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Conjugate addition of nitroalkanes to *N*-substituted maleimides. Synthesis of 3-alkylsuccinimides and pyrrolidines

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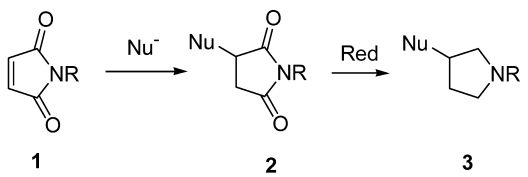
Abstract—3-Alkylidenesuccinimides obtained by conjugate addition of nitroalkanes to *N*-substituted maleimides can be reduced to the corresponding 3-alkyl derivatives by catalytic hydrogenation. 3-Alkylsuccinimides can be further reduced using $BH_3{\cdot}Me_2S$ complex to afford 3-alkylpyrrolidines in good yield.

1. Introduction

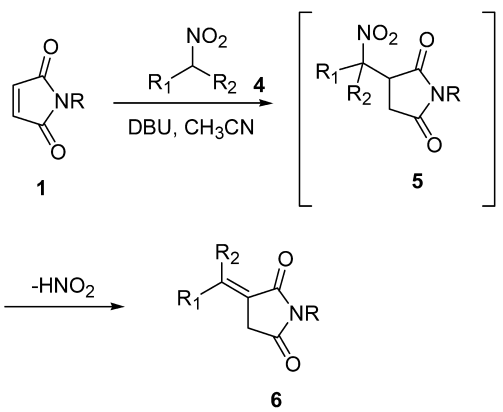
Substituted pyrrolidines are frequently included in many substances endowed of biological and industrial interest.[1] A large body of synthetic approaches leading to these five-membered heterocycles involves a ring closure process that can be carried out both intra- and intermolecularly.[2] An alternative procedure concerns functionalization of commercially available pyrrolidines and similar derivatives.[3] Partial reduction of *N*-acylpyrrolidin-2-ones and functionalized succinimides usually provides a rapid entry to 2-hydroxy or 2-alkoxypyrrolidines that can be used as precursors of *N*-acyliminium ions. These reactive intermediates can be suitably employed for the synthesis of 2-substituted pyrrolidines.[4] Reaction of enolates obtained from pyrrolidin-2-ones with various electrophilic reagents represents a viable route to 3-alkylpyrrolidines.[5] A complementary strategy involves conjugate addition to *N*-substituted maleimides **1** followed by a reduction of the obtained succinimides **2** to give the pyrrolidine ring system **3** (Scheme 1). Common organometallic reagents give exclusively (alkynyllithium) or consistent amounts (Grignard reagents) of 1,2-addition products with maleimides **1**.[6] Better results in terms of regioselectivity can be obtained adding carbon centered radicals[7] or exploiting 'ene' reactions to compounds **1**.[8] In this context, among various sources of stabilized carbanions, nitroalkanes occupy a prominent position since it is known that their reaction with α,β-unsaturated derivatives affords only 1,4-adducts.[9] Furthermore, the relatively high acidity of the hydrogens in adjacent position to the nitro group (CH_3NO_2: pK_a=10) makes the generation of the corresponding nitronate anion fully compatible with a large array of other functionalities such as hydroxy and carbonyl groups.



Scheme 1.

2. Results and discussion

Several years ago, we observed that nitroalkanes **4** react with *N*-substituted maleimides **1** in the presence of DBU to afford the corresponding adducts **5** that suffer elimination of nitrous acid by the excess of the base employed giving the unsaturated derivative **6** in good yield (Scheme 2).[10]



Scheme 2.

Keywords: addition reactions; imides; nitro compounds; pyrrolidines; reduction.

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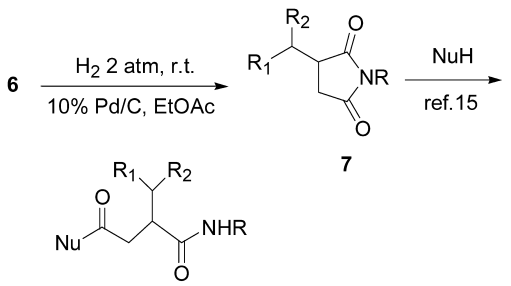


Scheme 3.

