

SYNTHESIS OF INDOLIZIDINE DERIVATIVES TRIFLUOROMETHYL-
ATED AT BRIDGEHEAD POSITION *VIA* ACYL IMINIUM ION
INTERMEDIATES DERIVED FROM RING-CHAIN TAUTOMERISM OF
5,5,5- TRIFLUORO- 4- OXOPENTANOYL ARYLETHYLAMIDES†

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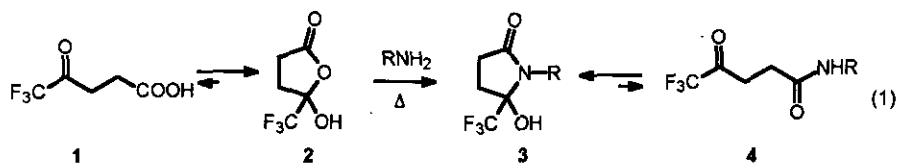
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Abstract- Acyliminium ion intermediates were generated from the stable
cyclic form of 5,5,5- trifluoro- 4- oxopentanoyl arylethylamides *via* acid cata-
lyzed dehydration. Electrophilic cyclization of aryl group led to fused
indolizidinones.

Preparation of trifluoromethylated heterocyclic compounds¹ is currently attracting wide interests because of their potential biological activities.² However, introduction of trifluoromethyl group into saturated nitrogen heterocycles such as pyrrolizidine, indolizidine, and quinolizidine has not been attracted much attention so far. There are many alkaloids with indolizidine skeleton known as biologically active compounds.³ Introduction of trifluoromethyl group near the nitrogen atom may modify or newly produces the biological activity due to the inductive effect affecting the basicity of the tertiary amine. In this paper, we report a facile preparation method for such a new class of trifluoromethylated fused indolizidine derivatives *via* acid- catalyzed cyclization of 5,5,5- trifluoro- 4- oxopentanoyl arylethylamides.

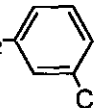
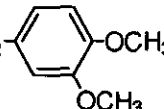
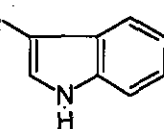
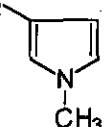
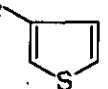
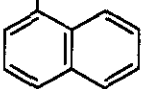
†Dedicated to Professor Shigeru Oae on the occasion of his 77th birthday.

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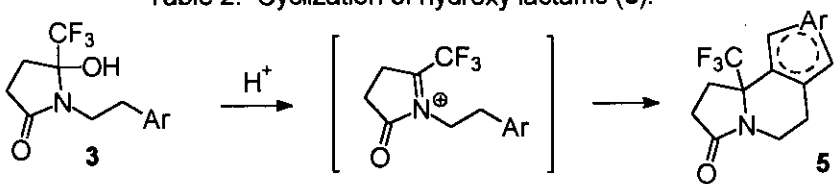
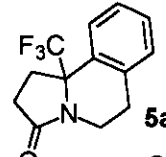
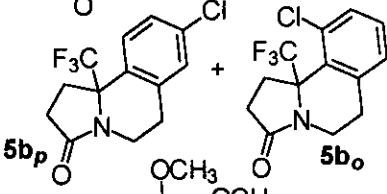
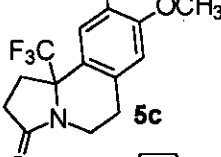
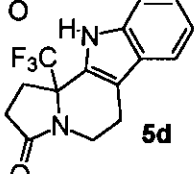
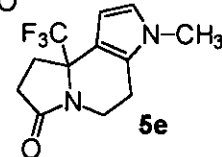
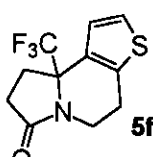
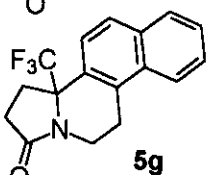
In the course of our study of preparation of fluorinated cyclic acyl imines,⁴ we found that 5,5,5-trifluoro-4-oxopentanoic acid (1)⁵ exists as a cyclic form⁶ of hydroxy lactone (2) due to highly electron-withdrawing effect of the CF₃ group which stabilized the hemiacetal structure. A facile reaction of 2 with phenethylamine gave hydroxy lactam (3a) (R = CH₂CH₂Ph) also as a stable

