Electrophilic *ipso*-Halocyclization of *N*-Arylpropynamides with Polyfluoroalkyl Alcohols: Selective Synthesis of 8-(Polyfluoroalkoxy)azaspiro[4.5]trienes

Zhi-Qiang Wang,[a] Bo-Xiao Tang,[a] Hong-Ping Zhang,[a,b] Feng Wang,[a] Jin-Heng Li*[a]

[a] Key Laboratory of Chemical Biology & Traditional Chinese Medicine Research (Ministry of Education), College of Chemistry and Chemical Engineering, Hunan Normal University, Changsha 410081, P. R. of China
Fax +86(731)8872101; E-mail: jhli@hunnu.edu.cn

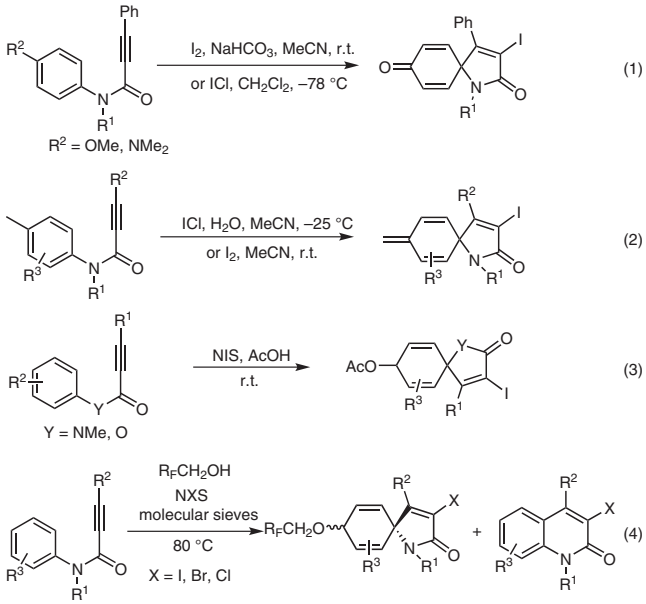
[b] Department of Biology and Chemical Engineering, Shaoyang University, Shaoyang 422000, P. R of China

Received 19 September 2008; revised 25 November 2008

Abstract: A novel and efficient method for the synthesis of 8-(polyfluoroalkoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-ones has been demonstrated via the electrophilic *ipso*-halocyclization of *N*-arylpropynamides with polyfluoroalkyl alcohols. In the presence of *N*-halosuccinimides (NXS), a variety of *N*-arylpropynamides underwent an electrophilic *ipso*-halocyclization reaction with polyfluoroalkyl alcohols to afford the corresponding 8-(polyfluoroalkoxy)spiro[4.5]trienes in good yields. Note that molecular sieves can improve the yield of the reaction.

Key words: electrophilic *ipso*-halocyclization, *N*-arylpropynamide, *N*-halosuccinimide, spiro[4.5]decane, polyfluoroalkoxy substitution

The intramolecular electrophilic cyclization of arylalkynes has recently attracted much attention and it is now widely recognized for its potential to synthesize a wide range of heterocycles and carbocycles under simple and mild conditions.[1–3] The electrophilic cyclization protocols are generally worked between alkyne and *ortho*-arene substituents to construct heterocycles and carbocycles.[1] Recently, the reaction between alkynes and *ipso*-arene substituents to give spirocyclic compound has been developed by the Fanghänel[2a] and Larock groups[2b] independently. 4-(4-Methoxyaryl)alk-1-ynes or 4-[4-(dimethylamino)aryl]alk-1-ynes, for example, underwent intramolecular electrophilic *ipso*-cyclization with iodine monochloride or iodine/sodium hydrogen carbonate to synthesize spiro[4.5]trienones in moderate to excellent yields (Scheme 1, equation 1). We have also reported that the intramolecular *ipso*-iodocyclization of 4-(4-alkylaryl)alk-1-ynes with iodine monochloride or iodine proceeded smoothly, providing the corresponding 8-methylene-1-azaspiro[4.5]trienes in moderate to good yields (Scheme 1, equation 2).[2c] However, the above *ipso*-cyclization method is limited to aryl compounds bearing active *para*-substituents, such as methoxy, dimethylamino, and alkyl groups, on the aryl ring. Very recently, we found that *N*-(*para*-unsubstituted aryl)propynamides and phenyl 3-phenylpropynoate underwent the intramolecular electrophilic *ipso*-iodocyclization/nucleophilic addition process with *N*-iodosuccinimide (NIS) and acetic acid to afford selectively spiro[4.5]trienyl acetates in moderate to good yields (Scheme 1, equation 3).[3] This prompted us to extend the new intramolecular electrophilic *ipso*-cyclization of (*para*-unsubstituted aryl)alkynes route to the synthesis of the important spiro[4.5]decanes.[4] It is well known that the trifluoromethyl group has a great effect on biological activity and often confers significant changes in chemical and physical properties.[5] Thus, we expected to induce a trifluoromethyl group into the spirocyclic motif using trifluoroacetic acid, but failed. Interestingly, we found that 2,2,2-trifluoroethanol was a suitable substrate for this purpose. Here, we wish to report that *para*-unactivated *N*-arylpropynamides can undergo electrophilic *ipso*-cyclization with polyfluoroalkyl alcohols and *N*-halosuccinimides (NXS) to synthesize selectively 8-(polyfluoroalkoxy)azaspiro[4.5]trienes in good yields (Scheme 1, equation 4).[6,7]



Scheme 1

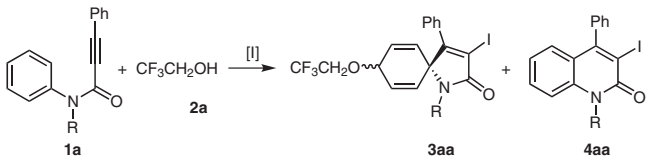
Stimulated by our previous studies on the electrophilic *ipso*-iodocyclization of *N*-(*para*-unsubstituted aryl)propynamides with *N*-iodosuccinimide and acetic acid,[3] we investigated the feasibility of the electrophilic *ipso*-iodocyclization of *N*-methyl-*N*,3-diphenylpropynamide (**1a**) with 2,2,2-trifluoroethanol (**2a**) because it was reported as

SYNTHESIS 2009, No. 6, pp 0891–0902
Advanced online publication: 24.02.2009
DOI: 10.1055/s-0028-1087972; Art ID: F20008SS

a special nucleophilic reagent for *ipso*-cyclizations.[6b,c,g] We found that the reaction temperature has a fundamental influence on the reaction. As shown in Table 1, trace amounts of three products were detected by GC-MS analysis from the reaction of *N*-methyl-*N*,3-diphenylpropynamide (**1a**) with 2,2,2-trifluoroethanol (**2a**) at room temperature (entry 1). At 80 °C, the target product **3aa** was enhanced to 51% total yield together with an *ortho*-cyclized side-product **4aa** in 23% yield (entry 2). Molecular sieves were found to improve the reaction, and the yield of **3aa** was enhanced to 67% when 100 mg of 3 Å molecular sieves were added (entry 3).[8] However, trace amounts of **3aa** or **4aa** were observed using iodine monochloride instead of *N*-iodosuccinimide (entry 4) and the product **4aa** was obtained as the major product in the presence of iodine (entry 5). Ethanol in place of 2,2,2-trifluoroethanol (**2a**) as the reaction partner was also tested, but failed (entry 6).[9] In the cases where the *N*-methyl group was replaced by *N*-benzyl or *N*-acetyl or an N-unsubstituted group, however, the reaction did not proceed and the starting material **1a** was recovered in >95% yield (entries 7–9).

A variety of substrates were examined by reacting with polyfluoroalkyl alcohols and *N*-iodosuccinimide to examine the scope of this intramolecular electrophilic *ipso*-iodocyclization process, and the results are summarized in Table 2.[8] We were pleased to find that the novel process

Table 1 Screening Optimal Conditions for the Electrophilic *ipso*-Iodocyclization Reaction[a]



Entry	R	[I]	Isolated yield (%)	
			cis/trans-**3**	**4**
1[b,c]	Me (**1a**)	NIS	trace (**3aa**)	trace (**4aa**)
2[c]	Me (**1a**)	NIS	26:25 (**3aa**)	23 (**4aa**)
3	Me (**1a**)	NIS	30:37 (**3aa**)	19 (**4aa**)
4[d]	Me (**1a**)	ICl	trace (**3aa**)	trace (**4aa**)
5	Me (**1a**)	I_2	trace (**3aa**)	53 (**4aa**)
6[e]	Me (**1a**)	NIS	0 (**3aa**)	trace (**4aa**)
7[f]	Bn (**1b**)	NIS	trace (**3ba**)	trace (**4ba**)
8[f]	Ac (**1c**)	NIS	trace (**3ca**)	trace (**4ca**)
9[f]	H (**1d**)	NIS	trace (**3da**)	trace (**4da**)

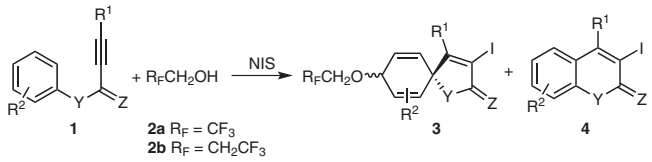
[a] Reagents and conditions: **1a** (0.3 mmol), **2a** (2 mL), [I] (1.5 equiv), 3 Å MS (100 mg), 80 °C, 8 h.
[b] At r.t.
[c] Without molecular sieves.
[d] Messy results were observed at –40 °C.
[e] EtOH instead of CF_3CH_2OH; >95% of **1a** was recovered.
[f] >95% of **1a** was recovered.

tolerated a wide range of functional groups, such as methyl, methoxy, chloro, bromo, iodo, and nitro groups in the aromatic nucleus. Initially, the reaction of substrate **1a** with another polyfluoroalkyl alcohol, 2,2,3,3,3-pentafluoropropan-1-ol (**2b**), was tested, and the results showed that it was still a suitable substrate to react with amide **1a** in good yield (entry 1). Subsequently, both the electronic and steric properties of the *N*-aryl group on the *ipso*-iodocyclization process were evaluated. Substrates **1e–i**, bearing electron-neutral or electron-rich groups on the *N*-aryl group, all worked well with polyfluoroalkyl alcohol **2a** or **2b** and *N*-iodosuccinimide in moderate to good yields (entries 2–7). *N*-Methyl-*N*-(2-methylphenyl)-3-phenylpropynamide (**1e**) bearing an *ortho*-methyl group on the *N*-aryl ring, for instance, underwent the reaction with **2a** and *N*-iodosuccinimide smoothly in 75% total yield (entry 2). To our surprise, substrate **1f** having a *meta*-methyl group provided the *ortho*-cyclized product **4fa** as the major product in 66% yield together with the *ipso*-product **3fa** in 28% yield (entry 4). We found that substrates **1j–l** bearing weakly electron-deficient halo groups also displayed high efficient for the *ipso*-iodocyclization reaction with *N*-iodosuccinimide and 2,2,2-trifluoroethanol (**2a**) providing **3ja–la** in good yields (entries 8–10). However, the reaction of amide **1m**, bearing an acetyl group on the *N*-aryl ring, did not take place under standard conditions (entry 11). *N*-Aryl groups bearing some active *para*-substituents were also evaluated (entries 12 and 13). *N*-Methyl-*N*-(4-methylphenyl)-3-phenylpropynamide (**1n**) did not undergo the reaction and *N*-(4-methoxyphenyl)-*N*-methyl-3-phenylpropynamide (**1o**) provided the spiro[4.5]trien-8-one **5oa** in 66% yield (Figure 1).