This reactivity is peculiar to enone systems and has been recently used for the synthesis of pyrroles,[11] furans,[12] cyclopentenones,[13] as well as 3-alkylidene pyrrolidines.[14]

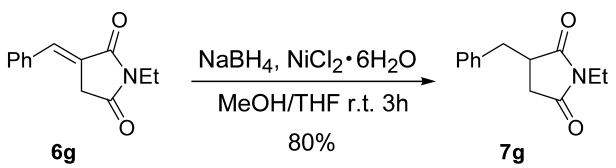
Reduction of the alkylidene moiety in compounds **6** allows the synthesis of 3-alkylsuccinimides **7**. These compounds are precursors of a wide range of functionalized open chain derivatives that can be obtained by nucleophilic ring opening reactions (Scheme 3).[15] Reduction of unsaturated succinimides **6** can be readily accomplished by catalytic hydrogenation in the presence of 10% Pd/C in very high yields (Table 1). Rather surprisingly, compound **6g** has been revealed practically inert towards these reductive conditions. Therefore, the double bond in compound **6g** has been reduced using the $NaBH_4/NiCl_2$ couple in 80% yield (Scheme 4).[16]

A large number of reducing agents are available in literature to carry out the conversion of cyclic imides into saturated nitrogen heterocycles.[17] $LiAlH_4$ is one of the most operationally simple reagents for this purpose. However, a preliminary test using succinimide **7d** revealed that $LiAlH_4$ in THF at reflux affords pyrrolidine **8d** and 3-pentyl-*N*-ethylpyrrole **9** in a 2:1 ratio (Scheme 5).

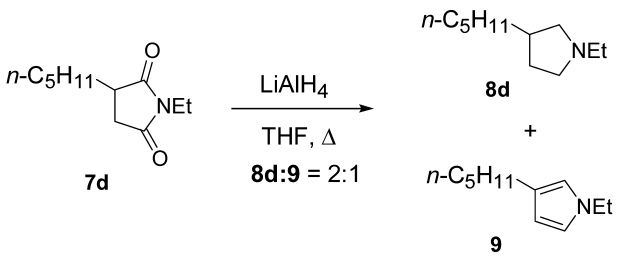
Table 1. Synthesis of 3-alkylsuccinimides **7**

Entry	Alkenylimide **6**		R	Alkylimide **7**, yield (%)[a]
	R_1	R_2		
a	CH_3	H	CH_3CH_2	95
b	CH_3CH_2	H	CH_3CH_2	98
c	$CH_3CH_2CH_2$	H	CH_3CH_2	96
d	$CH_3(CH_2)_2CH_2$	H	CH_3CH_2	99
e	$CH_3(CH_2)_3CH_2$	H	CH_3CH_2	97
f	$(CH_3)_2CH$	H	CH_3CH_2	96
g	Ph	H	CH_3CH_2	80[b]
h	$HO(CH_2)_4CH_2$	H	CH_3CH_2	98
i	CH_3	CH_3	CH_3CH_2	99
j	$-(CH_2)_5-$		CH_3CH_2	95
k	CH_3	H	Ph	94
l	$CH_3CH_2CH_2$	H	Ph	98
m	CH_3	CH_3	Ph	99

[a] Yields of pure, isolated products.
[b] Reduction has been carried out using $NaBH_4/NiCl_2$.

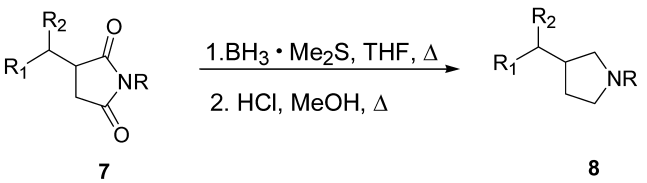


Scheme 4.



Scheme 5.

It is worth noting that the amount of pyrrole formed using borane reagents with compounds **7** is negligible even at reflux conditions. However, owing to the formation of an acid–base complex between boron and pyrrolidine nitrogen, strong hydrolytic conditions must be applied to the reaction mixture after reduction.



Scheme 6.

Table 2. Synthesis of 3-alkylpyrrolidines **8**

Entry	Alkylimide **7**	Alkylpyrrolidine **8**	Yield (%)[a]
1	**7a**	**8a**	63
2	**7b**	**8b**	67
3	**7c**	**8c**	72
4	**7d**	**8d**	78
5	**7e**	**8e**	83
6	**7f**	**8f**	76
7	**7 g**	**8 g**	81
8	**7 h**	**8 h**	73
9	**7i**	**8i**	70
10	**7j**	**8j**	80
11	**7k**	**8k**	85
12	**7l**	**8l**	79
13	**7m**	**8m**	77

[a] Yields of pure, isolated products.

