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One-Pot Cyclization of 2-Aminophenethyl Alcohols: A Novel and Direct Approach to the Synthesis of *N*-Acyl Indolines

Zengxue Wang,[†] Wen Wan,[†] Haizhen Jiang,[†] and Jian Hao*[,†,‡]

Department of Chemistry, Shanghai University, 99 Shangda Road, Shanghai 200444, China, and Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Road, Shanghai 200032, China

jhao@shu.edu.cn

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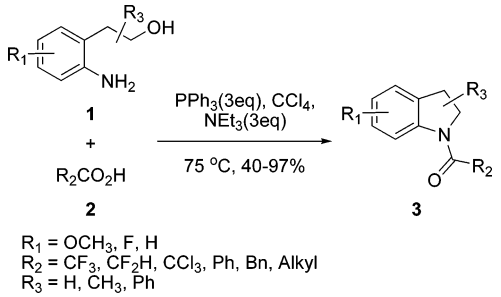
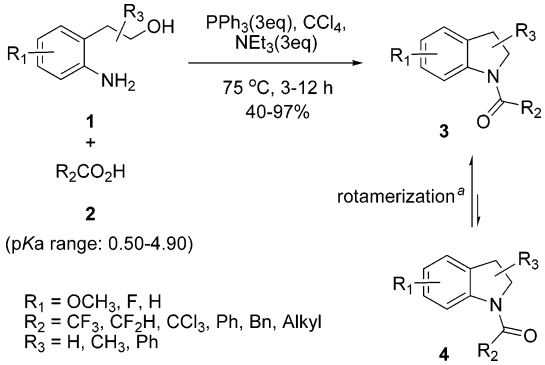


A unique one-pot cyclization of 2-aminophenethyl alcohols with carboxylic acids in the presence of PPh_3, CCl_4, and NEt_3 furnished the formation of *N*-acyl indolines in good to excellent yields. This new approach provides an efficient, scalable, low-cost, and direct access to the biologically important indolines which are further oxidizable to indoles and oxindoles.

Indoline frameworks are ubiquitous in natural products, as well as in a range of biologically active non-natural products.[1] A number of useful methodologies have been developed for the synthesis of various substituted indoline ring systems;[2−5] however, few synthetic methods provide efficient, scalable, and direct access to the biologically significant *N*-acyl indolines. Therefore, the discovery of novel and facile routes to the construction of such a nitrogen-containing bicyclic system is still one of the important issues in organic synthesis.

The synthetic strategy we disclose here is a one-pot cyclization of 2-aminophenethyl ethanols with common carboxylic acids in the presence of PPh_3, CCl_4, and NEt_3. This process provides a convenient modular, scalable, and well-suited approach for the direct synthesis of *N*-acyl indolines in one step (Scheme 1).

SCHEME 1. Synthesis of Indolines from Different Carboxylic Acids



[a] The ratio of rotamers **3** and **4** is determined by ^1H NMR or ^{19}F NMR. See ref 6 for the differentiation of rotamers **3** and **4**.

The initial purpose of this research was to prepare the fluoroalkyl-substituted benz-fused seven-membered-ring compound 4,5-dihydrobenzo-1,3-oxazepine (**5**) via our typical cyclization procedure for fluorinated imidoyl chloride intermediate (**6a**) that we previously communicated.[7] However, the imidoyl chloride intermediate **6a**, which was generated *in situ* from 2-aminophenethyl alcohol (**1a**) through the Uneyama procedure,[8] failed to yield the desired product **5**, instead, the cyclized *N*-trifluoroacetyl indoline (**3a**) was obtained in 97% yield (Scheme 2).

This unexpected result drew our attention to explore the mechanism of this one-pot cyclization process. It is clearly observed that during the model reaction with trifluoroacetic acid, the imidoyl chloride intermediate 2-[2-(1-chloro-2,2,2-trifluoroethylideneamino)phenyl]alcohol (**6a**) was formed at the initial stage, and with time going, **6a** disappeared gradually and instead the cyclized product **3a** was obtained as the final product. The rotamer **4a** was not clearly detected by ^{19}F NMR or ^1H NMR (500 MHz) in this case. Decreasing the quantity of NEt_3 that

[†] Shanghai University.
[‡] Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences.

