Preparation of 3-(Fluoroalkyl)-2-azadienes and Its Application in the Synthesis of (Fluoroalkyl)isoquinoline and -pyridine Derivatives

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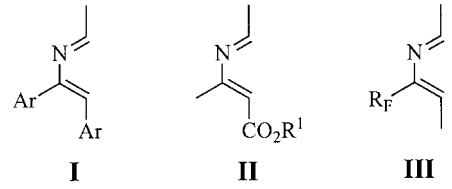
A method for the preparation of 3-(fluoroalkyl)-substituted 2-azabutadienes **5** by aza-Wittig reaction of *N*-vinylic 3-(fluoroalkyl)phosphazenes **4** and aldehydes is reported. Thermal 6π-electrocyclization of these azadienes gives 3-(fluoroalkyl)-substituted isoquinolines **6**. Also [4+2] cycloaddition of these heterodienes **5** with enamine **8** gives fluoroalkyl-substituted pyridine derivatives **10**–**16**. However, the reaction of azadienes **17** with azo compound **18** affords bicyclic heterocycles **19**.

Introduction

The development of efficient and mild methods for the synthesis of organofluorine compounds represents a broad area of research in organic chemistry since the incorporation of a fluorine-containing group into an organic molecule dramatically alters its physical, chemical and biological properties.[1] Special interest has been focused on the development of synthetic methods for the preparation of fluorinated building blocks which can be used in the efficient and/or selective preparation of fluorine-containing molecules with biological activity and commercial applications.[2] The synthetic methods used in the synthesis of these compounds include the introduction of fluorine into the preformed heterocycles or the formation of heterocyclic systems by using fluorinated precursors. Direct fluorination is the simplest way to prepare fluorinated heterocyclic compounds,[3] but usually the use of fluorinated precursors is of more interest due to the easy and regioselective formation of the products.[4]

Functionalized 2-azabutadiene systems have proved to be efficient key intermediates in the synthesis of heterocycles[5,6] and we have previously described new methods for the preparation of heterocycles,[7] as well as the synthesis of neutral azadienes **I**[8] or electron-poor 2-aza-1,3-butadienes derived from β-amino esters **II** (Figure 1),[9] all of which are useful in the preparation of nitrogen-containing heterocyclic compounds.[7–9]



I **II** **III**

Figure 1. 2-Aza-1,3-butadienes **I**–**III**.

Fluoroalkyl-substituted 2-aza-1,3-butadienes **III**, despite their potential interest as synthons in the construction of more complex fluoro-containing acyclic and cyclic compounds, have not received much attention, probably as a result of the lack of general methods available for the synthesis of these compounds. Indeed, as far as we know, only the synthesis of 4-alkoxy-1,4-bis(silyloxy)-1-(trifluoromethyl)-,[10a] 1,1-bis(trifluoromethyl)-[10b] and 4,4-difluoro- and 3-(trifluoromethyl)-2-aza-1,3-butadienes[10c] have been reported and only the reactions of 4-alkoxy-1,4-bis(silyloxy)-1-(trifluoromethyl)-2-aza-1,3-butadienes with carbonyl compounds[11a] and 1,1-bis(trifluoromethyl)-2-aza-1,3-butadiene with bromides, amines, mercaptans,[11b] diazomethane[11c] and phosphanes[11d] have been described. As a continuation of our work in the design of new building blocks and owing to the increasing importance of fluorine-containing heterocycles in biology, pharmacology and industry, we report herein an easy and versatile method for the synthesis of fluoroalkyl-substituted 2-azadienes **III** that involves the aza-Wittig reaction[12] of *N*-vinylic phosphazenes with aldehydes and the use of these substrates as starting materials for the construction of fluoroalkyl-functionalized heterocycles.[13]

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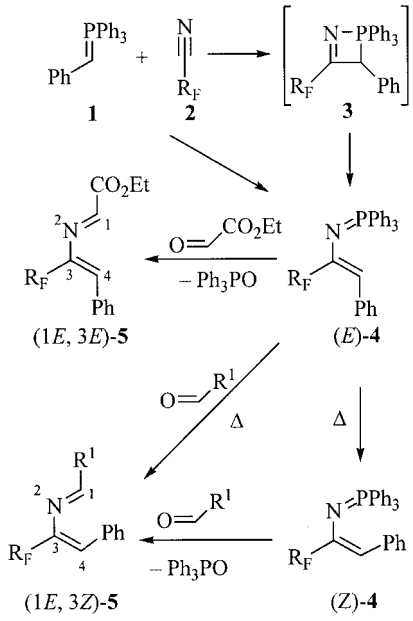
Results and Discussion

Synthesis of *N*-Vinylic Phosphazenes

Fluoroalkyl-substituted *N*-vinylic phosphazenes **4** were prepared by reaction of phosphorus ylides and perfluoroalkyl nitriles. Gaseous nitriles **2a** ($R_F = CF_3$) and **2b** ($R_F = C_2F_5$) were freshly generated[14] and bubbled through a cooled (0 °C) solution of phosphorus ylides **1** to afford the corresponding *N*-vinylic phosphazenes **4a** and **4b** (Scheme 1, Table 1, entries 1 and 3) in good yield, while commercially available nitrile **2c** ($R_F = C_7F_{15}$) was also used in the synthesis of phosphazene **4c** (Table 1, entry 5).



Scheme 1.

Table 1. *N*-Vinylic phosphazenes **4** obtained from the reaction of phosphorus ylides and perfluoroalkyl nitriles.

Entry		R_F	Time [h]	Solvent	Yield [%][a]	M.p. [°C]
1	(*E*)-**4a**	CF_3	12	Et_2O	90	134–135
2	(*Z*)-**4a**	CF_3	12[b]	toluene	98	121–122
3	(*E*)-**4b**	C_2F_5	24	Et_2O	61	105–106
4	(*Z*)-**4b**	C_2F_5	12[b]	toluene	98	97–98
5	(*E*)-**4c**	C_7F_{15}	12	Et_2O	83	oil
6	(*Z*)-**4c**	C_7F_{15}	12[b]	toluene	98	oil

[a] Yield of isolated compounds. [b] Obtained from the (*E*) isomer by heating at 110 °C.

Crystalline compounds **4** were characterized as exclusively pure *E* isomers by analysis of their spectroscopic data. The mass spectrum of compound **4a** gave the molecular-ion peak *m*/*z* = 447 as the base peak. The ^{31}P NMR spectrum of compound **4a** showed an absorption at δ_P = 7.94 ppm, in the ^1H NMR spectrum of **4a** the vinylic proton resonated at δ_H = 5.70 ppm as a well-resolved doublet with a long-range coupling constant of $^4J_{PH}$ = 3.2 Hz, while in the ^{13}C NMR spectrum of **4a** the olefinic CH (in the β position with respect to the nitrogen atom) gave a double doublet at δ_C = 113.8 ppm with coupling constants of $^3J_{PC}$ = 11.3 Hz and $^3J_{FC}$ = 1.7 Hz, the olefinic carbon in the α position with respect to the nitrogen atom gave a quadruplet at δ_C = 137.0 ppm with a coupling constant of $^2J_{FC}$ = 21.3 Hz and the CF_3 group appeared as a well-resolved double quadruplet at δ_C = 122.8 ppm with coupling constants of $^1J_{FC}$ = 278.0 Hz and $^3J_{PC}$ = 24.5 Hz.

The formation of the conjugated (*E*)-phosphazenes **4** can be explained in terms of a [2+2] cycloaddition reaction of phosphorus ylides **1** and nitriles **2** followed by ring opening of the unstable four-membered cyclic compounds **3**[8b,15] (Scheme 1). In this context, note that isomerization of the (*E*) isomer to the (*Z*) isomer was observed upon thermal treatment. ^1H NMR monitoring of (*E*)-phosphazene **4a** upon heating at 110 °C in toluene revealed that a new singlet appeared at δ_H = 6.23 ppm for the vinylic proton while the doublet corresponding to the (*E*) precursor (δ_H = 5.70 ppm, $^4J_{PH}$ = 3.2 Hz) disappeared. The configuration of the vinylic double bonds was determined on the basis of heteronuclear ^{19}F–^1H HOESY experiments which showed cross signals between fluorinated groups and vinylic protons suggesting the formation of the (*Z*) isomer (Table 1, entries 2, 4 and 6). Similar isomerization reactions have been observed previously by us[16] and by others.[17]

Aza-Wittig Reaction of Fluoroalkyl-Substituted *N*-Vinylic Phosphazenes 4 with Aldehydes

The aza-Wittig reaction[12] of the (*Z*) isomers of the *N*-vinylic (fluoroalkyl)phosphazenes **4**, derived from triphenylphosphane, with glyoxalate in $CHCl_3$ at room temperature (Scheme 1) gave fluoroalkyl-substituted (1*E*,3*Z*)-2-azadienes **5b** and **5h** (Table 2, entries 2 and 9) in which the (*Z*) configuration of the vinylic double bond was retained. These (1*E*,3*Z*)-heterodienes **5** were unstable to distillation and chromatography and therefore were not isolated and therefore were used in situ for subsequent reactions. However, the presence of the nonisolable compounds was established on the basis of the spectroscopic data of the crude product mixtures. Thus, in the ^1H NMR spectrum of the crude product of (1*E*,3*Z*)-heterodiene **5b** the olefinic hydrogen atom appeared as a singlet at δ_H = 7.04 ppm and the iminic hydrogen as a quadruplet at δ_H = 7.90 ppm with a coupling constant of $^5J_{FH}$ = 2.4 Hz. The structures of **5b** and **5h** were also studied by heteronuclear ^{19}F–^1H HOESY experiments which showed cross signals between the fluorinated groups and the vinylic and iminic protons confirming the (1*E*,3*Z*) configuration of heterodienes **5b** and **5h**, which means that the vinylic double bond retained the (*Z*) configuration of the starting phosphazenes.