3. Conclusions

Reaction of nitroalkanes to *N*-substituted maleimides affords 3-alkylidenesuccinimides **6** by a tandem conjugate addition–elimination process. Compounds **6** can be partially reduced to 3-alkyl derivatives **7** by catalytic hydrogenation. Further reduction of succinimides **7** with $BH_3{\cdot}Me_2S$ complex gives 3-alkylpyrrolidines **8** in good yield. This overall procedure provides a rapid entry to an important class of synthetic intermediates.

4. Experimental

4.1. General

^1H NMR were recorded at 300 MHz on a Varian VXR300 in $CDCl_3$ as solvent. ^{13}C NMR were recorded at 75 MHz in $CDCl_3$ as solvent. Microanalyses were performed with a CHNS-O analyzer Model EA 1108 from Fisons Instruments. IR spectra were recorded with a Perkin–Elmer Paragon 500 FT-IR. GLC analyses were performed on a Hewlett–Packard 5890 equipped with a capillary column of fused silica (0.32 mm×25 m), stationary phase SE54. Mass spectra were performed on a Hewlett–Packard GC/MS 5970 by means of the EI technique (70 eV). THF was dried by refluxing it over sodium wire then distilled. All chemicals used are available commercially. 3-Alkylidenesuccinimides **6** were prepared using a previously reported method.[10]

4.2. General procedure for the preparation of 3-alkylsuccinimides 7

3-Alkenylsuccinimide **6** (10 mmol) was dissolved in EtOAc (100 mL) and 10% Pd/C (0.2 g) was added. The suspension was hydrogenated at 2 atm at room temperature for 5 h and then filtered on a celite pad. The clear solution was evaporated at reduced pressure and the resulting alkylsuccinimides showed a purity >98% by glc analysis.

4.2.1. 1,3-Diethylpyrrolidin-2,5-dione, 7a. Yield 95%; oil; IR (cm^{-1}, neat) 1774, 1701, 1443, 1376; ^1H NMR δ (ppm) 1.08 (t, 3H, *J*=7.3 Hz), 1.16 (t, 3H, *J*=7.3 Hz), 1.60–1.85 (m, 1H), 1.95–2.15 (m, 1H), 2.50–2.70 (m, 1H), 2.89–3.11 (m, 2H), 3.55 (q, 2H, *J*=7.3 Hz). Anal. calcd for $C_8H_{13}NO_2$ (155.19) C, 61.91; H, 8.44; N, 9.03. Found C, 61.97; H, 8.48; N, 8.98.

4.2.2. 1-Ethyl-3-propylpyrrolidin-2,5-dione, 7b. Yield 98%; oil; IR (cm^{-1}, neat) 1774, 1701, 1443, 1376; ^1H NMR δ (ppm) 0.96 (t, 3H, *J*=7.3 Hz), 1.16 (t, 3H, *J*=7.3 Hz), 1.30–1.60 (m, 3H), 1.80–1.98 (m, 1H), 2.26–2.46 (m, 1H), 2.71–2.90 (m, 2H), 3.55 (q, 2H, *J*=7.3 Hz). Anal. calcd for $C_9H_{15}NO_2$ (169.22) C, 63.88; H, 8.93; N, 8.28. Found C, 63.82; H, 8.96; N, 8.24.

4.2.3. 3-Butyl-1-ethylpyrrolidin-2,5-dione, 7c. Yield 96%; oil; IR (cm^{-1}, neat) 1774, 1701, 1443, 1376; ^1H NMR δ (ppm) 0.92 (t, 3H, *J*=7.0 Hz), 1.15 (t, 3H, *J*=7.3 Hz), 1.30–1.60 (m, 4H), 1.80–2.00 (m, 2H), 2.25–2.47 (m, 1H), 2.69–2.90 (m, 2H), 3.55 (q, 2H, *J*=7.3 Hz). Anal. calcd for $C_{10}H_{17}NO_2$ (183.25) C, 65.54; H, 9.35; N, 7.64. Found C, 65.51; H, 9.38; N, 7.62.