Table 1

| R | method ^a | product | yield (%) |
|--|---------------------|-----------|-----------------|
| —CH ₂ CH ₂ C ₆ H ₅ | A | 3a | 74 |
| | B | 3a | 81 |
| —CH ₂ CH ₂ -  | B | 3b | 76 |
| —CH ₂ CH ₂ -  | A | 3c | 74 |
| | B | 3c | 79 |
| —CH ₂ CH ₂ -  | A | 3d | 74 ^b |
| —CH ₂ CH ₂ -  | B | 3e | 70 ^c |
| —CH ₂ CH ₂ -  | B | 3f | 89 |
| —CH ₂ CH ₂ -  | B | 3g | 91 |
| —CH ₂ C ₆ H ₅ | A | 3h | 72 |

a) Method A: heated at 140 °C without solvent. Method B: refluxing benzene solution. b) (5d) (23 %) was also yielded. c) (5e) (26 %) was also yielded.

Table 2. Cyclization of hydroxy lactams (3).

| substrate | conditions, ^a time | product | yield (%) |
|--|-------------------------------|---|---|
|  | | | |
| 3a | A, 2d C, 1d D, 4d |  5a | 85 100 0 |
| 3b | C, 7d |  5bp + 5bo | 100 (9 : 1) |
| 3c | A, 1d C, 1d |  5c | 97 97 |
| 3d^b | A, 8h B, 4d C, 1d |  5d | 57 ^c 91 ^c 77 ^c |
| 3e^d | C, 2d |  5e | 73 ^c |
| 3f | A, 1.5d C, 1d |  5f | 77 33 |
| 3g | A, 1.5d |  5g | 52 |

a) A: CF₃COOH (solvent), B: CF₃COOH (2eq) / CH₂Cl₂,

C: CF₃SO₃H (2eq) / CH₂Cl₂, D: 0.8M HCl / CH₃OH.

b) contaminated with 24% of (**5d**). c) yields based on ketoacid (**1**).

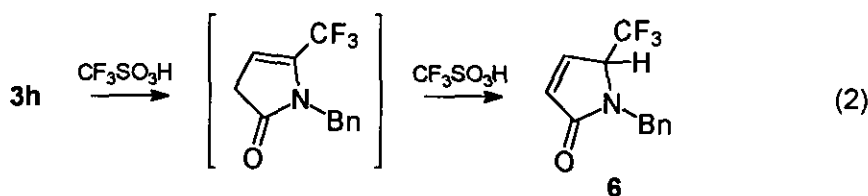
d) contaminated with 27% of (**5e**).

cyclic tautomer by just heating of the mixture at 140 °C (Method A) or refluxing of the benzene solution under neutral dehydration conditions (Method B) (eq. 1). Open-chain keto amide (**4a**) was not also observed in the reaction mixture unlike the corresponding acetyl derivative, which exists as open-chain structure as **4**.⁷ Various aryl derivatives were obtained from acid (**1**) and aryloethylamines and benzylamine in good yields as summarized in Table 1.

The structure of **3** is suitable for acid-catalyzed cyclization to indolizidinone skeletons (classical Pictet - Spengler conditions).⁸ Unlike usual aliphatic hydroxy lactams,⁷ (**3**) is considerably stable due to the electron-withdrawing effect of the CF₃ group and it could be treated with relatively strong acid such as CF₃COOH or CF₃SO₃H to dehydrate. For example, phenethylamide (**3a**) was treated with CF₃COOH as solvent at room temperature and led to tricyclic benzoindolizidinone (**5a**) in 85% yield (Table 2). Much better result was obtained by the reaction with 2-molar amount of CF₃SO₃H in CH₂Cl₂ at room temperature (quantitative yield). However, weaker 0.8 M HCl in methanol was not effective. Cyclized structure (**5a**) was readily assigned by the ¹H and ¹³C nmr spectra and absence of OH absorption in the ir spectrum.

