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Aza-Wittig reaction of fluoroalkylated *N*-vinylic phosphazenes with carbonyl compounds. Usefulness of 2-azadienes for the preparation of fluoroalkyl pyridine derivatives

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Abstract—A method for the preparation of 3-fluoroalkyl substituted 2-aza-butadienes **6** by aza-Wittig reaction of 3-fluoroalkyl-*N*-vinylic phosphazenes **4** and aldehydes **5** is reported. [4+2] Cycloaddition reaction of these heterodienes **6** with enamines **9** gives fluoroalkyl substituted pyridine **15**, **16**, **24**–**27** and isoquinoline **12**–**14**, **20** derivatives.

1. Introduction

Functionalized 2-azabutadiene systems have proved to be efficient key intermediates in organic synthesis for the preparation of heterocycles[1,2] although the great majority of 2-azadienes studied are substituted with electron-donating groups and are excellent reagents in normal Diels–Alder reactions with electron-poor dienophiles.[1–3] In this context, we have described new methods for the preparation of heterocycles,[4] as well as for the synthesis of neutral azadienes **I** (Fig. 1)[5] and of electron-poor 2-aza-1,3-butadienes derived from α- and β-amino esters **II** (Fig. 1)[6] and we have also reported their use in the preparation of nitrogen heterocyclic compounds.[4–6]

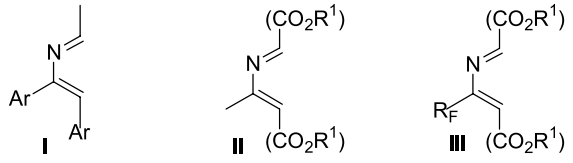

Figure 1.

Moreover, special interest has been focused on developing synthetic methods for the preparation of fluorinated building blocks since they are used for the efficient and/or selective preparation of fluorine-containing molecules with biological activity[7] and commercial applications.[8] Direct fluorination is the simplest way to prepare fluorinated heterocyclic compounds,[9] but usually the use of fluorinated precursors has been of more interest due to the easy formation of the products and to the regioselectivity of the fluorine substituents on the heterocyclic ring.[10] In this context, fluoroalkyl substituted 2-aza-1,3-butadienes **III** ($R_F = CF_3$, C_2F_5, … Fig. 1), despite their potential interest as synthons in organic synthesis for the construction of more complex fluoro-containing acyclic and cyclic compounds, have not received much attention, probably owing to the lack of general methods of synthesis of these compounds. Moreover, the presence of carboxylic groups in position 1 and 4 in compounds **III** (Fig. 1) may open new entries to the formation of heterodienes derived from α- and β-amino-acids. However, as far as we know, there has only been synthesis of 4-alkoxy-1,4-disilyloxy-1-trifluoromethyl-,[11a] 1,1-bis-(trifluoromethyl-),[11b] 4,4-difluoro- and 3-trifluoromethyl-2-aza-1,3-butadienes[11c] and reactions of 4-alkoxy-1,4-disilyloxy-1-trifluoromethyl-2-aza-1,3-butadienes with carbonyl compounds[12a] and 1,1-bis-(trifluoromethyl)-2-aza-1,3-butadiene with bromide, amines, mercaptans,[12b] diazomethane[12c] and phosphines[12d] have been described. As a continuation of our work on the design of new building blocks, we report herein an easy and versatile method for the synthesis of fluoroalkyl substituted 2-azadienes **III** involving aza-Wittig reaction[13] of *N*-vinylic phosphazenes **IV** with aldehydes and the use of these substrates as starting materials for the construction of fluoroalkyl functionalized heterocycles (Fig. 2).[14]

Keywords: *N*-vinylic phosphazenes; Aza-Wittig reaction; 2-Aza-1; 3-butadienes; Fluoroalkyl derivatives; Heterocycles.
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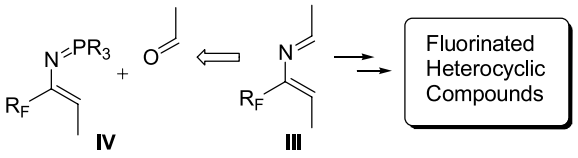
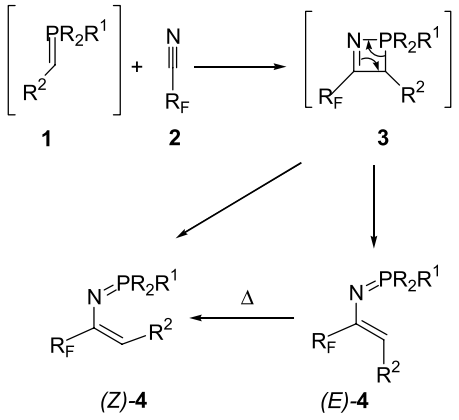


Figure 2.



Scheme 1.

2. Results and discussion

2.1. Synthesis of *N*-vinylic phosphazenes

Fluoroalkyl substituted *N*-vinylic phosphazenes **4** were prepared by reaction of phosphorus ylides and perfluoroalkyl nitriles.[15] Gas nitriles **2a** ($R_F=CF_3$) and **2b** ($R_F=C_2F_5$) were freshly generated[16] and bubbled through a solution of phosphorus ylides **1** (R^2=Ph, CO_2Me, CN),[17] affording the corresponding *N*-vinylic phosphazenes **4a**, **4b**, **4d**, **4e**, **4g**, **4i**, **4l** and **4m** (Scheme 1) in good yields (Table 1, entries 1, 2, 4, 5, 7, 9, 12 and 13). Commercially available nitrile **2c** ($R_F=C_7F_{15}$) was also used for the synthesis of phosphazenes **4c**, **4f**, **4h**, **4j**, **4k**, **4n** (Table 1, entries 3, 6, 8, 10, 11 and 14). Inorganic salts were eliminated by filtration and some phosphazenes were crystallized from ethyl acetate and isolated. However, other phosphazenes were less stable and, for this reason, were used without isolation (Table 1, entries 6–11) from the crude mixtures.

Crystalline compounds **4** were characterized on the basis of their spectroscopic data as *E* or *Z* isomers. Phosphazenes **4a–c** with a phenyl group (R^2=Ph) were exclusively obtained as *E* isomers (Table 1, entries 1–3), while phosphazenes **4d–h** derived from methoxycarbonyl ylides ($R^2=CO_2Me$) afforded phosphazenes whose HOESY ^{19}F–^{1}H experiments showed cross signals between fluorinated groups and vinylic protons, suggesting the formation of *Z* isomers (Table 1, entries 4–8).

However, when ylides containing a cyan substituent were employed (R^2=CN) either only *E* isomers (Table 1, entries 10, 11 and 14) or mixtures of *E* and *Z* isomers (Table 1, entries 9, 12 and 13) with a higher proportion of *E* isomers were obtained. Formation of conjugated phosphazenes **4** can be explained through [2+2] cycloaddition of phosphorus ylides **1** and nitriles **2** followed by ring opening of the unstable four-membered cyclic compounds **3**[5b,18] (Scheme 1). In this context, it is noteworthy that, isomerization of *E* isomer towards *Z* isomer was observed during purification (recrystallization or column chromatography) or thermal treatment.

For instance, spectroscopic analysis confirmed the total thermal isomerization to the new *Z* isomers when only the *E* isomers (phosphazenes **4a–c** and **4n**) as well as mixtures of *E*- and *Z*-isomers (phosphazenes **4i**, **4l** and **4m**) were heated at 110 °C in toluene. For example, ^{1}H NMR monitoring of *E*-phosphazene **4a** upon heating showed a singlet at δ_H 6.23 ppm for the vinylic proton of *Z*-phosphazene **4a**, instead of the doublet corresponding to the *E* precursor (δ_H=5.70 ppm, $^{4}J_{PH}$=3.2 Hz). Configuration of vinylic double bonds was also determined on the basis of heteronuclear HOESY ^{19}F–^{1}H experiments. Similar isomerizations have been observed previously by us[19] and by others.[20]

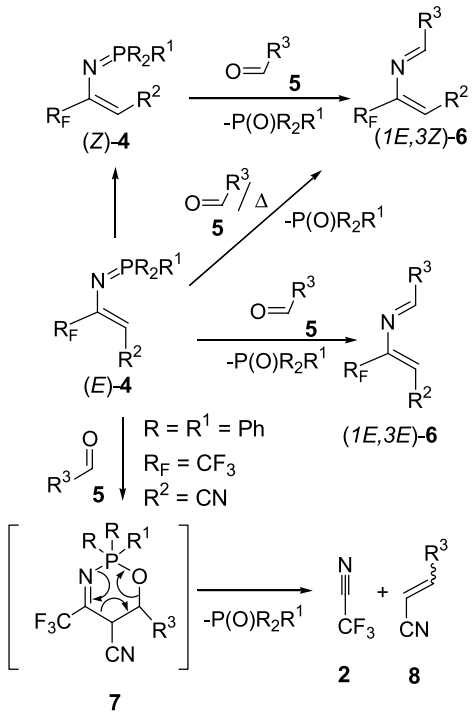
2.2. Aza-Wittig reaction of fluoroalkyl substituted *N*-vinylic phosphazenes 4 with carbonyl compounds 5