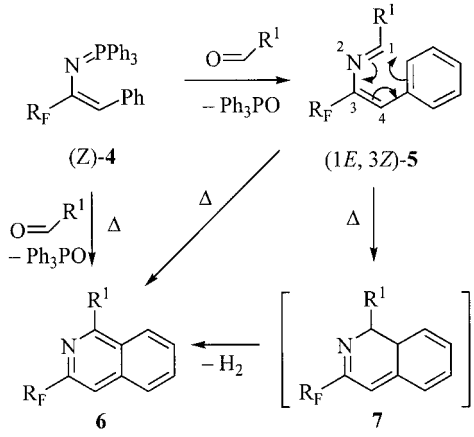
Similar behaviour was observed when this reaction was performed with the (*E*) isomers of fluoroalkyl *N*-vinylic phosphazenes **4** and glyoxalate at room temperature (Scheme 1) to give fluoroalkyl (1*E*,3*E*)-2-azadienes **5b**, **5f** and **5h** (Table 2, entries 3, 7 and 10). In these cases, the permanence of the (*E*) configuration of the vinylic double bond was corroborated by heteronuclear ^{19}F–^1H HOESY

Table 2. Azadienes **5** obtained from the aza-Wittig reaction of fluoroalkyl-substituted *N*-vinylic phosphazenes **4**.

Entry		R^1	R_F	Time [h]	Solvent	Yield [%]
1	(1*E*,3*Z*)-**5a**	2,4-$(NO_2)_2$-C_6H_3	CF_3	12	xylenes	–[a]
2	(1*E*,3*Z*)-**5b**	CO_2Et	CF_3	1	$CHCl_3$	–[a]
3	(1*E*,3*E*)-**5b**	CO_2Et	CF_3	1	$CHCl_3$	–[a]
4	(1*E*,3*Z*)-**5c**	C_6H_5	C_2F_5	96	xylenes	72[b]
5	(1*E*,3*Z*)-**5d**	2,4-$(NO_2)_2$-C_6H_3	C_2F_5	24	toluene	62[b]
6	(1*E*,3*Z*)-**5e**	3-Pyridyl	C_2F_5	96	xylenes	58[b]
7	(1*E*,3*E*)-**5f**	CO_2Et	C_2F_5	2	$CHCl_3$	–[a]
8	(1*E*,3*Z*)-**5g**	2,4-$(NO_2)_2$-C_6H_3	C_7F_{15}	144	xylenes	–[a]
9	(1*E*,3*Z*)-**5h**	CO_2Et	C_7F_{15}	0.5	$CHCl_3$	–[a]
10	(1*E*,3*E*)-**5h**	CO_2Et	C_7F_{15}	0.5	$CHCl_3$	–[a]

[a] Not isolated, used in situ. [b] Yield of isolated compounds.

experiments; in these experiments no cross signals were observed between the fluorinated groups and the vinylic proton. No aza-Wittig reaction was observed when the (*E*) isomers of *N*-vinylic (fluoroalkyl)phosphazenes **4** were treated with aromatic aldehydes at room temperature. However, thermal treatment of these (*E*) isomers with aromatic aldehydes gave (1*E*,3*Z*)-(fluoroalkyl)- 2-azadienes **5a**, **5c**–**e** and **g** (Scheme 1, Table 2, entries 1, 4–6 and 8). The formation of these (1*E*,3*Z*)-2-azadienes can be explained in terms of an initial isomerization of the (*E*)-phosphazene to the (*Z*) isomer followed by aza-Wittig reaction with the corresponding aldehydes.



Scheme 2.

6π-Electrocyclization of (1*E*,3*Z*)-3-(Perfluoroalkyl)-2-azadienes 5

Isoquinoline nuclei are widespread in the alkaloid family and constitute an important class of compound in pharmaceuticals.[18] For this reason, in order to test the synthetic usefulness of the new fluoroalkyl-substituted azadienes **5** as key intermediates in organic synthesis and especially in the preparation of new nitrogen-containing heterocycles, their electrocyclic ring-closure was explored. Thus, heating 3-fluoroalkyl-substituted (1*E*,3*Z*)-azadienes **5d** and **5e**, which contain an aryl and heteroaryl group at the 1-position [R^1 = 2,4-$(NO_2)_2$-C_6H_3, 3-pyridyl, respectively], in refluxing xylenes afforded the corresponding fluoroalkyl-substituted isoquinolines **6a** and **6b** in good yields (Scheme 2, Table 3, entries 1 and 2). The formation of the heterocycles **6** can be explained in terms of a 1,6-electrocyclic ring closure of the (1*E*,3*Z*) isomers of azadienes **5** followed by dehydrogenation of the nonisolable annelated compound **7** under the reaction conditions. Isoquinolines **6a**–**e** can also be prepared in a one-pot synthesis from (*Z*)-phosphazenes **4a**–**c** on heating with aldehydes without the isolation of the (1*E*,3*Z*)-azadienes **5b**, **5d**, **5e**, **5g** and **5h** (Table 3).

In order to check that the configuration of the carbon–carbon double bond of the azadienes **5** plays an important role in the process and that only the (3*Z*) isomers of the 2-azadienes **5** were precursors of the isoquinolines **6**, (1*E*,3*E*)-2-azadiene **5b** [generated in situ from (*E*)-phosphazene **4a** and ethyl glyoxalate] was heated in refluxing xylenes until total decomposition of the starting material had occurred with no formation of isoquinoline **6**. Note that although

Table 3. Synthesis of isoquinolines **6**.

Entry		R_F	R^1	Yield[a] [%]
1	**6a**	C_2F_5	2,4-$(NO_2)_2$-C_6H_3	54[b]/70[c]
2	**6b**	C_2F_5	3-Pyridyl	51[b]/62[c]
3	**6c**	C_7F_{15}	2,4-$(NO_2)_2$-C_6H_3	51[c]
4	**6d**	CF_3	CO_2Et	63[c]
5	**6e**	C_7F_{15}	CO_2Et	68[c]

[a] Yield of isolated compounds. [b] Obtained by heating the isolated azadienes. [c] Prepared by one-pot synthesis of (*Z*)-phosphazenes **4** and aldehydes.

several fluorine-substituted isoquinolines have been prepared,[7a,19] to the best of our knowledge this is the first report of the preparation of fluoroalkyl-substituted isoquinolines.

[4+2] Cycloaddition Reaction of 3-(Perfluoromethyl)-2-azadienes 5 Derived from α-Imino Esters

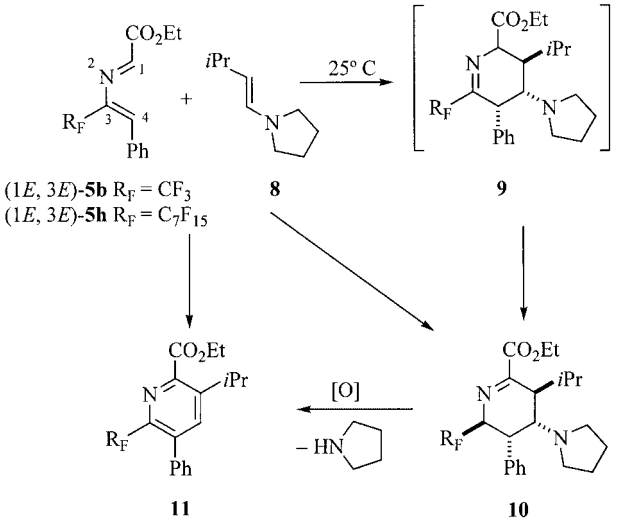
Owing to the interest in pyridine derivatives as pharmaceuticals, agrochemicals and dyestuffs,[20] we explored the cycloaddition reactions of these heterodienes **5** with electron-rich olefins such as enamines. Initially, we studied the reaction of the 2-azadiene **5b** because this substrate would be an interesting starting material for the preparation of pipecolic acid derivatives.[21] Thus, when the reaction of (1*E*,3*E*)-2-azadiene **5b** (R_F = CF_3) with *N*-(3-methyl)but-1-

enylpyrrolidine **8** in $CHCl_3$ was performed at room temperature a mixture of cycloaddition compounds was detected by ^1H NMR analysis of the crude product mixture from which tetrahydropyridine **10** and pyridine **11a** (Table 4, entries 1 and 2) were isolated. In order to simplify this mixture, an oxidant such as *p*-benzoquinone was added to the crude reaction mixture to afford only aromatic pyridine **11a** in good yield (Scheme 3, Table 4, entry 2).

