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Generation of 11-Fluoro-11*H*-indeno[1,2-*c*]quinolines *via* a Palladium-Catalyzed Three-Component Reaction of 2-Alkynylbromobenzenes, 2-Alkynylanilines, and *N*-Fluorobenzenesulfonimide

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Abstract: A novel and efficient synthesis of 11-fluoro-11*H*-indeno[1,2-*c*]quinolines has been developed *via* a palladium-catalyzed three-component reaction of 2-alkynylbromobenzenes, 2-alkynylanilines, and *N*-fluorobenzenesulfonimide. The reaction works well with high selectivity. Additionally, the diversity and complexity could be easily introduced *via* a simple operation from readily available starting materials. In the meantime, a fluorine atom could be incorporated into the scaffold during the reaction process.

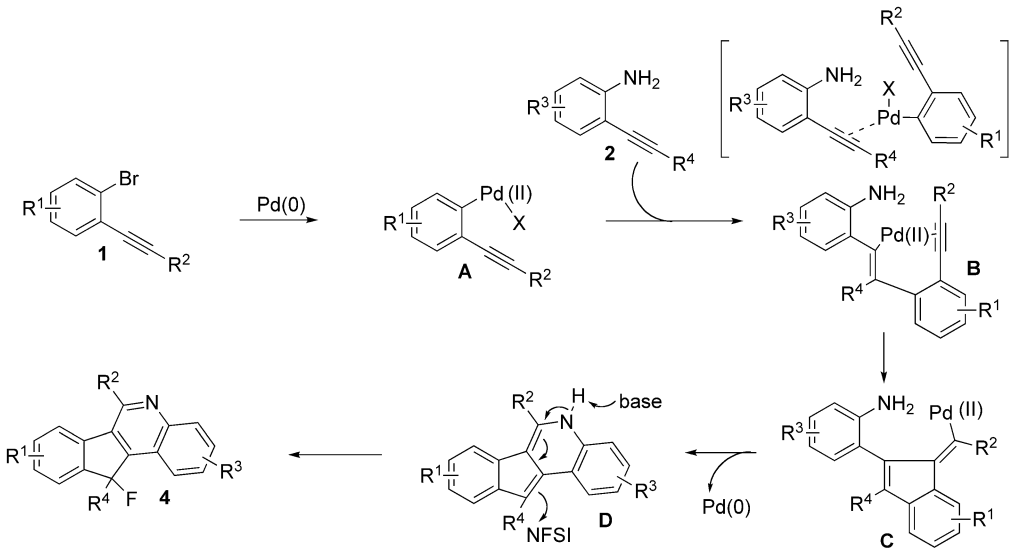
Keywords: 2-alkynylanilines; 2-alkynylbromobenzenes; homogeneous catalysis; *N*-fluorobenzenesulfonimide; 11-fluoro-11*H*-indeno[1,2-*c*]quinolines; palladium

Introduction

Molecules bearing a fluorine moiety are of great importance in pharmaceuticals since the fluorinated compounds can have significantly improved properties (such as solubility, bioavailability, and metabolic stability).[1] In the last decade, effort continues to be given to the methodological development for the synthesis of fluorinated molecules based on C–F bond formation.[2–5] For instance, Liu and co-workers achieved the generation of C–F bond *via* transition metal-catalyzed fluorination of unsaturated C–C bonds recently.[5] In the meantime, novel and efficient methods for the formation of natural product-like compounds are in great demand in the research on chemical genetics.[6] It would be of high interest to generate fluorinated natural product-like compounds for the further evaluation of different biological assays.

Quinoline is regarded as a privileged fragment, which is a ubiquitous subunit in many natural products and pharmaceuticals showing remarkable biological activities (finding use as antimalarial, anti-inflammatory agents, antiasthamatic, antibacterial, antihypertensive, and tyrosine kinase inhibiting agents).[7] Additionally, quinolines have been utilized as valuable synthons for the synthesis of nano- and mesostructures with enhanced electronic and photonic properties.[8] The indene scaffold is another kind of privileged structure, which can be observed in many drug candidates.[9] Applications of indenes have been demonstrated in materials science as well.[10] Inspired by the advance of diversity-oriented synthesis of natural product-like compounds, we conceived that a molecule which incorporated both quinoline and indene skeletons would be attractive. If a fluorine atom could be introduced to this scaffold, interesting biological activities would be expected from the corresponding focused library.

Recently, we have described an efficient and novel route for the generation of indeno[1,2-*c*]chromenes *via* a palladium-catalyzed cascade reaction[11] of 2-alkynylhalobenzenes with 2-alkynylphenols.[12a] Encouraged by this result, we envisioned that 2-alkynylanilines would be a good partner as well in the above transformation as a replacement for 2-alkynylphenols.



Scheme 1. A proposed synthetic route for the palladium-catalyzed three-component reaction of 2-alkynylbromobenzenes **1**, 2-alkynylanilines **2**, and *N*-fluorobenzenesulfonimide **3**.