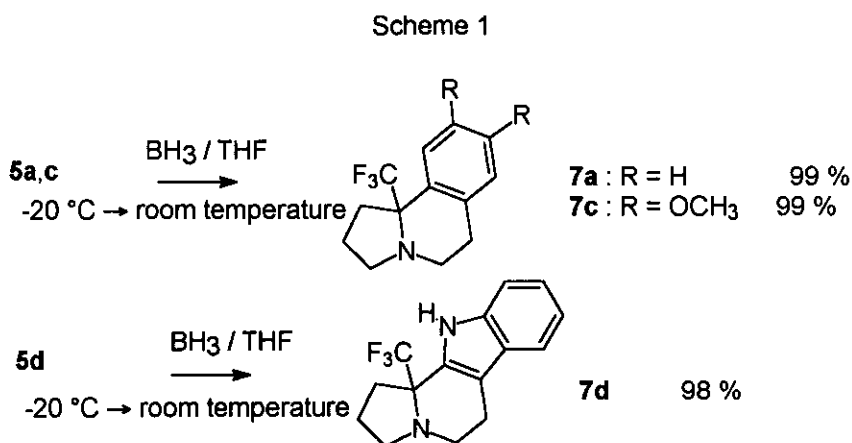
Other aryloethyl lactams (**3b-g**) were also converted into the corresponding fused indolizidinones (**5b-g**) in the same manner as that used for the preparation of **5a** (Table 2). Usually CF₃SO₃H (2 equiv) was the best reagent to dehydrative cyclization. However, in some cases (**3d,f**), strong acidity of the acid affected the heterocyclic aromatic ring to lower the yields of the products. While homoveratryl derivative (**3c**) gave sterically less hindered **5c** regioselectively, *m*-chlorophenethyl derivative (**3b**) gave a mixture of regioisomers (**5b_α**) and (**5b_β**) in 9 : 1 ratio. The reaction of α -naphthyl derivative (**3g**) led to 13-azasteroidal skeleton (**5g**).

If this cyclization was applied to the benzylamide derivative such as **3h**, pyrrolizidine derivative which is also a biologically interesting group of alkaloid-related compounds⁹ was expected to be obtained. However, **3h** unchanged under the similar reaction conditions (2 equiv CF₃SO₃H / CH₂Cl₂). When long reaction time (10 d) and high concentration of CF₃SO₃H (10 equiv) were



employed, dehydration and migration of a double bond led to pyrrolinone (**6**). The 5- *endo* cyclization of **3h** seems unlikely to occur (eq 2).¹⁰

Some of the obtained indolizidinones were readily converted into corresponding saturated tertiary amines (**7a,c,d**) with BH₃/THF complex¹¹ in good yields (Scheme 1).



EXPERIMENTAL

¹H (200 MHz) and ¹³C nmr (50 MHz) spectra were recorded on a Varian Gemini-200 spectrometer. Other spectral data for the new compounds were satisfactorily obtained.

Amide formation of 5,5,5-trifluoro-4-oxopentanoic acid (3). Method A: An amine (6.0 mmol) and **1** (850 mg, 5.0 mmol) was dissolved into Et₂O (15 ml), and the resulting mixture was allowed to stand overnight. The resulting precipitates were collected and washed with Et₂O several times. The collected solid was heated under Ar atmosphere at 140 °C for 2 h. Crude **3** was purified by recrystallization from Et₂O or SiO₂ column chromatography (1 : 1 hexane- EtOAc). Method B: An amine (6.0 mmol) and **1** (850 mg, 5.0 mmol) was dissolved into benzene (15 ml), and the resulting solution was refluxed with a Dean-Stark trap until deposition of water ceased. After removal of the solvent under reduced pressure, the residue was purified as above.

5-Hydroxy-1-(2-phenylethyl)-5-trifluoromethyl-2-pyrrolidinone (3a): mp 94 - 95 °C; ¹H nmr (CDCl₃) δ 1.93 - 2.07 (m, 1H), 2.42 - 2.62 (m, 3H), 2.80 (ddd, 1H, *J* = 13, 10, 5 Hz), 3.04 (ddd, 1H, *J* = 13, 10, 5 Hz), 3.39 (dddq, 1H, *J* = 14, 10, 7, 1 Hz), 3.64 (ddd, 1H, *J* = 14, 10, 5 Hz),

4.16 (brs, 1H), 7.15 - 7.36 (m, 5H); ^{13}C nmr (CDCl_3) δ 28.75, 29.79, 34.01, 42.42, 89.48 (q, $J=32$ Hz), 124.11 (q, $J=285$ Hz), 127.09, 129.07, 139.20, 175.82. Anal. Calcd for $\text{C}_{13}\text{H}_{14}\text{NO}_2\text{F}_3$: C, 57.14; H, 5.16; N, 5.13. Found: C, 56.95; H, 5.13; N, 5.18.

