

The synthesis of 7,8,9,10-tetrafluoroellipticine

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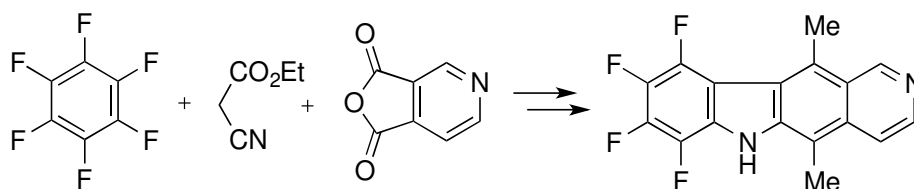
Received 11-29-2017

Accepted 01-21-2018

Published on line mm-02-05-2018

Abstract

We have synthesized a novel ellipticine analogue, 7,8,9,10-tetrafluoroellipticine, in nine steps from hexafluorobenzene and ethyl cyanoacetate, via 1-(phenylsulfonyl)-4,5,6,7-tetrafluoroindole. The key step is lithiation of the indole and subsequent coupling with 3,4-pyridinedicarboxylic acid anhydride to afford a keto-lactam. Reaction of the lactam with methyllithium followed by reduction with sodium borohydride yields 7,8,9,10-tetrafluoroellipticine.

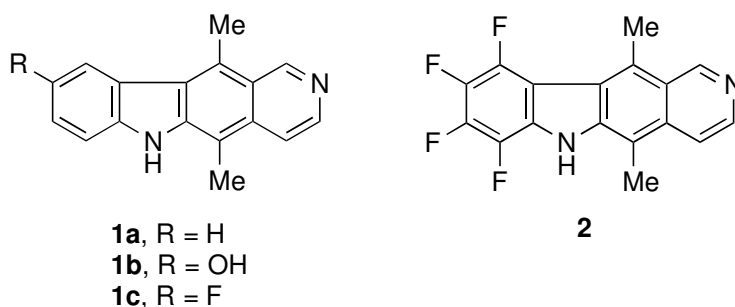


Keywords: Ellipticine, 7,8,9,10-tetrafluoroellipticine, 4,5,6,7-tetrafluoroindole, lithiation

Introduction

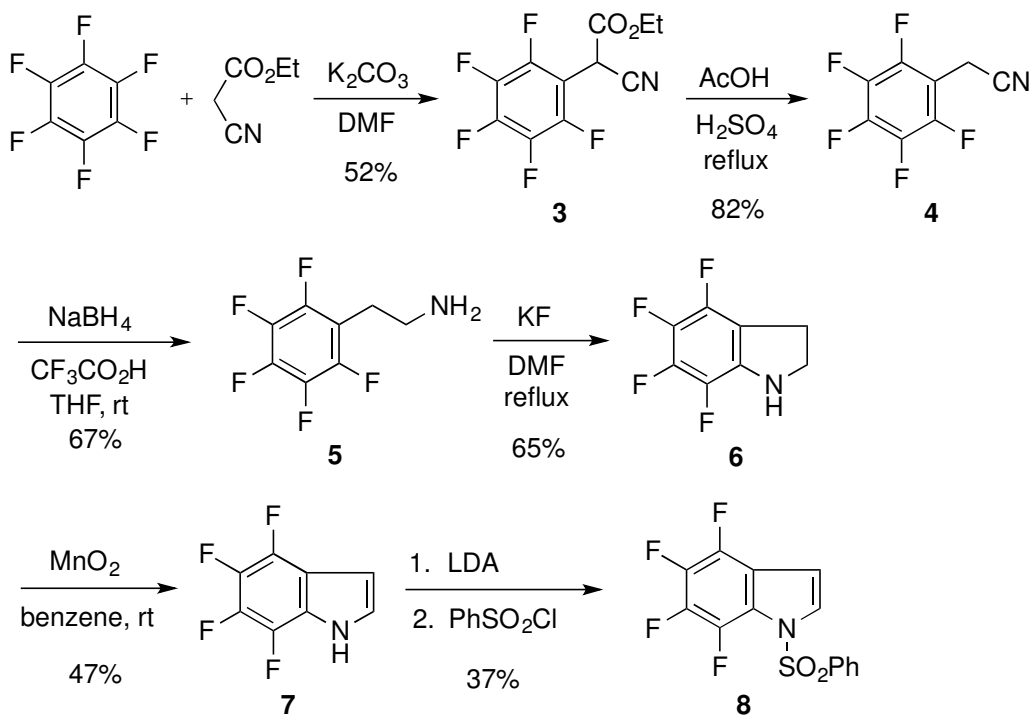
The synthesis and biological evaluation of substituted ellipticine (5,11-dimethyl-6*H*-pyrido[4,3-*b*]carbazole) derivatives has been of intense interest for several decades.¹⁻³ Notably, ring-A substitution can have a major impact on the biological activity of ellipticine (**1a**).⁴⁻¹¹ The prototypical example is 9-hydroxyellipticine (**1b**), which has a high affinity for DNA, high activity against L1210 mice leukemia, and low toxicity at a therapeutic dose.¹² Of special interest is 9-fluoroellipticine (**1c**), which inhibits aryl hydrocarbon hydroxylase without inducing mutagenicity.^{13,14}