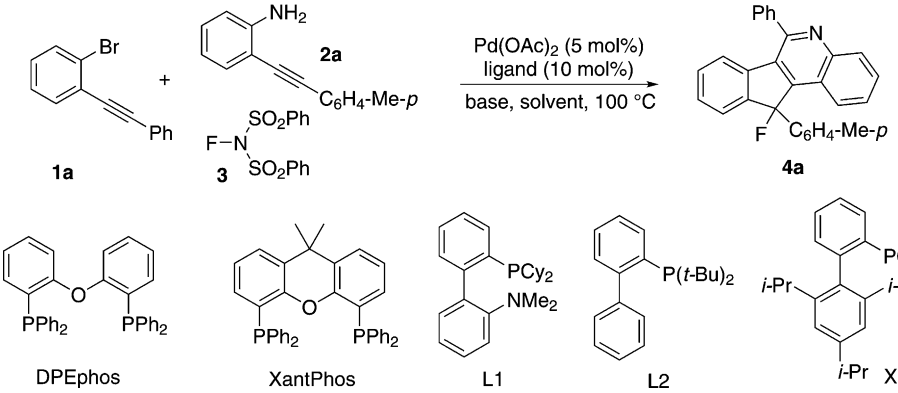
Therefore, 5*H*-indeno[1,2-*c*]quinoline would be obtained which incorporated both quinoline and indene skeletons as mentioned above. The proposed synthetic route is shown in Scheme 1. An oxidative addition of 2-alkynylbromobenzenes **1** to Pd(0) would occur to generate an intermediate **A**, which then coordinated with the triple bond of 2-alkynylanilines **2**. After double triple bond insertion, a vinyl Pd(II) species **C** would be formed, which subsequently undergoes an intramolecular C–N bond formation to afford 5*H*-indeno[1,2-*c*]quinoline **D**. In the presence of an electrophilic fluorine source (such as *N*-fluorobenzenesulfonimide **3**, NSFI), the fluorinated 11*H*-indeno[1,2-*c*]quinoline **4** would be furnished. Although several competitive reactions exist,[13] the attractiveness of 11-fluoro-11*H*-indeno[1,2-*c*]quinoline **4** and the challenge of the synthetic route described in Scheme 1 prompted us to explore the feasibility of this transformation.

Results and Discussion

To begin our study, 2-alkynylbromobenzene **1a** was first reacted with 2-alkynylaniline **2a** and *N*-fluorobenzenesulfonimide **3** catalyzed by palladium acetate (Table 1). A trace amount of the desired product **4a** was detected when PCy_3 was employed as the ligand in the presence of Na_2CO_3 in 1,4-dioxane (Table 1, entry 1). No reaction occurred when *t*-BuOK was used as a replacement for the base (Table 1, entry 2). Fortunately, the reaction proceeded as expected when NaOMe was utilized as base, albeit in low yield (Table 1, entry 3). With this promising preliminary result in hand, different ligands, bases, and solvents were screened. Finally, we realized that this reaction worked the most efficiently in the presence of $Pd(OAc)_2$, PCy_3 and *t*-BuONa in 1,4-dioxane, which generated the desired product **4a** in 73% yield. Another fluorinating reagent (such as Selectfluor) was employed in the above reaction as well. However, the reaction gave rise to the corresponding product **4a** in a lower yield. The reaction was retarded when the temperature was decreased or the catalytic amount of palladium acetate was reduced.

With the optimized reaction conditions in hand, we next investigated the scope of the reaction using different types of 2-alkynylbromobenzenes and 2-alkynylanilines. As shown in Table 2, this reaction proceeded with high selectivity to afford the desired products in moderate to good yields. 2-Alkynylanilines with both electron-donating and electron-withdrawing substituents could be smoothly converted into the desired products. For instance, 2-alkynylbromobenzene **1a** reacted with 2-alkynylaniline **2b** and *N*-fluorobenzenesulfonimide **3** leading to the corresponding product **4b** in 55% yield (Table 2, entry 2). A similar yield was obtained when 2-alkynylaniline **2c** with a *p*-methoxyphenyl group at the R^4 position was used as a replacement in the above reaction (50% yield, Table 2, entry 3). When 2-alkynylaniline **2d** with a *p*-chlorophenyl group at the R^4 position was utilized as a substrate, its reaction of 2-alkynylbromobenzene **1a** with *N*-fluorobenzenesulfonimide **3** gave rise to the expected product **4d** in a lower yield (Table 2, entry 4). Compared with the result from the reaction of 5-methyl-2-alkynylaniline **2e** (75% yield, Table 2, entry 5), an inferior yield was afforded when 5-chloro-2-alkynylaniline **2f** was employed as the substrate in the above reaction under the standard conditions (51% yield, Table 2, entry 6). Further explora-

Table 1. Initial studies for the palladium-catalyzed three-component reaction of 2-alkynylbromobenzene **1a**, 2-alkynylaniline **2a**, and *N*-fluorobenzenesulfonimide **3**.