Table 4. Pyridine derivatives **10**–**12**, **16** and bicyclic heterocycles **19** obtained from [4+2] cycloaddition reactions of azadienes **5** and **17**.

Entry		R_F	Time [h]	Solvent	Yield [%]
1	**10**	CF_3	24	$CHCl_3$	90[a] (36)[b]
2	**11a**	CF_3	24	$CHCl_3$	90[a] (54)[b] (48)[c]
3	**11b**	C_7F_{15}	24	$CHCl_3$	60[b]
4	**12**	CF_3	24	toluene	56[b]
5	**16**	C_2F_5	24	toluene	48[b]
6	**19a**	CF_3	12	acetonitrile	40[b]
7	**19b**	C_3F_7	12	acetonitrile	50[b]

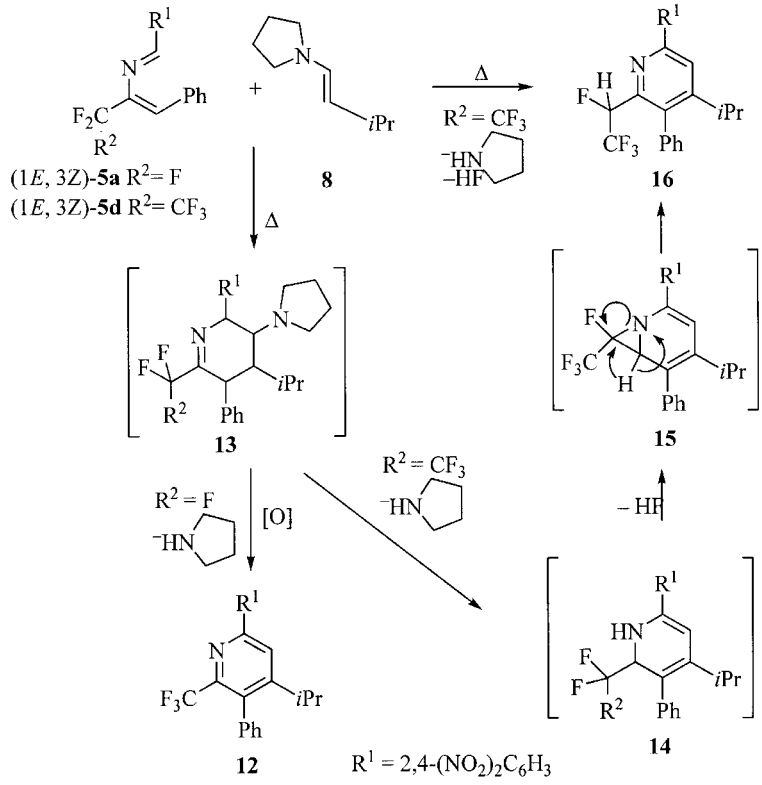
[a] Consumption [%] of the starting material determined by NMR analysis of the crude product mixture. [b] Isolated yield. [c] Obtained from the crude product mixture of **5** and **8** by oxidation with *p*-benzoquinone in dioxane at 80 °C.



Scheme 3.

The structure of compound **10** was elucidated on the basis of its 1D and 2D NMR spectroscopic data. The ^{13}C NMR spectrum provided enough evidence for the proposed structure of **10** because in this case the iminic carbon atom appeared as a singlet at δ_C = 171.6 ppm while the fluorine effect of the CF_3 substituent was observed in a CH carbon at δ_C = 63.0 ppm with a coupling constant of $^2J_{FC}$ = 26.4 Hz, which was assigned to the C-6 of the tetrahydropyridine ring on the basis of HMQC and HMBC experiments. The relative configurations of the stereogenic centers C-3, C-4, C-5 and C-6 were assigned on the basis of the observed 1D-NOESY correlations. Selective saturation at δ_H = 1.91–2.02 ppm (isopropyl CH) afforded significant NOEs (6%) with the proton (4-H) of the adjacent carbon atom at δ_H = 4.96 ppm confirming the *trans* relationship between 3-H and 4-H in the tetrahydropyridine ring, while selective saturation at δ_H = 2.41–2.46 ppm (pyrrolidine CH_2) afforded significant NOEs with 3-H at δ_H = 2.98–3.00 ppm (2%), with 6-H at δ_H = 4.79–4.84 ppm (2%) and with the aromatic protons of the phenyl group (1%) confirming the *cis* relationship between 3-H, pyrrolidine, the phenyl group and 6-H. The ^{13}C NMR spectrum of **11a** showed a quadruplet at δ_C = 161.4 ppm with a coupling constant of $^2J_{FC}$ = 32.0 Hz, which indicates that C-2 is the iminic carbon atom. The configurations of the C-3, C-4 and C-5 atoms of the tetrahydropyridine **10** are consistent with an *endo* approach of the enamine to the heterodiene to give cycloadduct **9** followed by tautomerization to **10**. This reaction can be extended to (1*E*,3*E*)-2-azadiene **5h** ($R_F = C_7F_{15}$) and in this case only aromatic pyridine **11b** was obtained regioselectively and in good yield (Scheme 3, Table 4, entry 3). As far as we know, this strategy describes the first synthesis of 2-(trifluoromethyl)pyridines derived from pipecolic esters **10** and **11**.

However, different behaviour was observed when azadiene **5a** with an aryl group in the 1-position [R^1 = 2,4-$(NO_2)_2$-C_6H_3] was heated with the same enamine **8**. At room temperature the starting materials were recovered, whilst refluxing heterodiene (1*E*,3*Z*)-**5a** and enamine **8** in toluene gave pyridine **12** (Scheme 4, Table 4, entry 4). The structure of compound **12** was determined on the basis of its 1D and 2D NMR data. In ^1H–^{13}C HMBC 2,3-bond correlation of compound **12**, proton 5-H of the pyridine ring showed cross signals with the same quaternary carbon as protons of the 2,4-(NO_2)-C_6H_3 group, while the CH of the isopropyl substituent and the aromatic protons of the phenyl substituent showed cross signals with the same quaternary carbon (C-3). Therefore, these data are in agreement with the proposed structure of **12** in which the fluoroalkyl, phenyl and isopropyl groups are substituents on C-2, C-3 and C-4, respectively. The substituent in the 1-position of the starting azadiene seems to play an important role, not only decreasing the reactivity of the heterodiene, but also changing its regioselectivity. The formation of compound **12** can be explained in terms of a [4+2] cycloaddition reaction of both substrates − heterodiene **5a** and dienophile **8** − with formation of cycloadduct **13** and subsequent aromatization. The regioselectivity of these processes can be controlled by substituents (FMO theory).[22] Analogous regioselectivity was observed in the reaction of (1*E*,3*Z*)-3-(perfluoroethyl)-2-azadiene **5d** with enamine **8**. However, the spectroscopic data for the adducts showed that defluorinated compound **16** was obtained (Scheme 4, Table 4, entry 5) instead of the expected perfluorinated compound. The mass spectra of isolated compound **16** showed a molecular ion [*m*/*z* = 463 (100%)] that corresponds to the loss of HF, while the ^1H and ^{13}C NMR spectra showed a proton (carbon) coupled to a CF–CF_3 moiety instead of a CF_2–CF_3 group. For instance, the ^1H NMR spectrum of compound **16** showed a double quadruplet at δ_H = 5.45 ppm for this proton with coupling constants of $^2J_{HF}$ = 44.4 and $^3J_{HF}$ = 5.8 Hz, and the ^{13}C NMR spectrum showed a double quadruplet at δ_C = 84.8 ppm with coupling constants of $^1J_{CF}$ = 188.4 and $^2J_{CF}$ = 34.4 Hz for the methane carbon atom directly

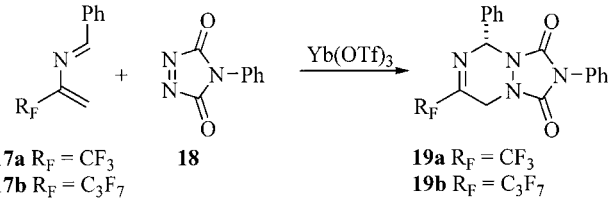


Scheme 4.

bonded to the fluorine atom. The formation of this fluoroalkyl heterocycle **16** can be explained in terms of intramolecular cyclocondensation of adduct **14** with the loss of HF and the formation of the polycyclic aziridine **15**, followed by ring opening of the aziridine and migration of the proton to the adjacent carbon atom bonded to the fluorine atom to give polysubstituted 2-(1,2,2,2-tetrafluoroethyl)pyridine **16** (Scheme 4). An exocyclic enaminic intermediate from dehydrofluorination of **14** could also justify the formation of compound **16**. To the best of our knowledge, cyclization reactions that afford heterocycles such as **16** have no precedent and therefore this is the first synthesis of fluoroalkyl-substituted pyridines.