4.2.4. 1-Ethyl-3-pentylpyrrolidin-2,5-dione, 7d. Yield 99%; oil; IR (cm^{-1}, neat) 1774, 1701, 1443, 1376; ^1H NMR δ (ppm) 0.81 (t, 3H, *J*=7.3 Hz), 1.08 (t, 3H, *J*=7.3 Hz), 1.18–1.48 (m, 7H), 1.76–1.90 (m, 1H), 2.22–2.36 (m, 1H), 2.64–2.80 (m, 2H), 3.46 (q, 2H, *J*=7.3 Hz). Anal. calcd for $C_{11}H_{19}NO_2$ (197.87) C, 66.97; H, 9.71; N, 7.10. Found C, 66.93; H, 9.73; N, 7.12.

4.2.5. 1-Ethyl-3-hexylpyrrolidin-2,5-dione, 7e. Yield 97%; oil; IR (cm^{-1}, neat) 1774, 1700, 1443, 1376; ^1H NMR δ (ppm) 0.85 (t, 3H, *J*=7.0 Hz), 1.12 (t, 3H, *J*=7.3 Hz), 1.20–1.36 (m, 7H), 1.38–1.54 (m, 2H), 1.80–1.93 (m, 1H), 2.26–2.40 (m, 1H), 2.68–2.83 (m, 2H), 3.51 (q, 2H, *J*=7.3 Hz). Anal. calcd for $C_{12}H_{21}NO_2$ (211.30) C, 68.21; H, 10.02; N, 6.63. Found C, 68.25; H, 10.04; N, 6.60.

4.2.6. 1-Ethyl-3-(2-methylpropyl)pyrrolidin-2,5-dione, 7f. Yield 96%; oil; IR (cm^{-1}, neat) 1774, 1701, 1443, 1376; ^1H NMR δ (ppm) 0.93 (d, 3H, *J*=6.2 Hz), 0.97 (d, 3H, *J*=6.2 Hz) 1.17 (t, 3H, *J*=7.3 Hz), 1.25–1.42 (m, 1H), 1.65–1.90 (m, 2H), 2.25–2.44 (m, 1H), 2.73–2.92 (m, 2H), 3.55 (q, 2H, *J*=7.3 Hz). Anal. calcd for $C_{10}H_{17}NO_2$ (183.25) C, 65.54; H, 9.35; N, 7.64. Found C, 65.58; H, 9.36; N, 7.63.

4.2.7. 1-Ethyl-3-(5-hydroxyhexyl)pyrroldin-2,5-dione, 7h. Yield 98%; oil; IR (cm^{-1}, neat) 1774, 1701, 1443, 1376; ^1H NMR δ (ppm) 1.12 (t, 3H, *J*=6.2 Hz), 1.28–1.41 (m, 5H), 1.42–1.58 (m, 4H), 1.80–1.94 (m, 1H), 2.25–2.39 (m, 2H), 2.68–2.84 (m, 2H), 3.51 (q, 2H, *J*=7.3 Hz), 3.61 (t, 2H, *J*=6.6 Hz). Anal. calcd for $C_{12}H_{21}NO_3$ (287.30) C, 63.41; H, 9.31; N, 6.16. Found C, 63.38; H, 9.34; N, 6.13.

4.2.8. 1-Ethyl-3-(1-methylethyl)pyrrolidin-2,5-dione, 7i.[10b] Yield 99%; oil; IR (cm^{-1}, neat) 1774, 1701, 1443, 1376; ^1H NMR δ (ppm) 1.01 (d, 3H, *J*=6.6 Hz), 1.09 (d, 3H, *J*=6.9 Hz), 1.12 (t, 3H, *J*=7.3 Hz), 2.36–2.54 (m, 1H), 2.58–2.71 (m, 1H), 2.81–2.88 (m, 1H), 2.95–3.04 (m, 1H), 3.55 (q, 2H, *J*=7.3 Hz). Anal. calcd for $C_9H_{15}NO_2$ (169.22) C, 63.88; H, 8.93; N, 8.28. Found C, 63.93; H, 8.95; N, 8.25.

4.2.9. 3-Cyclohexyl-1-ethylpyrrolidin-2,5-dione, 7j. Yield 95%; oil; IR (cm^{-1}, neat) 1774, 1701, 1443, 1376; ^1H NMR δ (ppm) 1.00–1.50 (m, 6H), 1.15 (t, 3H, *J*=7.3 Hz), 1.60–1.85 (m, 4H), 1.85–2.05 (m, 1H), 2.40–2.80 (m, 3H), 3.55 (q, 2H, *J*=7.3 Hz). Anal. calcd for $C_{12}H_{19}NO_2$ (209.28) C, 68.87; H, 9.15; N, 6.69. Found C, 68.83; H, 9.18; N, 6.71.