(1) (a) Ontoria, J. M.; Di Marco, S.; Conte, I.; Di Francesco, M. E.; Gardelli, C.; Koch, U.; Matassa, V. G.; Poma, M.; Steinkuhler, C.; Volpari, C.; Harper, S. *J. Med. Chem.* **2004**, *47*, 6443−6446. (b) Horton, D. A.; Bourne, G. T.; Smythe, M. L. *Chem. Rev*. **2003**, *103*, 893−930. (c) Boger, D. L.; Boyce, C. W.; Garbaccio, R. M.; Goldberg, J. A. *Chem. Rev.* **1997**, *97*, 787−828. (d) Bermudez, J.; Dabbs, S.; Joiner, K. A.; King, F. D. *J. Med. Chem.* **1990**, *33*, 1929−1932. (e) Glennon, R. A. *J. Med. Chem.* **1987**, *30*, 1−12.

(2) For palladium-catalyzed synthesis of indolines, see: (a) Alexanian, E. J.; Lee, C.; Sorensen, E. J. *J. Am. Chem. Soc.* **2005**, *127*, 7690−7691. (b) Ganton, M. D.; Kerr, M. A. *Org. Lett.* **2005**, *7*, 4777−4779. (c) Lira, R.; Wolfe, J. P. *J. Am. Chem. Soc.* **2004**, *126*, 13906−13907.

(3) For the copper-catalyzed synthesis of indolines, see: (a) Zabawa, T. P.; Kasi, D.; Chemler, S. R. *J. Am. Chem. Soc.* **2005**, *127*, 11250−11251. (b) Sherman, E. S.; Chemler, S. R.; Tan, T. B.; Gerlits, O. *Org. Lett.* **2004**, *6*, 1573−1575.

(4) For radical cyclization of indolines, see: (a) Viswanathan, R.; Prabhakaran, E. N.; Plotkin, M. A.; Johnston, J. N. *J. Am. Chem. Soc*. **2003**, *125*, 163−168. (b) Johnston, J. N.; Plotkin, M. A.; Viswanathan, R.; Prabhakaran, E. N. *Org. Lett.* **2001**, *3*, 1009−1011. (c) Gil, G. S.; Groth, U. M. *J. Am. Chem. Soc.* **2000**, *122*, 6789−6790.

(5) Other processes: (a) Yin, Y.; Zhao, G. *Heterocycles* **2006**, *68*, 23−31. (b) Hodges, J. C.; Wang, W.; Riley, F. *J. Org. Chem.* **2004**, *69*, 2504−2508. (c) Nicolaou, K. C.; Roecker, A. J.; Pfefferkorn, J. A.; Cao, G. Q. *J. Am. Chem. Soc.* **2000**, *122*, 2966−2967. (d) Tidwell, J. H.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 11797−11810.

(6) Helgen, C.; Bochet, C. G. *J. Org. Chem.* **2003**, *68*, 2483−2486.

(7) (a) Ge, F.; Wang, Z.; Wan, W.; Lu, W.; Hao, J. *Tetrahedron Lett.* **2007**, *48*, 3251−3254. (b) Ge, F.; Wang, Z.; Wan, W.; Hao, J. *Synlett*, **2007**, *3*, 447−450.

(8) Tamura, K.; Mizukami, H.; Maeda, K.; Watanabe, H.; Uneyama, K. *J. Org. Chem*. **1993**, *58*, 32−35.