Entry	Ligand	Base	Solvent	Yield [%][a]
1	PCy_3	Na_2CO_3	1,4-dioxane	trace
2	PCy_3	*t*-BuOK	1,4-dioxane	nr
3	PCy_3	NaOMe	1,4-dioxane	12
4	PCy_3	DABCO	1,4-dioxane	33
5	PCy_3	KOH	1,4-dioxane	64
6	PCy_3	K_3PO_4	1,4-dioxane	62
7	PCy_3	Cs_2CO_3	1,4-dioxane	52
8	PCy_3	*t*-BuONa	1,4-dioxane	73
9	PCy_3	*t*-BuONa	toluene	64
10	PCy_3	*t*-BuONa	DMF	42
11	DPPF[b]	*t*-BuONa	1,4-dioxane	trace
12	DPEphos	*t*-BuONa	1,4-dioxane	nr
13	XantPhos	*t*-BuONa	1,4-dioxane	nr
14	L1	*t*-BuONa	1,4-dioxane	nr
15	L2	*t*-BuONa	1,4-dioxane	nr
16	XPhos	*t*-BuONa	1,4-dioxane	trace

[a] Isolated yield based on 2-alkynylaniline **2a**.
[b] DPPF: 1,1′-bis(diphenylphosphino)ferrocene.

tion indicated that various 2-alkynylbromobenzenes **1** were suitable reactants in the transformation. The structure of compound **4j** was unambiguously determined by X-ray crystallography analysis in the meantime (see the Supporting Information). We also explored the reaction of 1-chloro-2-(2-phenylethynyl)-benzene **1g**, 2-alkynylaniline **2a** and *N*-fluorobenzenesulfonimide **3** under the standard conditions shown in Table 2. This reaction worked well to afford the expected product **4a** in 61% yield (Table 2, entry 18), which indicated aryl chloride was effective as well in this transformation.

Conclusions

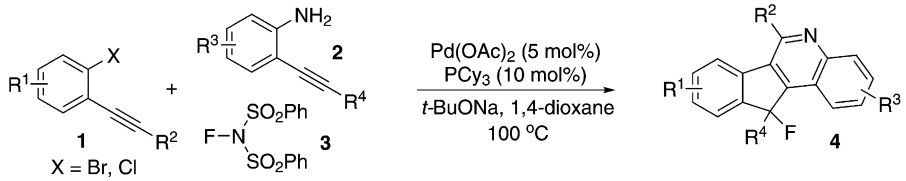
In conclusion, we have described a novel and efficient route for the generation of 11-fluoro-11*H*-indeno[1,2-*c*]quinolines *via* a palladium-catalyzed three-component reaction of 2-alkynylbromobenzenes, 2-alkynylanilines, and *N*-fluorobenzenesulfonimide. This transformation works well with high selectivity, and diversity and complexity could be easily introduced *via* a simple operation from readily available starting materials. During the reaction process, a fluorine atom could be incorporated into the scaffold. We believe that the interesting biological activities would be expected from the corresponding focused library. Further application of this strategy to explore new cascade reactions with the introduction of a fluorine atom is in progress.

Experimental Section

General Experimental Procedure for the Palladium-Catalyzed Three-Component Reaction of 2-Alkynylbromobenzenes, 2-Alkynylanilines and *N*-Fluorobenzenesulfonimide

2-Alkynylbromobenzene **1** (0.24 mmol) was added to a mixture of $Pd(OAc)_2$ (5 mol%), tricyclohexylphosphine

Table 2. Scope investigation for the palladium-catalyzed three-component reaction of 2-alkynylbromobenzenes **1**, 2-alkynylanilines **2**, and *N*-fluorobenzenesulfonimide **3**.



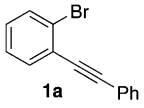
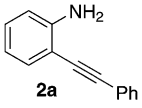
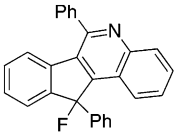
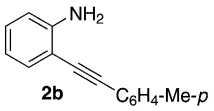
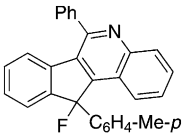
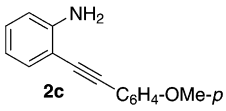
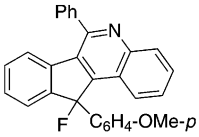
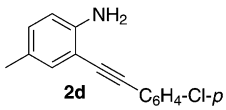
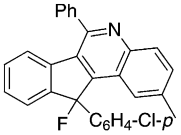
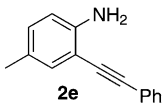
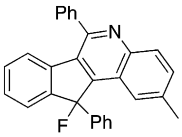
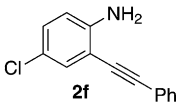
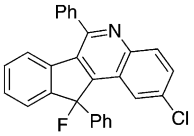
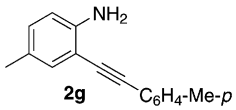
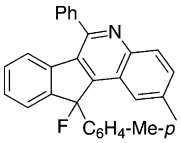
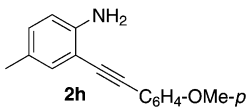
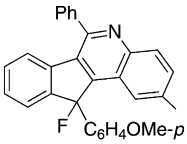
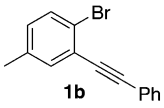
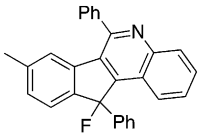
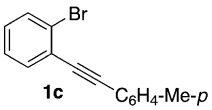
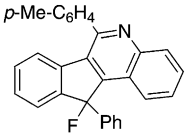
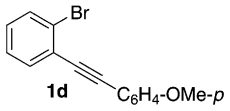
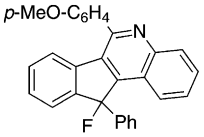
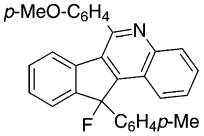
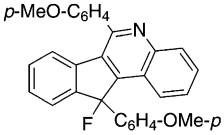
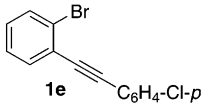
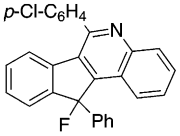
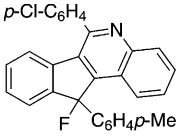
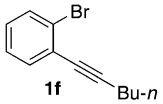
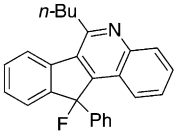
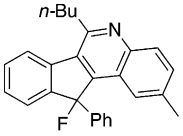
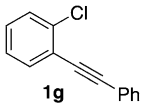
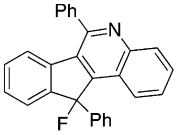
Entry	2-Alkynylhalobenzene	2-Alkynylaniline	Product		Yield [%][a]
1				**4a**	73
2	**1a**			**4b**	55
3	**1a**			**4c**	50
4	**1a**			**4d**	40
5	**1a**			**4e**	75
6	**1a**			**4f**	51
7	**1a**			**4g**	45
8	**1a**			**4h**	38
9		**2a**		**4i**	57
10		**2a**		**4j**	67