We then turned our attention to the preparation of

Table 1. *N*-Vinylic phosphazenes **4** obtained

Entry	Compound	R	R^1	R^2	R_F	Time (h)	Solvent	Yield (%)	Mp (°C)	*E*/*Z* (%)
1	**4a**	Ph	Ph	Ph	CF_3	12	Et_2O	90[a]	134–135	100:0[b,c]
2	**4b**	Ph	Ph	Ph	C_2F_5	24	Et_2O	81[a]	105–106	100:0[b,c]
3	**4c**	Ph	Ph	Ph	C_7F_{15}	12	Toluene	83[a]	120–121	100:0[c]
4	**4d**	Ph	Ph	CO_2Me	CF_3	12	Et_2O	65[a]	101–102	0:100
5	**4e**	Ph	Ph	CO_2Me	C_2F_5	24	Et_2O	99[a]	93–94	0:100
6	**4f**	Ph	Me	CO_2Me	C_7F_{15}	48	Toluene	—[d]	—	0:100
7	**4g**	Me	Me	CO_2Me	CF_3	12	Et_2O	—[d]	—	0:100
8	**4h**	Me	Me	CO_2Me	C_7F_{15}	12	Et_2O	—[d]	—	0:100
9	**4i**	Ph	Ph	CN	CF_3	24	Et_2O	—[d]	—	60:40[c]
10	**4j**	Ph	Ph	CN	C_7F_{15}	48	Toluene	—[d]	—	100:0
11	**4k**	Ph	Me	CN	C_7F_{15}	48	Toluene	—[d]	—	100:0
12	**4l**	Me	Me	CN	CF_3	12	THF	86[a]	—	80:20[c]
13	**4m**	Me	Me	CN	C_2F_5	12	THF	66[a]	—	75:25[c]
14	**4n**	Me	Me	CN	C_7F_{15}	12	THF	40[a]	98–99	100:0[c]

[a] Yield of isolated compounds.
[b] Isomerization towards *Z* isomer was observed when purification by column chromatography was performed (see Section 4).
[c] Isomerization of *E* isomer towards *Z* isomer was observed when a solution of *E* isomer or the *E*/*Z* mixture was heated at 110 °C in toluene (see Section 4).
[d] Not isolated, used in situ.



Scheme 2.

2-azadienes **III** (Fig. 2) containing a carboxylate group or a synthetic equivalent either in position 1 or in position 4, because these substrates are heterodienes derived from α- and β-amino acids respectively, containing fluoroalkyl substituents on 3 position. The aza-Wittig reaction[13] of fluoroalkyl *E*-*N*-vinylic phosphazenes **4a–c** derived from triphenylphosphine (R=R^1=Ph) with ethyl glyoxalate **5** (R^3=CO$_2$Et) at room temperature (Scheme 2) gave fluoroalkyl 2-azadienes **6a–c** (Table 2, entries 1–3) keeping the *E* configuration of the vinylic double bond (1,2-addition). These heterodienes **6a–c** were unstable to distillation or chromatography and therefore were not isolated and used in situ for the following reactions, but the presence of the non isolable compounds was established on the basis of the spectroscopic data of their crude mixtures. In the ^{1}H NMR spectrum of crude reaction of compound **6b** the olefinic hydrogen appeared as a singlet at δ 6.85 ppm and the iminic hydrogen as a singlet at δ 7.90 ppm. A significant signal enhancement (1.6% NOESY) was observed between the vinylic proton at δ 6.85 ppm of 2-azadiene and iminic proton at δ 7.90 ppm for compound **6b**. These data are consistent with the 1*E*,3*E*-configuration of heterodienes **6a–c**.

However, no aza-Wittig reaction (1,2-addition) was observed between ethyl glyoxalate or aromatic aldehydes **5** with fluoroalkyl *N*-vinylic phosphazenes derived from triphenylphosphine **4d**,**4e** (R=R^1=Ph, R^2=CO$_2$Me) or **4i**,**4j** (R=R^1=Ph, R^2=CN) or derived from diphenylmethylphosphine **4f** (R=Ph, R^1=Me, R^2=CO$_2$Me) and **4k** (R=Ph, R^1=Me, R^2=CN). The electron withdrawing effect of these groups (CN, CO$_2$Me) on 4 position seems to decrease the reactivity of conjugated phosphazenes **4** through the P=N linkage in the aza-Wittig reaction. Conversely, when phosphazene **4i** (R=R^1=Ph, R^2=CN, R$_F$=CF$_3$) was treated with *p*-nitrobenzaldehyde **5** (R^3=4-NO$_2$–C$_6$H$_4$), olefinic derivative **8a** (R^3=4-NO$_2$–C$_6$H$_4$)[21] and triphenylphosphine oxide were isolated from the crude mixture (Scheme 2). This result suggests an enaminic behaviour (1,4-addition) of the conjugated phosphazene **4i**. Formation of compound **8a** could be explained by an initial addition of aldehyde **5** to the β-carbon atom of phosphazene **4i** (1,4-addition) to give unstable 1,3,2-oxaazaphosphorane **7**, whose opening afforded the corresponding triphenylphosphine oxide (R=R^1=Ph), the very volatile nitrile **2** (R$_F$=CF$_3$) and alkene derivative **8a**.

Substitution in the phosphorus atom of phosphazenes of phenyl by methyl groups increases the reactivity of the phosphazene[6b] (1,2-addition) in a similar way to that observed for isosteric phosphorus ylides,[22] therefore more reactive phosphazenes derived from trimethylphosphine were used. Initially, we explored the reaction of *Z*-conjugated phosphazene with an ester group in 4 position **4g** (R=R^1=Me, R^2=CO$_2$Me, R$_F$=CF$_3$) with aromatic aldehydes **5** (R^3=4-NO$_2$–C$_6$H$_4$, 2,4-(NO$_2$)$_2$–C$_6$H$_3$). After heating the respective reaction mixtures in refluxing toluene the expected (1*E*,3*Z*)-2-azadienes **6d** (R^3=4-NO$_2$–C$_6$H$_4$) or **6e** (R^3=2,4-(NO$_2$)$_2$–C$_6$H$_3$) (Table 2, entries 4 and 5) were obtained, keeping the *Z*-configuration of the starting vinyl group from conjugated phosphazene **4g**. Similar results were observed when aza-Wittig reaction was attempted with *Z*-conjugated phosphazenes containing a cyano group **4l**

Table 2. 3-Fluoroalkyl-2-azadienes **6** obtained

	Compound	Starting material	R^2	R$_F$	R^3	*T* (°C)	Time (h)	Solvent	Yield (%)
1	(1*E*,3*E*)-**6a**	(*E*)-**4a**	Ph	CF$_3$	CO$_2$Et	20	1	CHCl$_3$	—[a]
2	(1*E*,3*E*)-**6b**	(*E*)-**4b**	Ph	C$_2$F$_5$	CO$_2$Et	20	1	CHCl$_3$	—[a]
3	(1*E*,3*E*)-**6c**	(*E*)-**4c**	Ph	C$_7$F$_{15}$	CO$_2$Et	20	0.5	CHCl$_3$	—[a]
4	(1*E*,3*Z*)-**6d**	(*Z*)-**4g**	CO$_2$Me	CF$_3$	4-NO$_2$–C$_6$H$_4$	110	3	Toluene	—[a]
5	(1*E*,3*Z*)-**6e**	(*Z*)-**4g**	CO$_2$Me	CF$_3$	2,4-(NO$_2$)$_2$–C$_6$H$_3$	110	3	Toluene	—[a]
6	(1*E*,3*Z*)-**6f**	(*Z*)-**4l**	CN	CF$_3$	4-NO$_2$–C$_6$H$_4$	110	2	Toluene	45[b]
7	(1*E*,3*Z*)-**6f**	(*E*)-**4l**	CN	CF$_3$	4-NO$_2$–C$_6$H$_4$	110	3	Toluene	35[b]
8	(1*E*,3*Z*)-**6g**	(*E*)-**4l**	CN	CF$_3$	2,4-(NO$_2$)$_2$–C$_6$H$_3$	110	6	Toluene	30[b]
9	(1*E*,3*Z*)-**6g**	(*E*+*Z*)-**4l**	CN	CF$_3$	2,4-(NO$_2$)$_2$–C$_6$H$_3$	61	12	CHCl$_3$	45[b]
10	(1*E*,3*Z*)-**6h**	(*E*+*Z*)-**4m**	CN	C$_2$F$_5$	4-NO$_2$–C$_6$H$_4$	110	120	Toluene	—[a]
11	(1*E*,3*Z*)-**6i**	(*Z*)-**4n**	CN	C$_7$F$_{15}$	4-NO$_2$–C$_6$H$_4$	110	120	Toluene	—[a]
12	(1*E*,3*Z*)-**6i**	(*E*)-**4n**	CN	C$_7$F$_{15}$	4-NO$_2$–C$_6$H$_4$	110	138	Toluene	—[a]
13	(1*E*,3*Z*)-**6j**	(*E*)-**4n**	CN	C$_7$F$_{15}$	2,4-(NO$_2$)$_2$–C$_6$H$_3$	110	192	Toluene	—[a]

[a] Not isolated, used in situ for the next reactions.
[b] Yield of isolated compounds by column chromatography.

