Novel Tandem Cyclizations/Reaction with Electrophiles of α-Aminoalkyl Radicals

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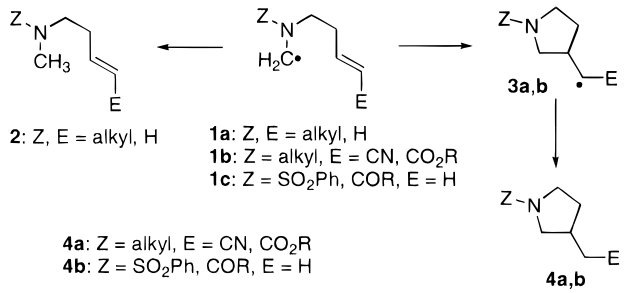
Construction of carbon−carbon bonds adjacent to nitrogen is of great importance for the synthesis of many nitrogen-containing compounds of biological significance, including interalia alkaloids and amino acids. Such carbon−carbon bond formation usually occurs via one of three different types of intermediates: (i) iminium ions,[1] (ii) α-amino-substituted carbanions,[2] and (iii) α-amino-substituted radicals.[3]

Regarding the last of these routes, electron-rich α-aminoalkyl radicals (**1a**,**b**, Scheme 1), which are strongly nucleophilic, react readily with electron-deficient C=C bonds (e.g., formation of products **4a**).[3,4,5b] However, attempted intramolecular additions of nonstabilized α-amino radicals (**1a**) to unactivated C=C bonds (Scheme 1) mostly give reduction products **2**[5] or very low yields of cyclization products[4a,6a] (for an exception see ref 6b). By contrast, α-amino radicals (**1c**) with stabilizing groups (e.g., acyl,[7] sulfonyl[5a,6]) or a quaternized[8] nitrogen undergo intramolecular cyclization to unactivated C=C bonds (Scheme 1).

The cyclization of an α-aminoalkyl radical onto an unactivated C=C bond is difficult due to (i) partial loss of the stabilization provided to the radical by the amino substituent in the transition state leading to cyclization, (ii) the nucleophilic nature of the radical, and (iii) the tendency for dimerization of the α-aminoalkyl radical. However, the previously reported[4a,6] formation of small amounts of the cyclized products and the dependence of the cyclization stereochemistry on the stability of the α-amino radical[5b] suggested to us that an equilibrium exists between the acyclic radical and the cyclized one (cf. **7** ↔ **8**, Scheme 2). Normally, the acyclic radical undergoes reduction[3,5] or dimerization.[5b,9] We reasoned that an additional driving force, such as the rapid reduction of the cyclized radical to the corresponding organosamarium (cf. **8** → **9**), could favor the formation of cyclized products. As justification of these speculations, we now report a novel reaction sequence comprising site specific formation of an α-aminoalkyl radical, regioselective addition of this radical to an unactivated double bond, further reduction to a carbanion, and finally carbanion trapping by an electrophile.[10]

N-(α-Aminobutyl)benzotriazole (**6a**) was prepared from the condensation of a secondary amine **5**,[11] butyraldehyde, and benzotriazole (Scheme 2). Crude **6a** was treated directly with samarium diiodide in THF−HMPA

Scheme 1

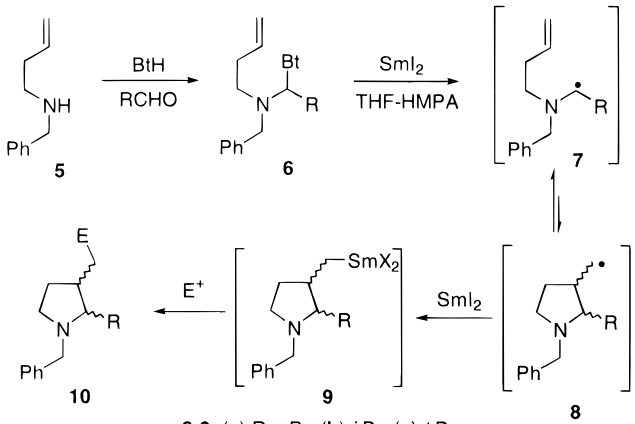


2: Z, E = alkyl, H

1a: Z, E = alkyl, H
1b: Z = alkyl, E = CN, CO_2R
1c: Z = SO_2Ph, COR, E = H

4a: Z = alkyl, E = CN, CO_2R
4b: Z = SO_2Ph, COR, E = H

Scheme 2



6-**9**: (**a**) R = Pr, (**b**) *i*-Pr, (**c**) *t*-Bu
10: see Table 1

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Table 1. Sequential Reactions from 6 to 10