In continuation of our synthetic efforts in this area, we now report the synthesis of the novel 7,8,9,10-tetrafluoroellipticine (**2**); the method is illustrative of its versatility in the construction of pyridocarbazoles.¹⁵⁻¹⁷ This ellipticine analogue seemed to be an attractive target given the profound biological effect that fluorine has both on ellipticine (i.e, **1c**) and in other biological molecules.¹⁸⁻²⁴ Thus, tetrafluorination should both increase the acidity of the NH and mitigate against metabolism of this ring. Moreover, the basicity of the pyridine nitrogen should be decreased by the strongly electron-withdrawing ability of multiple fluorines.



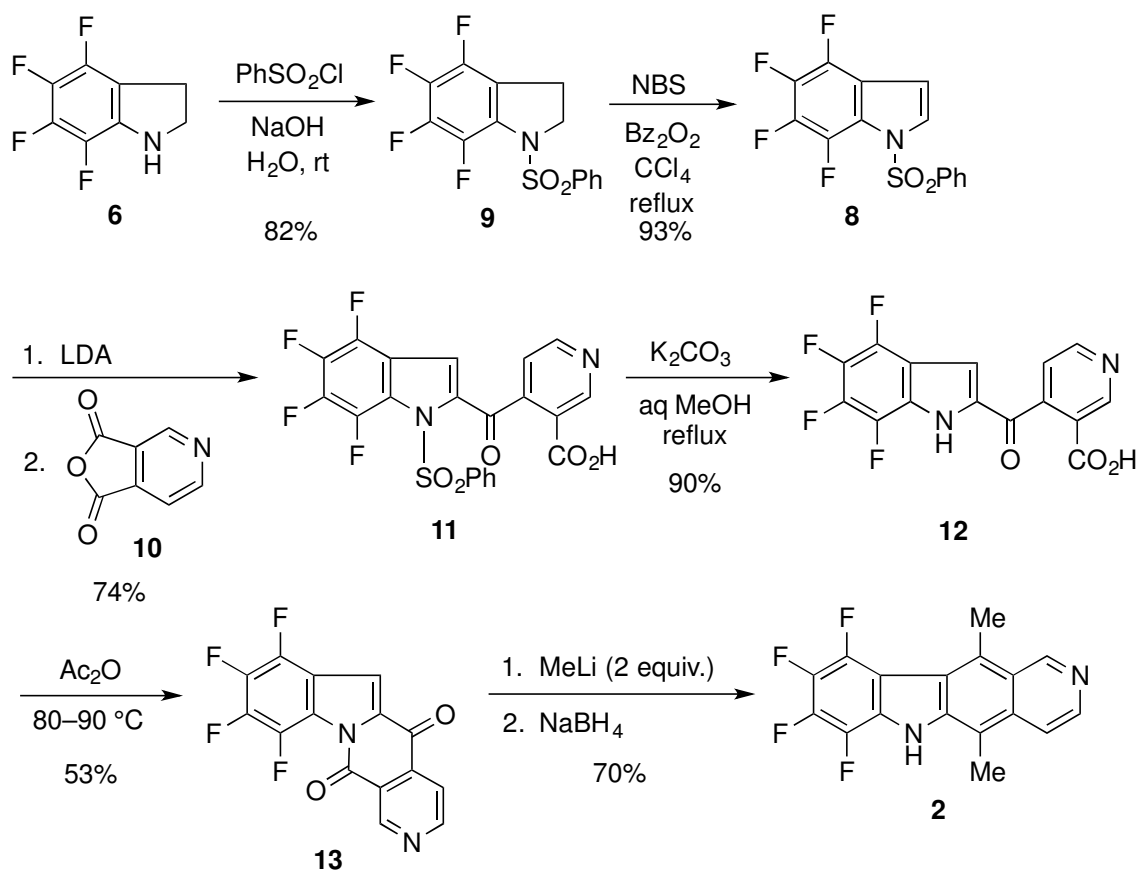
Results and Discussion

Our synthesis of **2** is summarized in Schemes 1 and 2. Our first goal became the synthesis of 4,5,6,7-tetrafluoroindole (**8**), which was first synthesized by Brooke in 1967.²⁵ The low yield from this procedure precluded its use here, so we adopted a method described by Petrov²⁶ and later by Filler.²⁷ Cyano-ester **3** was prepared by condensation of hexafluorobenzene with the anion of ethyl cyanoacetate to give ethyl α -cyano-(pentafluorophenyl)acetate (**3**) in 52% yield (Scheme 1). Hydrolysis and decarboxylation was achieved in refluxing acid to afford 2,3,4,5,6-pentafluorophenylacetonitrile (**4**) in 82% yield. Whereas Filler reduced the nitrile **4** to amine **5** using catalytic hydrogenation,²⁷ we employed sodium trifluoroacetoxyborohydride as reported by Umino,²⁸ which led to 2-(pentafluorophenyl)ethanamine (**5**) in 67% yield. Subjecting amine **5** to KF in hot DMF gave 4,5,6,7-tetrafluoroindoline (**6**) in 65% yield. Oxidation of indoline **6** to 4,5,6,7-tetrafluoroindole (**7**) using manganese dioxide as described by Filler proceeded