(R=R^1=Me, R^2=CN, R$_F$=CF$_3$) and **4n** (R=R^1=Me, R^2=CN, R$_F$=C$_7$F$_{15}$) to give (1*E*,3*Z*)-heterodienes **6f** and **6i** (Table 2, entries 6 and 11).

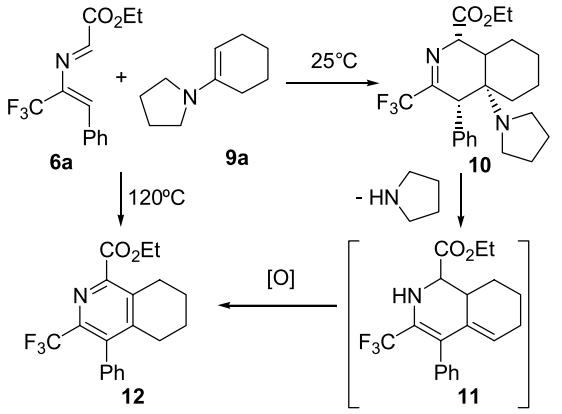
However, these azadienes **6f** and **6i** with the same configuration (1*E*,3*Z*) were also obtained when *E* isomers **4l** and **4n** were used, although longer reaction times were necessary than for 3-*Z* isomers (Table 2, entries 7 and 12). ^{1}H NMR monitoring of reaction of *E* isomer of phosphazene **4l** with *p*-nitrobenzaldehyde (R^3=4-NO$_2$–C$_6$H$_4$) was performed. Initially, signals corresponding to conversion of *E*-phosphazene towards *Z* isomer were observed, the latter being the precursor of corresponding (1*E*,3*Z*)-2-azadiene **6f**, whose signals began to be visible after isomerization. In a similar way, reaction *E* isomer of phosphazenes **4l** and **4n** with aromatic aldehyde **5** (R^3=2,4-(NO$_2$)$_2$–C$_6$H$_3$) (Table 2, entries 8 and 13) or reaction of *E*,*Z* mixtures of phosphazene **4l** (3*E*/3*Z*=80/20) with aromatic aldehyde **5** (R^3=2,4-(NO$_2$)$_2$–C$_6$H$_3$) or phosphazene **4m** (3*E*/3*Z*=75/25) with 4-nitrobenzaldehyde **5** (R^3=4-NO$_2$–C$_6$H$_4$) led to the formation of (1*E*,3*Z*)-azadienes **6g**,**h**,**j**, respectively (Table 2, entries 9, 10 and 13). HOESY ^{19}F–^{1}H experiment for compound **6j** showed cross signal between fluorinated group and vinylic proton, confirming the formation of (1*E*,3*Z*) isomer. As far as we know, this strategy describes the first synthesis[14] of 3-perfluoroalkyl-2-azabutadienes derived from α-amino esters **6a–c** (R$_F$=CF$_3$, C$_2$F$_5$, C$_7$F$_{15}$) and 3-perfluoroalkyl-2-azabutadienes derived from β-amino esters **6d**,**e** (R$_F$=CF$_3$) and from β-amino nitriles **6f–j** (R$_F$=CF$_3$, C$_2$F$_5$, C$_7$F$_{15}$).

2.3. Reaction of 3-fluoromethyl-2-azadienes 6 with enamines 9. [4+2] versus [2+2] cycloaddition processes

Pyridine nuclei are widespread in the alkaloid family and constitute an important class of compounds in pharmaceuticals, agrochemicals and dyestuffs.[23,24] For this reason, in order to test the synthetic usefulness of the new fluoroalkyl substituted azadienes **6** as key intermediates in organic synthesis and specially in the preparation of new nitrogen-containing heterocycles, the cycloaddition reaction of fluoroalkyl substituted 2-azadienes **6** was explored. Cycloaddition reactions with a range of dienophiles (diethyl ketomalonate, *trans*-cyclooctene, …) were inefficient. Indeed, even on prolonged heating and at higher temperature no significant cycloaddition was observed, and so the reaction of heterodienes **6** with electron-rich olefins such as enamines was studied.

Initially, the reaction of 2-azadiene derived from α-amino esters **6a** was explored, because this substrate would be an interesting starting material for the preparation of pipecolic acid derivatives.[25] When the reaction of 2-azadiene **6a** with *N*-cyclohex-1-enyl pyrrolidine **9a** was performed in refluxing toluene, only the aromatic bicyclic compound **12** (Scheme 3, 40%) was obtained.

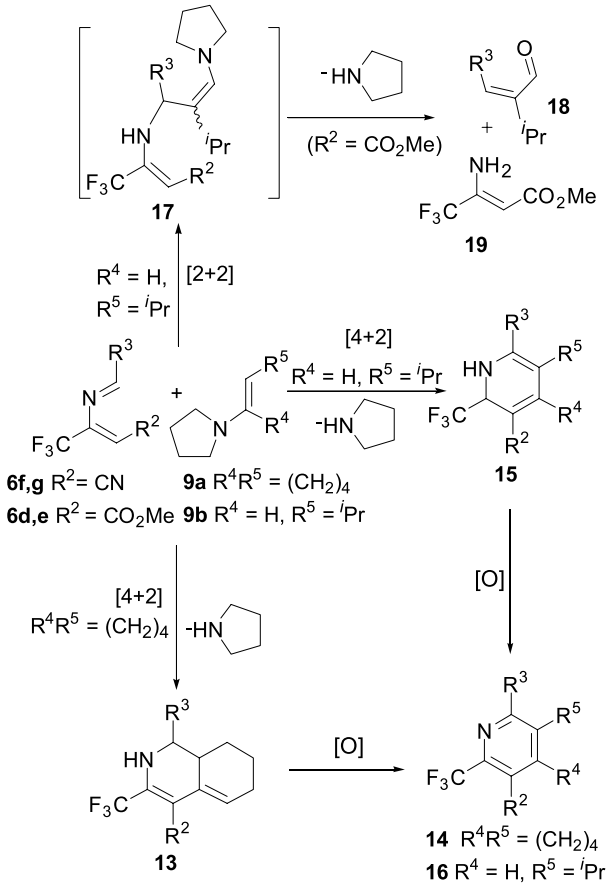
The formation of this tetrahydroisoquinoline can be explained through a [4+2] cycloaddition reaction of heterodiene **6a** with enamine **9a** and formation of cycloadduct **10** followed by the loss of pyrrolidine and oxidation. Then, we tried to stop the process in proposed intermediates when the reaction was achieved in very mild



Scheme 3.

reaction conditions. At room temperature in CHCl$_3$, alkylfluorinated 2-azadiene **6a**, underwent efficient regio- and stereoselective cycloaddition with enamine **9a** affording the *endo*-cycloadduct **10** (Scheme 3) in good yield (80%) in a regio- and stereoselective fashion. The structure of compound **10** was assigned on the basis of the 1D and 2D spectroscopy, including COSY, NOE, HMQC and HMBC experiments and mass spectral data. As far as we know, this strategy describes the first synthesis[14] of 3-trifluoromethyl-isoquinolines derived from α-amino esters **10** and **12**.

Then, we tried to extend the process to 3-trifluoromethyl-2-azadienes derived from β-amino nitrile. Thus, 2-azadiene **6f**



Scheme 4.

Table 3. Pyridine derivatives **13–16** obtained from azadienes **6** and enamines **9**

Entry	Compound	R^2	R^3	R^4	R^5	Time (h)	Yield (%)
1	**13a**	CN	4-NO_2–C_6H_4	–$(CH_2)_4$–		2	29[a]
2	**13b**	CN	2,4-$(NO_2)_2$–C_6H_3	–$(CH_2)_4$–		3	—[b,c]
3	**14a**	CN	4-NO_2–C_6H_4	–$(CH_2)_4$–		2/72[d]	29[a]/93[e]
4	**14b**	CN	2,4-$(NO_2)_2$–C_6H_3	–$(CH_2)_4$–		3/144[f]	—[b,c]/70[d]
5	**15a**	CO_2Me	2,4-$(NO_2)_2$–C_6H_3	H	^{i}Pr	3	35[a]
6	**15b**	CO_2Me	4-NO_2–C_6H_4	H	^{i}Pr	24	60[a]
7	**16a**	CO_2Me	2,4-$(NO_2)_2$–C_6H_3	H	^{i}Pr	3/24[i]	43[a]/98[f]
8	**16b**	CO_2Me	4-NO_2–C_6H_4	H	^{i}Pr	48[i]	72[f]
9	**16c**	CN	4-NO_2–C_6H_4	H	^{i}Pr	3	52[a]
10	**16d**	CN	2,4-$(NO_2)_2$–C_6H_3	H	^{i}Pr	3	64[a]

[a] Isolated by column chromatography.
[b] Not isolated.
[c] Proportion **13b**:**14b**, 6:1.
[d] Obtained by oxidation of the mixture of **13** and **14** with *p*-benzoquinone in dioxane at 80 °C.
[e] Obtained by oxidation of **13a** with *p*-benzoquinone in dioxane at 80 °C.
[f] Obtained by oxidation of **15** with *p*-benzoquinone in dioxane at 80 °C.