products **10**	R	electrophile	E	yield[a] (%)	cis/trans ratio[b] by GC by NMR
a	Pr	H_2O	H	58	2.6/1
b	Pr	MeOD	D	71	2.0/1
c	Pr	MeCOEt	MeC(OH)Et	60	2.4/1[c]
d	Pr	MeCOPr	MeC(OH)Pr	65	2.0/1[c]
e	Pr	EtCOEt	Et_2COH	46	2.2/1
f	Pr	$(CH_2)_5CO$	$(CH_2)_5COH$	53	2.3/1
f[d]	Pr	$(CH_2)_5CO$	$(CH_2)_5COH$	38	2.2/1
g	Pr	*i*-PrCHO	*i*-PrCHOH	41	5.8/1[c]
h	Pr	PhCHO	PhCHOH	43	4.1/1[c]
i	Pr	I_2	I	45	2.3/1
j	Pr	*i*-PrNCO	*i*-PrNHCO	37	2.5/1
k	*i*-Pr	H_2O	H	68	1.5/1
l	*i*-Pr	EtCOEt	Et_2CHOH	51	2.8/1
m	*t*-Bu	EtCOEt	Et_2CHOH	36	1/19.7
n[e]	*t*-Bu	EtCOEt	H	34	1/10.0

[a] Protonated pyrrolidines (**10a**,**n**, etc.) were always isolated with the expected products, sometimes in substantial amounts (e.g., 43% of **10a** with **10j**, 34% of **10n** with **10m**). [b] Determined by GC or ^{1}H NMR. [c] The ^{13}C spectra showed the presence of four isomers, but the GC separated only two peaks. [d] Benzotriazole substrate and cyclohexanone were added to SmI_2 solution simultaneously. [e] Obtained as a byproduct from the preparation of **10m**.

under argon to form, via radical intermediates **7a** and **8a**, carbanion **9a**, which was quenched by H_2O (Scheme 2). Pyrrolidine **10a** (Table 1) was isolated as a mixture of cis and trans isomers in 58% yield. When methyl alcohol-*d* was used as electrophile to trap carbanion **9a**, deuterium was incorporated to give *cis*- and *trans*-pyrrolidines **10b**. The cis and trans ratios (Table 1) were determined by GC or integration of the H-2 signals in the ^{1}H NMR spectrum. Ketones worked well in this sequence to form pyrrolidines **10c**−**f** in 38−65% yields, even when the ketone was added together with **6** to SmI_2 (Table 1). Symmetrical ketones gave mixtures of cis and trans isomers (Table 1). Unsymmetrical ketones formed four isomers for **10c** and **10d**: GC separated only the cis and trans forms, but the presence of the additional chiral center in the side chain was obvious from the ^{13}C spectra, which showed the presence of all four isomers. This general stepwise procedure was utilized with other electrophiles: aliphatic and aromatic aldehydes gave **10g** and **10h** (each as four isomers), iodine gave **10i**, and isopropyl isocyanate formed pyrrolidines **10j** in moderate yields (Table 1).

The yields reported in Table 1 are based on the amount of starting amine **5** used and are, therefore, overall yields for a two-pot, three-step process (a small amount of amine **5** was usually detected by NMR in crude benzotriazole derivatives **6**). The formation of **10b**−**j** was always accompanied by compound **10a** (ca. 10−43%), probably arising from protonation by traces of adventitious water of the intermediate organosamarium reagent **9** before it could be trapped by the electrophile; similar speculations have been proposed by Molander and Harris.[12] Alternatively, it could be the result of competitive enolization by the intermediate organosamarium, especially when aliphatic ketones were used. The cis derivative predominated in products **10a**−**j**. The cis:trans ratios for compounds **10a**−**f**,**i**,**j** were ca. 2:1, while those for pyrrolidines **10g**,**h** derived from aldehydes were higher at 4:1 and 6:1. The assignment of a cis stereochemistry for the major cyclized product followed from the observation that for the major isomers of **10a**−**j** C-2 and C-3 were shielded in the ^{13}C NMR spectrum when compared with the corresponding resonances of the minor isomers.[4a,13]