only in 47% yield despite several attempts. Therefore, we protected the indole NH using lithium diisopropylamide followed by benzenesulfonyl chloride to give the desired 1-(phenylsulfonyl)-4,5,6,7-tetrafluoroindole (**8**) in 37% yield. The disappointing two-step yield of only 17% urged us to seek an alternative route to **8** (Scheme 2).



Scheme 1

In the event, we treated indoline **6** with benzenesulfonyl chloride to give 1-(phenylsulfonyl)-4,5,6,7-tetrafluoroindoline (**9**) in 82% yield. Whereas oxidation to indole **8** failed using chloranil, *N*-bromosuccinimide worked beautifully to give 1-(phenylsulfonyl)-4,5,6,7-tetrafluoroindole (**8**) in 93% yield (Scheme 2).



Scheme 2

The key step in the final synthesis of **2** is the regioselective acylation of 2-lithio-1-(phenylsulfonyl)-4,5,6,7-tetrafluoroindole with 3,4-pyridinedicarboxylic acid (cinchomeric acid) anhydride (**10**).^{29,30} This sequence proceeded to give the keto acid **11** in 74% yield, after recrystallization to remove traces of the regioisomer. This material was directly hydrolyzed to keto acid **12** (90% yield) and, without purification, was cyclized to keto lactam **13** in hot acetic anhydride in 53% yield after recrystallization. Finally, treatment of **13** with methyllithium (2 equivalents) followed by work-up and treatment of the crude mixture of diols with NaBH₄ gave the desired 7,8,9,10-tetrafluoroellipticine (**2**) in 70% yield after flash chromatography. The overall yield of **2** from 1-(phenylsulfonyl)-4,5,6,7-tetrafluoroindole (**8**) is 25%. By comparison, our related synthesis of ellipticine from indole gave a yield of 54%.¹⁵ Not unexpectedly, the proton NMR spectrum of **2** shows long-range, through-space coupling (3.7 Hz) between the C-11 methyl group and the C-10 fluorine.³¹