Next, substituents at the terminal of the C≡C bond of anilines were also examined (entries 14–19). *N*-Methyl-*N*-phenylpropynamide (**1p**), a terminal alkyne, was an unsuitable substrate for the reaction with *N*-iodosuccinimide at 80 °C (entry 14). We found that the terminally substituted alkynes, with either alkyl groups or aryl groups, all worked well with *N*-iodosuccinimide to afford the corresponding target products **3qa–ua** in moderate yields (entries 15–19). Substrate **1q** having a methyl group at the terminal of the C≡C bond, for instance, gave the *cis*- and *trans*-spirocyclic products **3qa** in 77% total yield together with an *ortho*-cyclized byproduct in 15% yield (entry 15). The results demonstrated that both the electronic and steric properties of the aryl groups affected the chemoselectivity of the reaction to some extent. Although the *ortho*-cyclized product **4sa** was obtained as the major product from the reaction of the bulky substrate **1s**, the spirocyclic product **3sa** was still isolated in 38% yield (entry 17). Both the *ipso*-cyclized product **3ta** and the *ortho*-cyclized product **4ta** were observed in the reaction of the electron-rich substrate **1t** (entry 18), but only the *ipso*-cyclized product **3ua** was isolated from the electron-deficient substrate **1u** (entry 19). However, another product, 3-iodo-1-methyl-4-(thiophen-2-yl)-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione (**5va**) (Figure 1), was isolated from the re-

action of the heteroarylalkyne substrate **1v** with *N*-iodosuccinimide in 2,2,2-trifluoroethanol (**2a**) (entry 20). Unfortunately, amine **1w**, ester **1x**, and ether **1y** were found to be unsuitable substrates under the standard reaction conditions (entries 21–23).

Table 2 Electrophilic *ipso*-Iodocyclizations of *N*-Arylpropynamides **1** with Polyfluoroalkyl Alcohols **2** in the Presence of *N*-Iodosuccinimide[a]



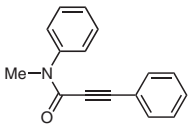
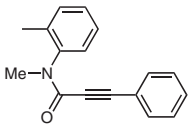
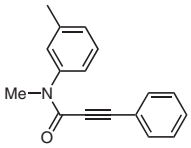
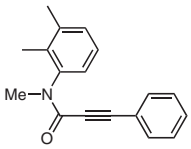
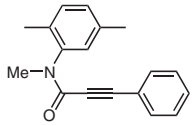
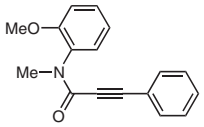
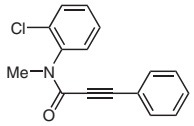
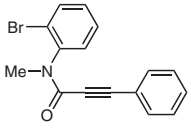
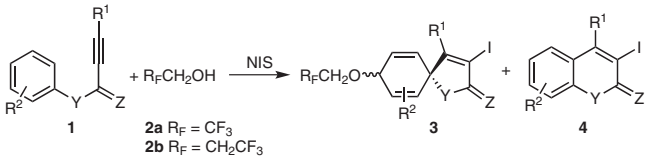
Entry	Substrate		Alcohol	Isolated yield (%) *cis*/*trans*-**3**	**4**
1	**1a**		**2b**	17:54 (**3ab**)	trace (**4ab**)
2	**1e**		**2a**	38:37 (**3ea**)	trace (**4ea**)
3	**1e**		**2b**	41:45 (**3eb**)	trace (**4eb**)
4	**1f**		**2a**	15:13 (**3fa**)	66 (**4fa**)[b]
5	**1g**		**2a**	35:28 (**3ga**)	trace (**4ga**)
6	**1h**		**2a**	55:42 (**3ha**)	trace (**4ha**)
7	**1i**		**2a**	44:33 (**3ia**)	trace (**3ia**)
8	**1j**		**2a**	46:44 (**3ja**)	trace (**4ja**)
9	**1k**		**2a**	43:41 (**3ka**)	trace (**4ka**)

Table 2 Electrophilic *ipso*-Iodocyclizations of *N*-Arylpropynamides **1** with Polyfluoroalkyl Alcohols **2** in the Presence of *N*-Iodosuccinimide[a] (continued)



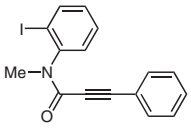
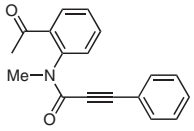
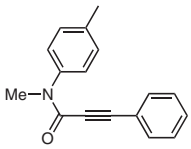
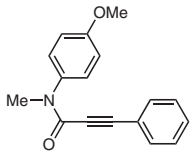
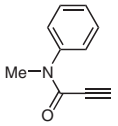
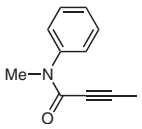
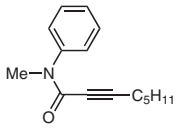
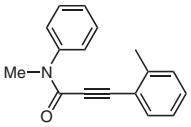
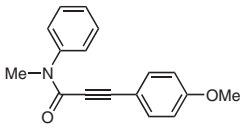
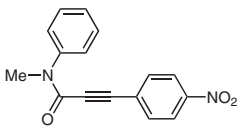
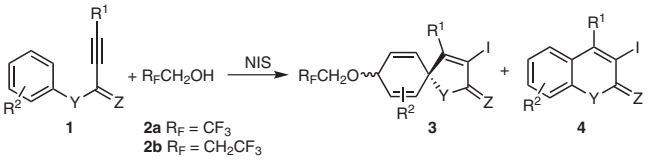
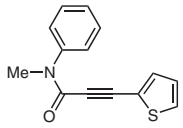
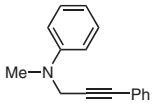
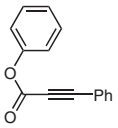
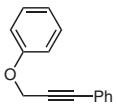
Entry	Substrate		Alcohol	Isolated yield (%) *cis*/*trans*-**3**	**4**
10	**1l**		**2a**	45:38 (**3la**)	trace (**3la**)
11[c]	**1m**		**2a**	trace (**3ma**)	trace (**4ma**)
12[c]	**1n**		**2a**	0 (**3na**)	trace (**4na**)
13[d]	**1o**		**2a**	0 (**3oa**)	0 (**4oa**)
14[c]	**1p**		**2a**	trace (**3pa**)	trace (**4pa**)
15[e]	**1q**		**2a**	32:45 (**3qa**)	15 (**4qa**)
16[e]	**1r**		**2b**	15:21 (**3ra**)	trace (**4ra**)
17	**1s**		**2a**	21:17 (**3sa**)	51 (**4sa**)
18	**1t**		**2a**	27:35 (**3ta**)	36 (**4ta**)
19	**1u**		**2a**	24:31 (**3ua**)	trace (**4ua**)

Table 2 Electrophilic *ipso*-Iodocyclizations of *N*-Arylpropynamides **1** with Polyfluoroalkyl Alcohols **2** in the Presence of *N*-Iodosuccinimide[a] (continued)



Entry	Substrate		Alcohol	Isolated yield (%)	
				cis/*trans*-**3**	**4**
20[f]	**1v**		**2a**	trace (**3va**)	trace (**4va**)
21[g]	**1w**		**2a**	trace (**3wa**)	trace (**4wa**)
22[g]	**1x**		**2a**	trace (**3xa**)	trace (**4xa**)
23[g]	**1y**		**2a**	trace (**3ya**)	trace (**4ya**)

[a] Reagents and conditions: **1** (0.3 mmol), **2a** (2 mL), 3 Å MS (100 mg), NIS (1.5 equiv), 80 °C, 8 h.
[b] 3-Iodo-1,5-dimethyl-4-phenylquinolin-2(1*H*)-one (**4fa**) and 3-iodo-1,7-dimethyl-4-phenylquinolin-2(1*H*)-one (**4fa′**); ratio **4fa**/**4fa′** 1:3.
[c] Messy results were observed, which was determined by GC-MS analysis.
[d] Another product **5oa** (Figure 1) was isolated in 66% yield.
[e] For 24 h.
[f] Another product **5va** (Figure 1) was isolated in 47% yield.
[g] >95% of substrate **1** was recovered.