1- [2- (3- Chlorophenyl)ethyl]- 5- hydroxy- 5- trifluoromethyl- 2- pyrrolidinone (3b): mp 104 - 105°C; ^1H nmr (CDCl_3) δ 2.00 - 2.15 (m, 1H), 2.45 - 2.67 (m, 3H), 2.77 (ddd, 1H, $J=13, 10, 5$ Hz), 2.99 (ddd, 1H, $J=13, 11, 6$ Hz), 3.39 (ddd, 1H, $J=14, 10, 6$ Hz), 3.58 (ddd, 1H, $J=14, 11, 5$ Hz), 4.34 (s, 1H), 7.06 - 7.13 (m, 1H), 7.17 - 7.26 (m, 3H); ^{13}C nmr (CDCl_3) δ 28.68, 29.73, 33.84, 41.99, 89.52 (q, $J=33$ Hz), 124.09 (q, $J=285$ Hz), 127.23, 127.41, 129.38, 130.27, 141.06, 175.86. Anal. Calcd for $\text{C}_{13}\text{H}_{13}\text{NO}_2\text{ClF}_3$: C, 50.75; H, 4.26; N, 4.55. Found: C, 50.88; H, 4.30; N, 4.53.

1- [2- (3,4- Dimethoxyphenyl)ethyl]- 5- hydroxy- 5- trifluoromethyl- 2- pyrrolidinone (3c): mp 108 - 109 °C; ^1H nmr (CDCl_3) δ 1.94 - 2.08 (m, 1H), 2.43 - 2.63 (m, 3H), 2.74 (ddd, 1H, $J=13, 9, 5$ Hz), 2.99 (ddd, 1H, $J=13, 10, 7$ Hz), 3.37 (ddd, 1H, $J=14, 9, 7$ Hz), 3.63 (ddd, 1H, $J=14, 10, 5$ Hz), 3.85 (s, 3H), 3.86 (s, 3H), 6.71 - 6.83 (m, 3H); ^{13}C nmr (CDCl_3) δ 28.74, 29.79, 33.59, 42.48, 56.09, 56.14, 89.45 (q, $J=32$ Hz), 111.82, 112.55, 121.19, 124.14 (q, $J=286$ Hz), 131.78, 138.18, 149.48, 175.65. Anal. Calcd for $\text{C}_{15}\text{H}_{18}\text{NO}_4\text{F}_3$: C, 54.05; H, 5.44; N, 4.20. Found: C, 54.09; H, 5.44; N, 4.16.

5- Hydroxy- 1- (2- thienyl)- 5- trifluoromethyl- 2- pyrrolidinone (3f): mp 87 - 88 °C; ^1H nmr (CDCl_3) δ 1.97 - 2.12 (m, 1H), 2.44 - 2.47 (m, 3H), 3.01 (ddd, 1H, $J=14, 9, 5$ Hz), 3.28 (ddd, 1H, $J=14, 9, 7$ Hz), 3.45 (ddd, 1H, $J=14, 9, 7$ Hz), 3.71 (ddd, 1H, $J=14, 9, 5$ Hz), 6.85 (dd, 1H, $J=3, 1$ Hz), 6.95 (dd, 1H, $J=5, 3$ Hz), 7.16 (dd, 1H, $J=5, 1$ Hz); ^{13}C nmr (CDCl_3) δ 28.00, 28.78, 29.84, 42.42, 89.46 (q, $J=32$ Hz), 124.10 (q, $J=285$ Hz), 124.48, 125.93, 127.54, 141.32, 175.80. Anal. Calcd for $\text{C}_{11}\text{H}_{12}\text{NO}_2\text{F}_3\text{S}$: C, 47.31; H, 4.33; N, 5.02. Found: C, 47.54; H, 4.34; N, 4.96.