Experimental Section

General. Melting points were determined in open capillaries with a Büchi 510 melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 599 instrument. ¹H NMR spectra were routinely obtained at 70 MHz with a Varian EM360A spectrometer, while ¹³C NMR spectra were obtained with a Varian XL-300 spectrometer. Chemical shifts are reported in parts per million downfield from tetramethylsilane as an internal reference. Low-resolution mass spectra were determined on a Finnegan EI-Cl gas chromatograph-mass spectrometer. Flash chromatography employed 230-400 mesh silica gel. Thin layer chromatography was performed on precoated (0.2 mm) silica gel 60 F₂₅₄ plastic sheets (E. Merck). Spots were visualized under 254 nm ultraviolet light. The alkyllithium reagents were purchased from Aldrich and were standardized by titration against diphenylacetic acid. Tetrahydrofuran was distilled from sodium metal/benzophenone, and diisopropylamine was distilled over sodium hydride. All reactions were performed in oven-dried (130 °C) or flame dried glassware under prepurified nitrogen or argon.

Ethyl α-cyanopentafluorophenylacetate (3). A mixture of spectral grade dimethylformamide (350 mL) and anhydrous K₂CO₃ (77 g, 0.55 mol) was heated to reflux in a 1 L, three-neck flask equipped with a mechanical stirrer, thermometer, an addition funnel, and a condenser. When the temperature of the mixture reached 150 °C, H₂O was allowed to flow through the condenser and ethyl cyanoacetate (62.0 g, 0.55 mol) was added dropwise rapidly without further heating. The temperature of the bright orange mixture was allowed to drop to 110–120 °C and maintained within this range while hexafluorobenzene (102.0 g, 0.55 mol) was added dropwise. The deep brown mixture was stirred, at the above temperature, for 3 h after the addition, then poured into 1 L of ice-cold H₂O and acidified with H₂SO₄ solution (20%) until all K₂CO₃ dissolved. A dark brown layer settled to the bottom, and after cooling for 2 h, the top layer was decanted and exhaustively extracted with Et₂O. The organic layer was dissolved in Et₂O, washed with H₂O, saturated NaHCO₃ solution, and dried (MgSO₄). The combined ethereal layers were then concentrated *in vacuo* to yield 107.9 g (52%) of **3** as a brown oil which formed yellow crystals when cooled to 0 °C. The solid was filtered off and recrystallized from 95% EtOH to yield white crystals: mp 34–35 °C (lit.²⁷ mp 32 °C); ¹H NMR (CDCl₃) δ 5.10 (s, 1H), 4.33 (q, 2H), 1.33 (t, 3H).

2,3,4,5,6-Pentafluorophenylacetonitrile (4). Ethyl α-cyanopentafluorophenylacetate (105.3 g, 397 mmol) was refluxed for 12 h in 50% AcOH (300 mL) containing H₂SO₄ (conc., 10 mL). The mixture was then cooled to rt, diluted with an equal volume of H₂O, stirred, and a viscous, dark layer settled to the bottom of the flask. The mixture was chilled in an ice bath, the top layer was decanted until the remaining mixture consisted mostly of

the dark layer, which was then transferred to a separatory funnel, where the remaining water layer was removed. The dark layer was then extracted with Et₂O, and the ethereal layers were combined, washed with H₂O, saturated NaHCO₃ solution, and dried (MgSO₄) to yield 79.74 g of crude pentafluorophenylacetonitrile. Distillation gave 67.1 g (324 mmol, 82%) of **4**: bp 65 °C (0.20 Torr) (lit.²⁷ bp 105–107 °C (8 Torr)). IR (neat) 2975, 2260, 1660, 1540, 1140 cm⁻¹; mass spectrum, *m/e* 207 (M⁺, 100%), 188, 181, 161, 157, 117, 93, 69.