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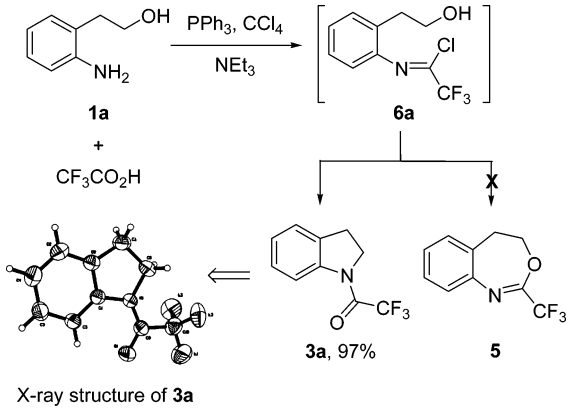
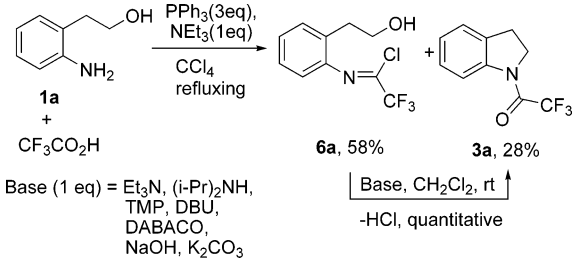
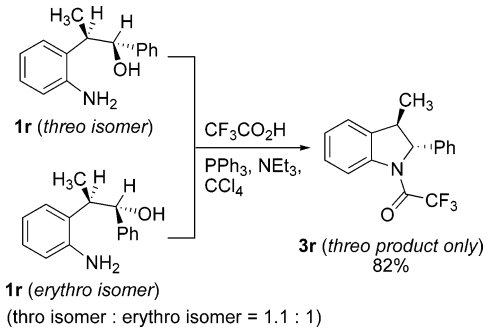
SCHEME 2. The Synthesis of *N*-Trifluoroacetylindoline 3a



SCHEME 3. The Ring Cyclization of 6a To Form 3a



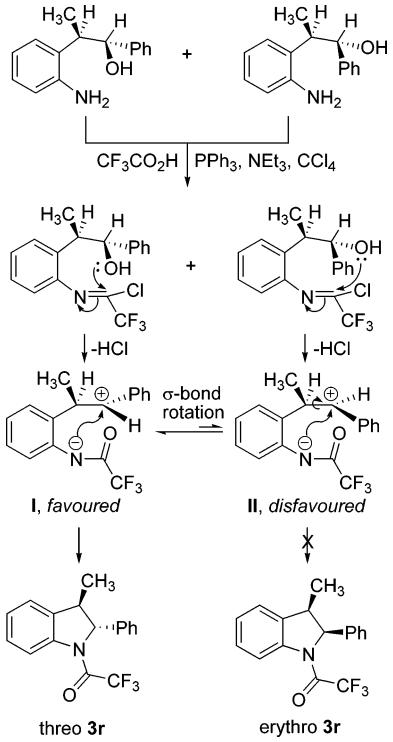
SCHEME 4. The Synthesis of Threo 3r



was used in this reaction to one-third of normal dosage could effectively prevent the subsequential cyclization from being complete. Thus, the intermediate **6a** was successfully isolated as a major and stable compound from the reaction mixture. The further cyclization of **6a** could be achieved quantitatively if **6a** is treated with an equivalent of base, such as NEt_3, DBU, and K_2CO_3, etc., in CH_2Cl_2 at ambient temperature. This result revealed clear evidence that the reaction initially generated imidoyl chloride intermediate **6a** *in situ*, which subsequentially underwent intramolecular addition of an hydroxy group to the imino carbon to form *N*-acetyl indoline **3a** under basic condition (Scheme 3).

An interesting phenomena was observed in the case of using a mixture of threo and erythro isomers of 2-(2-aminophenyl)-1-phenylpropan-1-ol (**1r**) (mole ratio of threo and erythro isomer = 1.1:1) as a starting material, where only threo **3r** was detected and isolated[9] and no erythro **3r** was tracked (Scheme 4). This result revealed that the carbon−oxygen bonds in the original

SCHEME 5. Proposed Mechanism for the Synthesis of 3r



compounds were possibly cleaved to form carbon cationic like intermediate **I** and **II** after hydroxy group attacked on the imino carbon. The equilibrium between intermediate **I** and **II** was established through a σ-bond rotation: intermediate **II** tended to transform into **I** to avoid the repulsion between the methyl group and the phenyl group (Scheme 5). This could be the reason why only threo **3r** was obtained as the final product even when an equal amount of threo and erythro isomers was employed in this reaction. The detailed mechanism for the formation of **3a** to **3p** is still under investigation.

The imidoyl chloride intermediates, such as **6a**, were clearly detected in all examined cases of using trifluoroacetic acid and difluoroacetic acids. However, in some cases other than with fluorinated acetic acids, imidoyl chloride intermediates were not clearly observed. It is possibly due to the good chemical stability that fluoroalkyl-substituted imidoyl chlorides have (the non-fluoroalkyl-substituted imidoyl chlorides are known to be less stable), once it formed, the subsequent cyclization could occur imediately under basic condition. This one-pot process is generally suitable to prepare various *N*-acyl indolines with different carboxylic acids in a range of pK_a values. Stronger acid facilitates this process to afford a higher yield of cyclized product with shorter reaction time, while weaker acid shows a little difficulty in generating the imidoyl chloride intermediate, and results in cyclized product in a lower yield. The reaction does not require the rigorous exclusion of air or moisture, and is generally clean with complete consumption of starting materials (Table 1).