Table 2. (Continued)

Entry	2-Alkynylhalobenzene	2-Alkynylaniline	Product		Yield [%][a]
11		**2a**		**4k**	56
12	**1d**	**2b**		**4l**	41
13	**1d**	**2c**		**4m**	43
14		**2a**		**4n**	86
15	**1e**	**2b**		**4a**	54
16		**2a**		**4p**	38
17	**1f**	**2e**		**4q**	42
18		**2a**		**4r**	61

[a] Isolated yield based on 2-alkynylaniline **2**.

(10 mol%), *t*-BuONa (0.8 mmol), and 2-alkynylaniline (0.20 mmol) in 1,4-dioxane (2.0 mL). The mixture was heated at 100 °C. After 2-alkynylaniline **2** was consumed completely, *N*-fluorobenzenesulfonimide (0.3 mmol) was added to the mixture. After completion of the reaction as indicated by TLC, the solvent was diluted by EtOAc (10 mL), washed with saturated brine (2×10 mL), and dried by anhydrous Na_2SO_4. Evaporation of the solvent followed by purification on silica gel provides the product **4**.

11-Fluoro-6,11-diphenyl-11*H*-indeno[1,2-*c*]quinoline (4a): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.20$ (d, $J = 8.8$ Hz, 1H), 7.79–7.76 (m, 3H), 7.67–7.58 (m, 4H), 7.44–7.40 (m, 3H), 7.39–7.31 (m, 4H), 7.21–7.13 (m, 2H), 6.98 (d, $J = 7.6$ Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$): $\delta = -166.7$; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 155.7$, 149.9 (d, $^2J_{C,F} = 17.3$ Hz), 146.7 (d, $^2J_{C,F} = 19.8$ Hz), 139.9, 139.4 (d, $^2J_{C,F} = 27.4$ Hz), 139.2 (d, $^4J_{C,F} = 3.0$ Hz), 131.9 (d, $^4J_{C,F} = 3.4$ Hz), 130.1, 129.9, 129.8, 129.7, 129.1, 128.8, 128.7, 128.5, 128.4, 127.4, 125.0, 124.3, 124.2, 123.3, 101.5 (d, $J_{C,F} = 183.6$ Hz): HR-MS (ESI): $m/z =$ 388.1500, calcd. for $C_{28}H_{18}FN$ ($M+H^+$): 388.1502.

11-Fluoro-6-phenyl-11-(*p*-tolyl)-11*H*-indeno[1,2-*c*]quinoline (4b): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.19$ (d, $J =$ 8.8 Hz, 1H), 7.78–7.76 (m, 3H), 7.67–7.59 (m, 4H), 7.43–7.39 (m, 1H), 7.36 (d, $J = 7.8$ Hz, 1H), 7.32–7.30 (m, 2H), 7.20–7.10 (m, 4H), 6.97 (d, $J = 7.6$ Hz, 1H), 2.33 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): $\delta = -165.9$; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 155.6$, 150.0 (d, $^3J_{C,F} = 6.6$ Hz), 148.1, 146.9 (d, $^2J_{C,F} = 20.0$ Hz), 139.9, 138.1, 136.4 (d, $^2J_{C,F} =$ 27.5 Hz), 131.8, 130.1, 129.8 (d, $^4J_{C,F} = 1.9$ Hz), 129.7, 129.5, 129.1, 128.9, 128.8, 128.5, 127.3, 124.9, 124.4, 124.2 (d, $^3J_{C,F} =$ 7.4 Hz), 123.4, 123.3, 101.6 (d, $J_{C,F} = 183.0$ Hz), 21.2; HR-MS (ESI): $m/z = 402.1663$, calcd. for $C_{29}H_{20}FN$ ($M+H^+$): 402.1658.