The introduction of larger isopropyl or *tert*-butyl groups at C-2 resulted in almost no difference in diastereoselectivity for the former (Table 1, 2.8:1 for **10l**, similar to compound **10e**) but a large increase for the latter (19.7:1 for **10m**). However the sense of the diastereoselection changed dramatically in the case of the *tert*-butyl group as the trans isomer was now found to predominate. The reaction also afforded significant amounts of byproduct **10n**, the result of protonation with high stereoselectivity (10:1) of a carbanionic intermediate **9** found in the second stage of the reaction. The trans stereochemistry in the major isomer **10n** was indicated by its downfield shifted C-2 when compared with the minor isomer; compound **10m** should possess the same stereochemistry of **10n** for mechanistic reasons (vide infra). The low yield obtained for **10m**, as well as the changes in the sense and amount of diastereoselectivity, should obviously be attributed to steric hindrance factors that render the formation of the normally preferred cis isomer a slow process. Thus, the generally preferred cis stereochemistry in products **10** was expected on the basis of Beckwith's model for radical ring closures,[14] and the only moderate diastereoselectivity observed for small R groups is in line with previous results obtained with the hex-5-enyl radical.[14] This relatively low stereoselectivity is in contrast to that found in related α-aminoalkyl radical ring closures leading to cyclopentylamines, which are much more selective.[4a] In this latter case, the *cis*-TS benefits additionally from a secondary stabilizing orbital interaction between SOMO and LUMO p-type orbitals that cannot take place during formation of pyrrolidines due to the endocyclic nature of the N−C bond throughout cyclization. For R = *t*-Bu, however, the greater steric congestion associated to the *cis*-TS overwhelms the normal stereoelectronic factors that usually favor cis products and high trans selectivity results.[15]

Two possible intermediates, a radical or a carbanion, could be involved in the cyclization step. Previously, we showed that *N*-(α-aminomethyl)benzotriazoles are easily transformed into the corresponding nonstabilized α-aminocarbanions by treatment with SmI_2.[16] However, when the NCH_2Bt methylene group carries an alkyl or aryl group substituent (e.g., compound **6**), the corresponding radical is more stable and cannot be further reduced by SmI_2;[17] rather, hydrogen transfer or dimerization is observed.[16] This appears to exclude the possibility of a carbanion cyclization in the present reaction, and we believe that the radical was the active intermediate in our new reactions. The whole process comprises the formation of an α-aminoalkyl radical **7**, addition of **7** to the C=C bond to generate the primary pyrrolidin-3-ylmethyl radical **8**, the reduction of **8** by SmI_2 to carban-

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(17) Secondary carbanions can be prepared from *N*-(α-aminoalkyl)-benzotriazoles by using the more powerful reducing agent Li/LiBr; see ref 16.

ion **9**, and the quenching of carbanion **9** by an electrophile to afford as final product pyrrolidine **10**.

In conclusion, we now report the tandem cyclization of α-aminoalkyl radicals, which provides a new strategy for the synthesis of pyrrolidines[18] with a functional group at C-3. The new reaction enlarges the synthetic potential of α-aminoalkyl radicals and suggests its potential scope in the preparation of alkaloids and other nitrogen-containing heterocycles.

Experimental Section

General Comments. Melting points were determined on a hot stage apparatus without correction. ^{1}H (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded in $CDCl_3$ with TMS, respectively, as the internal reference. Elemental analyses and high-resolution mass spectra were performed within the department. Column chromatography was carried out on MCB silica gel (200−425 mesh). Tetrahydrofuran (THF) was freshly distilled from sodium benzophenone. The commercial HMPA was used as received.

General Procedures for the Preparation of Pyrrolidines 10. A mixture of *N*-benzyl-*N*-but-3-en-1-ylamine (**5**, 2 mmol), butyraldehyde (3 mmol), and benzotriazole (3 mmol) in dry benzene (8 mL) was refluxed for 90 min with azeotropic separation of water. The reaction mixture was washed with aqueous Na_2CO_3 and vacuum-dried for 2 h to give crude **6**, which was dissolved in THF (20 mL) and added to SmI_2/THF−HMPA solution (60 mL 0.1 N SmI_2 in THF, 6 mL HMPA) at 0 °C over 30 min. The mixture was stirred for an additional 10 min, and then the appropriate electrophile (4 mmol) was added. The mixture was stirred overnight. Water was added to quench the reaction, followed by ether extraction. The residue, after solvent evaporation, was purified by column chromatography on silica gel (saturated with Et_3N, hexanes−EtOAc−Et_3N as eluent) to give the title compound.