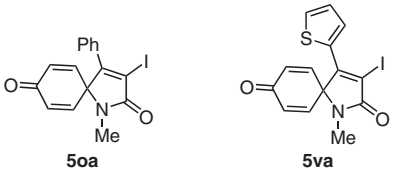
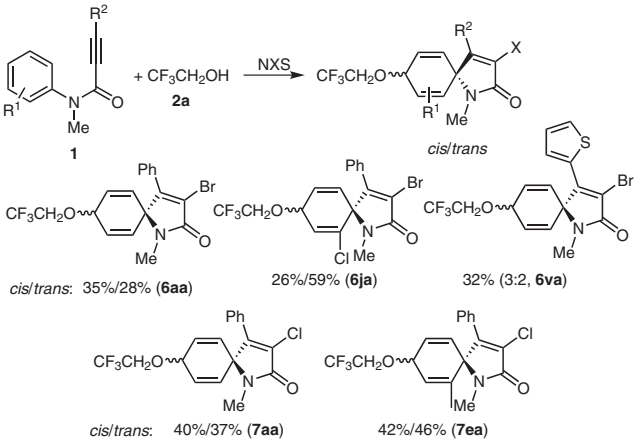


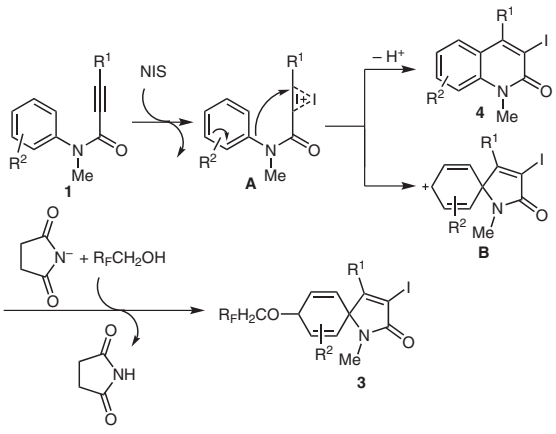
Figure 1

As listed in Scheme 2, the two other *N*-halosuccinimides, *N*-bromosuccinimide (NBS) and *N*-chlorosuccinimide (NCS), were used as the electrophilic reagents to react with anilines. To our delight, both *N*-bromosuccinimide and *N*-chlorosuccinimide are efficient for the electrophilic *ipso*-iodocyclizations. Substrate **1a**, for instance, underwent the electrophilic *ipso*-iodocyclization with either *N*-bromosuccinimide or *N*-chlorosuccinimide successfully to afford the corresponding *ipso*-cyclized products **6aa** and **7aa** in 62% and 77% yields, respectively. Gratifyingly, a 32% yield of the corresponding desired product **6va** was still achieved in the reaction of *N*-methyl-*N*-phenyl-3-(thiophen-2-yl)propynamide (**1v**) with *N*-bromosuccinimide. Interestingly, amides substrates bearing a group at the *ortho*-position of the *N*-aryl ring are still suitable substrates for the reaction with *N*-bromosuccinimide or *N*-chlorosuccinimide. For example, an 84% yield of the *ipso*-bromocyclized product **6ja** was obtained from the substrate **1j** having an *ortho*-chloro group.

A working mechanism as outlined in Scheme 3 was proposed on the basis of the present results and the previously reported mechanisms.[1–3] Initially, the iodonium intermediate **A** is generated by the interaction of the electrophilic *N*-iodosuccinimide with the alkyne moiety. The iodonium intermediate **A** can proceed via two routes including: (1) intramolecular electrophilic *ortho*-cyclization reaction to afford **4**, or (2) intramolecular electrophilic *ipso*-cyclization reaction to form intermediate **B**.[1,2] The reaction of intermediate **B** with R_FCH_2OH occurs to yield both *cis*- and *trans*-products **3**. Based on the mechanism, we deduced that both the steric hindrance and electron-withdrawing groups disfavored the stability of intermediate **B** resulting in lower yields.



Scheme 2 Electrophilic *ipso*-halocyclizations in the presence of *N*-bromosuccinimide or *N*-chlorosuccinimide. *Reagents and conditions*: **1** (3 mmol), **2a** (2 mL), 3 Å MS (100 mg), NXS (1.5 equiv), 80 °C, 8 h.



Scheme 3 A working mechanism

In summary, we have developed a novel and efficient electrophilic *ipso*-halocyclization method for the synthesis of 8-(polyfluoroalkoxy)azaspiro[4.5]trienes. In the presence of *N*-halosuccinimides, a variety of *N*-arylpropynamides underwent the electrophilic *ipso*-halocyclization reaction with polyfluoroalkyl alcohols to afford the corresponding 8-(polyfluoroalkoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-ones in good yields. Based on the results, two features were established: (1) The scope of the electrophilic *ipso*-halocyclization method was extended to substrates having no active *para*-substituents. (2) A wide range of functional groups, such as methyl, methoxy, chloro, bromo, iodo, and nitro groups, in the aromatic nucleus were tolerated well under the present reaction conditions. Efforts to explore new electrophilic *ipso*-halocyclization route and apply these protocols in organic synthesis are underway in our laboratory.

NMR spectroscopy was performed on an Inova-400 (Varian), or a Bruker-500 spectrometer operating at 400 MHz (^{1}H NMR) and 100 MHz (^{13}C NMR), or 500 MHz (^{1}H NMR) and 125 MHz (^{13}C NMR). TMS was used an internal standard and $CDCl_3$ was used as the solvent. MS analysis was performed on GC-MS analysis (Shimadzu GCMS-QP2010). Melting points are uncorrected.

Electrophilic *ipso*-Halocyclization; General Procedure

A mixture of aniline **1** (0.3 mmol), polyfluoroalkyl alcohol **2** (2 mL), NXS (1.5 equiv), and 3Å molecular sieve (100 mg) was stirred at 80 °C for the desired time (Table 2) until complete consumption of starting material (TLC and GC-MS analysis). The mixture was washed with sat. $Na_2S_2O_3$ soln and extracted with Et_2O. The combined organic layers were dried (anhyd Na_2SO_4) and evaporated under vacuum; the residue was purified by flash column chromatography (hexane or hexane–EtOAc) to afford the desired product.

***cis*-3-Iodo-1-methyl-4-phenyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*cis*-3aa)**

Pale yellow solid; mp 105.0–106.4 °C.

IR (KBr): 1695 cm^{-1}.

^{1}H NMR (400 MHz): δ = 7.40–7.34 (m, 3 H), 7.26 (d, *J* = 8.0 Hz, 2 H), 6.21 (d, *J* = 10.0 Hz, 2 H), 5.64 (d, *J* = 10.0 Hz, 2 H), 4.13 (s, 1 H), 3.83–3.77 (m, 2 H), 2.94 (s, 3 H).

^{13}C NMR (100 MHz): δ = 167.2, 162.0, 133.2, 131.2, 129.4, 128.5, 128.4, 127.9, 123.8 (q, *J* = 276.6 Hz, 1 C), 96.8, 69.4, 69.3, 65.0 (q, *J* = 34.4 Hz, 1 C), 26.6.

LR-MS (EI, 70 eV): *m*/*z* (%) = 461 (M$^+$, 3), 362 (2), 334 (100), 129 (66).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{18}H_{15}F_3INO_2$: 461.0100; found: 461.0098.

***trans*-3-Iodo-1-methyl-4-phenyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*trans*-3aa)**

Yellow solid; mp 179.6–180.4 °C.

IR (KBr): 1681 cm^{-1}.

^{1}H NMR (400 MHz): δ = 7.39–7.37 (m, 3 H), 7.22 (d, *J* = 8.0 Hz, 2 H), 6.20 (d, *J* = 10.0 Hz, 2 H), 5.71 (d, *J* = 10.0 Hz, 2 H), 4.69 (s, 1 H), 2.89–2.85 (m, 2 H), 2.83 (s, 3 H).

^{13}C NMR (100 MHz): δ = 167.0, 162.6, 133.2, 131.7, 130.1, 129.7, 128.5, 128.1, 125.0, 123.6 (q, *J* = 276.1 Hz, 1 C), 97.1, 68.8, 67.9, 61.5 (q, *J* = 34.4 Hz, 1 C), 26.3.

LR-MS (EI, 70 eV): *m*/*z* (%) = 461 (M$^+$, 18), 362 (3), 334 (100), 129 (60).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{18}H_{15}F_3INO_2$: 461.0100; found: 461.0099.

***cis*-3-Iodo-1-methyl-8-(2,2,3,3,3-pentafluoropropoxy)-4-phenyl-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*cis*-3ab)**

Yellow solid; mp 100.1 °C.

IR (KBr): 1672 cm^{-1}.

^{1}H NMR (500 MHz): δ = 7.40–7.37 (m, 3 H), 7.26 (d, *J* = 8.0 Hz, 2 H), 6.21 (d, *J* = 10.0 Hz, 2 H), 5.66 (d, *J* = 10.0 Hz, 2 H), 4.16 (s, 1 H), 3.88 (t, *J* = 12.5 Hz, 2 H), 2.95 (s, 3 H).

^{13}C NMR (125 MHz): δ = 167.1, 161.9, 133.1, 130.9, 129.4, 128.7, 128.3, 127.8, 118.6 (tt, *J* = 285.0, 35.0 Hz, 1 C), 113.7 (tq, *J* = 233.8, 37.5 Hz, 1 C), 96.7, 69.3, 69.2, 63.5 (q, *J* = 26.3 Hz, 1 C), 26.5.

LR-MS (EI, 70 eV): *m*/*z* (%) = 511 (M$^+$, 3), 384 (100), 129 (71).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{19}H_{15}F_5INO_2$: 511.0068; found: 511.0065.

***trans*-3-Iodo-1-methyl-8-(2,2,3,3,3-pentafluoropropoxy)-4-phenyl-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*trans*-3ab)**

Yellow solid; mp 159.2–160.0 °C.

IR (KBr): 1679 cm^{-1}.

^{1}H NMR (500 MHz): δ = 7.40–7.37 (m, 3 H), 7.24 (d, *J* = 8.0 Hz, 2 H), 6.20 (d, *J* = 10.0 Hz, 2 H), 5.74 (d, *J* = 10.0 Hz, 2 H), 4.70 (s, 1 H), 3.00 (t, *J* = 12.5 Hz, 2 H), 2.85 (s, 3 H).

^{13}C NMR (125 MHz): δ = 167.0, 162.5, 133.1, 131.4, 130.3, 129.7, 128.4, 128.0, 118.5 (tt, *J* = 284.0, 35.0 Hz, 1 C), 113.0 (tq, *J* = 235.0, 37.5 Hz, 1 C), 97.1, 68.7, 67.9, 60.7 (q, *J* = 26.3 Hz, 1 C), 26.3.

LR-MS (EI, 70 eV): *m*/*z* (%) = 511 (M$^+$, 121), 385 (23), 384 (100), 129 (69).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{19}H_{15}F_5INO_2$: 511.0068; found: 511.0068.

***cis*-3-Iodo-1,6-dimethyl-4-phenyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*cis*-3ea)**

Pale yellow solid; mp 93.0–94.5 °C.

IR (KBr): 1698 cm^{-1}.

^{1}H NMR (500 MHz): δ = 7.32–7.27 (m, 3 H), 7.22 (d, *J* = 8.0 Hz, 2 H), 6.14 (d, *J* = 10.0 Hz, 1 H), 5.87 (s, 1 H), 5.52 (d, *J* = 10.0 Hz, 1 H), 4.14 (s, 1 H), 3.74–3.69 (m, 2 H), 2.79 (s, 3 H), 1.51 (s, 3 H).

^{13}C NMR (125 MHz): δ = 167.6, 161.2, 133.7, 132.9, 130.7, 129.6, 129.0, 128.8, 128.5, 127.9, 127.6, 124.9, 123.8 (q, *J* = 277.5 Hz, 1 C), 96.6, 71.7, 70.6, 64.4 (q, *J* = 28.0 Hz, 1 C), 26.3, 17.0.