2-(Pentafluorophenyl)ethanamine (5). To a stirred suspension of NaBH₄ (12.4 g, 324 mmol) in dry THF (200 mL) under predried argon was added CF₃CO₂H (36.9 g, 324 mmol) in dry THF (30 mL) over a period of 10 min at 20 °C. 2,3,4,5,6-Pentafluorophenylacetonitrile (**4**) (67.07 g, 324 mmol) was then added dropwise in dry THF (30 mL), and the mixture was stirred at rt for 4 h after this addition. The excess reagent was then cautiously decomposed with H₂O below 10 °C in an ice bath, and the resulting mixture was concentrated to dryness *in vacuo*, and extracted with CH₂Cl₂. The extract was washed with saturated NaHCO₃ solution, H₂O, and dried over anhydrous Na₂SO₄. Concentration *in vacuo* yielded of **5** as a residual green oily layer (45.74 g, 67%), which was used without further purification for the preparation of 4,5,6,7-tetrafluoroindole. In order to characterize the amine, a small amount was distilled to give a colorless liquid; bp 96–102 °C (33 Torr) (lit.²⁷ bp 80–90 °C (20 Torr)); IR (neat) 3350, 2940, 2860, 1660, 1525, 1510 cm⁻¹; ¹H NMR (CDCl₃) δ 1.25 (m, 2H), 3.25 (m, 2H); UV (95% EtOH) λ_{max} 225, 247 nm.

4,5,6,7-Tetrafluoroindoline (6). Pentafluorophenylethylamine (6.5 g, 32 mmol) as the residual dark olive oil was taken up in spectroscopic grade DMF (300 mL). Anhydrous KF (3.0 g) was then added and the mixture was refluxed for 3 h with mechanical stirring under an atmosphere of dry N₂. The mixture was allowed to cool to rt and DMF (~250 mL) was removed by vacuum distillation. The reaction flask was transferred to a steam distillation apparatus and its contents were exhaustively steam distilled (~1 L condensed water collected). The cloudy effluent was filtered, then extracted with Et₂O (3 × 50 mL) to yield a combined product (3.82 g, 65%) as odiferous white crystals. Further purification by sublimation *in vacuo* yielded **6** as white crystals (3.52 g): mp 61–62 °C (lit.²⁶ mp 60–61 °C; lit.²⁷ mp 60 °C), IR (CCl₄) 3410, 2870, 1655, 1520, 1510 cm⁻¹; UV (95% EtOH) λ_{max} 223, 282 nm; ¹H NMR (CDCl₃) δ 3.70 (m, 3H), 3.13 (t, 2H).

4,5,6,7-Tetrafluoroindole (7). A magnetically stirred mixture of indoline **6** (4.50 g, 23.5 mmol), activated MnO₂ (22.0 g), type 4A molecular sieves, and 190 mL of dry benzene was stirred for 60 h during which time the temperature was maintained at 20 °C, occasionally reaching 30 °C. After the mixture was filtered using Filtercell, the solid residue was placed in a Soxhlet apparatus and extracted with 300 mL of dry benzene for 7 h. The filtrate and the extraction liquid were then combined and concentrated *in vacuo* to yield a brown oil. The oil was then purified by chromatography over neutral alumina (25 g) in hexanes (3 cm column), eluting first with hexanes (250 mL), then 50:50 hexane-Et₂O (250 mL), and finally, with Et₂O (250 mL). The hexane and hexane-ether fractions were concentrated *in vacuo* to yield 2.1 g (47%) of **7**: mp 92–94 °C (lit.²⁶ mp 93–93.5 °C; lit.²⁷ mp 91–92.5 °C). IR (KBr) 3470, 1540, 1480, 1420, 1390, 1350, 980, 880 cm⁻¹; UV (95% EtOH) λ_{max} 227, 250 nm; ¹H NMR (CDCl₃) δ 8.36 (s, broad, 1H), 7.20 (m, 1H), 6.62 (m, 1H).

1-(Phenylsulfonyl)-4,5,6,7-tetrafluoroindoline (9). A magnetically stirred solution of tetrafluoroindoline (**6**) (8.40 mg, 44.0 mmol) in aq NaOH solution (10%, 600 mL) was treated dropwise with benzenesulfonyl chloride (44.6 g, 0.264 mol, 33.7 mL) over 2 h at rt maintaining the temperature at ~20 °C with a cold water bath. Two more equivalents of benzenesulfonyl chloride (2 × 33.7 mL, 0.528 mol) were added over 8 h to drive the reaction to completion. NaOH (pellets, ~20 g) were also added to maintain a strongly alkaline solution, and the reaction mixture was stirred overnight to complete the hydrolysis of excess benzenesulfonyl chloride. The solution was then slowly acidified with 20% aq HCl (20%, ~500 mL) with adequate stirring and cooling, and the resulting aqueous mixture was exhaustively extracted with CH₂Cl₂ (6 × 200 mL). The combined extracts were washed with 10% HCl (3 × 200 mL), 5% NaHCO₃ (1 × 200 mL), H₂O (1 × 200 mL), brine (2 × 300 mL), and dried