***N*-Benzyl-2-propyl-3-methylpyrrolidine (10a):** obtained as a mixture of diastereoisomers; colorless oil; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.94−1.05 (m, 6H), 1.22−1.58 (m) and 2.35−2.42 (m, cis) (total 5H), 1.81−1.99 (m, 2H), 2.07−2.26 (m, 2H), 2.89−2.97 (ddd, J = 3.5, 8.1, 11.6 Hz, cis) and 2.81−2.87 (m, trans) (total 1H), 3.22 (d, J = 13.2 Hz, cis) and 3.14 (d, J = 12.9 Hz, trans) (total 1H), 4.05 (d, J = 13.2 Hz, cis) and 4.03 (d, J = 12.9 Hz, trans) (total 1H), 7.20−7.37 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.6, 14.7, 15.9, 18.6, 19.9, 20.5, 31.3, 31.5, 31.8, 34.4, 35.0, 37.3, 52.4, 52.7, 58.9, 66.6, 71.9, 126.4, 126.5, 127.9, 128.0, 128.6, 128.7, 139.9, 140.2; IR ($CHCl_3$) ν 2960, 2930, 2880, 2780, 1490, 1450, 1370, 1140, 1070, 1025, 910, 730, 700 cm^{-1}; LRMS (EI) *m*/*z* 216 (M^+), 174 (91), 91 (100); HRMS calcd for $C_{15}H_{23}N$ 216.1752, found 216.1751.

***N*-Benzyl-2-propyl-3-(methyl-*d*)pyrrolidine (10b):** obtained as a mixture of diastereoisomers; colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.80−1.09 (m, 5H), 1.15−2.45 (m, 9H), 2.75−2.98 (m, 1H), 3.12 (d, J = 12.9 Hz) and 3.20 (d, J = 13.2 Hz) (total 1H), 4.01 (d, J = 12.9 Hz) and 4.02 (d, J = 13.3 Hz) (total 1H), 7.12−7.42 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.7, 14.8, 15.4, 15.7, 16.0, 18.7, 20.0, 20.3, 20.6, 31.4, 31.5, 31.8, 34.4, 34.5, 35.1, 37.3, 37.4, 52.5, 52.8, 58.9, 59.0, 66.7, 72.0, 126.5, 126.6, 128.0, 128.1, 128.7, 128.8, 140.0, 140.3.

***N*-Benzyl-2-propyl-3-(2-hydroxy-2-methylbutyl)pyrrolidine (10c):** obtained as a mixture of four isomers; colorless oil; ^{1}H NMR (one single isomer was enriched by column chromatography, $CDCl_3$, 300 MHz) δ 0.78−1.03 (m, 6H), 1.17 (s, 3H), 1.22−1.76 (m, 10H), 1.85−2.06 (m, 1H), 2.23 (q, 2H, J = 8.5 Hz), 2.54−2.66 (m, 1H), 2.71−2.96 (m, 1H), 3.37 (d, 1H, J = 13.0 Hz), 3.99 (d, 1H, J = 13.1 Hz), 7.15−7.43 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 8.4, 14.6, 20.0, 27.2, 31.5, 32.4, 35.0, 36.3, 40.6, 52.8, 60.2, 67.0, 73.2, 126.6, 128.1, 128.7, 140.1. Anal. Calcd for $C_{19}H_{31}NO$: C, 78.84; H, 10.79; N, 4.84. Found: C, 78.70; H, 11.19; N, 4.95.