LR-MS (EI, 70 eV): *m*/*z* (%) = 475 (M$^+$, 32), 460 (16), 376 (5), 349 (23), 348 (100), 129 (61).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{19}H_{17}F_3INO_2$: 475.0256; found: 475.0254.

***trans*-3-Iodo-1,6-dimethyl-4-phenyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*trans*-3ea)**

Pale yellow solid; mp 154.5–155.3 °C.

IR (KBr): 1674 cm^{-1}.

^{1}H NMR (500 MHz): δ = 7.34–7.29 (m, 3 H), 7.21 (d, *J* = 8.0 Hz, 2 H), 6.12 (d, *J* = 10.0 Hz, 1 H), 5.90 (s, 1 H), 5.58 (d, *J* = 10.0 Hz, 1 H), 4.63 (s, 1 H), 2.98–2.90 (m, 2 H), 2.70 (s, 3 H), 1.56 (s, 3 H).

^{13}C NMR (125 MHz): δ = 167.4, 161.7, 135.5, 132.9, 131.0, 130.4, 129.9, 128.7, 128.6, 127.9, 123.8 (q, *J* = 276.3 Hz, 1 C), 97.2, 71.4, 69.5, 61.9 (q, *J* = 27.0 Hz, 1 C), 25.9, 17.3.

LR-MS (EI, 70 eV): *m*/*z* (%) = 475 (M^+, 52), 460 (17), 376 (6), 348 (100), 129 (66).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{19}H_{17}F_3INO_2$: 475.0256; found: 475.0256.

***cis*-3-Iodo-1,6-dimethyl-8-(2,2,3,3,3-pentafluoropropoxy)-4-phenyl-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*cis*-3eb)**
Pale yellow solid; mp 86.1 °C.

IR (KBr): 1699 cm^{-1}.

^{1}H NMR (500 MHz): δ = 7.40–7.35 (m, 3 H), 7.29 (d, *J* = 8.0 Hz, 2 H), 6.20 (d, *J* = 10.0 Hz, 1 H), 5.94 (s, 1 H), 5.60 (d, *J* = 10.0 Hz, 1 H), 4.23 (s, 1 H), 3.86 (t, *J* = 12.5 Hz, 2 H), 2.87 (s, 3 H), 1.59 (s, 3 H).

^{13}C NMR (125 MHz): δ = 167.6, 161.0, 133.8, 132.8, 130.5, 129.6, 129.1, 128.4, 127.6, 127.5, 118.6 (tt, *J* = 284.0 Hz, 35.0 Hz, 1 C), 114.1 (tq, *J* = 271.1 Hz, 36.3 Hz, 1 C), 96.5, 71.6, 70.4, 63.0 (t, *J* = 26.3 Hz, 1 C), 26.2, 17.0.

LR-MS (EI, 70 eV): *m*/*z* (%) = 525 (M^+, 11), 398 (38), 249 (10), 207 (13), 129 (40), 43 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{20}H_{17}F_5INO_2$: 525.0224; found: 525.0224.

***trans*-3-Iodo-1,6-dimethyl-8-(2,2,3,3,3-pentafluoropropoxy)-4-phenyl-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*trans*-3eb)**
Pale yellow solid; mp 152.9–153.4 °C.

IR (KBr): 1699 cm^{-1}.

^{1}H NMR (500 MHz): δ = 7.40–7.35 (m, 3 H), 7.29 (d, *J* = 10.0 Hz, 2 H), 6.18 (d, *J* = 10.0 Hz, 1 H), 5.96 (s, 1 H), 5.66 (d, *J* = 10.0 Hz, 1 H), 4.71 (s, 1 H), 3.16–3.09 (m, 2 H), 2.77 (s, 3 H), 1.64 (s, 3 H).

^{13}C NMR (125 MHz): δ = 167.3, 161.6, 135.6, 132.7, 130.7, 130.4, 129.8, 128.5, 128.4, 127.7, 118.5 (tt, *J* = 284.0 Hz, 35.0 Hz, 1 C), 113.9 (tq, *J* = 271.1 Hz, 36.3 Hz, 1 C), 97.2, 71.2, 69.4, 60.8 (t, *J* = 26.3 Hz, 1 C), 25.9, 17.3.

LR-MS (EI, 70 eV): *m*/*z* (%) = 525 (M^+, 43), 398 (100), 129 (71), 43 (62).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{20}H_{17}F_5INO_2$: 525.0224; found: 525.0224.

***cis*-3-Iodo-1,7-dimethyl-4-phenyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*cis*-3fa)**
Pale yellow solid; mp 149.5–150.7 °C.

IR (KBr): 1696 cm^{-1}.

^{1}H NMR (400 MHz): δ = 7.40–7.33 (m, 3 H), 7.22 (d, *J* = 8.0 Hz, 2 H), 6.15 (d, *J* = 10.0 Hz, 1 H), 5.61 (d, *J* = 10.0 Hz, 1 H), 5.36 (s, 1 H), 4.03 (s, 1 H), 3.77–3.65 (m, 2 H), 2.91 (s, 3 H), 1.85 (s, 3 H).

^{13}C NMR (100 MHz): δ = 167.1, 162.6, 138.9, 133.3, 130.7, 129.4, 129.0, 128.6, 128.3, 127.8, 123.8, 123.7 (q, *J* = 276.9 Hz, 1 C), 122.4, 96.4, 72.0, 70.3, 64.0 (q, *J* = 34.4 Hz, 1 C), 26.6, 19.5.

LR-MS (EI, 70 eV): *m*/*z* (%) = 475 (M^+, 49), 376 (7), 349 (23), 348 (100), 129 (84).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{19}H_{17}F_3INO_2$: 475.0256; found: 475.0256.

***trans*-3-Iodo-1,7-dimethyl-4-phenyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*trans*-3fa)**
Pale yellow solid; mp 160.4–160.9 °C.

IR (KBr): 1695 cm^{-1}.

^{1}H NMR (400 MHz): δ = 7.39–7.35 (m, 3 H), 7.16 (d, *J* = 8.0 Hz, 2 H), 6.14 (d, *J* = 10.0 Hz, 1 H), 5.70 (d, *J* = 10.0 Hz, 1 H), 5.42 (s, 1 H), 4.54 (s, 1 H), 2.81 (s, 3 H), 2.72–2.52 (m, 2 H), 1.83 (s, 3 H).

^{13}C NMR (100 MHz): δ = 166.9, 163.1, 139.3, 133.5, 131.2, 130.3, 129.6, 128.6, 128.5, 128.1, 127.8, 127.7, 125.3, 123.7 (q, *J* = 275.9 Hz, 1 C),, 96.8, 70.8, 70.1, 60.5 (q, *J* = 34.4 Hz, 1 C), 26.5, 15.9.

LR-MS (EI, 70 eV): *m*/*z* (%) = 475 (M^+, 10), 376 (2), 348 (100), 129 (47).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{19}H_{17}F_3INO_2$: 475.0256; found: 475.0253.

***cis*-3-Iodo-1,6,7-trimethyl-4-phenyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*cis*-3ga)**
Yellow solid; mp 100.2–101.5 °C.

IR (KBr): 1687 cm^{-1}.

^{1}H NMR (400 MHz): δ = 7.40–7.32 (m, 3 H), 7.20 (d, *J* = 8.0 Hz, 2 H), 6.14 (d, *J* = 10.0 Hz, 1 H), 5.57 (d, *J* = 10.0 Hz, 1 H), 4.10 (s, 1 H), 3.72–3.58 (m, 2 H), 2.84 (s, 3 H), 1.78 (s, 3 H), 1.49 (s, 3 H).

^{13}C NMR (100 MHz): δ = 167.6, 161.9, 133.3, 133.1, 130.4, 129.5, 128.4, 127.5, 127.1, 123.9 (q, *J* = 276.2 Hz, 1 C), 96.5, 73.0, 72.7, 63.3 (q, *J* = 34.4 Hz, 1 C), 26.3, 15.7, 12.4.

LR-MS (EI, 70 eV): *m*/*z* (%) = 489 (M^+, 38), 390 (7), 362 (100), 129 (55).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{20}H_{19}F_3INO_2$: 489.0413; found: 489.0412.

***trans*-3-Iodo-1,6,7-trimethyl-4-phenyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*trans*-3ga)**
Pale yellow solid; mp 155.1–155.2 °C.

IR (KBr): 1693 cm^{-1}.

^{1}H NMR (400 MHz): δ = 7.38–7.34 (m, 3 H), 7.14 (d, *J* = 8.0 Hz, 2 H), 6.12 (d, *J* = 10.0 Hz, 1 H), 5.63 (d, *J* = 10.0 Hz, 1 H), 4.54 (s, 1 H), 2.74 (s, 3 H), 2.71–2.59 (m, 2 H), 1.79 (s, 3 H), 1.55 (s, 3 H).

^{13}C NMR (100 MHz): δ = 167.4, 163.1, 134.1, 133.4, 130.5, 130.4, 129.8, 128.6, 128.5, 127.8, 123.8 (q, *J* = 276.0 Hz, 1 C), 97.3, 72.6, 72.3, 60.5 (q, *J* = 34.4 Hz, 1 C), 26.0, 15.5, 12.8.

LR-MS (EI, 70 eV): *m*/*z* (%) = 489 (M^+, 57), 390 (10), 362 (100), 129 (68).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{20}H_{19}F_3INO_2$: 489.0413; found: 489.0413.

***cis*-3-Iodo-1,6,9-trimethyl-4-phenyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*cis*-3ha)**
Yellow solid; mp 152.8–153.4 °C.

IR (KBr): 1672 cm^{-1}.

^{1}H NMR (400 MHz): δ = 7.40–7.33 (m, 3 H), 7.25 (d, *J* = 8.0 Hz, 2 H), 5.87 (s, 1 H), 5.31 (s, 1 H), 4.09 (s, 1 H), 3.75–3.62 (m, 2 H), 2.84 (s, 3 H), 1.84 (s, 3 H), 1.55 (s, 3 H).

^{13}C NMR (100 MHz): δ = 167.6, 161.9, 138.6, 134.1, 133.0, 129.6, 128.8, 128.7, 127.7, 127.6, 124.3, 123.9 (q, *J* = 276.6 Hz, 1 C), 96.2, 73.1, 72.7, 63.5 (q, *J* = 34.4 Hz, 1 C), 26.3, 19.2, 16.7.