4.2.10. 3-Ethyl-1-phenylpyrrolidin-2,5-dione, 7k. Yield 95%; oil; IR (cm^{-1}, neat) 1774, 1701, 1443, 1376; ^1H NMR δ (ppm) 1.08 (t, 3H, *J*=7.3 Hz), 1.60–1.85 (m, 1H), 1.95–2.15 (m, 1H), 2.50–2.70 (m, 1H), 2.89–3.11 (m, 2H), 7.24–7.60 (m, 5H). Anal. calcd for $C_{12}H_{13}NO_2$ (203.24) C, 70.92; H, 6.45; N, 6.89. Found C, 70.88; H, 6.47; N, 6.91.

4.2.11. 3-Butyl-1-phenylpyrrolidin-2,5-dione, 7l. Yield 98%; oil; IR (cm^{-1}, neat) 1774, 1701, 1443, 1376; ^1H NMR δ (ppm) 0.97 (t, 3H, *J*=7.0 Hz), 1.34–1.48 (m, 4H), 1.56–1.80 (m, 1H), 1.94–2.12 (m, 1H), 2.50–2.70 (m, 1H), 2.90–3.12 (m, 2H), 7.28–7.55 (m, 5H). Anal. calcd for

$C_{14}H_{17}NO_2$ (231.29) C, 72.70; H, 7.41; N, 6.06. Found C, 72.75; H, 7.40; N, 6.09.

4.2.12. 3-(1-Methylethyl)-1-phenylpyrrolidin-2,5-dione, 7m. Yield 99%; oil; IR (cm^{-1}, neat) 1774, 1701, 1443, 1376; ^1H NMR δ (ppm) 1.01 (d, 3H, J=6.6 Hz), 1.09 (d, 3H, J=6.9 Hz), 2.36–2.54 (m, 1H), 2.58–2.71 (m, 1H), 2.81–2.88 (m, 1H), 2.95–3.04 (m, 1H), 7.25–7.55 (m, 5H). Anal. calcd for $C_{13}H_{15}NO_2$ (217.26) C, 71.87; H, 6.96; N, 6.45. Found C, 71.91; H, 6.99; N, 6.43.

4.2.13. 1-Ethyl-3-phenylmethylpyrrolidin-2,5-dione, 7g. Alkenylimide **6g** (2 mmol) was added to a solution of $NiCl_2{\cdot}6H_2O$ (3.32 g) in MeOH–THF (3:1, 65 mL). The mixture was cooled at 0°C by ice bath and then $NaBH_4$ (40 mmol, 1.52 g) was added portionwise over 30 min. The black slurry was stirred at room temperature for 4 h and then filtered over a short pad of Florisil®. The Florisil® pad was washed with CH_2Cl_2 (3×10 mL) and then the collected solutions were evaporated at reduced pressure. The crude alkylimide **7g** was purified by column chromatography (8:2 hexanes–ethyl acetate) giving 0.35 g (80%) of pure product as an oil. IR (cm^{-1}, neat) 1774, 1701, 1443, 1376; ^1H NMR δ (ppm) 1.12 (t, 3H, J=7.3 Hz), 2.37–2.51 (m, 1H), 2.62–2.72 (m, 1H), 2.84–2.98 (m, 1H), 3.06–3.28 (m, 2H), 3.57 (q, 2H, J=7.3 Hz), 7.15–7.40 (m, 5H). Anal. calcd for $C_{13}H_{15}NO_2$ (217.26) C, 71.87; H, 6.96; N, 6.45. Found C, 71.90; H, 6.99; N, 6.47.

4.3. General procedure for the preparation of 3-alkylpyrrolidines 8

Succinimide **7** (5 mmol) was dissolved in dry THF (70 mL), and the solution was cooled at 0°C by ice bath. $BH_3{\cdot}Me_2S$ (25 mmol, 2.5 mL, 10 M in THF) was then added dropwise over 30 min and after removal of the cooling bath the mixture was refluxed for 3 h. The reaction mixture was then cooled at room temperature and the excess of BH_3 was eliminated by dropwise addition of MeOH (10 mL). After removal of the solvent at reduced pressure the residue was dissolved in MeOH (25 mL) and then 37% HCl (5 mL) was added. The mixture was refluxed for 3 h and the solvent was then evaporated at reduced pressure. The crude pyrrolidine hydrochloride was dissolved in 4N NaOH (15 mL) and the resulting solution was saturated with NaCl. The solution was extracted with CH_2Cl_2 (3×20 mL) and dried over Na_2SO_4. After evaporation of the solvent at reduced pressure the crude pyrrolidine was purified by column chromatography (8:4:1:0.1 hexane–ethyl acetate–ethanol–38% NH_4OH).