***N*-Benzyl-2-propyl-3-(2-hydroxy-2-methylpentyl)pyrrolidine (10d):** obtained as a mixture of four isomers; colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.78−1.07 (m, 6H), 1.08−1.20 (m, 3H), 1.21−1.75 (m, 12H), 1.86−2.68 (m, 4H), 2.78−2.98 (m, 1H), 3.06 (d, J = 12.8 Hz) and 3.37 (d, J = 13.2 Hz) (total 1H), 3.99 (d, J = 13.0 Hz) and 4.01 (d, J = 12.6 Hz) (total 1H), 7.13−7.43 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.5, 14.6, 14.8, 17.0, 17.2, 17.3, 17.4, 18.1, 19.9, 20.0, 27.1, 27.2, 27.4, 27.8, 30.7, 31.0, 31.2, 31.4, 32.4, 33.8, 36.3, 36.5, 38.1, 38.3, 41.0, 44.9, 45.1, 45.2, 46.0, 46.8, 47.0, 52.8, 58.8, 60.1, 66.9, 67.0, 70.8, 70.9, 72.9, 73.0, 73.2, 126.6, 128.1, 128.7, 128.8, 139.8, 139.9, 140.0. Anal. Calcd for $C_{20}H_{33}NO$: C, 79.15; H, 10.96; N, 4.62. Found: C, 78.74; H, 11.26; N, 5.09.

***N*-Benzyl-2-propyl-3-(2-hydroxy-2-ethylbutyl)pyrrolidine (10e):** obtained as a mixture of diastereoisomers; colorless oil; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.84−1.04 (m, 9H), 1.20−1.68 (m) and 2.59−2.67 (m, cis) (total 12H), 1.87−2.03 (m, 2H), 2.04−2.30 (m, 2H), 2.82−2.94 (m, 1H), 3.40 (d, J = 13.1 Hz, cis) and 3.08 (d, J = 12.8 Hz, trans) (total 1H), 3.99 (d, J = 13.1 Hz, cis) and 4.02 (d, J = 12.8 Hz, trans) (total 1H), 7.19−7.37 (m, 5H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 7.6, 7.8, 8.1, 14.6, 14.8, 18.0, 20.0, 30.5, 31.0, 31.3, 31.5, 31.8, 32.5, 33.7, 36.0, 37.6, 43.3, 52.8, 52.9, 58.8, 60.3, 66.9, 70.9, 74.9, 75.0, 126.6, 126.7, 128.1, 128.7, 128.8, 139.8, 140.1; HRMS calcd for $C_{20}H_{33}NO$ 303.2562, found 303.2549.

***N*-Benzyl-2-propyl-3-[(1-hydroxycyclohexyl)methyl]pyrrolidine (10f):** obtained as a mixture of diastereoisomers; colorless oil; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.93−0.96 (m, 3H), 1.21−1.69 (m, 17H), 1.85−2.04 (m, 2H), 2.10−2.33 (m, 2H), 2.58 (m, 1H), 2.90 (ddd, J = 3.1, 7.9, 10.9 Hz, cis) and 2.84 (m, trans) (total 1H), 3.36 (d, J = 13.1 Hz, cis) and 3.08 (d, J = 12.8 Hz, trans) (total 1H), 4.00 (d, J = 13.1 Hz, cis) and 4.02 (d, J = 12.8 Hz, trans) (total 1H), 7.21−7.36 (m, 5H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 14.6, 14.8, 18.2, 19.9, 22.1, 22.2, 25.8, 31.0, 31.4, 32.3, 33.9, 35.7, 37.5, 37.6, 37.8, 38.1, 38.7, 41.9, 48.1, 52.7, 52.8, 58.8, 60.0, 67.0, 70.9, 71.6, 71.8, 126.6,126.7, 128.1, 128.7, 128.8, 139.8, 140.0; IR ($CHCl_3$) ν 3420, 2930, 2860, 2780, 1495, 1450, 1360, 1250, 1140, 1070, 1025, 970, 700 cm^{-1}; LRMS (EI) *m*/*z* 315 (M^+), 272 (100); HRMS calcd for $C_{21}H_{33}NO$ 315.2562, found 315.2569.

***N*-Benzyl-2-propyl-3-(2-hydroxy-3-methylbutyl)pyrrolidine (10g):** obtained as a mixture of four isomers; colorless oil; ^{1}H NMR (one single isomer was enriched by column chromatography, $CDCl_3$, 300 MHz) δ 0.75−1.10 (m, 9H), 1.10−1.75 (m, 9H), 1.81−1.96 (m, 1H), 2.10−2.20 (m, 1H), 2.22−2.47 (m, 1H), 2.48−2.59 (m, 1H), 2.86−2.97 (m, 1H), 3.26 (d, 1H, J = 13.2 Hz), 3.32−3.45 (m, 1H), 4.02 (d, 1H, J = 13.2 Hz), 7.17−7.43 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.6, 17.5, 18.8, 20.1, 29.0, 32.2, 34.3, 34.5, 36.6, 52.9, 59.5, 66.6, 74.9, 126.6, 128.1, 128.8, 140.0. Anal. Calcd for $C_{19}H_{31}NO$: C, 78.84; H, 10.79; N, 4.84. Found: C, 78.61; H, 11.14; N, 5.18.