(R^2=CN, R^3=4-NO_2–C_6H_4) reacted with *N*-cyclohex-1-enylpyrrolidine **9a** at room temperature until disappearance of starting material, affording a mixture (1:1) of bicyclic cycloadduct **13a** (29%) and the corresponding aromatic heterocycle **14a** (29%) (Scheme 4, Table 3, entries 1 and 3). Oxidation of **13a** with *p*-benzoquinone in dioxane at 80 °C (72 h) gave only 3-trifluoromethyl-5,6,7,8-tetrahydro-isoquinoline **14a** in very high yield (93%). Similarly, azadiene **6g** (R^2=CN, R^3=2,4-$(NO_2)_2$–C_6H_3) was treated with enamine **9a** at room temperature to give an inseparable mixture of heterocyclic derivatives **13b** and **14b** (6:1) (Scheme 4, Table 3, entries 2 and 4). Oxidation of the mixture with *p*-benzoquinone in dioxane at 80 °C gave only the aromatic pyridine **14b** (Scheme 4, Table 3, entry 4).

Formation of compounds **13** and **14** (R^4R^5=$(CH_2)_4$) could be explained, as before, by formation of a [4+2]-cycloadduct followed by the loss of pyrrolidine and oxidation in a similar way to that described in Scheme 3.

The reaction was extended to *N*-(3-methyl)but-1-enyl-pyrrolidine **9b** (R^4=H, R^5=^{i}Pr). In this process, the electron-withdrawing effect of substituents at position 4 (CO_2Me, CN) seems to play an important role. 2-Azadiene **6e** derived from β-aminoester (R^2=CO_2Me, R^3=2,4-$(NO_2)_2$–C_6H_3) reacted with enamine **9b** in $CHCl_3$ at room temperature to give heterocycles **15a** (R^2=CO_2Me, R^3=2,4-$(NO_2)_2$–C_6H_3, R^4=H, R^5=^{i}Pr) and **16a** (R^2=CO_2Me, R^3=2,4-$(NO_2)_2$–C_6H_3, (Scheme 4, Table 3, entries 5 and 7) along with a small amount (<10%) of aldehyde **18a** (R^3=2,4-$(NO_2)_2$–C_6H_3) and enamine **19**.[26] Formation of heterocycles **15** and **16** (R^4=H, R^5=^{i}Pr) could be explained, as before, by formation of a [4+2]-cycloadduct followed by the loss of pyrrolidine and oxidation in a similar way to that described in Scheme 3. However, the formation of aldehyde **18a** (R^3=2,4-$(NO_2)_2$–C_6H_3) and primary enamine **19** could be explained by a competitive [2+2] cycloaddition of the enamine with the iminic double bond of heterodiene[27] followed by ring opening of the four-membered ring and formation of the intermediate **17** (Scheme 4), whose subsequent C–N bond cleavage gave pyrrolidine, carbonyl compound **18** and primary enamine **19**.

On the other hand, when 2-azadiene **6d** (R^2=CO_2Me, R^3=4-NO_2–C_6H_4) reacted in $CHCl_3$ at room temperature with the same enamine **9b** a complex mixture of several compounds including decomposition products of starting azadiene was obtained after very long period of time (10 days). Nevertheless, if the reaction was performed by heating in toluene, only the 1,2-dihydropyridine **15b** (R^2=CO_2Me, R^3=4-NO_2–C_6H_4, R^4=H, R^5=^{i}Pr) was obtained (Scheme 4, Table 3, entry 6). Oxidation of 1,2-dihydropyridines **15a**,**b** with *p*-benzoquinone in dioxane at 80 °C (for 24 and 48 h respectively) gave pyridines **16a**,**b** (98 and 72% see Table 3, entries 7 and 8).

Aromatic pyridines **16** can also be directly prepared in the case of 2-azadienes derived from β-amino nitriles **6f**,**g** (R^2=CN). Reactions of 2-azadienes **6f** (R^3=4-NO_2–C_6H_4) and **6g** (R^3=2,4-$(NO_2)_2$–C_6H_3) with enamine **9b** was performed in $CHCl_3$ at room temperature to give only

Table 4. Pyridine derivatives **20**, **24–27** obtained from azadienes **6** and enamines **9**

Entry	Compound	R^3	R^6	R^4	R^5	Yield
1	**20**	—	CF_3	–$(CH_2)_4$–	60[a]	
2	**24a**	—	CF_3	–$(CH_2)_3$–	42[a]	
3	**24b**	—	C_6F_{13}	–$(CH_2)_3$–	48[a]	
4	**25a**	4-NO_2–C_6H_4	CF_3	H	^{i}Pr	40[a]
5	**25b**	4-NO_2–C_6H_4	C_6F_{13}	H	^{i}Pr	35[a]
6	**25c**	2,4-$(NO_2)_2$–C_6H_3	C_6F_{13}	H	^{i}Pr	—[b]
7	**26a**	4-NO_2–C_6H_4	CF_3	H	^{i}Pr	18[a]
8	**26b**	4-NO_2–C_6H_4	C_6F_{13}	H	^{i}Pr	18[a]
9	**26c**	2,4-$(NO_2)_2$–C_6H_3	C_6F_{13}	H	^{i}Pr	—[b]
10	**27b**	4-NO_2–C_6H_4	C_6F_{13}	H	^{i}Pr	22[a]

[a] % Isolated by column chromatography.
[b] Obtained as an inseparable mixture of **25c** and **26c** (1:2).

pyridines **16c** and **16d**, respectively (Scheme 4, Table 3, entries 9 and 10).

2.4. Reaction of 3-perfluoroethyl-2-azadienes and 3-perfluorohepthyl-2-azadienes with enamines

In order to test the influence of perfluoroalkyl substituents at 3 position on the reactivity of heterodienes **6** derived from α-amino esters ($R^3=CO_2Et$), we tried to extend the study to the reaction of 3-perfluoroethyl-2-azadiene **6b** ($R^6=CF_3$) and 3-perfluorohepthyl-2-azadiene **6c** ($R^6=C_6F_{13}$) with enamines **9** (Scheme 5). However, an unexpected behaviour was observed when 2-azadiene derived from ethyl glyoxalate **6b** ($R^6=CF_3$) was treated with enamine **9a** ($R^4R^5=(CH_2)_4$). Spectroscopic data for the compounds obtained showed that pyridine **20** ($R^6=CF_3$, $R^4R^5=(CH_2)_4$) was obtained (Scheme 5, Table 4, entry 1) instead of the expected compound **21** ($R^4R^5=(CH_2)_4$).

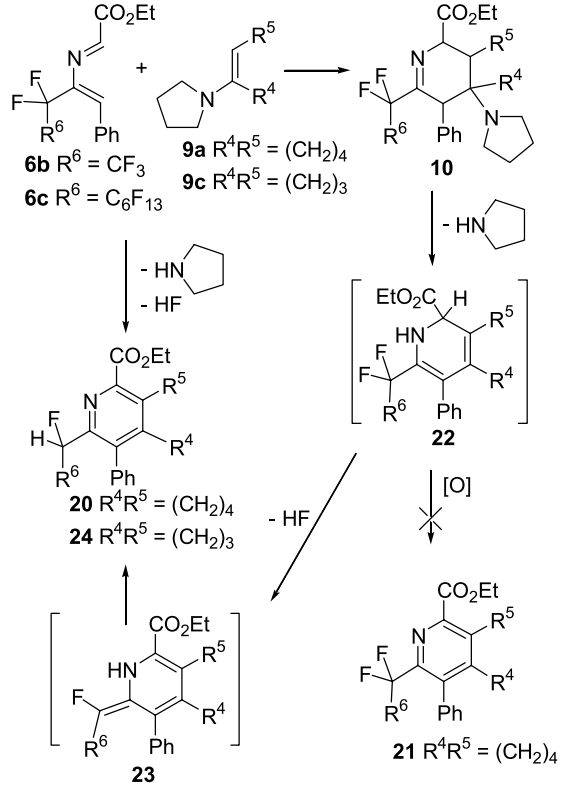
Mass spectrometry of compound **20** showed the molecular ion (*m*/*z* 381, 73%), which corresponds to the loss of HF from expected cycloadduct **22**, confirmed also by ^{1}H NMR and ^{13}C NMR spectra. Thus, ^{1}H NMR of compound **20** ($R^6=CF_3$, $R^4R^5=(CH_2)_4$) showed a double quadruplet at δ 5.45 ppm with coupling constants of $^2J_{HF}=46$ Hz and $^3J_{HF}=6$ Hz and ^{13}C NMR spectrum shows a double quadruplet at δ 122.0 ppm with coupling constants of $^1J_{CF}=281.0$ Hz and $^2J_{CF}=29.0$ Hz.