4.3.1. 1,3-Diethylpyrrolidine, 8a. Yield 63%; oil; ^1H NMR δ (ppm) 1.00 (t, 3H, J=7.3 Hz), 1.11 (t, 3H, J=7.3 Hz), 1.20–1.30 (m, 2H), 1.62–1.90 (m, 3H), 2.29–2.57 (m, 4H), 2.64–2.91 (m, 2H). ^{13}C NMR δ (ppm) 11.5, 12.2, 25.5, 32.1, 44.8, 47.7, 52.5, 61.5. MS m/z (%): 127 (M^+, 22), 126 (23), 112 (100), 82 (8), 71 (19), 55 (10), 42 (18), 29 (4). Anal. calcd for $C_8H_{17}N$ (127.23) C, 75.52; H, 13.47; N, 11.01. Found C, 75.47; H, 13.50; N, 11.04.

4.3.2. 1-Ethyl-3-propylpyrrolidine, 8b. Yield 67%; oil; ^1H NMR δ (ppm) 0.90 (t, 3H, J=7.0 Hz), 1.11 (t, 3H, J=7.3 Hz), 1.24–1.46 (m, 4H), 1.64–2.00 (m, 3H), 2.30–2.58 (m, 4H), 2.65–2.92 (m, 2H). ^{13}C NMR δ (ppm) 12.2, 13.8, 20.7, 33.5, 34.5, 43.1, 48.2, 52.9, 62.9. MS m/z (%): 141 (M^+, 15), 140 (18), 126 (100), 71 (25), 55 (16), 42 (16), 29 (5). Anal. calcd for $C_9H_{19}N$ (141.25) C, 76.53; H, 13.56; N, 9.92. Found C, 76.48; H, 13.53; N, 9.95.

4.3.3. 3-Butyl-1-ethylpyrrolidine, 8c. Yield 72%; oil; ^1H NMR δ (ppm) 0.90 (t, 3H, J=6.6 Hz), 1.11 (t, 3H, J=7.3 Hz), 1.20–1.43 (m, 6H), 1.90–2.20 (m, 3H), 2.26–2.56 (m, 4H), 2.64–2.90 (m, 2H). ^{13}C NMR δ (ppm) 12.2, 14.0, 22.5, 29.6, 30.1, 33.3, 43.1, 47.9, 52.8, 62.6. MS m/z (%): 155 (M^+, 14), 154 (15), 140 (100), 126 (8), 98 (8), 82 (15), 71 (24), 55 (18), 42 (21), 29 (11). Anal. calcd for $C_{10}H_{21}N$ (155.28) C, 77.35; H, 13.63; N, 9.03. Found C, 77.40; H, 13.59; N, 9.00.

4.3.4. 1-Ethyl-3-pentylpyrrolidine, 8d. Yield 78%; oil; ^1H NMR δ (ppm) 0.90 (t, 3H, J=6.2 Hz), 1.11 (t, 3H, J=7.3 Hz), 1.20–1.46 (m, 9H), 1.70–2.24 (m, 2H), 2.28–2.58 (m, 4H), 2.65–2.79 (m, 1H), 2.80–2.91 (m, 1H). ^{13}C NMR δ (ppm) 12.2, 14.1, 22.7, 28.5, 29.4, 31.0, 33.2, 41.7, 47.9, 52.3, 62.5. MS m/z (%): 169 (M^+, 14), 168 (15), 154 (100), 140 (12), 98 (6), 82 (13), 71 (20), 58 (14), 42 (14), 29 (8). Anal. calcd for $C_{11}H_{23}N$ (169.31) C, 78.03; H, 13.69; N, 8.27. Found C, 77.99; H, 13.72; N, 8.24.