***N*-Benzyl-2-propyl-3-(2-hydroxy-2-phenylethyl)pyrrolidine (10h):** obtained as a mixture of four isomers; colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.79−1.06 (m, 3H), 1.13−1.56 (m, 5H), 1.57−2.08 (m, 4H), 2.14 (q, 1H, J = 8.7 Hz), 2.32−2.60 (m, 2H), 2.81−3.05 (m, 1H), 3.03 (d, J = 12.4 Hz) and 3.25 (dd, J = 12.9 and 2.5 Hz) (total 1H), 4.00 (d, J = 13.1) and 4.27 (d, J = 12.4 Hz) (total 1H), 4.70 (dd, 1H, J = 8.9 and 2.3 Hz), 7.12−7.46 (m, 10H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.6, 19.9, 20.0, 25.0, 28.8, 29.8, 32.1, 36.9, 37.8, 39.6, 39.7, 52.6, 52.8, 58.2, 59.5, 66.4, 67.3, 70.1, 72.7, 125.6, 125.9, 126.6, 126.8, 127.1, 127.3, 128.1, 128.2, 128.3, 128.4, 128.7, 128.9, 138.2, 140.0, 145.7, 146.0. Anal. Calcd for $C_{22}H_{29}NO$: C, 81.69; H, 9.04; N, 4.33. Found: C, 81.28; H, 9.27; N, 4.75.

***N*-Benzyl-2-propyl-3-iodomethylpyrrolidine (10i):** obtained as a mixture of diastereoisomers; colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.78−1.08 (m, 3H), 1.20−1.78 (m, 5H), 1.88−2.08 (m, 1H), 2.10−2.35 (m, 2H), 2.44−2.70 (m, 2H), 2.77−3.04 (m, 1H), 3.05−3.46 (m, 2H), 3.97 (d, J = 12.9 Hz) and 3.99 (d, J = 13.2 Hz) (total 1H), 7.11−7.48 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 10.7, 14.5, 14.6, 18.6, 19.9, 30.7, 30.9, 31.3, 34.8, 44.1, 45.8, 51.8, 52.2, 58.6, 59.0, 67.0, 70.0, 126.7, 126.8, 128.1, 128.6, 128.7, 139.3, 139.6; HRMS calcd for $C_{15}H_{22}NI$ 343.0797, found 343.0796.

***N*-Benzyl-2-propyl-3-(isopropylcarbamoylmethyl)pyrrolidine (10j):** obtained as a mixture of diastereoisomers; white solid; mp 66−68 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.95 (t, 3H, J = 7.1 Hz), 1.08 (d, J = 6.6 Hz) and 1.13 (d, J = 6.5 Hz) (total 6H), 1.21−1.70 (m, 5H), 1.81−1.98 (m, 1H), 2.00−2.68 (m, 5H), 2.78−2.96 (m, 1H), 3.19 (d, 1H, J = 12.9 Hz), 3.93−4.18 (m, 1H), 4.03 (d, 1H, J = 13.3 Hz), 5.43 (d, J = 6.0 Hz) and 6.18 (d, J =

(18) For a recent survey of the synthesis of pyrrolidines, see: Denmark, S. E.; Marcin, L. R. *J. Org. Chem.* **1993**, *58*, 3857.

6.5 Hz) (total 1H), 7.15−7.38 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.5, 14.6, 18.4, 19.9, 22.7, 28.2, 29.1, 31.7, 34.7, 36.7, 37.6, 39.7, 41.0, 41.2, 42.4, 52.1, 52.7, 58.4, 58.8, 66.1, 69.3, 126.7, 128.1, 128.7, 128.8, 139.4, 170.9, 171.5. Anal. Calcd for $C_{19}H_{30}N_2O$: C, 75.45; H, 10.00; N, 9.26. Found: C, 75.07; H, 10.16; N, 9.47.