Reaction of 3-(Perfluoroalkyl)-2-azadienes 17 with 4-Phenyl-1,2,4-triazoline-3,5-dione 18

To further explore the behavior of fluoroalkyl-substituted 2-azadienes, we also studied the reactivity of heterodienes with no substituents at the 4-position. Nevertheless, the cycloaddition reaction of fluoroalkyl-substituted 2-azadienes **17** with a range of electron-rich (enamines, norbornadiene) and electron-poor dienophiles (maleic anhydride, tetracyanoethylene, diethyl acetylenedicarboxylate and ethyl glyoxalate) were inefficient at room temperature and, even on extended heating complex product mixtures and decomposition products were obtained. Cycloadducts **19** (Scheme 5, Table 4, entries 6 and 7) were isolated only when azadienes **17a** (R_F = CF_3)[10c] and **17b** (R_F = C_3F_7) were treated with a very reactive electron-poor dienophile such as 4-phenyl-1,2,4-triazoline-3,5-dione **18** in the presence of ytterbium triflate at room temperature. These bicyclic compounds **19** were characterized on the basis of their spectroscopic data. The mass spectrum of compound **19a** gave the molecular ion *m*/*z* = 374 (54%). The ^{19}F NMR spectrum of compound **19a** showed an absorption at δ_F = –72.8 ppm, and in the ^1H NMR spectrum of **19a** the methylene protons of the six-membered heterocycle resonated at δ_H = 4.40 and 4.80 ppm as well-resolved double doublets, while the ^{13}C NMR spectrum of **19a** revealed CF_3 as a quadruplet at δ_C = 118.7 ppm with a coupling constant of $^1J_{FC}$ = 279 Hz and the carbon atom directly bonded to this as a quadruplet at δ_C = 152.4 ppm with a coupling constant of $^2J_{FC}$ = 37 Hz. The formation of these bicyclic heterocycles **19** can be explained in terms of a [4+2] cycloaddition reaction of heterodienes **17** and dienophile **18**.



Scheme 5.

Conclusions

In summary, (*E*) and (*Z*) fluoroalkyl *N*-vinylic phosphazenes **4** can be prepared readily from fluoroalkyl nitriles **2**

and phosphorus ylides **1**. These conjugated phosphazenes **4** react cleanly and in good yields with aldehydes by means of an aza-Wittig reaction to afford (1*E*,3*E*) and (1*E*,3*Z*) fluoroalkyl-functionalized 2-azadienes **5** which are excellent building blocks for the preparation of fluorinated heterocycles. For instance, fluoroalkylated heterocycles such as isoquinolines **6** were obtained by 6π-electrocyclization of heterodienes **5**, while pyridines derived from pipecolic esters **10** and **11**, as well as polysubstituted pyridines **12** and **16** and bicyclic heterocycles **19**, can be prepared through a [4+2] cycloaddition strategy involving the reaction of heterodienes **5** or **17** with dienophiles. Most of these heterocycles have been prepared for the first time, thus showing that these fluoroalkylated 2-aza-1,3-butadienes may be important synthons in organic synthesis and in the preparation of fluoroalkyl-substituted acyclic and heterocycles.[1,5]

Experimental Section

General Remarks: Chemicals were purchased from Aldrich Chemical Company. Solvents for extraction and chromatography were technical grade. All the solvents used in the reactions were freshly distilled from appropriate drying agents before use. All other reagents were recrystallized or distilled as necessary. All reactions were performed under dry nitrogen. Analytical TLC was performed with Merck silica gel 60 F_{254} plates; visualization was accomplished with UV light. Flash chromatography was carried out using Merck silica gel 60 (230–400 mesh ASTM). Melting points were determined with an Electrothermal IA9100 Digital Melting Point Apparatus and are uncorrected. ^{1}H (400, 300 MHz), ^{13}C (100, 75 MHz), ^{19}F (376, 282 MHz) and ^{31}P NMR (120 MHz) spectra were recorded with a Bruker Avance 400 MHz and a Varian Unity 300 MHz spectrometer using $CDCl_3$ or CD_3OD solutions with TMS as an internal reference (δ = 0.00 ppm) for ^{1}H and ^{13}C NMR spectra, $CFCl_3$ as an internal reference (δ = 0.00 ppm) for ^{19}F NMR spectra, and phosphoric acid (85%) (δ = 0.00 ppm) for ^{31}P NMR spectra. Chemical shifts (δ) are reported in ppm and coupling constants (J) are in Hertz. Low-resolution mass spectra (MS) were obtained at 50–70 eV by electron impact (EIMS) with a Hewlett–Packard 5971 or 5973 spectrometer. Data are reported in the form *m*/*z* (intensity relative to base peak = 100). Infrared spectra (IR) were recorded with a Nicolet IRFT Magna 550 spectrometer and were obtained as solids in KBr or as neat oils. Peaks are reported in cm^{-1}. Elemental analyses were performed in a LECO CHNS-932 apparatus. Azadiene **17a** was prepared according to the literature procedure.[10c]

General Procedure for the Preparation of (*E*)-Phosphazenes 4: A 1.6 M solution of methyllithium in diethyl ether (3.125 mL, 5 mmol) was added dropwise to a solution of benzyltriphenylphosphonium iodide (2.40 g, 5 mmol) in diethyl ether (20 mL) cooled to 0 °C under N_2. The clear red solution was heated at reflux for 1 h. Fluoroalkylated nitrile was added dropwise or bubbled into the ylide solution at 0 °C and the mixture was stirred at room temperature. The mixture was filtered and concentrated to afford an oil.

(3*E*)-3-(Trifluoromethyl)-1,1,1,4-tetraphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (4a): The general procedure was followed, bubbling trifluoroacetonitrile in excess (CF_3CN). Crystallization from ethyl acetate gave a yellow solid (2.01 g, 90%); m.p. 134–135 °C (ethyl acetate). IR (KBr): $\tilde{\nu}$ = 1600, 1341 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.70 (d, J = 3.2 Hz, 1 H), 6.98–7.85 (m, 20 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 113.8 (dd, $^3J_{CP}$ = 11.3, $^3J_{CF}$ = 1.7 Hz), 122.8 (dq, $^1J_{CF}$ = 278.0, $^3J_{CP}$ = 24.5 Hz), 125.5–133.7 (m), 137.0 (q, $^2J_{CF}$ = 21.3 Hz) ppm. ^{31}P NMR (120 MHz, $CDCl_3$): δ = 7.94 ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –64.1 ppm. MS (EI): *m*/*z* = 447 (100) [M]$^+$. $C_{27}H_{21}F_3NP$ (447): calcd. C 72.48, H 4.73, N 3.13; found C 72.02, H 4.68, N 3.10.

(3*E*)-3-(Perfluoroethyl)-1,1,1,4-tetraphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (4b): The general procedure was followed, bubbling perfluoropropanenitrile in excess (C_2F_5CN) and the mixture was stirred for 24 h. Crystallization from ethyl acetate gave a yellow solid (2.01 g, 81%); m.p. 105–106 °C (ethyl acetate). IR (KBr): $\tilde{\nu}$ = 1608, 1203 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.73 (s, 1 H), 6.91–7.8 (m, 20 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 112.4 (tq, $^1J_{CP}$ = 259.9, $^2J_{CF}$ = 40.8 Hz), 119.3 (tq, $^1J_{CF}$ = 286.6, $^2J_{CF}$ = 40.8 Hz), 125.9–136.6 (m) ppm. ^{31}P NMR (120 MHz, $CDCl_3$): δ = 7.46 ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –64.3, –94.5 ppm. MS (EI): *m*/*z* = 497 (100) [M]$^+$. $C_{28}H_{21}F_5NP$ (497): calcd. C 67.61, H 4.25, N 2.82; found C 67.72, H 4.21, N 2.81.