5- Hydroxy- 1- [2- (1- naphthyl)ethyl]- 5- trifluoromethyl- 2- pyrrolidinone (3g): mp 132 - 134 °C; ^1H nmr (CDCl_3) δ 1.83 - 2.09 (m, 1H), 2.43 - 2.63 (m, 3H), 3.17 - 3.33 (m, 1H), 3.43 - 3.62 (m, 2H), 3.66 - 3.81 (m, 1H), 7.35 (dd, 1H, $J=12, 7$ Hz), 7.35 (d, 1H), 7.41 - 7.56 (m, 2H), 3.66 - 3.81 (m, 1H), 7.31 - 7.40 (m, 2H), 7.41 - 7.56 (m, 2H), 7.73 (dd, 1H, $J=7, 3$ Hz), 7.81 - 7.86 (m, 1H), 8.19 - 8.24 (m, 1H); ^{13}C nmr (CDCl_3) δ 28.52, 29.90, 31.36, 41.86, 89.48 (q, $J=33$ Hz), 124.15 (q, $J=286$ Hz), 124.15, 125.93, 126.20, 127.44, 127.85, 129.14, 132.34, 134.21, 135.40,

175.94. Anal. Calcd for $C_{17}H_{16}NO_2F_3$: C, 63.15; H, 4.99; N, 4.33. Found: C, 63.32; H, 4.34; N, 4.34.

1-Benzyl-5-hydroxy-5-trifluoromethyl-2-pyrrolidinone (3h): mp 101 - 103 °C; 1H nmr ($CDCl_3$) δ 2.01 - 2.13 (m, 1H), 2.37 - 2.55 (m, 3H), 4.36 (d, 1H, $J = 16$ Hz), 4.69 (d, 1H, $J = 16$ Hz), 7.20 (s, 5H); ^{13}C nmr ($CDCl_3$) δ 28.46, 29.15, 43.78, 90.00 (q, $J = 33$ Hz), 124.23 (q, $J = 286$ Hz), 127.86, 128.24, 128.85, 137.31, 176.37. Anal. Calcd for $C_{12}H_{12}NO_2F_3$: C, 55.60; H, 4.67; N, 5.40. Found: C, 55.67; H, 4.59; N, 5.40.

Acid-catalyzed cyclization of hydroxy lactams (3). Lactam (3) (0.5 mmol) was dissolved in CH_2Cl_2 (3 ml), and CF_3SO_3H (0.09 ml, 1.0 mmol) was added. The resulting mixture was stirred for the period given in Table 2 at room temperature. The solution was neutralized by saturated aq $NaHCO_3$ and extracted with Et_2O . The solution was dried over $MgSO_4$. After removal of the solvent under reduced pressure, recrystallization of the residual solid from Et_2O or SiO_2 column chromatography (1:1 hexane - $EtOAc$) gave pure cyclization product (5). When CF_3COOH as the solvent was used, just removal of the solvent under reduced pressure and purification as above was done.

1,5,6,10b-Tetrahydro-10b-trifluoromethylpyrrolo[2,1-*a*]isoquinolin-3(2*H*)-one (5a): mp 113 - 114 °C; 1H nmr ($CDCl_3$) δ 2.20 (dtq, 1H, $J = 13, 10, 1$ Hz), 2.47 (dd-pentaplet, 1H, $J = 17, 10, 1$ Hz), 2.66 - 3.09 (m, 4H), 3.27 - 3.43 (m, 1H), 4.41 (dddq, 1H, $J = 13, 7, 4, 1$ Hz), 7.16 - 7.38 (m, 4H); ^{13}C nmr ($CDCl_3$) δ 27.48, 29.43, 30.38, 35.30, 65.14 (q, $J = 34$ Hz), 126.85, 127.02 (q, $J = 288$ Hz), 127.34, 129.12, 129.84, 132.82, 134.71, 174.37. Anal. Calcd for $C_{13}H_{12}NOF_3$: C, 61.17; H, 4.74; N, 5.49. Found: C, 61.19; H, 4.69; N, 5.35.