Formation of this fluoroalkyl heterocycle **20** could be explained through a [4+2]-cycloadduct **10** followed by the loss of pyrrolidine, dehydrofluorination and formation of **23**. Enamine-imine tautomerization of **23** may give aromatic 1-ethoxycarbonyl-4-phenyl-3-(1,2,2,2-tetrafluoroethyl)-5,6,7,8-tetrahydroisoquinoline **20** (Scheme 5).[28]

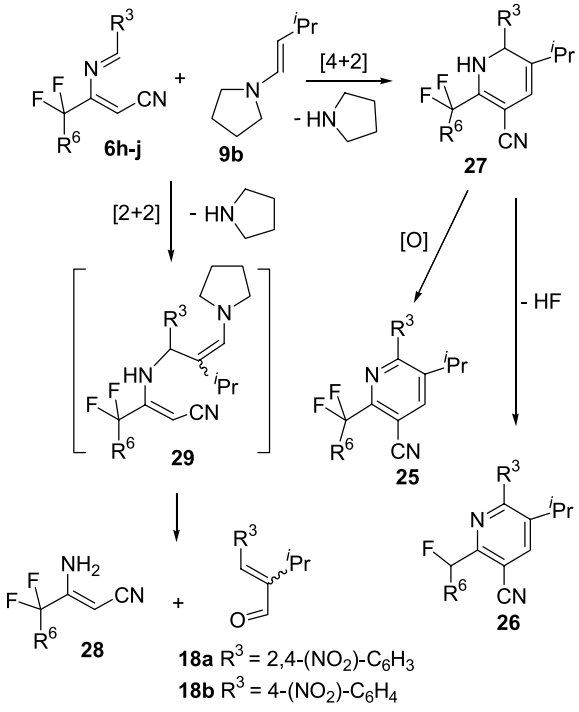
Likewise, heterodienes derived from glyoxalate **6b** ($R^6=CF_3$) and **6c** ($R^6=C_6F_{13}$) with *N*-cyclopent-1-enyl pyrrolidine **9c** ($R^4R^5=(CH_2)_3$) led also to the formation of bicyclic heterocycles **24a** ($R^6=CF_3$, $R^4R^5=(CH_2)_3$) and **24b** ($R^6=C_6F_{13}$, $R^4R^5=(CH_2)_3$) containing fluoroalkyl substituents at 3 position (Scheme 5, Table 4, entries 2 and 3). In these processes the presence of an electron-withdrawing group (CO_2Et) at 1 position seems to favour the [4+2] cycloaddition reaction with exclusive formation of aromatic pyridine derivatives **20** and **24**.

However, when heterodienes with an aryl group (1 position) and derived from β-amino nitriles ($R^2=CN$) such as 2-azadiene **6h** ($R^6=CF_3$, $R^3=4\text{-}NO_2\text{–}C_6H_4$) were treated with enamine **9b**, not only aromatic pyridines **25a** and **26a** (Scheme 6, Table 4, entries 4 and 7) but also unsaturated aldehydes **18b** ($R^3=4\text{-}NO_2\text{–}C_6H_5$, *E* and *Z*) and enamine **28a** ($R^6=CF_3$) were obtained (<10%, Scheme 6).

Similar behaviour was observed in the reaction of 2-azadienes **6i** ($R^6=C_6F_{13}$, $R^3=4\text{-}NO_2\text{–}C_6H_4$) and **6j** ($R^6=C_6F_{13}$, $R^3=2,4\text{-}(NO_2)_2\text{–}C_6H_3$) with this enamine **9b** to give mixtures of aromatic perfluoro substituted (position 2) pyridines **25b**,**c** (Scheme 6) and pyridines with only a fluorine atom in Cα of C-2 **26b**,**c** (Table 4, entries 5, 6, 8 and 9). Formation of compounds **25**, **26** could be explained, as before, through a normal [4+2] cycloaddition reaction of heterodienes and enamines with formation of cycloadducts **27**. These intermediates could give either pyridines **25**, by oxidation under reaction conditions, or pyridines **26** by dehydrofluorination, in a similar way to that observed before in Scheme 5. Moreover, in the case of the reaction of heterodiene **6i**, the dihydropyridine derivative **27b**



Scheme 5.



Scheme 6.

($R^6=C_6F_{13}$, $R^3=4$-(NO_2)–C_6H_4) can also be isolated (Table 4, entry 10). Spectroscopic data 1D and 2D, including HMQC and HMBC experiments were consistent with the structure of compound **27**. In these processes a small amount (<10%) of the corresponding unsaturated aldehydes **18b** ($R^3=4$-(NO_2)–C_6H_4) and **18a** ($R^3=2,4$-$(NO_2)_2$–C_6H_3) and enamine **28b** ($R^6=C_6F_{13}$, 6% and 8% respectively) were obtained. The formation of compounds **28** and **18** could also be explained by a competitive [2+2] cycloaddition of the enamine with the iminic double bond of heterodiene and formation of intermediate **29** in a similar manner to that reported in Scheme 4.

3. Conclusion

In summary, fluoroalkyl *N*-vinylic phosphazenes **4** can be prepared readily from fluoroalkyl nitriles **2** and phosphorus ylides **1**. These conjugated phosphazenes react cleanly and in good yields with aldehydes, by means of an aza-Wittig reaction, to afford fluoroalkyl functionalized 2-azadienes **6**, which are excellent building blocks for the preparation of fluorinated heterocycles. For instance, fluoroalkylated heterocycles esters such as 5,6,7,8-tetrahydroisoquinolines **12**, **14** and **20**, substituted pyridines derived from pipecolic esters **24**, as well as pyridine compounds derived from β-amino nitriles and β-amino esters such as 1,2,6,7,8,8a-hexahydroisoquinolines **13**, dihydropyridines **15** and **27** and substituted pyridines **16**, **25** and **26** can be prepared through a [4+2] cycloaddition strategy involving heterodienes **6** with electron-rich dienophiles such as enamines. Most of them are described for the first time. These fluoroalkylated 2-aza-1,3-butadienes may be important synthons in organic synthesis and in the preparation of fluoroalkyl substituted acyclic and heterocycles.[1,8]

4. Experimental

4.1. General

Chemicals were purchased from Aldrich, Lancaster, Fluorochem and Acros Chemical Companies. Solvents for extraction and chromatography were technical grade. All solvents used in reactions were freshly distilled from appropriate drying agents before use. All other reagents were recrystallized or distilled as necessary. All reactions were performed under an atmosphere of dry nitrogen. Analytical TLC was performed with Merck silica gel 60 F_{254} and aluminium oxide N/UV_{254} plates. Visualization was accomplished by UV light. Flash chromatography was carried out using Merck silica gel 60 (230–400 mesh ASTM) and aluminium oxide 90 active neutre (70–230 mesh ASTM). Melting points were determined with an Electrothermal IA9100 Digital Melting Point Apparatus and are uncorrected. ^{1}H (400, 300 and 250 MHz), ^{13}C (100 and 75 MHz), ^{19}F NMR (376 and 282 MHz) and ^{31}P NMR (120 MHz) spectra were recorded on a Bruker Avance 400 MHZ and a Varian VXR 300 MHz spectrometer using $CDCl_3$ or CD_3OD solutions with TMS as an internal reference ($\delta=0.00$ ppm) for ^{1}H and ^{13}C NMR spectra, $FCCl_3$ as an internal reference ($\delta=0.00$ ppm) for ^{19}F NMR spectra, and phosphoric acid (85%) ($\delta=0.0$ ppm) for ^{31}P NMR spectra. Chemical shifts (δ) are reported in ppm. Coupling constants (J) are reported in Hertz. Low-resolution mass spectra (MS) were obtained at 50–70 eV by electron impact (EIMS) on a Hewlett–Packard 5971 or 5973 spectrometer. Data are reported in the form *m/z* (intensity relative to base=100). Infrared spectra (IR) were taken on 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.

4.2. General procedure A for the preparation of phosphazenes 4

A 1.6 M solution of methyllithium (3.125 mL, 5 mmol) in ether was added dropwise to a solution of 5 mmol of phosphonium salt in ether or toluene (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 to the ylide solution at 0 or −35 °C and the mixture was stirred at room temperature. Inorganic salts were filtered under N_2 and filtrate was concentrated to afford an oil.

4.3. General procedure B for the preparation of phosphazenes 4

A 0.5 M solution of KHMDS in toluene (10 mL, 5 mmol) was added dropwise to a solution of 5 mmol of phosphonium salt in THF (20 mL) cooled to 0 °C under N_2 and was stirred for 4.5 h at room temperature. Inorganic salts were filtered under N_2 and fluoroalkylated nitrile was added dropwise or bubbled to the ylide solution at −35 °C. The mixture was stirred at room temperature overnight. Evaporation of solvent afforded an oil.