(3*E*)-3-(Perfluoroheptyl)-1,1,1,4-tetraphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (4c): The general procedure was followed using perfluorooctanenitrile ($C_7F_{15}CN$) (1.97 g, 5 mmol) and the mixture was stirred at room temperature for 12 h to give a yellow oil (83%); R_f = 0.41 (ethyl acetate/hexane. 1:10). IR (KBr): $\tilde{\nu}$ = 1611, 1206 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.74 (s, 1 H), 6.89–7.81 (m, 20 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 109.3–115.8 (m), 125.9–136.6 (m) ppm. ^{31}P NMR (120 MHz, $CDCl_3$): δ = 7.03 ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –81.2 (t, $^3J_{FF}$ = 9.2 Hz), –107.1 to –126.5 (m) ppm. MS (EI): *m*/*z* = 747 (40) [M]$^+$. $C_{33}H_{21}F_{15}NP$ (747): calcd. C 53.03, H 2.83, N 1.87; found C 53.20, H 2.80, N 1.82.

General Procedure for the Preparation of (*Z*)-Phosphazenes 4: A solution of (*E*)-phosphazene **4** (2 mmol) in toluene under N_2 was stirred at reflux (110 °C) overnight until ^{1}H NMR indicated the disappearance of the (*E*) isomer of the phosphazene.

(*Z*)-3-(Trifluoromethyl)-1,1,1,4-tetraphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (4a): The general procedure was followed using (3*E*)-3-(trifluoromethyl)-1,1,1,4-tetraphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (**4a**). Evaporation of the solvent and crystallization from ethyl acetate gave a yellow solid; m.p. 121–122 °C (ethyl acetate). IR (KBr): $\tilde{\nu}$ = 1613, 1467 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.23 (s, 1 H), 7.05–7.81 (m, 20 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 112.6–112.8 (m), 122.5 (dq, $^1J_{CF}$ = 279.0, $^3J_{CP}$ = 3.7 Hz), 125.9–133.7 (m), 133.7 (q, $^2J_{CF}$ = 29.5 Hz) ppm. ^{31}P NMR (120 MHz, $CDCl_3$): δ = 2.13 ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –68.2 ppm. MS (EI): *m*/*z* = 447 (100) [M]$^+$. $C_{27}H_{21}F_3NP$ (447): calcd. C 72.48, H 4.73, N 3.13; found C 72.22, H 4.70, N 3.10.

(*Z*)-3-(Perfluoroethyl)-1,1,1,4-tetraphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (4b): The general procedure was followed using (3*E*)-3-(perfluoroethyl)-1,1,1,4-tetraphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (**4b**). Evaporation of the solvent and crystallization from ethyl acetate gave a yellow solid; m.p. 97–98 °C (ethyl acetate). IR (KBr): $\tilde{\nu}$ = 1626, 1328, 1150 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.17 (s, 1 H), 7.08–7.67 (m, 20 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 112.4 (tq, $^1J_{CP}$ = 259.8, $^2J_{CF}$ = 36.7 Hz), 115.3 (t, $^3J_{CF}$ = 7.3 Hz), 119.4 (tq, $^1J_{CF}$ = 287.0, $^2J_{CF}$ = 39.8 Hz), 125.8–132.9 (m), 133.5 (t, $^2J_{CF}$ = 21.9 Hz) ppm. ^{31}P NMR (120 MHz, $CDCl_3$): δ = 2.35 ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –66.3, –96.5 ppm. MS (EI): *m*/*z* = 497 (76) [M]$^+$. $C_{28}H_{21}F_5NP$ (497): calcd. C 67.61, H 4.25, N 2.82; found C 67.70, H 4.29, N 2.79.

(*Z*)-3-(Perfluoroheptyl)-1,1,1,4-tetraphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (4c): The general procedure was followed using (3*E*)-3-

(perfluoroheptyl)-1,1,1,4-tetraphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (**4c**). Chromatographic separation (hexane/ethyl acetate, 10:1) gave a yellow oil; R_f = 0.13 (ethyl acetate/hexane, 1:10). IR (KBr): $\tilde{\nu}$ = 1612, 1438, 1206 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.07 (s, 1 H), 6.93–7.82 (m, 20 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 107.2–119.1 (m), 125.8–137.3 (m) ppm. ^{31}P NMR (120 MHz, $CDCl_3$): δ = 1.44 ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –81.15 to –82.3 (m), –109.8 (t, $^3J_{FF}$ = 15.2 Hz), –117.0 to –127.2 (m) ppm. MS (EI): *m*/*z* = 747 (69) $[M]^+$. $C_{33}H_{21}F_{15}NP$ (747): calcd. C 53.03, H 2.83, N 1.87; found C 52.90, H 2.86, N 1.86.

General Procedure for Preparation of 2-Azadienes 5: The appropriate aldehyde (2 mmol) was added to a solution of phosphazene **4** (2 mmol) in $CHCl_3$, toluene or xylenes at 0–10 °C under N_2, and the mixture was stirred at room temperature or reflux until TLC indicated the disappearance of the phosphazene.

(1*E*,3*Z*)-2-Azadiene 5a: The general procedure was followed using (3*E*)-3-(trifluoromethyl)-1,1,1,4-tetraphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (**4a**) (0.89 g) and 2,4-dinitrobenzaldehyde (0.39 g) for 12 h at 110 °C in xylenes. The reaction product was unstable to distillation and chromatography and therefore was not isolated and used in subsequent reactions. ^{1}H NMR (300 MHz, $CDCl_3$) of crude reaction mixture (**5a** + Ph_3PO): δ = 7.04 (s, 1 H), 7.12–8.17 (m, 6 H), 8.47 (s, 1 H), 8.55–9.04 (m, 2 H) ppm.

(1*E*,3*Z*)-2-Azadiene 5b: The general procedure was followed using (3*Z*)-3-(trifluoromethyl)-1,1,1,4-tetraphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (**4a**) (0.89 g) and ethyl glyoxalate (0.20 g) for 1 h at room temperature in $CHCl_3$. The reaction product was unstable to distillation and chromatography and therefore was not isolated and used in subsequent reactions. ^{1}H NMR (400 MHz, $CDCl_3$) of crude reaction mixture (**5b** + Ph_3PO): δ = 1.26 (t, *J* = 7.1 Hz, 3 H), 4.26 (q, *J* = 7.1 Hz, 2 H), 7.04 (s, 1 H), 7.11–7.79 (m, 5 H), 7.90 (q, *J* = 2.4 Hz, 1 H), 7.92–7.94 (m, 1 H) ppm.

(1*E*,3*E*)-2-Azadiene 5b: The general procedure was followed using (3*E*)-3-(trifluoromethyl)-1,1,1,4-tetraphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (**4a**) (0.89 g) and ethyl glyoxalate (0.20 g) for 1 h at room temperature in $CHCl_3$. The reaction product was unstable to distillation and chromatography and therefore was not isolated and used in subsequent reactions. ^{1}H NMR (400 MHz, $CDCl_3$) of crude reaction mixture (**5b** + Ph_3PO): δ = 1.26 (t, *J* = 7.1 Hz, 3 H), 4.26 (q, *J* = 7.1 Hz, 2 H), 6.89 (s, 1 H), 7.20–7.60 (m, 5 H), 7.82 (s, 1 H) ppm.

(1*E*,3*Z*)-2-Azadiene 5c: The general procedure was followed using (3*E*)-3-(perfluoroethyl)-1,1,1,4-tetraphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (**4b**) (0.99 g) and benzaldehyde (0.20 mL) for 96 h at 135 °C in xylenes. Evaporation of the solvent under reduced pressure afforded an oil that was purified by chromatography on neutral aluminium oxide (ethyl acetate/hexane, 1:20) to give 2-azadiene **5c** (0.47 g, 72%) as a yellow oil; R_f = 0.46 (ethyl acetate/hexane, 1:2). IR (KBr) $\tilde{\nu}$ = 1627, 1454, 1209 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.51 (s, 1 H), 7.21–7.86 (m, 10 H), 8.34 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 111.4 (tq, $^1J_{CF}$ = 254.7, $^2J_{CF}$ = 38.5 Hz), 118.9 (t, $^3J_{CF}$ = 7.5 Hz), 119.0 (tq, $^1J_{CF}$ = 285.5, $^2J_{CF}$ = 38.5 Hz), 128.1–135.2 (m), 137.7 (t, $^2J_{CF}$ = 23.0 Hz), 166.3 ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –60.4, –94.2 ppm. MS (70 eV): *m*/*z* = 325 (90) $[M]^+$. $C_{17}H_{12}F_5N$ (325): calcd. C 62.77, H 3.69, N 4.31; found C 67.06, H 4.41, N 3.71.