9 : 1 Mixture of 8- and 10-chloro-1,5,6,10b-tetrahydro-10b-trifluoromethylpyrrolo[2,1-*a*]isoquinolin-3(2*H*)-one (5b). 1H Nmr ($CDCl_3$) δ 2.15 (dtq, 0.9H, $J = 13, 10, 1$ Hz), 2.39 - 2.60 (m, 1H), 2.65 - 3.07 (m, 4H), 3.23 - 3.40 (m, 1H), 4.30 - 4.40 (m, 0.1H), 4.41 (dddq, 0.9H, $J = 13, 7, 3, 1$ Hz), 7.13 (ddt, 0.1H, $J = 8, 2, 1$ Hz), 7.19 - 7.36 (m, 3H); ^{13}C nmr ($CDCl_3$) δ 27.42, 29.38, 30.29, 34.93, 64.87 (q, $J = 28$ Hz), 126.42 (q, $J = 250$ Hz), 127.71, 128.29 (q, $J = 2$ Hz), 129.71, 131.29, 135.12, 136.78, 174.20; minor peaks: 27.91, 28.90, 30.02, 34.63, 130.15, 130.80, 135.4. Anal. Calcd for $C_{13}H_{11}NO_2ClF_3$: C, 53.90; H, 3.83; N, 4.84. Found: C, 53.57; H, 3.91; N, 4.77.

1,5,6,10b-Tetrahydro-8,9-dimethoxy-10b-trifluoromethylpyrrolo[2,1-*a*]isoquinolin-3(2*H*)-one (5c): mp 69 - 71 °C; 1H nmr ($CDCl_3$) δ 2.09 - 2.25 (m, 1H), 2.39 - 2.53 (m, 1H), 2.65 - 3.01 (m,

4H), 3.22 - 3.38 (s, 6H), 4.35 - 4.46 (m, 1H), 6.63 (s, 1H), 6.77 (q, $J = 1$ Hz); ^{13}C nmr (CDCl_3) δ 27.15, 29.38, 30.38, 35.30, 56.00, 56.28, 64.92 (q, $J = 28$ Hz), 109.27 (q, $J = 2$ Hz), 111.7, 124.29, 127.07 (q, $J = 288$ Hz), 127.28, 148.45, 149.79, 174.32. Anal. Calcd for $\text{C}_{15}\text{H}_{16}\text{NO}_3\text{F}_3$: C, 57.14; H, 5.12; N, 4.44. Found: C, 57.27; H, 5.14; N, 4.47.

1,5,6,9b-Tetrahydro-9b-trifluoromethylindolizino[8,7-*b*]indol-3(2*H*)-one (5d). The reaction of tryptamine with acid (1) gave a mixture of 3d and 5d. The mixture was treated as above: mp 221 - 222 °C; ^1H nmr (CDCl_3) δ 2.16 - 2.33 (m, 1H), 2.50 (ddq, 1H, $J = 15, 10, 1$ Hz), 2.70 - 2.93 (m, 4H), 3.26 - 3.41 (m, 1H), 4.61 (ddd, 1H, $J = 14, 5, 3$ Hz), 7.16 (ddd, $J = 8, 7, 1$ Hz), 7.27 (ddd, 1H, $J = 8, 7, 1$ Hz), 7.40 (ddd, 1H, $J = 8, 1, 1$ Hz), 7.54 (ddd, 1H, $J = 8, 1, 1$ Hz), 8.31 (brs, 1H); ^{13}C nmr (CDCl_3) δ 20.67, 27.93, 30.41, 36.60, 63.76 (q, $J = 30$ Hz), 111.71, 117.36, 120.59, 123.86, 126.36, 126.58 (q, $J = 287$ Hz), 127.62, 137.09, 174.61. Anal. Calcd for $\text{C}_{15}\text{H}_{13}\text{N}_2\text{OF}_3$: C, 61.22; H, 4.45; N, 9.52. Found: C, 61.46; H, 4.41; N, 9.33.