This procedure can also be scaled up and applicable to synthesize the desired products even in the hundreds of grams scale. One-pot cyclization with trichloroacetic acid (entry 2, Table 1) was comparatively complicated due to the cleavage of the carbon−chlorine bond by PPh_3 during the process, no *N*-trichloroacetyl indoline product was detected from the reaction

(9) The assignment for stereochemistry of threo and erythro **3r** is based on their J_{2H-3H} value in ^1H NMR according to the reference: McComas, C. C.; Gilbert, E. J.; Van Vranken, D. L. *J. Org. Chem.* **1997**, *62*, 8600−8603.

TABLE 1. Synthesis of *N*-Acyl Indolines with 2-Aminophenethyl Ethanols and Carboxylic Acids

entry	R_1	R_2	R_3	pK_a of acid	yield of **3** + **4** (%)[a]	
1	H	CF_3	H	0.50	**3a**	97
2	H	CCl_3	H	0.52	**3b**	40[b]
3	H	CF_2H	H	1.33	**3c**	94
4	H	H	H	3.75	**3d** + **4d**	74[c]
5	H	Ph	H	4.21	**3e**	83
6	H	$PhCH_2$	H	4.31	**3f**	80
7	H	CH_3	H	4.75	**3g** + 4g	79[c]
8	H	C_3H_7	H	4.82	**3h** + **4h**	77[c]
9	H	C_5H_{11}	H	4.85	**3i** + **4i**	75[c]
10	5-OCH_3	CF_3	H	0.50	**3j**	95
11	5-OCH_3	CF_2H	H	1.33	**3k**	91
12	5-OCH_3	$PhCH_2$	H	4.31	**3*l***	81
13	5-F	CF_3	H	0.50	**3m**	89
14	5-F	C_2H_5	H	4.87	**3n** + **4n**	79[d]
15	H	CF_3	3-CH_3	0.50	**3o**	92
16	H	$PhCH_2$	3-CH_3	4.31	**3p**	83
17	H	CF_3	2-Ph	0.50	**3q**	90
18	H	CF_3	3-CH_3, 2-Ph	0.50	**3r**	82[e]

[a] All the yields listed here are isolated yields. [b] **3b** is *N*-dichloroacetylindoline. [c] The ratio of **3** and **4** is determined by ^{1}H NMR: **3d**:**4d** = 82:18, **3g**:**4g** =85:15, **3h**:**4h** = 89:11, **3i**:**4i** = 90: 11. [d] The ratio of **3n** and **4n** is determined by ^{19}F NMR: **3n**:**4n** = 93:7. [e] Only threo **3r** was detected and isolated.

mixture, and only *N*-dichloroacetyl indoline product (**3b**) was obtained in 40% yield.

The starting 2-aminophenethyl alcohols (**1**) are commercially available. For specific structure demands, such as **1r**, the desired product can also be simply prepared through a reaction of 1-alkyl-2-nitrobenzene with aldehyde,[10] followed by the reduction of the nitro group.[11]

The cyclized indoline products can further be simply oxidized to the biologically important indoles and oxindoles according to the known procedures.[12,13]

In conclusion, a unique and concise one-pot synthesis of *N*-acyl indolines from of 2-aminophenethyl alcohols and carboxylic acids has been developed. This new approach provides an efficient, scalable, low-cost, and direct access to the biologically important indolines which are further oxidizable to indoles and oxindoles.

Experimental Section

General Procedure. To a 100-mL three-necked round-bottomed flask equipped with a condenser and a magnetic stir bar was added Ph_3P (7.86 g, 30 mmol), NEt_3 (4.2 mL, 30 mmol), CCl_4 (40 mL, 419 mmol), and carboxylic acid (10 mmol) at 0 °C under nitrogen atmosphere and the solution was then stirred for 10 min. A solution of 2-aminophenethyl alcohol (10 mmol) dissolved in CCl_4 (21 mL, 220 mmol) was added dropwisely to the reaction mixture. Once the addition was completed, the reaction mixture was allowed to reflux for 3−12 h. After cooling, the solvent was removed by rotary evaporator, the residue was then carefully washed with mixture solvent (4:1 hexane:ethyl acetate) 3 times, and the precipitate was removed via filtration. The filtrate was combined and concentrated by rotary evaporator. The residue was then purified by column chromatography or distillation under reduced pressure to offer the product **3**.