(1*E*,3*Z*)-2-Azadiene 5d: The general procedure was followed using (3*E*)-3-(perfluoroethyl)-1,1,1,4-tetraphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (**4b**) (1.00 g) and 2,4-dinitrobenzaldehyde (0.39 g) for 24 h at 110 °C in toluene. Evaporation of the solvent under reduced pressure afforded an oil that was purified by chromatography on neutral aluminium oxide (ethyl acetate/hexane, 1:20) to give 2-azadiene **5d** (0.51 g, 62%) as a yellow oil; R_f = 0.55 (ethyl acetate/hexane, 1:5). IR (KBr) $\tilde{\nu}$ = 1539, 1339, 1213 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.80 (s, 1 H), 7.07–8.61 (m, 7 H), 8.94 (s, 1 H), 8.95 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 120.4, 102.9–124.1 (m), 127.1–149.3 (m), 159.7 ppm. MS (70 eV): *m*/*z* = 415 (20) $[M]^+$. $C_{17}H_{10}F_5N_3O_4$ (415): calcd. C 49.17, H 2.43, N 10.12; found C 49.11, H 2.39, N 10.16.

(1*E*,3*Z*)-2-Azadiene 5e: The general procedure was followed using (3*E*)-3-(perfluoroethyl)-1,1,1,4-tetraphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (**4b**) (0.99 g) and 3-pyridylcarboxaldehyde (0.92 g) for 96 h at 135 °C in xylenes. Evaporation of the solvent under reduced pressure afforded an oil that was purified by chromatography on neutral aluminium oxide (ethyl acetate/hexane, 1:10) to give 2-azadiene **5e** (0.38 g, 58%) as a yellow oil; R_f = 0.31 (ethyl acetate/hexane, 1:2). IR (KBr) $\tilde{\nu}$ = 1636, 1202 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.58 (s, 1 H), 7.21–8.22 (m, 7 H), 8.39 (s, 1 H), 8.70 (dd, $^3J_{HH}$ = 4.7, $^3J_{HH}$ = 1.7 Hz), 8.70 (d, $^3J_{HH}$ = 1.7 Hz) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 111.0 (tq, $^1J_{CF}$ = 255.9, $^2J_{CF}$ = 38.6 Hz), 118.8 (tq, $^1J_{CF}$ = 285.5, $^2J_{CF}$ = 38.1 Hz), 120.1 (t, $^3J_{CF}$ = 7.1 Hz), 123.8–135.0 (m), 137.7 (t, $^2J_{CF}$ = 19.3 Hz), 150.9, 152.8, 163.4 ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –60.5, –94.0 ppm. MS (70 eV): *m*/*z* = 326 (90) $[M]^+$. $C_{16}H_{11}F_5N_2$ (326): calcd. C 58.90, H 3.40, N 8.59; found C 59.12, H 3.48, N 8.63.

(1*E*,3*E*)-2-Azadiene 5f: The general procedure was followed using (3*E*)-3-(perfluoroethyl)-1,1,1,4-tetraphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (**4b**) (0.99 g) and ethyl glyoxalate (0.20 g) for 2 h at room temperature in $CHCl_3$. The reaction product was unstable to distillation and chromatography and therefore was not isolated and used in subsequent reactions. ^{1}H NMR (400 MHz, $CDCl_3$) of crude reaction mixture (**5f** + Ph_3PO): δ = 1.46 (t, *J* = 7.2 Hz, 3 H), 4.45 (q, *J* = 7.2 Hz, 2 H), 6.85 (s, 1 H), 7.40–7.80 (m, 5 H), 7.90 (s, 1 H) ppm.

(1*E*,3*Z*)-2-Azadiene 5g: The general procedure was followed using (3*E*)-3-(perfluoroheptyl)-4-phenyl-1,1,1-triphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (**4c**) (1.50 g) and 2,4-dinitrobenzaldehyde (0.39 g) for 144 h at 135 °C in xylenes. The reaction product was unstable to distillation and chromatography and therefore was not isolated and used in subsequent reactions. ^{1}H NMR (300 MHz, $CDCl_3$) of crude reaction mixture (**5g** + Ph_3PO): δ = 7.25 (s, 1 H), 7.37–8.12 (m, 6 H), 8.22 (s, 1 H), 8.01–9.07 (m, 2 H) ppm.

(1*E*,3*Z*)-2-Azadiene 5h: The general procedure was followed using (3*Z*)-3-(perfluoroheptyl)-4-phenyl-1,1,1-triphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (**4c**) (1.50 g) and ethyl glyoxalate (0.20 g) for 0.5 h at room temperature in $CHCl_3$. The reaction product was unstable to distillation and chromatography and therefore was not isolated and used in subsequent reactions. ^{1}H NMR (400 MHz, $CDCl_3$) of crude reaction mixture (**5h** + Ph_3PO): δ = 1.38 (t, *J* = 7.1 Hz, 3 H), 4.37 (q, *J* = 7.1 Hz, 2 H), 6.75 (s, 1 H), 7.09–7.70 (m, 5 H), 7.80 (s, 1 H) ppm.

(1*E*,3*E*)-2-Azadiene 5h: The general procedure was followed using (3*E*)-3-(perfluoroheptyl)-4-phenyl-1,1,1-triphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (**4c**) (1.50 g) and ethyl glyoxalate (0.20 g) for 0.5 h at room temperature in $CHCl_3$. The reaction product was unstable to distillation and chromatography and therefore was not isolated and used in subsequent reactions. ^{1}H NMR (400 MHz, $CDCl_3$) of crude reaction mixture (**5h** + Ph_3PO): δ = 1.22 (t, *J* = 7.2 Hz, 3 H), 4.21 (q, *J* = 7.2 Hz, 2 H, CH_2), 6.63 (s, 1 H), 7.16–7.59 (m, 5 H), 7.70 (s, 1 H) ppm.

General Procedure A for the Preparation of Isoquinolines 6: A solution of the (1*E*,3*Z*) isomer of 2-azadiene **5** (1 mmol) was heated in

xylenes (10 mL) at reflux under N_2 until TLC indicated the disappearance of the azadiene.

General Procedure B for the Preparation of Isoquinolines 6: The appropriate aldehyde (1 mmol) was added to a solution of phosphazene **4** (1 mmol) in xylenes at 0–10 °C under N_2, and the mixture was stirred at reflux until TLC indicated the disappearance of 2-azadiene.

1-(2,4-Dinitrophenyl)-3-(perfluoroethyl)isoquinoline (6a): The general procedure A was followed by using (1*E*,3*Z*)-2-azadiene **5d** (0.42 g) and by heating for 72 h. Evaporation of the solvent under reduced pressure and chromatographic separation (hexane/ethyl acetate, 10:1) gave 0.22 g (54%) of **6a** as a yellow solid. The general procedure B was followed using (3*Z*)-3-(perfluoroethyl)-1,1,1,4-tetraphenyl-2-aza-1λ^5-phosphabuta-1,3-diene **4b** (0.50 g) and 2,4-dinitrobenzaldehyde (0.19 g) and by stirring for 90 h. Evaporation of the solvent under reduced pressure and chromatographic separation (hexane/ethyl acetate, 10:1) gave 0.29 g (70%) of **6a** as a yellow solid; m.p. 97–98 °C (ethyl acetate/hexane). IR (KBr): $\tilde{\nu}$ = 1540, 1354 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28–8.14 (m, 6 H), 8.65 (dd, J = 8.4, J = 2.3 Hz, 1 H), 8.66 (d, J = 2.3 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 108.7–120.1 (m), 120.4–155.9 (m) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –82.0, –113.6 ppm. MS (EI): m/z = 413 (100) $[M]^+$. $C_{17}H_8F_5N_3O_4$ (413): calcd. C 49.41, H 1.95, N 10.17; found C 49.38, H 1.90, N 10.15.