(Na₂SO₄). Concentration *in vacuo* yielded **9** (11.98 g, 82%) as a bright orange product. Recrystallization from Et₂O yielded **9** (9.60 g, 66%) as light orange fluffy crystals: mp 127 °C; UV (95% EtOH) λ_{max} 240, 271 (sh), 273 (sh) nm; ¹H NMR (CDCl₃) δ 7.66 (m, 5H), 4.22 (t, 2H), 2.75 (t, 2H); ¹³C NMR (CDCl₃) δ 139.2, 138.7, 137.0, 135.6, 135.5, 131.0, 130.8, 130.6, 130.5, 128.8, 128.5, 128.4, 126.6, 118.0, 117.6; mass spectrum, *m/e* 331 (M⁺), 190, 189, 170, 163, 141, 77 (100%), 51; HRMS (ES⁺) *m/z* calcd for C₁₄H₉F₄NO₂S (M+1) 332.0368, found 332.0371.

1-(Phenylsulfonyl)-4,5,6,7-tetrafluoroindole (**8**)

(a) from the indoline **9.** A mixture of the protected tetrafluoroindoline **9** (7.95 g, 24.0 mmol), *N*-bromosuccinimide (4.28 g, 24.0 mmol), and benzoyl peroxide (0.60 g) in reagent grade CCl₄ (500 mL) was heated to reflux. After 12 h of refluxing, the reaction mixture was allowed to cool to rt, and then evaporated to dryness *in vacuo*. The residue was dissolved in Et₂O (500 mL), washed with H₂O (3 × 100 mL), aq NaHCO₃ (10%, 2 × 100 mL), and dried (Na₂SO₄). The combined ethereal layers were then concentrated *in vacuo* to yield 9.24 g of a crude brown solid. Flash chromatography over silica gel with hexane:Et₂O (20:1) yielded 7.35 g (93%) of **8** as off-white crystals. Recrystallization from diethyl ether gave **8** as white crystals in three crops: mp 124–125 °C; ¹H NMR (CDCl₃) δ 7.66 (m, 6H), 6.83 (q, 1H); UV (95% EtOH) λ_{max} 213, 245 (sh), 276, 286 nm; mass spectrum, *m/e* 329 (M⁺), 188, 161, 141, 78, 77 (100%), 69, 51, 50; HRMS (ES⁺) *m/z* calcd for C₁₄H₈F₄NO₂S (M+1) 330.0212, found 330.0228.

(b) from the indole **7.** To a magnetically stirred solution of lithium diisopropylamide (LDA) (11.8 mmol, 1.1 equiv) prepared from diisopropylamine (1.31 g, 12.9 mmol, 1.81 mL), and *n*-butyllithium (2.22 M in hexane, 5.32 mL, 11.8 mmol) in dry THF (50 mL) at -78 °C was added via syringe over 40 min a solution of **7** (2.03 g, 10.7 mmol) in dry THF (35 mL). The temperature of the solution was not allowed to rise above -70 °C during the addition, and then the red mixture was allowed to warm to rt over 8 h. The solution was then recooled to -78 °C and treated via syringe with neat benzenesulfonyl chloride (1.89 g, 10.7 mmol, 1.36 mL) over 15 min while keeping the internal temperature below -70 °C. The reaction mixture was then allowed to warm slowly to rt overnight, and then poured into aq NaHCO₃ (2%, 100 mL) and extracted with Et₂O (2 × 100 mL). The combined ethereal layers were washed with 10% NaHCO₃ solution (2 × 100 mL), H₂O (2 × 50 mL), brine (2 × 75 mL), dried (Na₂SO₄), and concentrated *in vacuo* to yield 4.07 g of a crude brown oil that solidified. Recrystallization from Et₂O gave **8** (1.02 g, 37%) as a tan powder in three crops, mp 126 °C. This material was identical to the sample prepared above by mp, ¹H NMR, UV and IR spectra.