***N*-Trifluoroacetylindoline (3a). 3a** was obtained as a white solid in 97% yield by column chromatography (4:1 hexane:ethyl acetate) on neutral aluminum oxide: mp 51−52 °C; ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.14 (d, J = 8.0 Hz, 1H), 7.07−7.23 (m, 3H), 4.22 (t, J = 8.5 Hz, 2H), 3.20 (t, J = 8.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.4 (q, $^2J_{C-F}$ = 37.5 Hz), 141.8, 131.8, 128.0, 126.1, 125.0, 118.1, 116.3 (q, $^1J_{C-F}$ = 286.3 Hz), 47.9 (q, $^4J_{C-F}$ = 4.2 Hz), 28.6; ^{19}F NMR (470 MHz, $CFCl_3$) δ −75.69 (s); IR (KBr, cm^{-1}) 3023, 1683, 1606, 1492, 1433, 1222, 1201, 1138, 765.

***N*-Difluoroacetylindoline (3c). 3c** was obtained as a yellow solid in 94% yield by column chromatography (4:1 hexane:ethyl acetate) on neutral aluminum oxide: mp 63−64 °C; ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.20 (d, J = 8.0 Hz, 1H), 7.10−7.26 (m, 3H), 6.12 (t, J = 53.5 Hz, 1H), 4.26 (t, J = 8.5 Hz, 2H), 3.24 (t, J = 8.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.7 (t, $^2J_{C-F}$ = 25.0 Hz), 142.0, 131.6, 127.8, 125.4, 124.9, 117.7, 110.1 (t, $^1J_{C-F}$ = 252.5 Hz), 46.7, 28.5; ^{19}F NMR (470 MHz, $CFCl_3$) δ −124.25 (d, J = 53.5 Hz); IR (KBr, cm^{-1}) 3018, 1675, 1489, 1458, 1148, 1043, 759; HRMS calcd for (M^+) $C_{10}H_9F_2NO$:197.0652, found 197.0656.

***N*-Trifluoroacetyl-5-methoxyindoline (3j). 3j** was obtained as a white solid in 95% yield by column chromatography (4:1 hexane:ethyl acetate) on neutral aluminum oxide: mp 96−98 °C; ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.12 (d, J = 8.5 Hz, 1H), 6.77−6.81 (m, 2H), 4.27 (t, J = 8.0 Hz, 2H), 3.81 (s, 3H), 3.23 (t, J = 8.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.0, 153.7 (q, $^2J_{C-F}$ = 37.5 Hz), 135.3, 133.5, 118.8, 116.4 (q, $^1J_{C-F}$ = 286.3 Hz), 112.6, 111.0, 55.8, 48.1 (q, $^4J_{C-F}$ = 3.8 Hz), 28.8; ^{19}F NMR (470 MHz, $CFCl_3$) δ −72.32 (s); IR (KBr, cm^{-1}) 3016, 2954, 2847, 1682, 1607, 1494, 1437, 1233, 1200, 1142, 1078, 832; HRMS calcd for (M^+) $C_{11}H_{10}F_3NO_2$ 245.0664, found 245.0665.

***N*-Difluoroacetyl-5-methoxyindoline (3k). 3k** was obtained as a pink solid in 91% yield by column chromatography (4:1 hexane:ethyl acetate) on neutral aluminum oxide: mp 97−99 °C; ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.11 (d, J = 8.5 Hz, 1H), 6.75−6.81 (m, 2H), 6.12 (t, J = 53.5 Hz, 1H), 4.26 (t, J = 8.5 Hz, 2H), 3.80 (s, 3H), 3.22 (t, J = 8.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.1 (t, $^2J_{C-F}$ = 25.0 Hz), 157.7, 135.7, 133.3, 118.4, 112.4, 111.0, 110.6 (t, $^1J_{C-F}$ = 252.5 Hz), 55.8, 47.0 (t, $^4J_{C-F}$ = 5 Hz), 28.8; ^{19}F NMR (470 MHz, $CFCl_3$) δ −123.91 (d, J = 53.5 Hz); IR (KBr, cm^{-1}) 2972, 2923, 2845, 1678, 1495, 1438, 1272, 1197, 1148, 1087, 1048, 823; HRMS calcd for (M^+) $C_{11}H_{11}F_2NO_2$ 227.0758, found 227.0763.