3-(Perfluoroethyl)-1-(3-pyridyl)isoquinoline (6b): The general procedure A was followed using (1*E*,3*Z*)-2-azadiene **5e** (0.326 g) and by heating for 144 h. Evaporation of the solvent under reduced pressure and chromatographic separation (hexane/ethyl acetate, 10:1) gave 0.20 g (62%) of **6b** as a yellow solid. The general procedure B was followed using (3*Z*)-3-(perfluoroethyl)-1,1,1,4-tetraphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (**4b**) (0.50 g) and 3-pyridylcarboxaldehyde (0.46 g) and by stirring for 240 h. Evaporation of the solvent under reduced pressure and chromatographic separation (hexane/ethyl acetate, 10:1) gave 0.16 g (51%) of **6b** as a yellow solid; m.p. 98–99 °C (ethyl acetate/hexane). IR (KBr): $\tilde{\nu}$ = 1739, 1189 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28–8.20 (m, 7 H), 8.80 (dd, J = 4.8, J = 1.7 Hz, 1 H), 9.02 (dd, J = 2.2, J = 0.8 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 111.7 (tq, $^1J_{CF}$ = 254.4, $^2J_{CF}$ = 37.8 Hz), 119.1 (tq, $^1J_{CF}$ = 286.8, $^2J_{CF}$ = 37.9 Hz), 119.9 (t, $^3J_{CF}$ = 4.2 Hz), 121.0–137.6 (m), 140.8 (t, $^2J_{CF}$ = 25.7 Hz), 150.2, 150.7, 158.2 ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –83.2, –117.0 ppm. MS (EI): m/z 324 (67) $[M]^+$. $C_{16}H_9F_5N_2$ (324): calcd. C 59.27, H 2.80, N 8.64; found C 59.09, H 2.82, N 8.61.

1-(2,4-Dinitrophenyl)-3-(perfluoroheptyl)isoquinoline (6c): The general procedure B was followed using (3*Z*)-3-(perfluoroheptyl)-4-phenyl-1,1,1-triphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (**4c**) (0.75 g) and 2,4-dinitrobenzaldehyde (0.20 g) and by stirring for 250 h. Evaporation of the solvent under reduced pressure and chromatographic separation (hexane/ethyl acetate, 10:1) gave 0.34 g (51%) of **6c** as a yellow solid; m.p. 119–120 °C (ethyl acetate/hexane). IR (KBr): $\tilde{\nu}$ = 1540, 1348 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66–8.13 (m, 6 H), 8.23 (s, 1 H), 8.65 (dd, J = 8.4, J = 2.3 Hz, 1 H), 9.09 (d, J = 2.3 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 110.6–120.3 (m), 120.5–141.0 (m), 148.3, 149.3, 155.9 ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –81.1 (t, J = 11 Hz), –109.8. to –126.4 (m) ppm. MS (EI): m/z = 663 (50) $[M]^+$. $C_{22}H_8F_{15}N_3O_4$ (663): calcd. C 39.84, H 1.22, N 6.34; found C 39.58, H 1.19, N 6.15.

Ethyl 3-(Trifluoromethyl)isoquinoline-1-carboxylate (6d): The general procedure B was followed using (3*Z*)-3-(trifluoromethyl)-1,1,1,4-tetraphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (**4a**) (0.45 g) and ethyl glyoxalate (0.10 g) and by stirring for 24 h. Evaporation of the solvent under reduced pressure and chromatographic separation (hexane/ethyl acetate, 10:1) gave 0.17 g (63%) of **6d** as an orange oil; R_f = 0.29 (ethyl acetate/hexane, 1:5). IR (KBr): $\tilde{\nu}$ = 1727, 1146 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.53 (t, J = 7.1 Hz, 3 H), 4.62 (q, J = 7.1 Hz, 2 H), 7.81–8.40 (m, 5 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 62.5, 117.7–150.9 (m), 165.4 ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –67.5 ppm. MS (EI): m/z = 269 (5) $[M]^+$. $C_{13}H_{10}F_3NO_2$ (269): calcd. C 58.00, H 3.74, N 5.20; found C 57.97, H 3.50, N 5.17.

Ethyl 3-(Perfluoroheptyl)isoquinoline-1-carboxylate (6e): The general procedure B was followed using (3*Z*)-3-(perfluoroheptyl)-4-phenyl-1,1,1-triphenyl-2-aza-1λ^5-phosphabuta-1,3-diene **4c** (0.75 g) and ethyl glyoxalate (0.10 g) and by stirring for 144 h. Evaporation of the solvent under reduced pressure and chromatographic separation (hexane/ethyl acetate, 10:1) gave 0.39 g (68%) of **6e** as a white solid; m.p. 39–40 °C (ethyl acetate/hexane). IR (KBr): $\tilde{\nu}$ = 1734, 1135 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.37 (t, J = 7.1 Hz, 3 H), 4.49 (q, J = 7.1 Hz, 2 H), 7.72–7.94 (m, 5 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 62.4, 102.0–120.0 (m), 123.3–150.6 (m), 165.5 ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –81.6 (t, J = 10.8 Hz), –113.6 to –127.0 (m) ppm. MS (EI): m/z = 569 (2) $[M]^+$. $C_{19}H_{10}F_{15}NO_2$ (569): calcd. C 40.09, H 1.77, N 2.46; found C 40.18, H 1.80, N 2.12.

General Procedure for the [4+2] Cycloaddition Reactions: The dienophile (5 mmol) was added to a solution of azadiene **5** (5 mmol) in $CHCl_3$ or toluene (15 mL) at 0–10 °C under N_2 and the mixture was stirred at an adequate temperature until TLC indicated the disappearance of the azadiene.

Ethyl 3-Isopropyl-6-(perfluoromethyl)-5-phenyl-4-pyrrolidinyl-3,4,5,6-tetrahydropyridine-2-carboxylate (10) and Ethyl 3-Isopropyl-6-(perfluoromethyl)-5-phenylpyridine-2-carboxylate (11a): The general procedure was followed using (1*E*,3*E*)-2-azadiene **5b** prepared in situ and *trans*-3-methyl-1-pyrrolidinylbut-1-ene (0.67 g) at room temperature and by stirring for 24 h in $CHCl_3$. Chromatographic separation (hexane/ethyl acetate, 15:1) gave 0.63 g (31%) of **10** as a yellow oil [R_f = 0.16 (ethyl acetate/hexane, 1:10)] and 0.82 g (49%) of **11a** as a yellow oil [R_f = 0.35 (ethyl acetate/hexane, 1:10)]. For compound **10**: IR (KBr): $\tilde{\nu}$ = 1719, 1121 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.06 (d, J = 6.8 Hz, 3 H), 1.10 (d, J = 6.8 Hz, 3 H), 1.41 (t, J = 7.2 Hz, 3 H), 1.61–1.67 (m, 4 H), 1.91–2.02 (m, 1 H), 2.26–2.31 (m, 2 H), 2.41–2.46 (m, 2 H), 2.98–3.00 (m, 1 H), 3.10 (s, 1 H), 3.12–3.14 (m, 1 H), 4.27–4.50 (m, 2 H), 4.79–4.84 (m, 1 H), 7.25–7.34 (m, 5 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 20.8, 21.6, 23.6, 31.1, 40.4, 41.8, 50.7, 58.3, 62.3, 63.0 (q, $^2J_{CF}$ = 26.4 Hz), 125.3 (q, $^1J_{CF}$ = 286.6 Hz), 126.7–139.9 (m), 165.4, 171.6 ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –72.1 ppm. MS (70 eV): m/z = 410 (5) $[M]^+$. $C_{22}H_{29}F_3N_2O_2$ (410): calcd. C 64.37, H 7.12, N 6.82; found C 64.31, H 7.16, N 6.79. For compound **11a**: IR (KBr): $\tilde{\nu}$ = 1734 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.33 (d, J = 6.9 Hz, 6 H), 1.47 (t, J = 7.1 Hz, 3 H), 3.51–3.55 (m, 1 H), 4.51 (q, J = 7.1 Hz, 2 H), 7.28–7.50 (m, 5 H), 7.74 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 23.4, 29.1, 62.1, 121.3 (q, $^1J_{CF}$ = 275.8 Hz), 126.8–138.8 (m), 142.3 (q, $^2J_{CF}$ = 33.4 Hz), 145.6, 147.3, 166.1 ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –61.5 ppm. MS (70 eV): m/z = 337 (35) $[M]^+$. $C_{18}H_{18}F_3NO_2$ (337): calcd. C 64.09, H 5.38, N 4.15; found C 64.13, H 5.39, N 4.19.

Ethyl 3-Isopropyl-6-(perfluoroheptyl)-5-phenylpyridine-2-carboxylate (11b): The general procedure was followed using (1*E*,3*E*)-2-azadiene **5h** prepared in situ and *trans*-3-methyl-1-pyrrolidinylbut-1-ene (0.67 g) in $CHCl_3$ at room temperature and by stirring for 24 h. Chromatographic separation (hexane/ethyl acetate, 15:1) gave

1.91 g (60%) of **11b** as a yellow oil; R_f = 0.53 (ethyl acetate/hexane, 1:5). IR (KBr): $\tilde{\nu}$ = 1735, 1197 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.35 (d, J = 6.9 Hz, 6 H), 1.47 (t, J = 7.1 Hz, 3 H), 3.50–3.57 (m, 1 H), 4.52 (q, J = 7.1 Hz, 2 H), 7.28–7.48 (m, 5 H), 7.83 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 23.3, 29.2, 62.1, 104.5–122.3 (m), 127.1–153.8 (m), 166.1 ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –81.2, –117.9 to –163.6 (m) ppm. MS (70 eV): m/z = 637 (1) $[M]^+$. $C_{24}H_{18}F_{15}NO_2$ (637): calcd. C 45.23, H 2.85, N 2.20; found C 45.30, H 2.80, N 2.22.