4.3.1. (3*E*)-1,1,1,4-Tetraphenyl-3-trifluoromethyl-2-aza-1λ^5-phosphabuta-1,3-diene (4a). The general procedure A was followed using benzyltriphenylphosphonium iodide (2.40 g) in ether and bubbling trifluoroacetonitrile (CF_3CN) in excess at 0 °C for 12 h. Crystallization from ethyl acetate gave the (*E*) isomer of **4a** as a yellow solid (2.01 g, 90%) mp 134–135 °C (ethyl acetate). IR (KBr) ν 1600, 1341 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.70 (d, $^4J_{PH}=3.2$ Hz, 1H), 6.98–7.85 (m, 20H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 113.8 (dd, $^3J_{CP}=11.3$ Hz, $^3J_{CF}=1.7$ Hz), 122.8 (dq, $^1J_{CF}=278.0$ Hz, $^3J_{CP}=24.5$ Hz), 125.5–133.7 (m), 137.0 (q, $^2J_{CF}=21.3$ Hz). ^{31}P NMR (120 MHz, $CDCl_3$) δ: 7.94. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −64.1. MS (EI) *m/z* 447 (M^+, 100). Anal. Calcd for $C_{27}H_{21}F_3NP$ (447): C, 72.48; H, 4.73; N, 3.13. Found: C, 72.02; H, 4.68; N, 3.10.

4.3.2. (3*E*)-3-Perfluoroethyl-1,1,1,4-tetraphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (4b). The general procedure A was followed using benzyltriphenylphosphonium iodide (2.40 g) in ether and bubbling perfluoropropanenitrile (C_2F_5CN) in excess at 0 °C for 24 h. Crystallization from ethyl acetate gave the (*E*) isomer of **4b** as a yellow solid (2.01 g, 81%) mp 105–106 °C (ethyl acetate). IR (KBr) ν 1608, 1203 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.73 (s, 1H), 6.91–7.8 (m, 20H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 112.4 (tq, $^1J_{CP}=259.9$ Hz, $^2J_{CF}=40.8$ Hz), 119.3 (tq, $^1J_{CF}=286.6$ Hz, $^2J_{CF}=40.8$ Hz), 125.9–136.6 (m). ^{31}P NMR (120 MHz, $CDCl_3$) δ: 7.46. ^{19}F NMR (282 MHz,

$CDCl_3$) δ: −64.3, −94.5; MS (EI) *m/z* 497 (M^+, 100). Anal. Calcd for $C_{28}H_{21}F_5NP$ (497): C, 67.61; H, 4.25; N, 2.82. Found: C, 67.72; H, 4.21; N, 2.81.

4.3.3. (3*E*)-3-Perfluorohepthyl-1,1,1,4-tetraphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (4c). The general procedure A was followed using benzyltriphenylphosphonium iodide (2.40 g) at 0 °C in toluene and adding dropwise 1.97 g (5 mmol) of perfluorooctanenitrile ($C_7F_{15}CN$). The mixture was stirred at room temperature for 12 h. Crystallization from ethyl acetate gave the (*E*) isomer of **4c** as a yellow solid (3.10 g, 83%) mp 120–121 °C (ethyl acetate) IR (KBr) ν 1611, 1206 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 5.74 (s, 1H), 6.89–7.81 (m, 20H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 109.3–115.8 (m), 125.9–136.6 (m). ^{31}P NMR (120 MHz, $CDCl_3$) δ: 7.03. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −81.2 (t, $^3J_{FF}$=9.2 Hz), −107.1–126.5 (m); MS (EI) *m/z* 747 (M^+, 40). Anal. Calcd for $C_{33}H_{21}F_{15}NP$ (747): C, 53.03; H, 2.83; N, 1.87. Found: C, 53.20; H, 2.80; N, 1.82.

4.3.4. (3*Z*)-4-Methoxycarbonyl-3-trifluoromethyl-1,1,1-triphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (4d). Trifluoroacetonitrile in excess (CF_3CN) was bubbled to a suspension of commercial ylide (methoxycarbonyl-methylen)-triphenylphosphoran ($Ph_3P{=}CHCO_2CH_3$) in Et_2O at 0 °C and the mixture was stirred at room temperature for 12 h. Filtration and evaporation of solvent afforded the (*Z*) isomer of **4d** as an orange solid (1.39 g, 65%) mp 101–102 °C ($CHCl_3$). IR (KBr) ν 1702, 1208 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 3.17, (s, 3H), 5.41 (s, 1H), 7.31–7.58 (m, 15H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 50.2, 96.7, 120.9 (q, $^1J_{CF}$=280 Hz), 128.2–132.5 (m), 167.1. ^{31}P NMR (120 MHz, $CDCl_3$) δ: 10.2. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −71.3. MS (EI) *m/z* 429 (M^+, 18). Anal. Calcd for $C_{23}H_{19}F_3NO_2P$ (429): C, 64.34; H, 4.46; N, 3.26. Found: C, 64.58; H, 4.51; N, 3.13.

4.3.5. (3*Z*)-4-Methoxycarbonyl-3-perfluoroethyl-1,1,1-triphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (4e). A solution of commercial (methoxycarbonylmethylen)-triphenylphosphorane (1.672 g, 5 mmol) in CH_2Cl_2 was cooled to 0 °C under N_2. Perfluoropropanenitrile in excess (C_2F_5CN) was bubbled and the mixture was stirred for 24 h. Crystallization from ethyl acetate gave the (*Z*) isomer of **4e** as a white solid (2.37 g, 99%) mp 93–94 °C (ethyl acetate). IR (KBr) ν 1709, 1178 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 3.13, (d, $^4J_{PH}$=0.97 Hz, 3H), 5.43 (s, 1H), 7.40–7.71 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 50.0, 95.8 (d, $^3J_{PC}$=4.5 Hz), 111.1 (tq, $^1J_{CF}$=258 Hz, $^2J_{CF}$=31 Hz) 119.2 (tq, $^1J_{CF}$=287 Hz, $^2J_{CF}$=37.8 Hz), 127.7–132.4 (m), 149.1 (t, $^2J_{CF}$=27.7 Hz), 167.0. ^{31}P NMR (120 MHz, $CDCl_3$) δ: 9.56. ^{19}F NMR (282 MHz, $CDCl_3$) δ −59.6, −95.0. MS (EI) *m/z* 479 (M^+, 100). Anal. Calcd for $C_{24}H_{19}F_5NO_2P$ (479): C, 60.13; H, 3.99; N, 2.92. Found: C, 60.21; H, 3.88; N, 2.86.

4.3.6. (3*Z*)-1,1-Diphenyl-4-methoxycarbonyl-3-perfluorohepthyl-1-methyl-2-aza-1λ^5-phosphabuta-1,3-diene (4f). The general procedure A was followed using methoxycarbonylmethyldiphenylphosphonium bromide (1.76 g) at 0 °C in toluene and adding dropwise 1.97 g (5 mmol) of perfluorooctanenitrile ($C_7F_{15}CN$). The mixture was stirred at room temperature for 48 h. The reaction product is unstable to distillation or chromatography and therefore was not isolated and used in situ for the following reactions. Spectroscopic data of crude reaction mixture [(3*Z*)-**4f**]: ^1H NMR (300 MHz, $CDCl_3$) δ: 2.36 (d, $^2J_{PH}$= 13.4 Hz, 3H), 3.34 (s, 3H), 5.37 (s, 1H), 7.26–7.76 (m, 10H). ^{31}P NMR (120 MHz, $CDCl_3$) δ: 11.2.

4.3.7. (3*Z*)-4-Methoxycarbonyl-3-trifluoromehyl-1,1,1-trimethyl-2-aza-1λ^5-phosphabuta-1,3-diene (4g). The general procedure A was followed using (methoxycarbonyl)-tetramethylphosphonium bromide (1.15 g) at −35 °C in ether and bubbling trifluoroacetonitrile in excess (CF_3CN) for 12 h. The reaction product is unstable to distillation or chromatography and therefore was not isolated and used in situ for the following reactions. Spectroscopic data of crude reaction mixture [(3*Z*)-**4g**]: ^1H NMR (400 MHz, $CDCl_3$) δ: 1.81 (d, $^2J_{PH}$=12.8 Hz, 9H), 3.67 (s, 3H), 5.44 (d, $^4J_{PH}$=1.4 Hz, 1H). ^{31}P NMR (120 MHz, $CDCl_3$) δ: 22.2. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −71.4.

4.3.8. (3*Z*)-4-Methoxycarbonyl-3-perfluorohepthyl-1,1,1-trimethyl-2-aza-1λ^5-phosphabuta-1,3-diene (4h). The general procedure A was followed using (methoxycarbonyl)-tetramethylphosphonium bromide (1.15 g) in ether at 0 °C and adding dropwise 1.97 g (5 mmol) of perfluorooctanenitrile ($C_7F_{15}CN$). The mixture was stirred at room temperature for 12 h. The reaction product is unstable to distillation or chromatography and therefore was not isolated and used in situ for the following reactions. Spectroscopic data of crude reaction mixture [(3*Z*)-**4h**]: ^1H NMR (300 MHz, $CDCl_3$) δ: 1.70 (d, $^2J_{PH}$=12.8 Hz, 9H), 3.63 (s, 3H), 5.40 (s, 1H). ^{31}P NMR (120 MHz, $CDCl_3$) δ: 19.8. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −81.0, −114.4 to −126.4 (m).