11-Fluoro-2-methoxy-6,11-diphenyl-11*H*-indeno[1,2-*c*]-quinoline (4c): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.19 (d, J = 8.4 Hz, 1H), 7.80–7.76 (m, 3H), 7.68–7.64 (m, 1H), 7.61–7.57 (m, 3H), 7.44–7.40 (m, 1H), 7.37–7.33 (m, 3H), 7.21–7.17 (m, 1H), 7.14–7.10 (m, 1H), 6.97 (d, J = 7.6 Hz, 1H), 6.87 (d, J = 8.4 Hz, 2H), 3.78 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ = −164.7; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.5, 155.7, 150.0, 148.2, 146.9 (d, $^2J_{C,F}$ = 20.2 Hz), 140.0, 138.0 (d, $^4J_{C,F}$ = 3.1 Hz), 131.4 (d, $^2J_{C,F}$ = 28.0 Hz), 129.7 (d, $^4J_{C,F}$ = 1.9 Hz), 129.7, 129.1, 128.8, 128.7, 128.4 (d, $^4J_{C,F}$ = 1.6 Hz), 127.3, 125.6 (d, $^3J_{C,F}$ = 7.5 Hz), 124.9, 124.4, 123.4, 123.3, 114.2, 101.5 (d, $J_{C,F}$ = 182.6 Hz), 55.2; HR-MS (ESI): m/z = 418.1607, calcd. for $C_{29}H_{20}FNO$ ($M+H^+$): 418.1607.

11-(4-Chlorophenyl)-11-fluoro-2-methyl-6-phenyl-11*H*-indeno[1,2-*c*]quinoline (4d): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.09 (d, J = 8.8 Hz, 1H), 7.77–7.75 (m, 2H), 7.60–7.58 (m, 3H), 7.51–7.49 (m, 1H), 7.46 (s, 1H), 7.38–7.30 (m, 5H), 7.22–7.12 (m, 2H), 6.97 (d, J = 7.6 Hz, 1H), 2.42 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ = −166.5; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.7, 147.0, 146.3 (d, $^2J_{C,F}$ = 19.8 Hz), 140.0, 138.3 (d, $^2J_{C,F}$ = 19.8 Hz), 140.0, 138.3 (d, $^4J_{C,F}$ = 2.8 Hz), 138.1, 137.6, 134.1, 132.3, 130.0 (d, $^4J_{C,F}$ = 1.9 Hz), 129.9, 129.1, 129.0, 128.9, 128.8, 128.5 (d, $^4J_{C,F}$ = 1.8 Hz), 125.8 (d, $^3J_{C,F}$ = 7.6 Hz), 124.9, 123.4, 122.7, 101.3 (d, $J_{C,F}$ = 184.5 Hz), 22.0; HR-MS (ESI): m/z = 436.1262, calcd. for $C_{29}H_{19}ClFN$ ($M+H^+$): 436.1268.

11-Fluoro-2-methyl-6,11-diphenyl-11*H*-indeno[1,2-*c*]quinoline (4e): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08 (d, J = 8.8 Hz, 1H), 7.77–7.75 (m, 2H), 7.59–7.57 (m, 3H), 7.51–7.46 (m, 2H), 7.44–7.42 (m, 2H), 7.35–7.32 (m, 4H), 7.19–7.10 (m, 2H), 6.97 (d, J = 7.6 Hz, 1H), 2.38 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ = −166.8; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.7, 149.1 (d, $^2J_{C,F}$ = 17.2 Hz), 146.9, 146.7, 140.0, 139.5 (d, $^2J_{C,F}$ = 27.4 Hz), 138.3 (d, $^4J_{C,F}$ = 2.8 Hz), 137.4, 132.2, 129.8, 129.0, 128.9, 128.7 (d, $^3J_{C,F}$ = 5.9 Hz), 128.3 (d, $^4J_{C,F}$ = 1.6 Hz), 128.2, 124.9, 124.2 (d, $^3J_{C,F}$ = 7.6 Hz), 123.3, 123.1 (d, $^2J_{C,F}$ = 30.4 Hz), 101.6 (d, $J_{C,F}$ = 183.6 Hz), 21.9; HR-MS (ESI): m/z = 402.1652, calcd. for $C_{29}H_{20}FN$ ($M+H^+$): 402.1658.

2-Chloro-11-fluoro-6,11-diphenyl-11*H*-indeno[1,2-*c*]quinoline (4f): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12 (d, J = 9.2 Hz, 1H), 7.77–7.72 (m, 3H), 7.61–7.60 (m, 4H), 7.40–7.36 (m, 6H), 7.23–7.13 (m, 2H), 7.00 (d, J = 7.26 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$): δ = −167.4; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.9, 146.7, 146.6, 139.6, 139.0, 138.7, 137.7 (d, $^4J_{C,F}$ = 3.0 Hz), 134.0, 133.2, 131.7, 130.7, 130.0 (d, $^4J_{C,F}$ = 1.8 Hz), 129.1 (d, $^2J_{C,F}$ = 31.8 Hz), 128.8, 128.7, 128.5, 125.1, 124.2 (d, $^3J_{C,F}$ = 7.6 Hz), 123.9, 123.5, 123.0, 101.4 (d, $J_{C,F}$ = 184.1 Hz); HR-MS (ESI): m/z = 422.1096, calcd. for $C_{28}H_{17}ClFN$ ($M+H^+$): 422.1112.