1,5,6,9b-Tetrahydro-7-methyl-9b-trifluoromethylpyrrolo[2,3-*g*]indolizin-3(2*H*)-one (5e). The reaction of 2-(2-aminoethyl)pyrrole with 1 gave a mixture of 3e and 5e. The mixture was treated as above: mp 115 - 116 °C; ^1H nmr (CDCl_3) δ 1.93 - 2.16 (m, 1H), 2.36 - 2.47 (m, 1H), 2.56 - 2.79 (m, 4H), 3.16 - 3.33 (m, 1H), 3.51 (s, 3H), 4.49 - 4.59 (m, 1H), 6.06 (dq, $J = 3, 1$ Hz), 6.59 (m, 1H); ^{13}C nmr (CDCl_3) δ 20.97, 29.42, 30.64, 33.19, 35.59, 64.30 (q, $J = 29$ Hz), 104.28, 114.63, 122.28, 126.94, 127.16 (q, $J = 286$ Hz), 174.98. Anal. Calcd for $\text{C}_{12}\text{H}_{13}\text{N}_2\text{OF}_3$: C, 55.81; H, 5.07; N, 10.85. Found: C, 55.70; H, 5.09; N, 10.73.

1,5,6,9b-Tetrahydro-9b-trifluoromethylindolizino[7,8-*b*]thiophen-3(2*H*)-one (5f): ^1H Nmr (CDCl_3) δ 1.96 - 2.20 (m, 1H), 2.37 - 2.55 (m, 1H), 2.64 - 2.84 (m, 2H), 2.92 (dd, 1H, $J = 8, 4$ Hz), 3.21 - 3.37 (m, 1H), 4.54 (dt, 1H, $J = 13, 2$ Hz), 6.96 (dq, 1H, $J = 5, 2$ Hz), 7.23 (dq, 1H, $J = 5, 1$ Hz); ^{13}C nmr (CDCl_3) 24.11, 28.60, 30.41, 35.81, 64.90 (q, $J = 29$ Hz), 124.55 (q, $J = 2$ Hz), 124.70, 126.66 (q, $J = 287$ Hz), 130.94, 137.06, 174.52. Anal. Calcd for $\text{C}_{11}\text{H}_{10}\text{NOF}_3\text{S}$: C, 50.57; H, 3.86; N, 5.36. Found: C, 50.50; H, 3.94; N, 5.23.

1,5,6,12b-Tetrahydro-12b-trifluoromethylnaphtho[1,2-*g*]indolizin-3(2*H*)-one (5g): mp 146 - 149 °C; ^1H nmr (CDCl_3) δ 2.21 (dtq, 1H, $J = 12, 11, 1$ Hz), 2.49 (dd-pent, 1H, $J = 16, 10, 1$ Hz), 2.69 - 2.88 (m, 1H), 2.99 (ddd, 1H, $J = 13, 9, 2$ Hz), 3.10 - 3.54 (m, 3H), 4.58 - 4.69 (m, 1H), 7.43 (dq, 1H, $J = 9, 2$ Hz), 7.52 - 7.47 (m, 2H), 7.79 - 7.89 (m, 2H), 7.95 - 8.02 (m, 1H); ^{13}C nmr (CDCl_3) δ 24.00, 29.36, 30.43, 34.62 (q, $J = 2$ Hz), 65.24 (q, $J = 28$ Hz), 123.62 (q, $J = 3$ Hz),

123.72, 127.17 (q, $J=288$ Hz), 127.43, 127.98, 129.02, 129.70, 130.84, 131.84, 133.35, 174.05.

Anal. Calcd for $C_{17}H_{14}NOF_3$: C, 66.88; H, 4.62; N, 4.59. Found: C, 66.85; H, 4.75; N, 4.49.

1-Benzyl-5-trifluoromethylpyrrol-2(5*H*)-one (6): 1H Nmr ($CDCl_3$) δ 4.12 (d, 1H, $J=15$ Hz), 4.37 (ddq, 1H, $J=6, 2, 1$ Hz), 5.35 (d, 1H, $J=15$ Hz), 6.44 (dd, 1H, $J=6, 2$ Hz), 6.97 (dd, 1H, $J=6, 1$ Hz), 7.19 - 7.40 (m, 5H); ^{13}C NMR δ 44.99, 61.92 (q, $J=33$ Hz), 123.69 (q, $J=282$ Hz), 128.52, 129.34, 131.71, 136.53, 139.27 (q, $J=3$ Hz), 171.86. Anal. Calcd for $C_{12}H_{10}NOF_3$: C, 59.75; H, 4.18; N, 5.81. Found: C, 59.75; H, 4.17; N, 5.81.