4.3.5. 1-Ethyl-3-hexylpyrrolidine, 8e. Yield 83%; ^1H NMR δ (ppm) 0.90 (t, 3H, J=6.2 Hz), 1.11 (t, 3H, J=7.3 Hz), 1.22–1.45 (m, 11H), 1.80–2.20 (m, 2H), 2.28–2.56 (m, 4H), 2.64–2.89 (m, 2H). ^{13}C NMR δ (ppm) 12.2, 14.1, 22.7, 26.9, 29.1, 30.3, 31.9, 32.9, 43.1, 47.9, 52.3, 62.3. MS m/z (%): 183 (M^+, 13), 184 (14), 168 (100), 154 (9), 126 (4), 98 (6), 82 (10), 71 (17), 58 (14), 29 (5). Anal. calcd for $C_{12}H_{25}N$ (183.33) C, 78.62; H, 13.74; N, 7.64. Found C, 78.57; H, 13.71; N, 7.66.

4.3.6. 1-Ethyl-3-(2-methylpropyl)pyrrolidine, 8f. Yield 76%; oil; ^1H NMR δ (ppm) 0.88 (d, 3H, J=6.6 Hz), 0.89 (d, 3H, J=6.6 Hz), 1.11 (t, 3H, J=7.3 Hz), 1.65–1.80 (m, 4H), 1.85–1.95 (m, 2H), 2.25–2.54 (m, 4H), 2.68–2.79 (m, 2H). ^{13}C NMR δ (ppm) 12.2, 22.3, 22.5, 27.9, 33.7, 40.3, 41.2, 47.9, 52.7, 63.0. MS m/z (%): 155 (M^+, 20), 154 (17), 140 (100), 112 (5), 96 (7), 71 (22), 58 (25), 42 (14), 29 (5). Anal. calcd for $C_{10}H_{21}N$ (155.28) C, 77.35; H, 13.63; N, 9.03. Found C, 77.31; H, 13.60; N, 9.05.

4.3.7. 1-Ethyl-3-phenylmethylpyrrolidine, 8g. Yield 81%; oil; ^1H NMR δ (ppm) 1.07 (t, 3H, J=7.3 Hz), 1.42–1.54 (m, 1H), 1.88–2.01 (m, 1H), 2.15–2.30 (m, 1H), 2.37–2.54 (m, 4H), 2.59–2.73 (m, 4H), 7.12–7.28 (m, 5H). ^{13}C NMR δ (ppm) 14.1, 30.7, 39.0, 41.8, 50.6, 53.9, 60.0, 126.0, 128.4, 128.9, 141.2. MS m/z (%): 189 (M^+, 33), 188 (28), 174 (100), 131 (24), 111 (14), 97 (47), 91 (42), 82 (25), 71 (20), 65 (16), 42 (19). Anal. calcd for $C_{13}H_{19}N$ (189.30) C, 82.48; H, 10.12; N, 7.40. Found C, 82.43; H, 10.15; N, 7.38.

4.3.8. 1-Ethyl-3-(5-hydroxyhexyl)pyrrolidine, 8h. Yield 73%; ^1H NMR δ (ppm) 1.06 (t, 3H, J=7.3 Hz), 1.20–1.40 (m, 10H), 1.46–1.57 (m, 2H), 1.62–1.53 (m, 1H), 1.79–2.14 (m, 2H), 2.20 (bs, 1H), 2.27–2.50 (m, 2H), 2.61–2.71 (m, 1H), 2.76–2.83 (m, 1H), 3.58 (t, 2H, J=6.7 Hz). ^{13}C NMR δ (ppm) 13.5, 25.5, 28.1, 29.2, 30.5, 32.5, 35.3, 37.1,

50.2, 53.4, 60.0, 62.5. MS *m/z* (%): 199 (M^+, 9), 198 (15), 184 (100), 140 (12), 100 (39), 71 (34), 58 (31), 43 (37), 44 (37), 32 (44). Anal. calcd for $C_{12}H_{25}NO$ (199.33) C, 72.31; H, 12.64; N, 7.03. Found C, 72.29; H, 12.61; N, 7.00.

4.3.9. 1-Ethyl-3-(1-methylethyl)pyrrolidine, 8i. Yield 70%; oil; ^{1}H NMR δ (ppm) 1.00 (d, 6H, J=6.2 Hz), 1.11 (t, 3H, J=7.3 Hz), 1.50–1.75 (m, 2H), 1.87–2.06 (m, 1H), 2.08–2.23 (m, 1H), 2.30–2.58 (m, 4H), 2.65–2.92 (m, 2H). ^{13}C NMR δ (ppm) 12.2, 18.6, 20.6, 26.8, 31.1, 32.1, 48.0, 53.3, 59.8. MS *m/z* (%): 141 (M^+, 20), 140 (20), 126 (100), 83 (12), 71 (18), 55 (11), 42 (11), 29 (4). Anal. calcd for $C_9H_{19}N$ (141.25) C, 76.53; H, 13.56; N, 9.92. Found C, 76.59; H, 13.59; N, 9.89.