3,4-Pyridinedicarboxylic acid anhydride (10**).** A magnetically stirred mixture of 3,4-pyridinedicarboxylic acid (25.0 g, 0.15 mol) and Ac₂O (100 mL) was refluxed for 45 min. All of the solid material dissolved to form a black colored solution. The Ac₂O was removed by distillation at 40 °C (15 Torr) and the product was distilled to afford **10** (19.6 g (88%)) as a white solid: mp 77–78 °C (lit.³⁰ mp 76–77 °C).

4-[[1-(Phenylsulfonyl)-4,5,6,7-tetrafluoroindol-2-yl]carbonyl]pyridine-3-carboxylic acid (11**).** To a magnetically stirred solution of lithium diisopropylamide (LDA) (18.8 mmol, 1.1 equiv) prepared from diisopropylamine (2.08 g, 20.5 mmol, 288 mL), and *n*-butyllithium (2.22 M in hexane, 8.49 mL, 18.8 mmol) in dry THF (50 mL) at -50 °C was added via syringe over 5 min a solution of **8** (5.64 g, 17.1 mmol) in dry THF (45 mL). The orange-red mixture was then allowed to warm to rt over 4 h. The solution was then cooled to -100 °C (dry ice/pentane/liquid nitrogen bath) and treated as rapidly as possible with a solution of 3,4-pyridinedicarboxylic acid anhydride (**10**) (2.81 g, 18.8 mol) in dry THF (40 mL) while maintaining efficient stirring at -100 °C for 1 h, and then allowed to warm slowly to rt overnight. Removal of the solvent *in vacuo* left a dark solid, which was dissolved in H₂O (300 mL), and slowly acidified to pH 2–3 with 20% HCl. The resulting white precipitate was filtered, and dried *in vacuo* at 80 °C/0.5 Torr to yield a tan solid (7.84, 96%). Recrystallization in Me₂CO gave 6.02 g (74%) of **11** as an off-white powder in three crops: mp 181–182 °C; UV

(95% EtOH) λ_{\max} 220, 269 (sh), 276 (sh), 292 nm; IR (KBr) 3400, 3100, 1690, 1555, 1505, 1490, 1450, 1340, 1225, 1045, 1015, 750, 720 cm^{-1} ; mass spectrum, m/e (M^+ 478) 320, 264, 187, 161, 78, 77 (100%), 51. This crude material was used directly in the next step.

4-[(4,5,6,7-Tetrafluoroindol-2-yl)carbonyl]pyridine-3-carboxylic acid (12). A magnetically stirred mixture of the protected keto acid **11** (3.00 g, 6.26 mmol), K_2CO_3 (3.45 g, 25.0 mmol), H_2O (80 mL), and MeOH (240 mL) was refluxed under N_2 for 4.5 h. After cooling, the solvents were removed to give a dark brown oil, which was dissolved in distilled H_2O (250 mL), and acidified to pH ~2–4 with 20% HCl while maintaining efficient cooling and stirring. The aqueous portion was then saturated with NaCl, and extracted with EtOAc (4 \times 200 mL). The combined extracts were washed with H_2O (2 \times 150 mL), brine (2 \times 150 mL), and dried (Na_2SO_4). Rotary evaporation of the solution afforded 1.90 g (90%) of **12** as a yellow solid. This product was difficult to purify, and was used crude in the next step: mp 178–182 $^\circ\text{C}$; UV (95% EtOH) λ_{\max} 223, 301 nm; IR (KBr) 3100, 1715, 1550, 1495, 1380, 1340, 1230, 750 cm^{-1} ; mass spectrum, m/e 320 (M^+ , 100%) 264, 187, 161, 105, 78, 77, 50.