11-Fluoro-2-methyl-6-phenyl-11-(*p*-tolyl)-11*H*-indeno[1,2-*c*]quinoline (4g): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08 (d, J = 8.4 Hz, 1H), 7.77–7.75 (m, 2H), 7.59–7.54 (m, 4H), 7.49–7.47(m, 1H), 7.35–7.30 (m, 3H), 7.19–7.09 (m, 4H), 6.96 (d, J = 7.6 Hz, 1H), 2.40 (s, 3H), 2.33 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ = −166.5; ^{13}C NMR (100 MHz, $CDCl_3$); δ = 154.7, 146.9, 140.1, 138.2 (d, $^4J_{C,F}$ = 2.3 Hz), 137.9, 137.3, 136.5 (d, $^2J_{C,F}$ = 27.5 Hz), 132.1, 129.8, 129.7 (d, $^4J_{C,F}$ = 1.8 Hz), 129.5, 129.0, 128.9, 128.7, 128.3, 124.9, 124.2 (d, $^3J_{C,F}$ = 7.3 Hz), 123.4, 123.1 (d, $^2J_{C,F}$ = 18.1 Hz), 101.7 (d, $J_{C,F}$ = 183.1 Hz), 21.9, 21.2; HR-MS (ESI): m/z = 416.1803, calcd. for $C_{30}H_{22}FN$ ($M+H^+$): 416.1815.

11-Fluoro-11-(4-methoxyphenyl)-2-methyl-6-phenyl-11*H*-indeno[1,2-*c*]quinoline (4h): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08 (d, J = 8.4 Hz, 1H), 7.77–7.75 (m, 2H), 7.59–7.58 (m, 3H), 7.54–7.48 (m, 2H), 7.35–7.33 (m, 3H), 7.20–7.17 (m, 1H), 7.13–7.10 (m, 1H), 6.95 (d, J = 8.0 Hz, 1H), 6.88 (d, J = 8.8 Hz, 2H), 3.79 (s, 3H), 2.41 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ = −166.4; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.4, 154.7, 148.9, 146.9, 140.1, 138.2, 137.3, 132.2, 131.5 (d, $^2J_{C,F}$ = 28.1 Hz), 129.8, 129.7, 129.0, 128.9, 128.7, 128.3, 125.6 (d, $^3J_{C,F}$ = 7.4 Hz), 124.8, 123.4, 123.2, 123.1, 114.2, 110.8, 101.6 (d, $J_{C,F}$ = 183.0 Hz), 55.2, 22.0; HR-MS (ESI): m/z = 432.1759, calcd. for $C_{30}H_{22}FNO$ ($M+H^+$): 432.1764.

11-Fluoro-8-methyl-6,11-diphenyl-11*H*-indeno[1,2-*c*]quinoline (4i): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.22 (dd, J = 8.4, 2.6 Hz, 1H), 7.78–7.76 (m, 3H), 7.61–7.59 (m, 4H), 7.51–7.22 (m, 7H), 7.04–6.99 (m, 1H), 6.77–6.76 (m, 1H), 2.16 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ = −165.5; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.8 (d, $^2J_{C,F}$ = 31.8 Hz), 153.4, 148.6, 148.1 (d, $^3J_{C,F}$ = 8.1 Hz), 144.0 (d, $^2J_{C,F}$ = 20.1 Hz), 139.9, 138.6, 135.9, 130.3, 130.1, 129.6 (d, $^3J_{C,F}$ = 10.8 Hz), 129.4, 129.1, 128.8 (d, $^2J_{C,F}$ = 19.5 Hz), 128.2 (d, $^3J_{C,F}$ = 10.9 Hz), 127.3, 127.0, 126.7, 125.1 (d, $^3J_{C,F}$ = 11.0 Hz), 124.8, 124.3, 123.3, 122.8, 101.3 (d, $J_{C,F}$ = 183.3 Hz), 21.7; HR-MS (ESI): m/z = 402.1662, calcd. for $C_{29}H_{20}FN$ ($M+H^+$): 402.1658.

11-Fluoro-11-phenyl-6-(*p*-tolyl)-11*H*-indeno[1,2-*c*]quinoline (4j): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.18 (d, J = 8.4 Hz, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.68–7.62 (m, 3H), 7.43–7.39 (m, 5H), 7.36–7.30 (m, 4H), 7.20–7.12 (m, 2H), 7.07 (d, J = 7.6 Hz, 1H), 2.51 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ = −166.3; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.8, 148.2, 146.8, 139.5 (d, $^2J_{C,F}$ = 27.3 Hz), 139.0, 138.4, 137.0, 134.3, 130.1, 129.8 (d, $^4J_{C,F}$ = 1.7 Hz), 129.6, 129.4, 128.8 (d, $^3J_{C,F}$ = 5.9 Hz), 128.3 (d, $^2J_{C,F}$ = 18.3 Hz), 127.2, 125.0, 124.3 (d, $^3J_{C,F}$ = 7.6 Hz), 124.2, 123.4, 123.2, 101.5 (d, $J_{C,F}$ = 183.5 Hz); HR-MS (ESI): m/z = 402.1652, calcd. for $C_{29}H_{20}FN$ ($M+H^+$): 402.1658.