***N*-Benzyl-2-isopropyl-3-methylpyrrolidine (10k):** obtained as a mixture of diastereoisomers; colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.75−1.15 (m, 9H), 1.18−2.57 (m, 6H), 2.75−3.02 (m, 1H), 3.20 (d, J = 13.2 Hz) and 3.37 (d, J = 13.7 Hz) (total 1H), 4.00 (d, J = 13.5 Hz) and 4.04 (d, J = 13.5 Hz) (total 1H), 7.12−7.50 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 15.8, 16.9, 19.6, 19.9, 21.1, 22.6, 29.7, 29.9, 32.5, 32.8, 32.9, 36.4, 52.5, 53.3, 59.7, 61.9, 71.9, 77.6, 126.4, 126.5, 128.1, 128.3, 128.5, 140.8, 141.2. Anal. Calcd for $C_{15}H_{23}NO$: C, 82.89; H, 10.67; N, 6.44. Found: C, 82.83; H, 10.86; N, 7.02.

***N*-Benzyl-2-isopropyl-3-(2-hydroxy-2-ethylbutyl)pyrrolidine (10l):** obtained as a mixture of diastereoisomers; colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.71−0.92 (m, 6H), 0.93−1.15 (m, 6H), 1.17−1.32 (m, 1H), 1.35−1.65 (m, 7H), 1.66−1.95 (m, 2H), 2.08 (br s, 1H), 2.15−3.01 (m, 3H), 3.24 (d, J = 13.2 Hz) and 3.57 (d, J = 13.6 Hz) (total 1H), 3.99 (d, J = 13.2 Hz) and 4.09 (d, J = 13.6 Hz) (total 1H), 7.09−7.45 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 7.8, 7.9, 8.0, 8.1, 18.1, 18.5, 19.6, 22.3, 26.9, 30.5, 30.6, 31.0, 31.5, 31.6, 31.7, 33.4, 34.6, 37.3, 37.4, 45.3, 49.6, 52.9, 54.3, 60.3, 63.4, 71.5, 75.2, 75.4, 77.5, 126.4, 126.5, 127.6, 128.1, 128.2, 128.5, 130.8, 140.8, 141.2. Anal. Calcd for $C_{20}H_{33}NO$: C, 79.15; H, 10.96; N, 4.62. Found: C, 79.47; H, 10.93; N, 4.75.

***N*-Benzyl-2-*tert*-butyl-3-(2-hydroxy-2-ethylbutyl)pyrrolidine (10m):** obtained as a mixture of diastereoisomers; colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.87 (t, 6H, J = 7.4 Hz), 0.96 (s, 9H), 1.06−1.35 (m, 2H), 1.37−1.59 (m, 5H), 1.60−1.73 (m, 1H), 1.74−1.93 (m, 1H), 2.08−2.25 (m, 2H), 2.35−2.48 (m, 1H), 2.77−2.90 (m, 1H), 3.55 (d, 1H, J = 14.0 Hz), 4.07 (d, 1H, J = 14.0 Hz), 7.18 (m, 1H), 7.29 (t, 2H, J = 7.3 Hz), 7.39 (d, 2H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 7.8, 8.1, 27.2, 30.8, 31.7, 32.0, 36.0, 36.7, 45.8, 53.6, 63.6, 75.5, 82.3, 126.4, 128.1, 141.4. Anal. Calcd for $C_{21}H_{35}NO$: N, 4.41. Found: N, 4.51.

***N*-Benzyl-2-*tert*-butyl-3-methylpyrrolidine (10n):** obtained as a mixture of diastereoisomers; colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.94 (br s, 9H),1.01 (d, 3H, J = 6.0 Hz), 1.30−1.44 (m, 1H), 1.55−1.92 (m, 1H), 2.03−2.58 (m, 3H), 2.77−3.03 (m, 1H), 3.54 (d, 1H, J = 14.0 Hz), 4.15 (d, 1H, J = 14.0 Hz), 7.14−7.53 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.8, 27.0, 28.5, 33.0, 35.0, 53.6, 63.8, 81.7, 126.4, 126.8, 128.0, 128.1, 141.6. Anal. Calcd for $C_{16}H_{25}N$: C, 83.06; H, 10.89; N, 6.05. Found: C, 82.38; H, 10.81; N, 6.04.

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