N*-Benzoacetyl-5-methoxyindoline (3*l*). 3*l was obtained as a white solid in 81% yield by column chromatography (4:1 hexane:ethyl acetate) on neutral aluminum oxide: mp 159−161 °C; ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.18 (d, J = 8.5 Hz, 1H), 7.24−7.36 (m, 5H), 6.71 (m, 2H), 4.05 (t, J = 8.5 Hz, 2H), 3.79 (s, 2H), 3.77 (s, 3H), 3.12 (t, J = 8.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.5, 156.5, 137.0, 134.6, 132.9, 129.2 (2 carbon), 128.9 (2 carbon), 127.1, 117.9, 112.0, 111.0, 55.8, 48.5, 43.5, 28.4; IR (KBr, cm^{-1}) 3031, 3010, 2972, 2837, 1652, 1592, 1487, 1399, 1267, 815, 746, 708; HRMS calcd for (M^+) $C_{17}H_{17}NO_2$ 267.1259, found 267.1268.

***N*-Trifluoroacetyl-5-fluoroindoline (3m). 3m** was obtained as a golden solid in 89% yield by column chromatography (4:1 hexane:ethyl acetate) on neutral aluminum oxide: mp 52−54 °C; ^{1}H NMR (500 MHz, $CDCl_3$, ppm) 8.17 (dd, J = 8.5, 4.5 Hz, 1H), 6.93−6.98 (m, 2H), 4.31 (t, J = 8.5 Hz, 2H), 3.26 (t, J = 8.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.7 (d, $^1J_{C-F}$ = 245 Hz), 154.1 (q, $^2J_{C-F}$ = 37.5 Hz), 137.9 (d, $^4J_{C-F}$ = 2.5 Hz), 134.0 (d, $^3J_{C-F}$ = 8.8 Hz), 119.1 (d, $^3J_{C-F}$ = 8.8 Hz), 116.3 (q, $^1J_{C-F}$ = 286.3 Hz), 114.4 (d, $^2J_{C-F}$ = 22.5 Hz), 112.3 (d, $^2J_{C-F}$ = 22.5 Hz), 48.2 (q, $^4J_{C-F}$ = 4.2 Hz), 28.6; ^{19}F NMR (470 MHz, $CFCl_3$) δ −72.51 (s), −116.04 (m); IR (KBr, cm^{-1}) 2926, 2855, 1693, 1610, 1487, 1428, 1246, 1208, 1146, 1077, 832; HRMS calcd for (M^+) $C_{10}H_7F_4NO$ 233.0464, found 233.0466.

***N*-Propionyl-5-fluoroindoline (3n). 3n** was obtained as a pink solid in 79% yield by column chromatography (4:1 hexane:ethyl

(10) Morimoto, T.; Hashimoto, I.; Yamaoka, H. Japanese patent 77108941, 1977; *Chem. Abstr*. **1978**, *88*, 104878.
(11) Bavin, P. M. G. *Org. Synth.* **1973**, *5*, 30.
(12) Dunetz, J. R.; Danheiser, R. L. *J. Am. Chem. Soc*. **2005**, *127*, 5776−5777.
(13) Yadav, J. S.; Subba, Reddy, B. V.; Suresh Reddy, Ch.; Krishna, A. D. *Tetrahedron Lett.* **2007**, *48*, 2029−2032.

