Synthesis of 6-fluoroalkylbenzo[*h*]cyclopenta[*c*]quinoline and -benzo[*c*]phenanthridine derivatives

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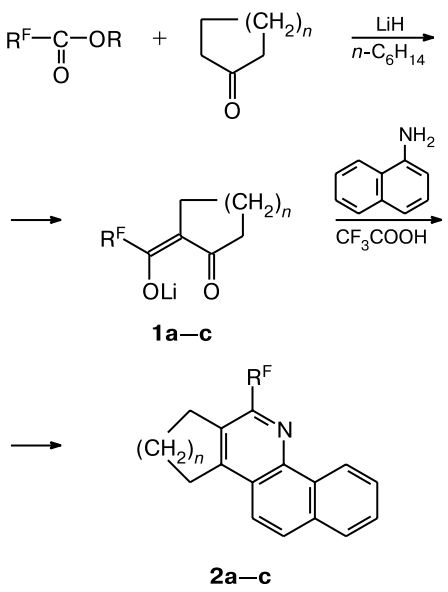
Cyclization of 2-fluoroacylcycloalkanone lithium enolates (**1a—c**, Scheme 1) with α-naphthylamine afforded 6-fluoroalkylbenzo[*h*]dihydrocyclopenta[*c*]quinoline (**2a**) and -benzo[*c*]tetrahydrophenanthridine derivatives (**2b,c**).

Scheme 1



R^F = HCF_2, *n* = 1 (**a**); R^F = HCF_2, *n* = 2 (**b**); R^F = CF_3, *n* = 2 (**c**)
R = Me, Et

Enolates **1a—c** were synthesized using a known procedure.[1] ^{1}H, ^{19}F, and ^{13}C-{^{1}H} NMR spectra were recorded on a Bruker DRX-400 spectrometer (400 (^{1}H), 376 (^{19}F), and 100 MHz (^{13}C)) using $CDCl_3$ as the solvent and Me_4Si (^{1}H and ^{13}C) and C_6F_6 (^{19}F) as the internal standards. The reaction course was monitored by TLC on Silufol UV-254 plates using $CHCl_3$ as the eluent.

6-Difluoromethyl-8,9-dihydro-7*H*-benzo[*h*]cyclopenta[*c*]quinoline (2a). A solution of enolate **1a** (2 g, 12 mmol) and α-naphthylamine (1.7 g, 12 mmol) in CF_3COOH (10 mL) was refluxed until the starting compounds disappeared. The reaction mixture was poured on ice, and a precipitate was filtered off and recrystallized from *n*-hexane. The yield of compound **2a** was 1.5 g (47%), m.p. 146 °C. Found (%): C, 75.98; H, 4.91; F, 14.11; N, 5.23. $C_{17}H_{13}F_2N$. Calculated (%): C, 75.82; H, 4.87; F, 14.11; N, 5.20. ^{1}H NMR, δ: 2.26 (tt, 2 H, H(8), J = 7.6 Hz); 3.20 (t, 2 H, H(9), J = 7.6 Hz); 3.31 (tt, 2 H, H(7), J = 7.6 Hz, $J_{H,F}$ = 1.6 Hz); 6.87 (t, 1 H, HCF_2, $J_{H,F}$ = 55.0 Hz); 7.59 (d, 1 H, H(10), J = 9.0 Hz); 7.65 (ddd, 1 H, H(2), J = 7.8 Hz, J = 6.9 Hz, J = 1.5 Hz); 7.70 (ddd, 1 H, H(3), J = 8.1 Hz, J = 6.9 Hz, J = 1.4 Hz); 7.77 (d, 1 H, H(11), J = 9.0 Hz); 7.85 (dd, 1 H, H(1), J = 7.8 Hz, J = 1.4 Hz); 9.25 (dd, 1 H, H(4), J = 8.1 Hz, J = 1.5 Hz). ^{13}C NMR, δ: 24.56 (C(8)); 30.50 (t, C(7), $^4J_{C,F}$ = 2.0 Hz); 30.77 (C(9)); 117.08 (t, HCF_2, $^1J_{C,F}$ = 239.7 Hz); 121.72 (C(10)); 124.49 (C(9b)); 124.70 (C(4)); 127.23 (C(3)); 127.86 (C(1)); 127.94 (C(2)); 128.83 (C(11)); 131.69 (C(4a)); 133.20 (C(11a)); 135.13 (C(6a)); 143.76 (t, C(4b)), $^4J_{C,F}$ = 1.4 Hz); 146.86 (t, C(6), $^2J_{C,F}$ = 27.3 Hz); 153.09 (t, C(9a), $^4J_{C,F}$ = 1.4 Hz). ^{19}F NMR, δ: 47.95 (dt, HCF_2, $^2J_{H,F}$ = 55.0 Hz, $^5J_{H,F}$ = 1.6 Hz).