4.3.10. 3-Cyclohexyl-1-ethylpyrrolidine, 8j. Yield 85%; oil; ^{1}H NMR δ (ppm) 1.07 (t, 3H, J=7.3 Hz), 1.55–1.95 (m, 14H), 1.99–2.10 (m, 1H), 2.20–2.52 (m, 3H), 2.70–2.86 (m, 2H). ^{13}C NMR δ (ppm) 13.6, 26.2, 28.6, 30.0, 31.7, 32.0, 44.9, 50.5, 53.6, 58.4, 61.8. MS *m/z* (%): 181 (M^+, 17), 180 (16), 166 (100), 98 (5), 81 (13), 71 (20), 58 (17), 41 (10). Anal. calcd for $C_{12}H_{23}N$ (181.32) C, 79.49; H, 12.79; N, 7.72. Found C, 79.45; H, 12.82; N, 7.75.

4.3.11. 3-Ethyl-1-phenylpyrrolidine, 8k. Yield 85%; oil; ^{1}H NMR δ (ppm) 0.98 (t, 3H, J=7.5 Hz), 1.42–1.70 (m, 3H), 2.09–2.28 (m, 2H), 2.86–2.92 (m, 1H), 3.22–3.47 (m, 3H), 6.50–6.68 (m, 3H), 7.18–7.27 (m, 2H). ^{13}C NMR δ (ppm) 12.8, 26.8, 31.4, 40.6, 47.5, 53.3, 111.4, 115.27, 129.12, 148.0. MS *m/z* (%): 175 (M^+, 68), 174 (68), 144 (9), 119 (33), 104 (30), 91 (100), 77 (44), 51 (13), 41 (9). Anal. calcd for $C_{12}H_{17}N$ (175.27) C, 82.23; H, 9.78; N, 7.99. Found C, 82.18; H, 9.82; N, 8.03.

4.3.12. 3-Butyl-1-phenylpyrrolidine, 8l.[19] Yield 79%; oil; ^{1}H NMR δ (ppm) 0.92 (t, 3H, J=6.2 Hz), 1.25–1.58 (m, 4H), 1.62–1.97 (m, 3H), 2.12–2.40 (m, 2H), 2.90–3.06 (m, 1H), 3.33–3.60 (m, 3H), 6.50–6.68 (m, 3H), 7.18–7.27 (m, 2H). ^{13}C NMR δ (ppm) 14.0, 22.5, 29.9, 30.4, 34.6, 44.3, 47.5, 54.3, 111.5, 115.4, 129.1, 148.0. MS *m/z* (%): 203 (M^+, 88), 202 (72), 144 (16), 119 (38), 106 (57), 91 (100), 77 (42), 55 (12), 41 (12), 29 (10). Anal. calcd for $C_{14}H_{21}N$ (203.32) C, 82.70; H, 10.41; N, 6.89. Found C, 82.65; H, 10.38; N, 6.86.

4.3.13. 3-(1-Methylethyl)-1-phenylpyrrolidine, 8m. Yield 77%; waxy solid; ^{1}H NMR δ (ppm) 1.00 (d, 6H, J=6.2 Hz), 1.50–1.75 (m, 2H), 1.87–2.06 (m, 1H), 2.08–2.23 (m, 1H), 2.90–3.00 (m, 1H), 3.22–3.50 (m, 3H), 6.50–6.68 (m, 3H), 7.18–7.27 (m, 2H). ^{13}C NMR δ (ppm) 21.4, 21.8, 30.5, 32.7, 46.7, 48.1, 52.5, 112.5, 115.4, 129.3, 148.1. MS *m/z* (%): 189 (M^+, 67), 188 (56), 146 (12), 119 (36), 104 (31), 91 (100), 77 (46), 51 (11), 41 (16). Anal. calcd for $C_{13}H_{19}N$ (189.30) C, 82.48; H, 10.12; N, 7.40. Found C, 82.51; H, 10.08; N, 7.38.

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