acetate) on neutral aluminum oxide: mp 110−112 °C; ^{1}H NMR (500 MHz, $CDCl_3$, ppm) major rotamer (93:7) δ 8.20 (dd, J = 9.5, 4.5 Hz, 1H), 6.85−6.89 (m, 2H), 4.06 (t, J = 8.5 Hz, 2H), 3.18 (t, J = 8.5 Hz, 2H), 2.43 (q, J = 7.5 Hz, 2H), 1.23 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.8, 159.2 (d, $^1J_{C-F}$ = 240 Hz), 139.4, 133.1 (d, $^3J_{C-F}$ = 8.8 Hz), 117.6 (d, $^3J_{C-F}$ = 7.5 Hz), 113.7 (d, $^2J_{C-F}$ = 22.5 Hz), 111.8 (d, $^2J_{C-F}$ = 23.8 Hz), 48.1, 29.0, 28.1, 8.8; ^{19}F NMR (470 MHz, $CFCl_3$) δ −119.80 (m); IR (KBr, cm^{-1}) 2976, 2935, 1658, 1605, 1484, 1411, 1244, 844; HRMS calcd for (M^+) $C_{11}H_{12}FNO$ 193.0903, found 193.0907.

***N*-Trifluoroacetyl-3-methylindoline (3o). 3o** was obtained as a yellowy liquid in 92% yield by column chromatography (4:1 hexane:ethyl acetate) on neutral aluminum oxide: ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.18 (d, J = 8.5 Hz, 1H), 7.16−7.29 (m, 3H), 4.43 (m, 1H), 3.77 (m, 1H), 3.55 (m, 1H), 1.38 (d, J = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.1 (q, $^2J_{C-F}$ = 37.5 Hz), 141.2, 137.0, 128.0, 126.1, 123.8, 117.9, 116.2 (q, $^1J_{C-F}$ = 286.3 Hz), 55.7 (q, $^4J_{C-F}$ = 3.8 Hz), 35.3, 19.5; ^{19}F NMR (470 MHz, $CFCl_3$) δ −72.45 (s); IR (neat, cm^{-1}) 2969, 2933, 1696, 1601, 1485, 1437, 1254, 1203, 1144, 1084, 759, 715; HRMS calcd for (M^+) $C_{11}H_{10}F_3NO$ 229.0714, found 229.0717.

***N*-Trifluoroacetyl-2-phenylindoline (3q). 3q** was obtained as a white solid in 90% yield by column chromatography (4:1 hexane: ethyl acetate) on neutral aluminum oxide: mp 113−116 °C; ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.30 (d, J = 8.5 Hz, 1H), 7.07−7.37 (m, 8H), 5.74 (d, J = 9.0 Hz, 1H), 3.83 (dd, J = 15.5, 9.0 Hz, 1H), 3.03 (d, J = 15.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.2 (q, $^2J_{C-F}$ = 37.5 Hz), 142.6, 142.2, 130.1, 129.0 (2 carbon), 128.1, 127.9 (2 carbon), 126.5, 125.5, 124.5, 118.2, 116.1 (q, $^1J_{C-F}$ = 286.3 Hz), 63.1 (d, $^4J_{C-F}$ = 2.5 Hz), 39.6; ^{19}F NMR (470 MHz, $CFCl_3$) δ −70.54 (s); IR (KBr, cm^{-1}) 3032, 2963, 2923, 1690, 1601, 1481, 1461, 1250, 1203, 1159, 760, 701; HRMS calcd for (M^+) $C_{16}H_{12}F_3NO$ 291.0871, found 291.0876.

***N*-Trifluoroacetyl-3-mehtyl-2-phenylindoline (3r). 3r** was obtained as a yellowy liquid in 82% yield by column chromatography (8:1 hexane:ethyl acetate) on neutral aluminum oxide: ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.30 (d, J = 8.0 Hz, 1H), 7.05−7.37 (m, 8H), 5.25 (s, 1H), 3.24 (q, J = 7.0 Hz, 1H), 1.43 (d, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.5 (q, $^2J_{C-F}$ = 37.5 Hz), 142.0, 141.3, 136.0, 129.0 (2 carbon), 128.4, 127.9 (2 carbon), 126.6, 124.9, 124.4, 118.2, 116.1 (q, $^1J_{C-F}$ = 286.3 Hz), 71.1, 47.2, 22.5; ^{19}F NMR (470 MHz, $CFCl_3$) δ −70.47 (s); IR (neat, cm^{-1}) 3029, 2960, 2923, 1687, 1601, 1483, 1458, 1229, 1200, 1137, 758, 707; HRMS calcd for (M^+) $C_{17}H_{14}F_3NO$ 305.1027, found 305.1036.

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Supporting Information Available: Experimental procedures, characterization data, and X-ray crystal structure and CIF file of **3a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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