2-(2,4-Dinitrophenyl)-4-isopropyl-6-(perfluoromethyl)-5-phenylpyridine (12): The general procedure was followed using (1*E*,3*Z*)-2-azadiene **5a** obtained in situ and *trans*-3-methyl-1-pyrrolidinylbut-1-ene (0.21 g) in toluene at 110 °C and by stirring for 24 h. When the 2-azadiene had disappeared (12 h), *p*-benzoquinone (0.16 g) was added and the mixture was heated to 80 °C for 48 h. Chromatographic separation (hexane/ethyl acetate, 1:10) gave 0.36 g (56%) of **12** as a yellow solid; m.p. 161–162 °C. IR (KBr): $\tilde{\nu}$ = 1534, 1348 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.18 (d, J = 6.9 Hz, 6 H), 2.86 (dq, J = 6.9 Hz, 1 H), 7.27–7.51 (m, 4 H), 7.69 (s, 1 H), 8.03 (d, J = 8.5 Hz, 1 H), 8.58 (dd, J = 8.5, J = 2.3 Hz, 1 H), 8.82 (d, J = 2.3 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.5, 30.0, 123.6 (q, $^1J_{CF}$ = 278.0 Hz) 120.4–151.6 (m), 161.1 ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –62.2 ppm. MS (70 eV): m/z = 431 (5) $[M]^+$. $C_{21}H_{16}F_3N_3O_4$ (431): calcd. C 58.47, H 3.74, N 9.74; found C 58.30, H 3.80, N 9.62.

2-(2,4-Dinitrophenyl)-4-isopropyl-5-phenyl-6-(1,2,2,2-tetrafluoroethyl)pyridine (16): The general procedure was followed using (1*E*,3*Z*)-2-azadiene **5d** (2.08 g) and *trans*-3-methyl-1-pyrrolidinylbut-1-ene (0.21 g) at 110 °C in toluene and by stirring for 24 h. Chromatographic separation (hexane/ethyl acetate, 20:1) gave 1.11 g (48%) of **16** as a yellow oil; R_f = 0.61 (ethyl acetate/hexane, 1:5). IR (KBr): $\tilde{\nu}$ = 1534, 1358 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.18 (d, J = 6.9 Hz, 3 H), 1.20 (d, J = 6.9 Hz, 3 H), 2.83 (dq, J = 6.9 Hz, 1 H), 5.49 (dq, J = 44.4, J = 5.8 Hz), 7.23–7.63 (m, 5 H), 7.99 (d, J = 8.5 Hz, 1 H), 8.56 (dd, J = 8.5, J = 2.2 Hz 1 H), 8.79 (d, J = 2.3 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.2, 23.3, 30.2, 84.8 (dq, $^1J_{CF}$ = 188.4, $^2J_{CF}$ = 34.4 Hz), 120.4–139.9 (m), 147.7, 147.9, 149.5, 152.6, 159.2 ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –75.5 (d, J = 15 Hz), –190.8 (dq, J = 44, J = 15 Hz) ppm. MS (70 eV): m/z = 463 (100) $[M]^+$. $C_{22}H_{17}F_4N_3O_4$ (463): calcd. C 57.02, H 3.70, N 9.07; found C 57.10, H 3.67, N 9.10.

(1*E*)-3-(Perfluoropropyl)-1-phenyl-2-azabuta-1,3-diene (17b): This azadiene was prepared by a modification of the method of Soloshonok and co-workers.[10c] First, *N*-(3,3,4,4,5,5,5-heptafluoropent-2-ylidene)benzylamine was obtained by condensation of methyl heptafluoropropyl ketone and benzylamine. NBS bromination of this imine in CCl_4 produced *N*-(1-bromo-3,3,4,4,5,5,5-heptafluoropent-2-yliden)benzylamine which was treated (0.64 g, 2.3 mmol) with triethylamine (5 mL) at room temperature for 24 h. Elimination of triethylamine under reduced pressure afforded an oil that was purified by chromatography on silica gel (ethyl acetate/hexane, 1:40) to give 2-azadiene **17b** (0.27 g, 40%) as a yellow oil; R_f = 0.21 (ethyl acetate/hexane, 1:4). IR (NaCl): $\tilde{\nu}$ = 2924, 1657 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 5.14 (m, 2 H), 7.42–7.84 (m, 5 H), 8.35 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 103.4, 108.7–119.8 (m), 129.3–132.3 (m), 135.0, 149.2 (q, $^2J_{CF}$ = 21.3 Hz), 161.9 ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –81.4, –116.0, –127.0 ppm. MS (EI): m/z = 299 (46) $[M]^+$. $C_{12}H_8F_7N$ (299): calcd. C 48.17, H 2.70, N 4.68; found C 48.30, H 2.50, N 4.54.

General Procedure for the [4+2] Cycloaddition Reactions of Azadienes 17 with 4-Phenyl-1,2,4-triazoline-3,5-dione (18): 4-Phenyl-1,2,4-triazoline-3,5-dione (about 1 mmol) was added to a solution of an equimolecular amount of azadiene **17** and a catalytic amount of ytterbium triflate in acetonitrile (5 mL) under N_2 and the mixture was stirred at room temperature until TLC indicated the disappearance of the starting azadiene. The reaction mixture was treated with water, extracted with dichloromethane, dried and the solvent removed under reduced pressure to yield a residue that was crystallized from hexane.

7-(Perfluoromethyl)-2,5-diphenyl-5,8-dihydro[1,2,4]triazolo[1,2-*a*]-[1,2,4]triazine-1,3-dione (19a): The general procedure was followed using (1*E*)-3-(perfluoromethyl)-1-phenyl-2-azabuta-1,3-diene (**17a**) (0.25 g, 1.26 mmol) and by stirring for 12 h. Work up of the reaction and crystallization yielded 0.19 g (40%) of **19a** as a white solid; m.p. 115–116 °C (hexane). IR (NaCl): $\tilde{\nu}$ = 1724, 1601 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.40 (dd, J = 18.3, J = 3.0 Hz, 1 H), 4.80 (dd, J = 18.0, J = 0.9 Hz, 1 H), 6.85 (s, 1 H), 7.25–7.64 (m, 10 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 72.9, 118.7 (q, $^1J_{CF}$ = 279 Hz), 125.2–129.8 (m), 130.0, 132.7, 134.4, 150.4, 152.4 (q, $^2J_{CF}$ = 36.7 Hz), 152.8 ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –72.8 ppm. MS (70 eV): m/z = 374 (54) $[M]^+$. $C_{18}H_{13}F_3N_4O_2$ (374): calcd. C 57.76, H 3.50, N 14.97; found C 57.66, H 3.59, N 14.33.

7-(Perfluoropropyl)-2,5-diphenyl-5,8-dihydro[1,2,4]triazole[1,2-*a*]-[1,2,4]triazine-1,3-dione (19b): The general procedure was followed using (1*E*)-3-(perfluoropropyl)-1-phenyl-2-azabuta-1,3-diene (**17b**) (0.25 g, 0.84 mmol) and by stirring for 12 h. Work up of the reaction and crystallization yielded 0.20 g (50%) of **19b** as a white solid; m.p. 110–111 °C (hexane). IR (NaCl): $\tilde{\nu}$ = 1727, 1602 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.30 (dd, J = 18.3, J = 3.0 Hz, 1 H), 4.60 (dd, J = 18.3, J = 1.3 Hz, 1 H), 6.77 (s, 1 H), 7.15–7.34 (m, 10 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 73.3, 104.4–119.5 (m), 125.1–129.0 (m), 132.4, 132.5, 134.2, 150.2, 152.5, 154.1 (q, $^2J_{CF}$ = 35.3 Hz), 152.8 ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –80.3, –116.4 (d, $^2J_{FF}$ = 285.3 Hz), –118.1 (d, $^2J_{FF}$ = 285.3 Hz), –125.7 ppm. MS (70 eV): m/z = 474 (56) $[M]^+$. $C_{20}H_{13}F_7N_4O_2$ (474): C 50.64, H 2.76, N 11.81; found C 50.76, H 2.59, N 11.33.

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