6-Difluoromethyl-7,8,9,10-tetrahydrobenzo[*c*]phenanthridine (2b). Compound **2b** was synthesized similarly from enolate **1b** (1.5 g, 9 mmol) and α-naphthylamine (1.27 g, 9 mmol), yield 1.3 g (51%), m.p. 146—147 °C. Found (%): C, 76.17; H, 5.30; F, 13.49; N, 5.30. $C_{18}H_{15}F_2N$. Calculated (%): C, 76.31; H, 5.33; F, 13.41; N, 4.94. ^{1}H NMR, δ: 1.89—2.02 (m, 4 H, H(8), H(9)); 3.10 (m, 2 H, H(10)); 3.14 (m, 2 H, H(7)); 6.93 (t, 1 H, HCF_2, $J_{H,F}$ = 54.9 Hz); 7.63 (ddd, 1 H, H(2), J = 7.7 Hz, J = 6.8 Hz, J = 1.5 Hz); 7.68 (ddd, 1 H, H(3), J = 8.1 Hz, J = 6.8 Hz, J = 1.6 Hz); 7.72, 7.76 (both d, 1 H each, H(11), H(12), J = 9.1 Hz); 7.83 (dd, 1 H, H(1), J = 7.7 Hz, J = 1.6 Hz); 9.25 (dd, 1 H, H(4), J = 8.1 Hz, J = 1.5 Hz). ^{13}C NMR, δ: 21.88 (C(8)); 22.04 (C(9)); 24.33 (t, C(7), $^4J_{C,F}$ = 3.5 Hz); 26.10 (C(10)); 118.64 (t, HCF_2, $^1J_{C,F}$ = 242.4 Hz); 120.15 (C(11)); 124.50 (C(4)); 125.96 (C(10b)); 127.16 (C(3)); 127.59 (C(1)); 127.86 (C(2)); 128.76 (C(12)); 129.25 (C(4a)); 131.74 (C(12a)); 132.87 (C(6a)); 142.32 (t, C(4b), $^4J_{C,F}$ = 1.4 Hz); 143.77 (C(10a)); 148.57 (t, C(6), $^2J_{C,F}$ = 25.1 Hz). ^{19}F NMR, δ: 49.23 (d, HCF_2, $^2J_{H,F}$ = 54.9 Hz).

6-Trifluoromethyl-7,8,9,10-tetrahydrobenzo[*c*]phenanthridine (2c). Compound **2c** was obtained similarly from enolate **1c** (2 g, 1 mmol) and α-naphthylamine (1.43 g, 1 mmol), yield 1.81 g (61%), m.p. 142 °C. Found (%): C, 71.75; H, 4.70; F, 19.17; N, 4.65. $C_{18}H_{14}F_3N$. Calculated (%): C, 71.75; H, 4.68;

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F, 18.92; N, 4.65. ^{1}H NMR, δ: 1.86—1.97 (m, 4 H, H(8), H(9)); 3.06 (tq, 2 H, H(7), J = 6.2 Hz, $J_{H,F}$ = 1.3 Hz); 3.16 (t, 2 H, H(10)); 7.66 (ddd, 1 H, H(2), J = 7.7 Hz, J = 7.0 Hz, J = 1.6 Hz); 7.71 (ddd, 1 H, H(3), J = 8.2 Hz, J = 7.0 Hz, J = 1.5 Hz); 7.76, 7.82 (both d, 1 H each, H(11), H(12), J = 9.1 Hz); 7.85 (dd, 1 H, H(1), J = 7.7 Hz, J = 1.5 Hz); 9.29 (dd, 1 H, H(4), J = 8.2 Hz, J = 1.6 Hz). ^{13}C NMR, δ: 21.90 (C(8), C(9)); 24.95 (q, C(7), $^4J_{C,F}$ = 3.1 Hz); 26.27 (C(10)); 119.95 (C(11)); 122.72 (q, CF_3, $^1J_{C,F}$ = 276.5 Hz); 124.82 (C(4)); 126.43 (C(10b)); 127.43 (C(3)); 127.56 (C(1)); 128.16 (C(2)); 128.61 (C(12)); 129.44 (C(4a)); 131.81 (C(12a)); 132.96 (C(6a)); 142.06 (C(4b)); 144.38 (q, C(6)), $^2J_{C,F}$ = 32.0 Hz); 144.39 (C(10a)). ^{19}F NMR, δ: 96.84 (t, CF_3, $^5J_{H,F}$ = 1.3 Hz).

References

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