4.3.9. (3*E*/3*Z*)-4-Cyano-3-trifluoromethyl-1,1,1-triphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (4i). The general procedure A was followed using cyanomethyltriphenylphosphonium chloride obtained in situ [from triphenylposphine 1.31 g (5 mmol) and 1-chloroacetonitrile 0.80 mL (12.5 mmol) the mixture was stirred at 70 °C for 12 h] in ether and bubbling trifluoroacetonitrile in excess (CF_3CN) for 24 h to give **4i** as a mixture of isomers 3*E*/3*Z* (60/40). The reaction product is unstable to distillation or chromatography and therefore was not isolated and used in situ for the following reactions. Spectroscopic data of crude reaction mixture [(3*E* and 3*Z*)-**4i**]: ^1H NMR (300 MHz, $CDCl_3$) δ: 3.87 (s, 1H), 4.86 (s, 1H), 7.50–7.78 (m, 30H). ^{31}P NMR (120 MHz, $CDCl_3$) δ: 9.1, 12.8. ^{19}F NMR (282 MHz, $CDCl_3$) δ −67.2, −71.2.

4.3.10. (3*E*)-4-Cyano-3-perfluorohepthyl-1,1,1-triphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (4j). The general procedure A was followed using cyanomethyltriphenylphosphonium chloride (1.69 g) in toluene at 0 °C and adding dropwise 1.97 g (5 mmol) of perfluorooctanenitrile ($C_7F_{15}CN$). The mixture was stirred at room temperature for 48 h. The reaction product is unstable to distillation or chromatography and therefore was not isolated and used in situ for the following reactions. Spectroscopic data of crude reaction mixture [(3*E*)-**4j**]: ^1H NMR (300 MHz, $CDCl_3$) δ: 4.77 (d, $^4J_{PH}$=1.07 Hz, 1H),

7.14–7.79 (m, 15H). ^{31}P NMR (120 MHz, $CDCl_3$) δ: 11.1. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −81.1, −113.8 to −126.5 (m).

4.3.11. (3*E*)-4-Cyano-1,1-diphenyl-1-methyl-3-perfluorohepthyl-2-aza-1λ^5-phosphabuta-1,3-diene (4k). The general procedure B was followed using cyanomethylmethyldiphenyl phosphonium chloride (1.20 g) at 0 °C in toluene and adding dropwise 1.97 g (5 mmol) of perfluorooctanenitrile ($C_7F_{15}CN$). The mixture was stirred at room temperature for 48 h. The reaction product is unstable to distillation or chromatography and therefore was not isolated and used in situ for the following reactions. Spectroscopic data of crude reaction mixture [(3*E*)-**4k**]: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.14 (d, $^2J_{PH}$=13.3 Hz, 3H), 4.74 (s, 1H), 7.18–7.79 (m, 10H). ^{31}P NMR (120 MHz, $CDCl_3$) δ: 14.4. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −81.1 (t, $^3J_{FF}$=10.7 Hz) −111.9 to −126.5 (m).

4.3.12. 4-Cyano-3-trifluoromethyl-1,1,1-trimethyl-2-aza-1λ^5-phosphabuta-1,3-diene (4l). The general procedure B was followed using cyanotetramethylphosphonium chloride (0.76 g) in THF and bubbling trifluoroacetonitrile in excess (CF_3CN) for 12 h to give **4l** (0.90 g, 86%) as a mixture of isomers 3*E*/3*Z* (80/20). ^{1}H NMR (300 MHz, $CDCl_3$) of crude reaction mixture [(3*E* and 3*Z*)-**4l**] δ: 1.72 (d, $^2J_{PH}$=12.8 Hz, 9H), 1.80 (d, $^2J_{PH}$=12.9 Hz, 9H), 4.02 (d, $^4J_{PH}$=0.6 Hz, 1H), 4.71 (s, 1H). Chromatographic separation (10/1, hexane/ethyl acetate) gave 0.54 g (52%) of *E* isomer **4l** as a white solid; mp 133–134 °C ($CHCl_3$/hexane). IR (KBr) ν 2195, 1360 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.72 (d, $^2J_{PH}$=12.8 Hz, 9H), 4.02 (d, $^4J_{PH}$=0.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 13.5 (d, $^1J_{CP}$=68.0 Hz), 70.5, 116.5 (q, $^1J_{CF}$=279 Hz), 117.7, 155.4 (q, $^2J_{CF}$=32 Hz). ^{31}P NMR (120 MHz, $CDCl_3$) δ: 21.5. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −68.5. MS (EI) *m*/*z* 210 (M^+, 100). Anal. Calcd for $C_7H_{10}F_3N_2P$ (210): C, 40.01; H, 4.80; N, 13.33. Found C, 39.96; H, 4.56; N, 13.12.

4.3.13. 4-Cyano-3-perfluoroethyl-1,1,1-trimethyl-2-aza-1λ^5-phosphabuta-1,3-diene (4m). The general procedure B was followed using cyanotetramethylphosphonium chloride (0.76 g) in THF and bubbling perfluoropropanenitrile in excess (C_2F_5CN) for 12 h to give **4m** (0.86 g, 66%) as a mixture of isomers 3*E*/3*Z* (75/25). ^{1}H NMR (300 MHz, $CDCl_3$) of crude reaction mixture [(3*E* and 3*Z*)-**4m**] δ: 1.71 (d, $^2J_{PH}$=12.8 Hz, 9H), 1.80 (d, $^2J_{PH}$=13.0 Hz, 9H), 4.09 (d, $^4J_{PH}$=0.6 Hz, 1H), 4.73 (s, 1H). Chromatographic separation (10/1, hexane/ethyl acetate) gave 0.56 g (43%) of *E* isomer **4m** as a brown solid; mp 143–144 °C ($CHCl_3$/hexane). IR (KBr) 2199, 1371 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.71 (d, $^2J_{PH}$=12.8 Hz, 9H), 4.09 (d, $^4J_{PH}$=0.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 13.8 (d, $^1J_{CP}$=68 Hz), 72.0 (d, $^3J_{CF}$=16 Hz), 111.7 (tq, $^1J_{CF}$=143 Hz, $^3J_{CF}$=37 Hz), 117.7, 118.8 (tq, $^1J_{CF}$=288 Hz, $^3J_{CF}$=37 Hz), 156.3. ^{31}P NMR (120 MHz, $CDCl_3$) δ: 21.3. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −82.4, −115.6 (d, $^2J_{FF}$=7.6 Hz); MS (CI) *m*/*z* 261 (M^++1, 100). Anal. Calcd for $C_8H_{10}F_5N_2P$ (260): C, 36.94; H, 3.87; N, 10.77. Found: C, 36.65; H, 3.58; N, 10.63.

4.3.14. (3*E*)-4-Cyano-3-perfluoroheptyl-1,1,1-trimethyl-2-aza-1λ^5-phosphabuta-1,3-diene (4n). The general procedure B was followed using cyanotetramethylphosphonium chloride (0.76 g) in THF at 0 °C and adding dropwise 1.97 g (5 mmol) of perfluorooctanenitrile ($C_7F_{15}CN$). The mixture was stirred at room temperature for 12 h to give the (*E*) isomer of **4n** as a brown solid (1.02 g, 40%) mp 98–99 °C ($CHCl_3$). IR (KBr) ν 2196, 1379 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.70 (d, $^2J_{PH}$=12.8 Hz, 9H), 4.09 (d, $^4J_{PH}$=0.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2 (d, $^1J_{CP}$=68 Hz), 72.7 (d, $^3J_{CF}$=16 Hz), 110.5–115.7 (m), 117.5, 155.0–157.2 (m). ^{31}P NMR (120 MHz, $CDCl_3$) δ: 21.1. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −81.1, −112.1 to −126.4 (m). MS (CI) *m*/*z* 511 (M^++1, 100). Anal. Calcd for $C_{13}H_{10}F_{15}N_2P$ (510): C, 30.60; H, 1.98; N, 5.49. Found: C, 30.49; H, 1.86; N, 5.47.

4.4. General procedure A for isomerization of (*E*) isomer towards (*Z*) isomer of phosphazenes 4

Purification by colum chromatography of (*E*)-phosphazene **4** (2 mmol) on neutral alumina using ethyl acetate as eluent.

4.5. General procedure B for isomerization of (*E*) isomer towards (*Z*) isomer of phosphazenes 4

A solution of (*E*)-phosphazene **4** or a mixture of *E*/*Z* isomers of phosphazene (2 mmol) in toluene under N_2, was stirred at reflux (110 °C), until ^{1}H NMR of crude reaction mixture indicated the disappearance of (*E*)-isomer of phosphazene.