LR-MS (EI, 70 eV): *m*/*z* (%) = 489 (M^+, 23), 390 (6), 362 (100), 129 (54).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{20}H_{19}F_3INO_2$: 489.0413; found: 489.0413.

***trans*-3-Iodo-1,6,9-trimethyl-4-phenyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*trans*-3ha)**
Pale yellow solid; mp 165.7–166.6 °C.

IR (KBr): 1674 cm^{-1}.

^{1}H NMR (400 MHz): δ = 7.38–7.35 (m, 3 H), 7.19 (d, *J* = 8.0 Hz, 2 H), 5.90 (s, 1 H), 5.35 (s, 1 H), 4.55 (s, 1 H), 2.85–2.78 (m, 1 H), 2.74 (s, 3 H), 2.70–2.63 (m, 1 H), 1.82 (s, 3 H), 1.62 (s, 3 H).

^{13}C NMR (100 MHz): δ = 167.3, 162.3, 138.7, 135.7, 133.3, 129.8, 128.6, 128.4, 127.8, 125.6, 123.8 (q, *J* = 276.1 Hz, 1 C), 97.1, 72.6, 72.3, 60.8 (q, *J* = 34.4 Hz, 1 C), 26.0, 19.2, 17.1.

LR-MS (EI, 70 eV): *m*/*z* (%) = 489 (M^+, 28), 390 (5), 362 (100), 129 (52).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{20}H_{19}F_3INO_2$: 489.0413; found: 489.0411.

***cis*-3-Iodo-6-methoxy-1-methyl-4-phenyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*cis*-3ia)**
Yellow solid; mp 76.0 °C.

IR (KBr): 1700 cm^{-1}.

^{1}H NMR (500 MHz): δ = 7.41–7.34 (m, 3 H), 7.18 (d, *J* = 8.0 Hz, 2 H), 6.14 (d, *J* = 10.0 Hz, 1 H), 5.51 (d, *J* = 10.0 Hz, 1 H), 5.09 (s, 1 H), 4.51 (s, 1 H), 3.83–3.73 (m, 2 H), 3.59 (s, 3 H), 2.87 (s, 3 H).

^{13}C NMR (125 MHz): δ = 167.9, 160.7, 151.9, 132.8, 130.7, 129.5, 129.3, 128.3, 127.8, 127.6, 129.2 (q, *J* = 276.0 Hz, 1 C), 98.8, 96.6, 71.9, 70.6, 63.6 (q, *J* = 33.4 Hz, 1 C), 54.9, 26.3.

LR-MS (EI, 70 eV): *m*/*z* (%) = 491 (M^+, 34), 392 (24), 377 (19), 364 (18), 129 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{19}H_{17}F_3INO_3$: 491.0205; found: 491.0204.

***trans*-3-Iodo-6-methoxy-1-methyl-4-phenyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*trans*-3ia)**
White solid; mp 147.0–148.6 °C.

IR (KBr): 1696 cm^{-1}.

^{1}H NMR (500 MHz): δ = 7.39–7.38 (m, 3 H), 7.11 (d, *J* = 8.0 Hz, 2 H), 6.09 (d, *J* = 10.0 Hz, 1 H), 5.56 (d, *J* = 10.0 Hz, 1 H), 5.06 (s, 1 H), 4.98 (s, 1 H), 3.62 (s, 3 H), 2.78 (s, 3 H), 2.74–2.64 (m, 2 H).

^{13}C NMR (125 MHz): δ = 167.7, 161.6, 153.1, 133.0, 131.0, 129.6, 129.1, 128.5, 127.8, 129.0 (q, *J* = 276.1 Hz, 1 C), 99.5, 97.0, 70.7, 70.4, 59.9 (q, *J* = 33.8 Hz, 1 C), 54.8, 26.1.

LR-MS (EI, 70 eV): *m*/*z* (%) = 491 (M^+, 36), 460 (21), 392 (26), 364 (24), 234 (7), 129 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{19}H_{17}F_3INO_3$: 491.0205; found: 491.0205.

***cis*-6-Chloro-3-iodo-1-methyl-4-phenyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*cis*-3ja)**
Pale yellow solid; mp 92.9–94.0 °C.

IR (KBr): 1697 cm^{-1}.

^{1}H NMR (400 MHz): δ = 7.43–7.35 (m, 3 H), 7.26 (d, *J* = 8.0 Hz, 2 H), 6.32 (s, 1 H), 6.21 (d, *J* = 10.0 Hz, 1 H), 5.67 (d, *J* = 10.0 Hz, 1 H), 4.31 (s, 1 H), 3.84–3.78 (m, 2 H), 2.91 (s, 3 H).

^{13}C NMR (100 MHz): δ = 167.5, 159.7, 132.4, 132.2, 130.2, 129.8, 129.6, 128.8, 127.9, 127.8, 123.6 (q, *J* = 276.8 Hz, 1 C), 98.2, 71.9, 71.7, 65.0 (q, *J* = 33.4 Hz, 1 C), 26.2.

LR-MS (EI, 70 eV): *m*/*z* (%) = 497 (M^+ + 2, 9), 495 (M^+, 29), 460 (M – Cl, 30), 396 (4), 368 (50), 332 (31), 129 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{18}H_{14}ClF_3INO_2$: 494.9710; found: 494.9709.

***trans*-6-Chloro-3-iodo-1-methyl-4-phenyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*trans*-3ja)**
Pale yellow solid; mp 162.1–163.3 °C.

IR (KBr): 1700 cm^{-1}.

^{1}H NMR (500 MHz): δ = 7.44–7.41 (m, 3 H), 7.28 (d, *J* = 8.0 Hz, 2 H), 6.34 (s, 1 H), 6.18 (d, *J* = 10.0 Hz, 1 H), 5.76 (d, *J* = 10.0 Hz, 1 H), 4.86 (s, 1 H), 2.85 (s, 3 H), 2.82–2.80 (m, 2 H).

^{13}C NMR (125 MHz): δ = 167.3, 160.3, 133.5, 132.5, 130.7, 130.5, 130.0, 129.9, 128.7, 123.4 (q, *J* = 276.3 Hz, 1 C), 98.8, 71.8, 70.3, 61.5 (q, *J* = 35.0 Hz, 1 C), 26.1.

LR-MS (EI, 70 eV): *m*/*z* (%) = 497 (M^+ + 2, 9), 495 (M^+, 29), 460 (M – Cl, 30), 368 (54), 129 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{18}H_{14}ClF_3INO_2$: 494.9710; found: 494.9709.

***cis*-6-Bromo-3-iodo-1-methyl-4-phenyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*cis*-3ka)**
Pale yellow solid; mp 117.8–119.5 °C.

IR (KBr): 1697 cm^{-1}.

^{1}H NMR (500 MHz): δ = 7.35–7.30 (m, 3 H), 7.23 (d, *J* = 8.0 Hz, 2 H), 6.48 (s, 1 H), 6.16 (d, *J* = 10.0 Hz, 1 H), 5.65 (d, *J* = 10.0 Hz, 1 H), 4.14 (s, 1 H), 3.77–3.72 (m, 2 H), 2.85 (s, 3 H).

^{13}C NMR (125 MHz): δ = 167.3, 159.8, 133.8, 132.3, 130.2, 129.7, 128.5, 127.8, 127.7, 124.0, 123.4 (q, *J* = 276.3 Hz, 1 C), 98.3, 72.3, 71.9, 64.9 (q, *J* = 33.8 Hz, 1 C), 26.2.

LR-MS (EI, 70 eV): *m*/*z* (%) = 541 (M^+ + 2, 9), 539 (M^+, 10), 461 (12), 460 (M – Br, 58), 412 (10), 332 (52), 333 (22), 234 (9), 129 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{18}H_{14}BrF_3INO_2$: 538.9205; found: 538.9205.

***trans*-6-Bromo-3-iodo-1-methyl-4-phenyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*trans*-3ka)**
Pale yellow solid; mp 164.6–165.8 °C.

IR (KBr): 1699 cm^{-1}.

^{1}H NMR (500 MHz): δ = 7.35–7.34 (m, 3 H), 7.24 (d, *J* = 8.0 Hz, 2 H), 6.50 (s, 1 H), 6.12 (d, *J* = 10.0 Hz, 1 H), 5.73 (d, *J* = 10.0 Hz, 1 H), 4.67 (s, 1 H), 2.79–2.77 (m, 5 H).

^{13}C NMR (125 MHz): δ = 167.2, 160.4, 134.0, 132.5, 130.4, 130.0, 129.8, 128.8, 128.6, 128.2, 125.4, 123.1 (q, *J* = 276.1 Hz, 1 C), 99.0, 72.2, 70.6, 61.7 (q, *J* = 35.0 Hz, 1 C), 26.1.

LR-MS (EI, 70 eV): *m*/*z* (%) = 541 (M^+ + 2, 23), 539 (M^+, 26), 461 (2), 460 (M – Br, 9), 412 (11), 333 (22), 332 (52), 234 (9), 129 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{18}H_{14}BrF_3INO_2$: 538.9205; found: 538.9205.

***cis*-3,6-Diiodo-1-methyl-4-phenyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*cis*-3la)**
Pale yellow solid; mp 114.0–115.2 °C.

IR (KBr): 1691 cm^{-1}.

^{1}H NMR (500 MHz): δ = 7.44–7.39 (m, 3 H), 7.35 (d, *J* = 8.0 Hz, 2 H), 6.87 (s, 1 H), 6.30 (d, *J* = 10.0 Hz, 1 H), 5.81 (d, *J* = 10.0 Hz, 1 H), 4.11 (s, 1 H), 3.86–3.80 (m, 2 H), 2.92 (s, 3 H).

^{13}C NMR (125 MHz): δ = 167.1, 160.3, 141.8, 132.3, 130.3, 129.7, 128.4, 127.8, 123.5 (q, *J* = 277.5 Hz, 1 C), 102.7, 98.5, 73.0, 71.9, 64.9 (q, *J* = 33.8 Hz, 1 C), 26.3.

LR-MS (EI, 70 eV): *m*/*z* (%) = 588 (M^+, 3), 587 (15), 460 (100), 333 (25), 250 (29), 234 (20), 129 (96).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{18}H_{14}F_3I_2NO_2$: 586.9066; found: 586.9065.

***trans*-3,6-Diiodo-1-methyl-4-phenyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*trans*-3la)**
Pale yellow solid; mp 164.6–165.8 °C.

IR (KBr): 1699 cm^{-1}.