1,2,3,5,6,10b-Hexahydro-10b-trifluoromethylpyrrolo[2,1-*a*]isoquinoline (7a). To a THF solution (15 ml) of (5a) (765 mg, 3.00 mmol), BH_3 -THF (1.0 M, 30 ml, 30 mmol) was added dropwise at $-20^\circ C$, and the resulting solution was stirred for 3 h. To the solution, MeOH (8ml) was added, and then the solvents were removed under reduced pressure. The residue was chromatographed on SiO_2 column (1 : 1 hexane - EtOAc) to give colorless oil which was treated with HCl (g) to form hydrochloride as colorless solid (633 mg, 100 %): mp $169 - 170^\circ C$; 1H nmr (free amine, $CDCl_3$) δ 1.73 - 2.17 (m, 3H), 2.64 - 2.91 (m, 5H), 3.26 - 3.36 (m, 1H), 3.52 (m, 1H), 7.12 - 7.37 (m, 4H); ^{13}C nmr (free amine, $CDCl_3$) δ 23.86, 26.50, 36.83, 47.09, 54.78, 67.50 (q, $J=26$ Hz), 127.78 (q, $J=284$ Hz), 127.89, 128.53, 128.78, 135.25, 137.58. Anal. Calcd for $C_{13}H_{14}NF_3 \cdot HCl$: C, 56.22; H, 5.44; N, 5.04. Found: C, 56.13; H, 5.34; N, 5.21.

1,2,3,5,6,10b-Tetrahydro-8,9-dimethoxy-10b-trifluoromethylpyrrolo[2,1-*a*]isoquinoline (7c). 1H Nmr ($CDCl_3$) δ 1.75 - 2.14 (m, 3H), 2.58 - 2.96 (m, 3H), 2.58 - 2.96 (m, 5H), 3.25 (ddd, 1H, $J=9, 6, 2$ Hz), 3.40 (ddd, 1H, $J=13, 9, 5$ Hz), 3.87 (s, 3H), 3.88 (s, 3H), 6.62 (s, 1H), 6.82 (q, 1H, $J=1$ Hz); ^{13}C nmr ($CDCl_3$) δ 23.75, 25.12, 36.98, 46.33, 54.05, 55.95, 56.26, 66.93 (q, $J=27$ Hz), 111.07, 111.59 (q, $J=285$ Hz), 126.74, 129.80, 147.96, 148.85. Hydrochloride: mp $30^\circ C$ (decomp.). Anal. Calcd for $C_{15}H_{18}NF_3 \cdot HCl$: C, 53.34; H, 5.67; N, 4.15. Found: C, 53.03; H, 6.00; N, 4.13.

1,2,3,5,6,11b-Tetrahydro-11b-trifluoromethyl-(1*H*)-indolizino[8,7-*b*]indole (7d): mp $105 - 107^\circ C$; 1H nmr ($CDCl_3$) δ 1.75 - 2.08 (m, 3H), 2.49 - 2.65 (m, 2H), 2.95 (ddd, 2H, $J=16, 10, 7$ Hz), 3.08 - 3.16 (m, 1H), 3.31 - 3.38 (m, 2H), 7.13 (ddd, 1H, $J=8, 7, 1$ Hz), 7.22 (ddd, 1H, $J=8, 7, 1$ Hz), 7.36 (ddd, 1H, $J=8, 1, 1$ Hz), 7.55 (ddd, 1H, $J=8, 1, 1$ Hz), 7.91 (br s, 1H); ^{13}C nmr ($CDCl_3$) δ 15.96, 23.78, 35.34, 44.26, 51.38, 63.77 (q, $J=28$ Hz), 111.40, 111.81, 119.10, 120.07, 123.14, 126.80, 127.49 (q, $J=284$ Hz), 130.71, 136.78. Anal. Calcd for $C_{15}H_{15}N_2F_3$: C, 64.28;

H, 5.39; N, 9.99. Found: C, 64.33; H, 5.50; N, 9.82. Hydrochloride: mp 120 °C (decomp.).

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