11-Fluoro-8-methoxy-6,11-diphenyl-11*H*-indeno[1,2-*c*]-quinoline (4k): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.18 (d, J = 8.8 Hz, 1H), 7.75–7.73 (m, 3H), 7.66–7.62 (m, 1H), 7.44–7.33 (m, 7H), 7.20–7.16 (m, 2H), 7.14–7.11 (m, 3H), 3.94 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ = −166.3; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.4, 155.4, 150.0, 148.2, 146.7 (d, $^2J_{C,F}$ = 19.8 Hz), 139.5 (d, $^2J_{C,F}$ = 27.3 Hz), 138.4 (d, $^4J_{C,F}$ = 3.0 Hz), 132.3, 131.9 (d, $^4J_{C,F}$ = 3.2 Hz), 130.2, 130.0, 129.9 (d, $^4J_{C,F}$ = 1.9 Hz), 129.8 (d, $^2J_{C,F}$ = 29.5 Hz), 128.8, 128.4, 128.2, 127.2, 125.0, 124.3 (d, $^3J_{C,F}$ = 7.1 Hz), 123.4, 123.2, 114.1, 101.5 (d, $J_{C,F}$ = 183.5 Hz), 55.4; HR-MS (ESI): m/z = 418.1601, calcd. for $C_{29}H_{20}FNO$ ($M+H^+$): 418.1607.

11-Fluoro-6-(4-methoxyphenyl)-11-(*p*-tolyl)-11*H*-indeno-[1,2-*c*]quinoline (4l): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.18 (d, J = 8.4 Hz, 1H), 7.78–7.72 (m, 3H), 7.66–7.62 (m, 1H), 7.41–7.35 (m, 2H), 7.31–7.29 (m, 2H), 7.19–7.11 (m, 7H), 3.94 (s, 3H), 2.33 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ = −165.8; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.4, 155.4, 148.2, 146.9 (d, $^2J_{C,F}$ = 20.1 Hz), 138.3 (d, $^4J_{C,F}$ = 2.9 Hz),138.0, 136.5 (d, $^2J_{C,F}$ = 27.2 Hz), 134.2, 132.4, 131.9 (d, $^4J_{C,F}$ = 3.3 Hz), 130.3, 129.9, 129.7 (d, $^4J_{C,F}$ = 1.8 Hz), 129.6, 129.5, 128.4, 127.1, 124.9, 124.4, 124.2 (d, $^3J_{C,F}$ = 7.4 Hz), 123.3, 123.2, 114.1, 101.6 (d, $J_{C,F}$ = 182.8 Hz), 55.4, 21.2; HR-MS (ESI): m/z = 432.1771, calcd. for $C_{30}H_{22}FNO$ ($M+H^+$): 432.1764.

11-Fluoro-6,11-bis(4-methoxyphenyl)-11*H*-indeno[1,2-*c*]-quinoline (4m): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.18$ (d, $J = 8.4$ Hz, 1H), 7.78 (d, $J = 8.0$ Hz, 1H), 7.73 (d, $J = 8.8$ Hz, 2H), 7.66–7.63 (m, 2H), 7.42–7.33 (m, 4H), 7.20–7.10 (m, 5H), 6.87 (d, $J = 8.8$ Hz, 1H), 3.94 (s, 3H), 3.78 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): $\delta = -164.7$; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 160.4$, 159.5, 155.4, 148.2, 146.9 (d, $^2J_{C,F} = 20.2$ Hz), 138.2, 134.3, 131.4 (d, $^2J_{C,F} = 28.1$ Hz), 130.3, 130.0, 129.7 (d, $^4J_{C,F} = 1.8$ Hz), 129.6, 128.4, 127.1, 125.7 (d, $^3J_{C,F} = 7.3$ Hz), 125.3, 124.9, 124.4, 123.3, 123.2, 114.1 (d, $^3J_{C,F} = 5.1$ Hz), 101.5 (d, $J_{C,F} = 182.4$ Hz), 55.4, 55.2; HR-MS (ESI): $m/z = 448.1708$, calcd. for $C_{30}H_{22}FNO_2$ ($M+H^+$): 448.1713.

6-(4-Chlorophenyl)-11-fluoro-11-phenyl-11*H*-indeno[1,2-*c*]quinoline (4n): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.16$ (d, $J = 8.4$ Hz, 1H), 7.77–7.73 (m, 3H), 7.67–7.63 (m, 1H), 7.59–7.57 (m, 1H), 7.42–7.40 (m, 3H), 7.38–7.31 (m, 4H), 7.22–7.15 (m, 2H), 7.06–7.04 (m, 1H), 2.87 (s, 1H); ^{19}F NMR (376 MHz, $CDCl_3$): $\delta = -166.2$; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 154.3$, 150.1 (d, $^2J_{C,F} = 17.3$ Hz), 148.2, 146.7 (d, $^2J_{C,F} = 19.9$ Hz), 139.3 (d, $^4J_{C,F} = 27.4$ Hz), 138.4, 137.9 (d, $^4J_{C,F} = 3.0$ Hz), 135.2, 130.4, 130.1, 129.9 (d, $^4J_{C,F} = 1.8$ Hz), 129.8, 129.0, 128.8, 128.7, 128.6, 128.3, 127.6, 125.2, 124.3, 124.4 (d, $^3J_{C,F} = 7.7$ Hz), 123.3, 123.1, 101.4 (d, $J_{C,F} = 183.7$ Hz); HR-MS (ESI): $m/z = 422.1107$, calcd. for $C_{28}H_{17}ClFN$ ($M+H^+$): 422.1112.