7,8,9,10-Tetrafluoroindolo[2,1-g]isoquinoline-5,12-dione (13). A mixture of the crude keto acid **12** (1.80 g, 5.31 mmol) was heated under N_2 with magnetic stirring in neat Ac_2O (300 mL) at 80–90 $^\circ\text{C}$ for 24 h. The Ac_2O was almost completely removed by distillation at 40 $^\circ\text{C}$ (~15 Torr). The cooled residue was treated with H_2O (250 mL), stirred, and filtered to afford a crude yellow-brown product. Recrystallization from Me_2CO gave 0.91 g (53%) of keto lactam (**13**) as dark yellow prisms: mp 240 $^\circ\text{C}$. UV (95% EtOH) λ_{\max} 215 (sh), 232, 307, 370 nm, addition of 3 drops 10% NaOH gave UV λ_{\max} 219, 240 (sh), 270, 332 nm; IR (KBr) 3100, 1715, 1670, 1560, 1520, 1365, 1340, 1140, 1045, 1020, 995, 870, 800, 720; ^1H NMR (d_6 -DMSO) δ 9.52 (s, 1H), 9.19 (d, 1H), 8.06 (d, 2H) cm^{-1} ; ^{13}C NMR (d_6 -DMSO) δ 110.7, 118.2, 136.2, 138.2, 150.4, 155.6, 155.7, 156.5, 174.5; mass spectrum, m/e 321, 320 (M^+ , 100%), 292, 264, 237, 187, 77, 50. *Anal.* Calcd for $\text{C}_{15}\text{H}_4\text{F}_4\text{N}_2\text{O}_2$: C, 56.27; H, 1.26; N, 8.75. Found: C, 56.00; H, 1.21; N, 8.68.

7,8,9,10-Tetrafluoroellipticine (2). A magnetically stirred solution of the fluoro keto lactam **13** (0.50 g, 1.55 mmol) in dry THF (60 mL) was cooled to -100 $^\circ\text{C}$ and treated over 10 sec with methyllithium (0.176 M CH_3Li in Et_2O , 17.6 mL, 3.10 mmol). The resulting tan mixture was stirred at -100 $^\circ\text{C}$ for 1 h, and was allowed to warm rt over 5 h. Distilled H_2O (5 mL) was added the mixture was stirred for 15 min, and the THF was removed *in vacuo* to give a brown yellow residue. This material was immediately treated with absolute EtOH (100 mL), and excess NaBH_4 (5 pellets, *ca.* 1.25 g), and then refluxed with magnetic stirring for 18 h. The NaBH_4 was added in four portions during the 18 h reaction time. After 1 h, the reaction mixture became yellow, and was brightly fluorescent. The reaction mixture was then cooled, and the solvents were removed *in vacuo*. The resulting tan solid was dissolved in CHCl_3 (200 mL), stirred for 15 min, and then treated with distilled H_2O (200 mL). The phases were separated and the aqueous portion was extracted with additional CHCl_3 (3 \times 50 mL). The aqueous layer was then partitioned over fresh CHCl_3 (75 mL), and slowly acidified to pH 2–4 with 20% HCl, and then basified with aqueous 2 M NaOH to pH ~10. The aqueous layer was further extracted with CHCl_3 (1 \times 100 mL), and the organic layers were combined, washed with H_2O (1 \times 150 mL), and dried (Na_2SO_4). The compound was then absorbed onto silica gel *in vacuo*, and flash chromatography over silica gel (25 cm column) with EtOAc gave 0.34 g (70%) of 7,8,9,10-tetrafluoroellipticine **2** as a bright yellow solid which fluoresces light blue under UV (254 nm) light: mp 281–282 $^\circ\text{C}$; UV (95% EtOH) λ_{\max} 212, 232 (sh), 274, 312 (sh), 325 (sh), 395 nm, addition of 2 drops 20% HCl to the cuvette gave UV λ_{\max} 212, 240, 290, 343 (sh), 425 nm; IR (KBr) 3450, 3000, 1665, 1600, 1530, 1315, 1005, 860, 800 cm^{-1} ; ^1H NMR (d_4 -MeOH) δ 9.58 (s, 1H), 8.41 (d, 1H, J = 6.2 Hz), 8.22 (d, 1H, J = 6.2 Hz), 3.21 (d, 3H, J = 3.7 Hz, through-space coupling to fluorine at C-10), 3.01 (s, 3H); mass spectrum, m/e 318 (M^+ , 100%) 317, 303, 81, 73, 69, 60, 55; HRMS (ES+) m/z calcd for $\text{C}_{17}\text{H}_{11}\text{F}_4\text{N}_2$ ($M+1$) 319.0858, found 319.0867.

Acknowledgements

We thank Dartmouth College for support, and Drs. Milind Rajopadhye for technical assistance.

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