^1H NMR (500 MHz): δ = 7.44–7.41 (m, 3 H), 7.39–7.37 (m, 2 H), 6.91 (s, 1 H), 6.27 (d, *J* = 10.0 Hz, 1 H), 5.89 (d, *J* = 10.0 Hz, 1 H), 4.63 (s, 1 H), 2.94–2.90 (m, 2 H), 2.84 (s, 3 H).

^{13}C NMR (125 MHz): δ = 166.9, 160.8, 143.0, 132.4, 130.5, 130.0, 128.8, 128.5, 128.3, 127.9, 123.4 (q, *J* = 276.3 Hz, 1 C), 104.4, 99.2, 72.8, 70.6, 61.8 (q, *J* = 33.8 Hz, 1 C), 26.1.

LR-MS (EI, 70 eV): *m*/*z* (%) = 588 (M^+, 9), 587 (43), 503 (5), 460 (25), 333 (25), 250 (21), 129 (77), 57 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{18}H_{14}F_3I_2NO_2$: 586.9066; found: 586.9066.

***cis*-3-Iodo-1,4-methyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*cis*-3qa)**
Yellow solid; mp 84.1–85.9 °C.

IR (KBr): 1699 cm^{-1}.

^1H NMR (500 MHz): δ = 6.29 (d, *J* = 12.5 Hz, 2 H), 5.48 (d, *J* = 12.5 Hz, 2 H), 4.65 (s, 1 H), 3.89–3.84 (m, 2 H), 2.91 (s, 3 H), 1.81 (s, 3 H).

^{13}C NMR (125 MHz): δ = 167.3, 160.7, 130.6, 129.2, 123.7 (q, *J* = 276.3 Hz, 1 C), 94.5, 69.0, 68.7, 64.2 (q, *J* = 35.0 Hz, 1 C), 26.6, 15.4.

LR-MS (EI, 70 eV): *m*/*z* (%) = 399 (M^+, 44), 587 (15), 272 (44), 111 (31), 97 (45), 57 (89), 43 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{13}H_{13}F_3INO_2$: 398.9943; found: 398.9943.

***trans*-3-Iodo-1,4-methyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*trans*-3qa)**
Yellow solid; mp 88.6 °C.

IR (KBr): 1694 cm^{-1}.

^1H NMR (500 MHz): δ = 6.36 (d, *J* = 12.5 Hz, 2 H), 5.48 (d, *J* = 12.5 Hz, 2 H), 4.63 (s, 1 H), 3.92–3.88 (m, 2 H), 2.78 (s, 3 H), 1.90 (s, 3 H).

^{13}C NMR (125 MHz): δ = 167.2, 160.6, 131.1, 129.9, 123.5 (q, *J* = 276.3 Hz, 1 C), 69.3, 68.3, 64.8 (q, *J* = 35.0 Hz, 1 C), 26.2, 15.8.

LR-MS (EI, 70 eV): *m*/*z* (%) = 399 (M^+, 17), 300 (4), 503 (5), 272 (28), 111 (37), 57 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{13}H_{13}F_3INO_2$: 398.9943; found: 398.9941.

***cis*-3-Iodo-1-methyl-8-(2,2,3,3,3-pentafluoropropoxy)-4-pentyl-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*cis*-3rb)**
Yellow oil.

IR (KBr): 1699 cm^{-1}.

^1H NMR (500 MHz): δ = 6.28 (d, *J* = 11.0 Hz, 2 H), 5.49 (d, *J* = 11.0 Hz, 2 H), 4.68 (s, 1 H), 3.92 (t, *J* = 13.0 Hz, 2 H), 2.86 (s, 3 H), 2.09–2.05 (m, 2 H), 1.49–1.40 (m, 2 H), 1.29–1.25 (m, 4 H), 0.88 (t, *J* = 6.5 Hz, 3 H).

^{13}C NMR (125 MHz): δ = 167.4, 164.3, 130.3, 129.2, 118.6 (tt, *J* = 284.0, 35.0 Hz, 1 C), 114.0 (tq, *J* = 233.8, 36.3 Hz, 1 C), 94.5, 69.0, 68.8, 63.1 (t, *J* = 27.5 Hz, 1 C), 31.8, 29.5, 27.4, 26.3, 22.0, 13.6.

LR-MS (EI, 70 eV): *m*/*z* (%) = 505 (M^+, 7), 434 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{18}H_{21}F_5INO_2$: 505.0537; found: 505.0535.

***trans*-3-Iodo-1-methyl-8-(2,2,3,3,3-pentafluoropropoxy)-4-pentyl-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*trans*-3rb)**
Yellow oil.

IR (KBr): 1699 cm^{-1}.

^1H NMR (500 MHz): δ = 6.33 (d, *J* = 11.0 Hz, 2 H), 5.50 (d, *J* = 11.0 Hz, 2 H), 4.63 (s, 1 H), 3.94 (t, *J* = 13.0 Hz, 2 H), 2.75 (s, 3 H), 2.021–2.12 (m, 2 H), 1.49–1.40 (m, 2 H), 1.31–1.25 (m, 4 H), 0.89 (t, *J* = 6.5 Hz, 3 H).

^{13}C NMR (125 MHz): δ = 167.2, 164.1, 130.5, 130.0, 118.5 (tt, *J* = 283.8, 35.0 Hz, 1 C), 113.9 (tq, *J* = 271.3, 36.3 Hz, 1 C), 94.6, 69.1, 68.5, 63.6 (t, *J* = 27.5 Hz, 1 C), 31.6, 29.8, 27.5, 26.0, 21.9, 13.6.

LR-MS (EI, 70 eV): *m*/*z* (%) = 505 (M^+, 17), 434 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{18}H_{21}F_5INO_2$: 505.0537; found: 505.0537.

***cis*-3-Iodo-1-methyl-4-(2-methylphenyl)-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*cis*-3sa)**
Pale yellow solid; mp 118.4 °C.

IR (KBr): 1694 cm^{-1}.

^1H NMR (500 MHz): δ = 7.28 (t, *J* = 7.5 Hz, 1 H), 7.22 (d, *J* = 7.5 Hz, 1 H), 7.14 (t, *J* = 7.5 Hz, 1 H), 6.88 (d, *J* = 7.5 Hz, 1 H), 6.27 (d, *J* = 12 Hz, 1 H), 6.05 (d, *J* = 12 Hz, 1 H), 5.70 (d, *J* = 12 Hz, 1 H), 5.65 (d, *J* = 12 Hz, 1 H), 3.84 (s, 1 H), 3.77–3.72 (m, 2 H), 2.97 (s, 3 H), 2.19 (s, 3 H).

^{13}C NMR (125 MHz): δ = 167.1, 163.0, 135.9, 1, 129.8, 129.1, 128.0, 127.7, 125.1, 123.7 (q, *J* = 276.3 Hz, 1 C), 98.5, 70.7, 69.3, 64.5 (q, *J* = 33.8 Hz, 1 C), 26.9, 20.0.

LR-MS (EI, 70 eV): *m*/*z* (%) = 475 (M^+, 21), 376 (4), 348 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{19}H_{17}F_3INO_2$: 475.0256; found: 475.0256.

***trans*-3-Iodo-1-methyl-4-(2-methylphenyl)-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*trans*-3sa)**
Pale yellow solid; mp 163.3–164.1 °C.

IR (KBr): 1682 cm^{-1}.

^1H NMR (500 MHz): δ = 7.32–7.26 (m, 2 H), 7.21 (t, *J* = 7.5 Hz, 1 H), 6.93 (d, *J* = 7.5 Hz, 1 H), 6.25 (d, *J* = 12 Hz, 1 H), 6.09 (d, *J* = 12 Hz, 1 H), 5.82 (d, *J* = 10 Hz, 1 H), 5.76 (d, *J* = 10 Hz, 1 H), 4.74 (s, 1 H), 2.90 (s, 3 H), 2.61–2.57 (m, 1 H), 2.46–2.42 (m, 1 H), 2.26 (s, 3 H).

^{13}C NMR (125 MHz): δ = 166.8, 163.1, 135.8, 132.0, 131.8, 131.0, 130.7, 130.5, 129.7, 128.4, 125.3, 123.5 (q, *J* = 276.3 Hz, 1 C), 98.8, 70.0, 67.5, 60.1 (q, *J* = 33.8 Hz, 1 C), 26.6, 19.9.

LR-MS (EI, 70 eV): *m*/*z* (%) = 475 (M^+, 3), 376 (2), 348 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{19}H_{17}F_3INO_2$: 475.0256; found: 475.0255.

***cis*-3-Iodo-4-(4-methoxyphenyl)-1-methyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*cis*-3ta)**
Yellow solid; mp 133.3–135.0 °C.

IR (KBr): 1697 cm^{-1}.

^1H NMR (500 MHz): δ = 7.23 (d, *J* = 7.0 Hz, 2 H), 6.88 (d, *J* = 7.0 Hz, 2 H), 6.21 (d, *J* = 10.5 Hz, 2 H), 5.69 (d, *J* = 10.5 Hz, 2 H), 4.68 (s, 1 H), 3.78 (s, 3 H), 3.05–3.00 (m, 2 H), 2.81 (s, 3 H).

^{13}C NMR (125 MHz): δ = 167.2, 162.1, 160.6, 131.4, 130.3, 129.6, 125.1, 123.6 (q, *J* = 277.5 Hz, 1 C), 113.9, 96.4, 68.8, 68.0, 61.9 (q, *J* = 33.8 Hz, 1 C), 55.2, 26.3.

LR-MS (EI, 70 eV): *m*/*z* (%) = 491 (M^+, 36), 364 (69), 159 (100).

HRMS (EI): *m/z* [M]$^+$ calcd for $C_{19}H_{17}F_3INO_3$: 491.0205; found: 491.0205.

***trans*-3-Iodo-4-(4-methoxyphenyl)-1-methyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*trans*-3ta)**
Yellow solid; mp 135.0 °C.

IR (KBr): 1682 cm^{-1}.

^{1}H NMR (500 MHz): δ = 7.28 (d, *J* = 9.0 Hz, 2 H), 6.87 (d, *J* = 8.5 Hz, 2 H), 6.22 (d, *J* = 10.0 Hz, 2 H), 5.62 (d, *J* = 10.0 Hz, 2 H), 4.24 (s, 1 H), 3.83–3.81 (m, 5 H), 2.92 (s, 3 H).

^{13}C NMR (125 MHz): δ = 167.3, 161.4, 160.4, 130.9, 129.3, 128.9, 125.2, 123.8 (q, *J* = 277.5 Hz, 1 C), 113.8, 95.9, 69.4, 69.1, 64.6 (q, *J* = 33.8 Hz, 1 C), 55.3, 26.9.

