}_3$, J = 6.9 Hz); 1.37 (s, 3 H, CH_3); 2.0—2.5 (m, 4 H, CH_2CH_2); 2.92—3.05 (m, 1 H, $OC\underline{H}_aH_bCH_3$);

3.18—3.30 (m, 1 H, $OCH_a\underline{H}_bCH_3$); 4.21 (d, 1 H, $C\underline{H}_aH_bPh$, J = 15.2 Hz); 4.63 (d, 1 H, $CH_a\underline{H}_bPh$, J = 15.2 Hz); 7.21—7.33 (m, 5 H, Ph).

1-Benzyl-5-methyl-5-(2,2,2-trifluoroethoxy)pyrrolidin-2-one (5″). ^{1}H NMR (CDCl), δ: 1.42 (s, 3 H, CH_3); 1.95—2.06 (m, 1 H, $C(O)CH_2C\underline{H}_aH_b$); 2.15—2.25 (m, 1 H, $C(O)CH_2CH_a\underline{H}_b$); 2.48—2.57 (m, 2 H, $C(O)C\underline{H}_2CH_aH_b$); 3.21—3.38 (m, 1 H, $OC\underline{H}_aH_bCF_3$); 3.45—3.55 (m, 1 H, $OCH_a\underline{H}_bCF_3$); 4.19 (m, 1 H, $C\underline{H}_aH_bPh$, J = 15.3 Hz); 4.71 (m, 1 H, $CH_a\underline{H}_bPh$, J = 15.3 Hz); 7.20—7.33 (m, 5 H, Ph).

Deuterolysis of hydroxy lactam **1a** was carried out similarly to hydrogenolysis. Reaction conditions: 1% Pd/Sibunite, toluene, deuterium pressure of 20 atm., 50 °C, 2 h. For products D_n-**4a**, the percentage of deuterium bonded to the carbon atoms were as follows: C(3), 0; C(4), 70; C(5), 60; C(6), 30; Bn, 0 (^{1}H NMR data).

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