6-(4-Chlorophenyl)-11-fluoro-11-(*p*-tolyl)-11*H*-indeno[1,2-*c*]quinoline (4o): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.16$ (d, $J = 8.4$ Hz, 1H), 7.79–7.73 (m, 3H), 7.68–7.63 (m, 1H), 7.59–7.57 (m, 2H), 7.43–7.36 (m, 2H), 7.31–7.28 (m, 2H), 7.21–7.19 (m, 1H), 7.17–7.14 (m, 3H), 7.04 (d, $J = 7.2$ Hz, 1H), 2.32 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): $\delta = -165.8$; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 153.3$, 150.2 (d, $^3J_{C,F} = 7.2$ Hz), 148.2, 146.9 (d, $^2J_{C,F} = 20.0$ Hz), 138.5, 138.1 137.9 (d, $^4J_{C,F} = 3.1$ Hz), 136.3 (d, $^2J_{C,F} = 27.7$ Hz), 135.2, 131.6 (d, $^4J_{C,F} = 3.4$ Hz), 130.4, 130.1, 129.8, 129.5, 129.0, 128.6 (d, $^4J_{C,F} = 1.6$ Hz),127.5, 125.1, 124.4 (d, $^3J_{C,F} = 7.4$ Hz), 123.4, 123.1, 109.0, 101.5 (d, $J_{C,F} = 183.1$ Hz), 21.2; HR-MS (ESI): $m/z = 436.1267$, calcd. for $C_{29}H_{19}ClFN$ ($M+H^+$): 436.1268.

6-Butyl-11-fluoro-11-phenyl-11*H*-indeno[1,2-*c*]quinoline (4p): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.10$ (d, $J = 8.4$ Hz, 1H), 7.82 (d, $J = 7.6$ Hz, 1H), 7.68 (d, $J = 8.4$ Hz, 1H), 7.63–7.59 (m, 1H), 7.48–7.44 (m, 1H), 7.40–7.39 (m, 1H), 7.34–7.29 (m, 7H), 3.43–3.39 (m, 2H), 1.97–1.91 (m, 2H), 1.67–1.62 (m, 2H), 1.06 (t, $J = 7.6$ Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): $\delta = -167.9$; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 158.0$, 149.2 (d, $^2J_{C,F} = 17.1$ Hz), 148.1, 146.9 (d, $^2J_{C,F} = 20.0$ Hz), 139.6 (d, $^2J_{C,F} = 27.3$ Hz), 138.5 (d, $^4J_{C,F} = 2.9$ Hz), 132.3 (d, $^4J_{C,F} = 3.4$ Hz), 130.4, 129.4, 129.3, 128.8, 128.2 (d, $^3J_{C,F} = 10.7$ Hz), 126.6, 125.3, 124.3, 124.2, 124.1, 123.1, 123.0, 101.4 (d, $J_{C,F} = 183.2$ Hz), 37.6, 30.6, 23.0, 14.1; HR-MS (ESI): $m/z = 368.1825$, calcd. for $C_{26}H_{22}FN$ ($M+H^+$): 368.1815.

6-Butyl-11-fluoro-2-methyl-11-phenyl-11*H*-indeno[1,2-*c*]-quinoline (4q): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.99$ (d, $J = 8.4$ Hz, 1H), 7.81 (d, $J = 7.6$ Hz, 1H), 7.45–7. 43 (m, 3H), 7.39–7.38 (m, 1H), 7.33–7.21 (m, 6H), 3.41–3.36 (m, 2H), 2.35 (s, 3H), 1.95–1.89 (m, 2H), 1.66–1.61(m, 2H), 1.05 (t, $J = 7.2$ Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): $\delta = -169.1$; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 157.0$, 146.7, 139.6 (d, $^2J_{C,F} = 27.3$ Hz), 138.5 (d, $^4J_{C,F} = 3.1$ Hz), 136.5, 131.8, 130.3 (d, $^4J_{C,F} = 1.6$ Hz), 128.9, 128.8, 128.7, 128.2, 128.1, 125.2, 124.2 (d, $^3J_{C,F} = 7.6$ Hz), 123.0 (d, $^3J_{C,F} = 7.1$ Hz), 101.6 (d, $J_{C,F} = 183.1$ Hz), 37.5, 30.7, 23.0, 21.8, 14.1; HR-MS (ESI): $m/z = 382.1960$, calcd. for $C_{27}H_{24}FN$ ($M+H^+$): 382.1971.

Crystallographic data for the structure **4j** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 827084. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif or on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax.: (internat.) +44-1223/336-033; e-mail: deposit@ccdc.cam.ac.uk].

Supporting Information

Experimental procedure, characterization data as well as ^{1}H, ^{19}F and ^{13}C NMR spectra of compounds **4** are available as Supporting Information.

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