LR-MS (EI, 70 eV): *m/z* (%) = 491 (M$^+$, 44), 364 (69), 265 (11), 253 (6), 159 (100).

HRMS (EI): *m/z* [M]$^+$ calcd for $C_{19}H_{17}F_3INO_3$: 491.0205; found: 491.0205.

***cis*-3-Iodo-1-methyl-4-(4-nitrophenyl)-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*cis*-3ua)**
Yellow solid; mp 175.5–176.3 °C.

IR (KBr): 1690 cm^{-1}.

^{1}H NMR (500 MHz): δ = 8.17 (d, *J* = 9.0 Hz, 2 H), 7.40 (d, *J* = 8.5 Hz, 2 H), 6.21 (d, *J* = 10.5 Hz, 2 H), 5.59 (d, *J* = 10.5 Hz, 2 H), 4.08 (s, 1 H), 3.79–3.74 (m, 2 H), 2.89 (s, 3 H).

^{13}C NMR (125 MHz): δ = 166.4, 159.7, 148.2, 139.7, 131.7, 129.1, 127.7, 123.7, 123.6 (q, *J* = 276.3 Hz, 1 C), 99.1, 69.1 (2 C), 65.0 (q, *J* = 35.0 Hz, 1 C), 26.6.

LR-MS (EI, 70 eV): *m/z* (%) = 506 (M$^+$, 3), 406 (3), 379 (100).

HRMS (EI): *m/z* [M]$^+$ calcd for $C_{18}H_{14}F_3IN_2O_4$: 505.9950; found: 505.9950.

***trans*-3-Iodo-1-methyl-4-(4-nitrophenyl)-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*trans*-3ua)**
Yellow solid; mp 121.9–123.4 °C.

IR (KBr): 1682 cm^{-1}.

^{1}H NMR (500 MHz): δ = 8.19 (d, *J* = 8.5 Hz, 2 H), 7.46 (d, *J* = 8.5 Hz, 2 H), 6.24 (d, *J* = 10.0 Hz, 2 H), 5.65 (d, *J* = 9.0 Hz, 2 H), 4.55 (s, 1 H), 3.15–3.10 (m, 2 H), 2.79 (s, 3 H).

^{13}C NMR (125 MHz): δ = 166.4, 159.7, 148.2, 139.4, 132.0, 129.4, 129.0, 123.6, 123.4 (q, *J* = 277.5 Hz, 1 C), 99.0, 68.7, 68.3, 63.2 (q, *J* = 35.0 Hz, 1 C), 26.3.

LR-MS (EI, 70 eV): *m/z* (%) = 506 (M$^+$, 3), 407 (3), 380 (20), 379 (100).

HRMS (EI): *m/z* [M]$^+$ calcd for $C_{18}H_{14}F_3IN_2O_4$: 505.9950; found: 505.9948.

3-Iodo-1-methyl-4-phenylquinolin-2(1*H*)-one (4aa)[1]
Pale yellow solid; mp 173.2 °C.

IR (KBr): 1737, 1637, 1597 cm^{-1}.

^{1}H NMR (400 MHz): δ = 7.62–7.50 (m, 4 H), 7.43 (d, *J* = 8.4 Hz, 1 H), 7.22 (d, *J* = 6.8 Hz, 2 H), 7.15 (d, *J* = 8.0 Hz, 1 H), 7.08 (t, *J* = 7.2 Hz, 1 H), 3.90 (s, 3 H).

^{13}C NMR (100 MHz): δ = 159.1, 156.3, 141.2, 139.6, 131.1, 128.8, 128.9, 128.6, 128.4, 122.4, 121.5, 65.8, 31.7.

LR-MS (EI, 70 eV): *m/z* (%) = 361 (M$^+$, 100).

3-Iodo-1,5-dimethyl-4-phenylquinolin-2(1*H*)-one (4fa) and 3-Iodo-1,7-dimethyl-4-phenylquinolin-2(1*H*)-one (4fa′)
Pale yellow solid; ratio **4fa/4fa′** 1:3.

IR (KBr): 1644 cm^{-1}.

^{1}H NMR (400 MHz): δ = 7.41–7.35 (m, 4 H), 7.26 (d, *J* = 6.8 Hz, 0.31 H), 7.13–7.08 (m, 4 H), 6.92 (d, *J* = 6.4 Hz, 0.69 H), 6.86 (d, *J* = 5.6 Hz, 0.28 H), 6.80 (d, *J* = 6.8 Hz, 0.72 H), 3.81 (s, 0.29 H), 3.78 (s, 0.71 H), 2.38 (s, 3 H).

^{13}C NMR (100 MHz): δ = 159.2, 158.7, 156.2, 156.0, 146.0, 142.0, 141.6, 140.8, 139.0, 137.0, 128.7, 128.4, 127.1, 123.8, 119.8, 119.4, 114.4, 113.3, 105.3, 99.8, 32.8, 31.7, 24.9, 22.2.

LR-MS (EI, 70 eV): *m/z* (%) = 375 (M$^+$, 100).

3-Iodo-1,4-dimethylquinolin-2(1*H*)-one (4qa)[1]
Yellow solid; mp 121.0 °C.

IR (KBr): 1633 cm^{-1}.

^{1}H NMR (500 MHz): δ = 7.83 (d, *J* = 8.0 Hz, 1 H), 7.62 (t, *J* = 8.0 Hz, 1 H), 7.40 (d, *J* = 8.5 Hz, 1 H), 7.28–7.25 (m, 1 H), 2.83 (s, 3 H), 2.82 (s, 3 H).

^{13}C NMR (100 MHz): δ = 150.8, 139.0, 130.9, 129.1, 126.0, 122.4, 120.6, 114.4, 102.7, 31.6, 26.2.

LR-MS (EI, 70 eV): *m/z* (%) = 299 (M$^+$, 100).

3-Iodo-1-methyl-4-(2-methylphenyl)quinolin-2(1*H*)-one (4sa)
Pale yellow solid; mp 109.6–121.0 °C.

IR (KBr): 1637 cm^{-1}.

^{1}H NMR (500 MHz): δ = 7.61 (t, *J* = 8.5 Hz, 1 H), 7.46–7.41 (m, 2 H), 7.36 (t, *J* = 8.0 Hz, 2 H), 7.10–7.04 (m, 3 H), 3.91 (s, 3 H), 2.05 (s, 3 H).

^{13}C NMR (125 MHz): δ = 159.1, 156.3, 140.5, 139.4, 134.8, 131.1, 130.3, 128.8, 128.2, 128.0, 126.3, 122.5, 120.9, 114.3, 101.5, 31.6, 19.3.

LR-MS (EI, 70 eV): *m/z* (%) = 375 (M$^+$, 100).

HRMS (EI): *m/z* [M]$^+$ calcd for $C_{17}H_{14}INO$: 375.0120; found: 375.0120.

3-Iodo-4-(4-methoxyphenyl)-1-methylquinolin-2(1*H*)-one (4ta)
Yellow solid; mp 145.1 °C.

IR (KBr): 1631 cm^{-1}.

^{1}H NMR (500 MHz): δ = 7.26 (t, *J* = 8.0 Hz, 1 H), 7.21 (d, *J* = 8.0 Hz, 1 H), 7.14 (d, *J* = 8.5 Hz, 1 H), 7.10 (d, *J* = 10.5 Hz, 2 H), 7.07–7.05 (m, 3 H), 3.90 (s, 3 H), 3.89 (s, 3 H).

^{13}C NMR (125 MHz): δ = 159.8, 159.1, 156.2, 139.6, 133.6, 130.9, 129.8, 129.0, 122.3, 121.8, 114.1, 102.1, 55.3, 31.7.

LR-MS (EI, 70 eV): *m/z* (%) = 391 (M$^+$, 100).

HRMS (EI): *m/z* [M]$^+$ calcd for $C_{17}H_{14}INO_2$: 391.0069; found: 391.0069.

3-Iodo-1-methyl-4-phenyl-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione (5oa)[3]
White solid; mp 195.6–197.3 °C.

IR (KBr): 1699, 1662, 1361 cm^{-1}.

^{1}H NMR (400 MHz): δ = 7.40–7.34 (m, 3 H), 7.28 (d, *J* = 8.0 Hz, 2 H), 6.52, 6.46 (dd, *J* = 10.4 Hz, 10.4 Hz, 4 H), 2.95 (s, 3 H).

^{13}C NMR (100 MHz): δ = 183.8, 167.4, 158.0, 144.1, 133.3, 131.9, 130.1, 128.7, 127.7, 98.2, 70.4, 27.1.

LR-MS (EI, 70 eV): *m/z* (%) = 377 (M$^+$, 14), 248 (94), 129 (100).

3-Iodo-1-methyl-4-(thiophen-2-yl)-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione (5va)
White solid; mp 179.3–180.1 °C.

IR (KBr): 1695, 1662 cm^{-1}.

^{1}H NMR (500 MHz): δ = 7.68 (s, 1 H), 7.53 (d, *J* = 5.0 Hz, 2 H), 7.10 (d, *J* = 5.0 Hz, 2 H), 6.62–6.53 (m, 4 H) 2.93 (s, 3 H).

^{13}C NMR (125 MHz): δ = 183.9, 167.6, 149.5, 145.1, 133.2, 132.7, 129.7, 129.4, 127.5, 93.5, 69.1, 26.3.

LR-MS (EI, 70 eV): *m*/*z* (%) = 383 (M^+, 27), 256 (18), 135 (100).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{14}H_{10}INO_2S$: 382.9477; found: 382.9477.

***cis*-3-Bromo-1-methyl-4-phenyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*cis*-6aa)**
Pale yellow solid; mp 88.2 °C.

IR (KBr): 1697 cm^{-1}.

^{1}H NMR (500 MHz): δ = 7.39–7.35 (m, 5 H), 6.25 (d, *J* = 10.0 Hz, 2 H), 5.64 (d, *J* = 10.0 Hz, 2 H), 4.27 (s, 1 H), 3.85–3.80 (m, 2 H), 2.92 (s, 3 H).

^{13}C NMR (125 MHz): δ = 165.6, 154.8, 131.2, 130.3, 129.5, 128.9, 128.4, 127.8, 123.7 (q, *J* = 276.3 Hz, 1 C), 118.4, 69.2, 67.2, 64.6 (q, *J* = 33.8 Hz, 1 C), 26.2.

LR-MS (EI, 70 eV): *m*/*z* (%) = 415 (M^+ + 2, 3), 413 (M^+, 3), 334 (100), 129 (42).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{18}H_{15}BrF_3NO_2$: 413.0238; found: 413.0237.

***trans*-3-Bromo-1-methyl-4-phenyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*trans*-6aa)**
White solid; mp 173.9–174.7 °C.

IR (KBr): 1693 cm^{-1}.

^{1}H NMR (500 MHz): δ = 7.42–7.36 (m, 3 H), 7.32 (d, *J* = 7.0 Hz, 2 H), 6.24 (d, *J* = 10.0 Hz, 2 H), 5.73 (d, *J* = 10.0 Hz, 2 H), 4.72 (s, 1 H), 3.02–3.00 (m, 2 H), 2.82 (s, 3 H).

^{13}C NMR (125 MHz): δ = 165.5, 155.3, 131.8, 131.2, 129.9, 129.8, 128.4, 128.3, 123.6 (q, *J* = 276.3 Hz, 1 C), 118.8, 73.1, 66.8, 62.0 (q, *J* = 33.8 Hz, 1 C), 25.9.

LR-MS (EI, 70 eV): *m*/*z* (%) = 415 (M^+ + 2, 12), 413 (M^+, 12), 334 (100), 129 (64).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{18}H_{15}BrF_3NO_2$: 413.0238; found: 413.0238.

***cis*-3-Bromo-6-chloro-1-methyl-4-phenyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*cis*-6ja)**
Yellow oil.

IR (KBr): 1716 cm^{-1}.

^{1}H NMR (500 MHz): δ = 7.41–7.33 (m, 5 H), 6.35 (d, *J* = 7.5 Hz, 1 H), 6.24 (t, *J* = 7.5 Hz, 1 H), 5.68 (d, *J* = 7.5 Hz, 1 H), 4.11 (d, *J* = 7.5 Hz, 1 H), 3.85–3.83 (m, 2 H), 2.90 (s, 3 H).

^{13}C NMR (100 MHz): δ = 166.0, 152.7, 132.2, 130.6, 130.3, 129.8, 129.7, 128.6, 128.0, 127.8, 123.5 (q, *J* = 276.9 Hz, 1 C), 120.0, 71.6, 70.1, 64.9 (q, *J* = 35.1 Hz, 1 C), 25.9.

LR-MS (EI, 70 eV): *m*/*z* (%) = 451 (6), 450 (5), 449 (M^+ + 2, 25), 448 (5), 447 (M^+, 18), 414 (40), 368 (33), 332 (16), 312 (13), 268 (19), 234 (19), 129 (100).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{18}H_{14}BrClF_3NO_2$: 446.9849; found: 446.9849.

***trans*-3-Bromo-6-chloro-1-methyl-4-phenyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*trans*-6ja)**
Yellow solid; mp 94.9 °C.

IR (KBr): 1708 cm^{-1}.

^{1}H NMR (500 MHz): δ = 7.43–7.34 (m, 5 H), 6.36 (d, *J* = 10.0 Hz, 1 H), 6.21 (t, *J* = 10.0 Hz, 1 H), 5.75 (d, *J* = 10.0 Hz, 1 H), 4.86 (s, 1 H), 2.98–2.94 (m, 2 H), 2.82 (s, 3 H).

^{13}C NMR (125 MHz): δ = 165.7, 153.2, 132.3, 130.8, 130.4, 130.0, 129.6, 129.4, 128.5, 127.6, 123.5 (q, *J* = 276.3 Hz, 1 C), 120.4, 71.3, 70.0, 61.9 (q, *J* = 35.0 Hz, 1 C), 25.6.

LR-MS (EI, 70 eV): *m*/*z* (%) = 451 (5), 450 (4), 449 (M^+ + 2, 15), 448 (4), 447 (M^+, 9), 414 (9), 368 (13), 332 (10), 268 (7), 234 (10), 129 (90), 77 (9), 43 (100).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{18}H_{14}BrClF_3NO_2$: 446.9849; found: 446.9848.

3-Bromo-1-methyl-4-(thiophen-2-yl)-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (6va)
Yellow solid; ratio *cis*/*trans* 3:2; mp 147.2 °C.

IR (KBr): 1694 cm^{-1}.

^{1}H NMR (500 MHz): δ = 7.66–7.36 (m, 2 H), 7.12–7.05 (m, 1 H), 6.40–6.36 (m, 2 H), 5.67–5.63 (m, 2 H), 4.75–4.72 (m, 1 H), 3.98–3.93 (m, 2 H), 2.91 (s, 1.9 H), 2.89 (m, 1.1 H).

^{13}C NMR (125 MHz): δ = 165.5, 165.2, 147.1, 146.2, 134.0, 132.4, 131.2, 131.0, 130.2, 130.0, 129.9, 129.7, 129.6, 129.1, 127.3, 123.8 (q, *J* = 276.3 Hz, 1 C), 117.4, 115.3, 114.9, 70.1, 69.9, 66.0–64.8 (qq, 2 C), 25.9, 25.8.

LR-MS (EI, 70 eV): *m*/*z* (%) = 422 (7), 421 (M^+ + 2, 38), 420 (9), 419 (M^+, 36), 375 (2), 341 (13), 340 (66), 241 (21), 204 (19), 135 (100), 77 (21).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{16}H_{13}BrF_3NO_2S$: 418.9803; found: 418.9800.

***cis*-3-Chloro-1-methyl-4-phenyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*cis*-7aa)**
Yellow solid; mp 73.0 °C.

IR (KBr): 1700 cm^{-1}.

^{1}H NMR (400 MHz): δ = 7.41–7.26 (m, 5 H), 6.26 (d, *J* = 10.0 Hz, 2 H), 5.61 (d, *J* = 10.0 Hz, 2 H), 4.35 (s, 1 H), 3.87–3.80 (m, 2 H), 2.89 (s, 3 H).

^{13}C NMR (100 MHz): δ = 165.0, 150.6, 131.2, 130.3, 129.6, 128.7, 128.4, 127.9, 127.0, 123.7 (q, *J* = 277.0 Hz, 1 C), 69.3, 65.5, 64.7 (q, *J* = 34.3 Hz, 1 C), 27.8.

LR-MS (EI, 70 eV): *m*/*z* (%) = 371 (M^+ + 2, 3), 369 (M^+, 9), 334 (M – Cl, 100).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{18}H_{15}ClF_3NO_2$: 369.0743; found: 369.0741.

***trans*-3-Chloro-1-methyl-4-phenyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*trans*-7aa)**
Yellow solid; mp 129.7 °C.

IR (KBr): 1719 cm^{-1}.

^{1}H NMR (400 MHz): δ = 7.40–7.36 (m, 5 H), 6.26 (d, *J* = 10.0 Hz, 2 H), 5.71 (d, *J* = 10.0 Hz, 2 H), 4.72 (s, 1 H), 31.8–3.11 (m, 2 H), 2.80 (s, 3 H).

^{13}C NMR (100 MHz): δ = 164.9, 151.0, 131.8, 130.1, 129.9, 129.8, 128.6, 128.4, 128.3, 127.3, 123.6 (q, *J* = 276.1 Hz, 1 C), 68.0, 65.2, 62.3 (q, *J* = 34.3 Hz, 1 C), 25.6.

LR-MS (EI, 70 eV): *m*/*z* (%) = 371 (M^+ + 2, 11), 369 (M^+, 33), 334 (M – Cl, 100).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{18}H_{15}ClF_3NO_2$: 369.0743; found: 369.0743.

***cis*-3-Chloro-1,6-dimethyl-4-phenyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*cis*-7ea)**
Yellow solid; mp 90.0 °C.

IR (KBr): 1699 cm^{-1}.

^1H NMR (400 MHz): δ = 7.44–7.36 (m, 5 H), 6.24 (d, *J* = 10.0 Hz, 1 H), 6.00 (s, 1 H), 5.58 (d, *J* = 10.0 Hz, 1 H), 4.43 (s, 1 H), 3.86–3.80 (m, 2 H), 2.82 (s, 3 H), 1.55 (s, 3 H).

^{13}C NMR (100 MHz): δ = 165.4, 149.8, 134.1, 130.6, 129.7, 129.3, 128.7, 128.5, 128.0, 127.9, 127.6, 123.8 (q, *J* = 276.9 Hz, 1 C), 70.6, 67.8, 64.5 (q, *J* = 34.4 Hz, 1 C), 25.6, 16.9.

LR-MS (EI, 70 eV): *m*/*z* (%) = 385 (M^+ + 2, 7), 383 (M^+, 21), 348 (M – Cl, 22), 284 (7), 234 (7), 207 (14), 129 (13), 77 (8), 43 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{19}H_{17}ClF_3NO_2$: 383.0900; found: 383.0899.

***trans*-3-Chloro-1,6-dimethyl-4-phenyl-8-(2,2,2-trifluoroethoxy)-1-azaspiro[4.5]deca-3,6,9-trien-2-one (*trans*-7ea)**
Yellow solid; mp 182.1 °C.

IR (KBr): 1720 cm^{-1}.

^1H NMR (400 MHz): δ = 7.43–7.40 (m, 2 H), 7.36–7.30 (m, 3 H), 6.19 (d, *J* = 10.0 Hz, 1 H), 5.97 (s, 1 H), 5.57 (d, *J* = 10.0 Hz, 1 H), 3.28–3.24 (m, 2 H), 2.67 (s, 3 H), 1.53 (s, 3 H).

^{13}C NMR (100 MHz): δ = 165.3, 150.1, 135.3, 131.0, 130.1, 130.0, 129.9, 128.7, 128.5, 128.2, 128.0, 123.7 (q, *J* = 276.9 Hz, 1 C), 69.7, 67.6, 62.8 (q, *J* = 34.3 Hz, 1 C), 25.2, 17.2.

LR-MS (EI, 70 eV): *m*/*z* (%) = 385 (M^+ + 2, 6), 383 (M^+, 17), 348 (M – Cl, 15), 284 (8), 207 (20), 129 (12), 77 (9), 43 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{19}H_{17}ClF_3NO_2$: 383.0900; found: 383.0900.

Acknowledgment

The authors thank the National Natural Science Foundation of China (No. 20572020 and 20872112), Scientific Research Fund of Hunan Provincial Education Department (No. 08A037), and Program for New Century Excellent Talents in University (No. NCET-06-0711) for financial support.

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(9) A set of other reagents, including NaOEt, NaOAc, NH_4Cl, 4-nitrophenol, and TfOH, instead of TFA were examined. The results showed that no reaction was observed using NaOEt, NaOAc, NH_4Cl, or 4-nitrophenol, and the electrophilic *ortho*-cyclization product **4aa** was obtained in 90% yield in the presence of TfOH.