4.5.1. (3*Z*)-3-Trifluoromethyl-1,1,1,4-tetraphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (4a). The general procedure A was followed using (3*E*)-1,1,1,4-tetraphenyl-3-trifluoromethyl-2-aza-1λ^5-phosphabuta-1,3-diene (**4a**) and 0.54 g (60%) of (3*Z*)-**4a** were obtained. When the general procedure B was followed for 12 h, 0.88 g (98%) of (3*Z*)-**4a** were obtained. In both cases evaporation of solvent and crystallization from ethyl acetate give a yellow solid mp 121–122 °C. IR (KBr) ν 1613, 1467 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.23 (s, 1H), 7.05–7.81 (m, 20H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 112.6–112.8 (m), 122.5 (dq, $^1J_{CF}$=279.0 Hz, $^3J_{CP}$=3.7 Hz), 125.9–133.7 (m), 133.7 (q, $^2J_{CF}$=29.5 Hz). ^{31}P NMR (120 MHz, $CDCl_3$) δ: 2.13; ^{19}F NMR (282 MHz, $CDCl_3$) δ −68.2. MS (EI) *m*/*z* 447 (M^+, 100). Anal. Calcd for $C_{27}H_{21}F_3NP$ (447): C, 72.48; H, 4.73; N, 3.13. Found: C, 72.22; H, 4.70; N, 3.10.

4.5.2. (3*Z*)-3-Perfluoroethyl-1,1,1,4-tetraphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (4b). The general procedure A was followed using (3*E*)-3-perfluoroethyl-1,1,1,4-tetraphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (**4b**) and 0.61 g (62%) of (3*Z*)-**4b** were obtained. When the general procedure B was followed for 12 h, 0.97 g, (98%)of (3*Z*)-**4b** were obtained. In both cases evaporation of solvent and crystallization from ethyl acetate give a yellow solid mp 97–98 °C (ethyl acetate). IR (KBr): ν 1626, 1328, 1150 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.17 (s, 1H), 7.08–7.67 (m, 20H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 112.4 (tq, $^1J_{CP}$=259.8 Hz, $^2J_{CF}$=36.7 Hz), 115.3 (t, $^3J_{CF}$=7.3 Hz), 119.4 (tq, $^1J_{CF}$=287.0 Hz, $^2J_{CF}$=39.8 Hz), 125.8–132.9 (m), 133.5 (t, $^2J_{CF}$=21.9 Hz). ^{31}P NMR (120 MHz, $CDCl_3$) δ: 2.35. ^{19}F NMR (282 MHz, $CDCl_3$) δ : −66.3, −96.5. MS (EI) *m*/*z* 497 (M^+, 76). Anal. Calcd for $C_{28}H_{21}F_5NP$ (497):

C, 67.61; H, 4.25; N, 2.82. Found: C, 67.70; H, 4.29; N, 2.79.

4.5.3. (3*Z*)-3-Perfluorohepthyl-1,1,1,4-tetraphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (4c). The general procedure B was followed using (3*E*)-3-perfluorohepthyl-1,1,1,4-tetraphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (**4c**) for 12 h, and 1.46 g (98%) of (3*Z*)-**4c** were obtained. Evaporation of solvent give a yellow oil; R_f=0.13 (1/10, ethyl acetate/hexane). IR (KBr) ν 1612, 1438, 1206 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.07 (s, 1H), 6.93–7.82 (m, 20H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 107.2–119.1 (m), 125.8–137.3 (m). ^{31}P NMR (120 MHz, $CDCl_3$) δ: 1.44. ^{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). MS (EI) *m*/*z* 747 (M^+, 69). Anal. Calcd for $C_{33}H_{21}F_{15}NP$ (747): C, 53.03; H, 2.83; N, 1.87. Found: C, 52.90; H, 2.86; N, 1.86.

4.5.4. (3*Z*)-4-Cyano-3-trifluoromethyl-1,1,1-triphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (4i). The general procedure B was followed for 24 h using a mixture of 3*E*/3*Z* (60/40) of 4-cyano-3-trifluoromethyl-1,1,1-triphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (**4i**) prepared in situ. Evaporation of solvent and crystallization gave the (*Z*) isomer of **4i** (0.68 g, 86%) as a white solid mp 122–123 °C (hexane/ethyl acetate). IR (KBr) ν 2207, 1432 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.86 (s, 1H), 7.50–7.78 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 75.8, 119.1, 120.5 (q, $^1J_{CF}$=280 Hz), 128.6–132.7 (m), 152.6 (q, $^2J_{CF}$=32 Hz). ^{31}P NMR (120 MHz, $CDCl_3$) δ: 9.03. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −71.2. MS (EI) *m*/*z* 396 (M^+, 100). Anal. Calcd for $C_{22}H_{16}F_3N_2P$ (396): C, 66.67; H, 4.07; N, 7.07. Found: C, 66.76; H, 3.86; N, 7.17.

4.5.5. (3*Z*)-4-Cyano-3-trifluoromethyl-1,1,1-trimethyl-2-aza-1λ^5-phosphabuta-1,3-diene (4l). The general procedure B was followed for 4 h using (3*E*)-4-cyano-3-trifluoromethyl-1,1,1-trimethyl-2-aza-1λ^5-phosphabuta-1,3-diene (**4l**). Evaporation of solvent gave the (*Z*) isomer of **4l** (0.38 g, 91%) as a yelow oil; R_f=0.17 (ethyl acetate). IR (KBr) ν 2175, 1295 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.80 (d, $^2J_{PH}$=12.9 Hz, 9H), 4.71 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.8 (d, $^1J_{CP}$=69 Hz), 69.8 (dd, $^3J_{CP}$=11 Hz, $^3J_{CF}$=4 Hz), 121.8 (dq, $^1J_{CF}$=253 Hz, $^3J_{CP}$=27 Hz), 121.6, 154.7 (q, $^2J_{CF}$=31 Hz). ^{31}P NMR (120 MHz, $CDCl_3$) δ: 19.7. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −72.5. M/S (EI) *m*/*z* 210 (M^+, 84). Anal. Calcd for $C_7H_{10}F_3N_2P$ (210): C, 40.01; H, 4.80; N, 13.33. Found C, 40.09; H, 4.65; N, 13.27.

4.5.6. (3*Z*)-4-Cyano-3-perfluoroethyl-1,1,1-trimethyl-2-aza-1λ^5-phosphabuta-1,3-diene (4m). The general procedure B was followed for 120 h using (3*E*)-4-cyano-3-perfluoroethyl-1,1,1-trimethyl-2-aza-1λ^5-phosphabuta-1,3-diene (**4m**). Evaporation of solvent and crystallization gave the (*Z*) isomer of **4m** (0.49 g, 95%) as a brown solid; mp 43–44 °C (ethyl acetate). IR (KBr) ν 2189, 1326 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.80 (d, $^2J_{PH}$=13 Hz, 9H), 4.73 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ =17.9 (d, $^1J_{CP}$=69 Hz), 70.7, 110.2–111.5 (m), 118.8 (tq, $^1J_{CF}$=287 Hz, $^2J_{CF}$=38 Hz), 121.9, 154.4–155.1 (m). ^{31}P NMR (120 MHz, $CDCl_3$) δ: 18.8. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −81.9, −118.2. MS (EI) *m*/*z* 260 (M^+, 85). Anal. Calcd for $C_8H_{10}F_5N_2P$ (260): C, 36.94; H, 3.87; N, 10.77. Found C, 36.89; H, 3.75; N, 10.72.

4.5.7. (3*Z*)-4-Cyano-3-perfluorohepthyl-1,1,1-trimethyl-2-aza-1λ^5-phosphabuta-1,3-diene (4n). The general procedure B was followed for 120 h using (3*E*)-4-cyano-3-perfluorohepthyl-1,1,1-trimethyl-2-aza-1λ^5-phosphabuta-1,3-diene (**4n**). Evaporation of solvent and crystallization gave the (*Z*) isomer of **4n** (0.87 g, 85%) as a white solid; mp 90–91 °C ($CHCl_3$). IR (KBr) ν 2211, 1248 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.80 (d, $^2J_{PH}$=12.9 Hz, 9H), 4.71 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 18.0 (d, $^1J_{CP}$=69 Hz), 70.8, 110.5–115.7 (m), 122, 157.0–157.5 (m). ^{31}P NMR (120 MHz, $CDCl_3$) δ: 18.9. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −81.1 (t, $^3J_{FF}$=9 Hz), −118.1 to −126.4 (m). MS (EI) *m*/*z* 510 (M^+, 95). Anal. Calcd for $C_{13}H_{10}F_{15}N_2P$ (510): C, 30.60; H, 1.98; N, 5.49. Found: C, 30.69; H, 2.02; N, 5.51.

4.6. General procedure for preparation of azadienes 6

Aldehyde (2 mmol) was added to a 0–10 °C solution of phosphazene **4** (2 mmol) in $CHCl_3$, toluene or xylenes under N_2, and the mixture was stirred at room temperature or reflux, until TLC indicated the disappearance of phosphazene.

4.6.1. (1*E*,3*E*)-1-Ethoxycarbonyl-4-phenyl-3-trifluoromethyl-2-azabuta-1,3-diene (6a). The general procedure was followed using (3*E*)-3-trifluoromethyl-1,1,1,4-tetraphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (0.89 g) **4a** and ethyl glyoxalate (0.20 g) for 1 h at room temperature in $CHCl_3$. The reaction product is unstable to distillation or chromatography and therefore was not isolated and used in situ for the following reactions. Spectroscopic data of crude reaction mixture (**6a**+Ph_3PO): ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.26 (t, *J*=7.1 Hz, 3H), 4.26 (q, *J*=7.1 Hz, 2H), 6.89 (s, 1H), 7.09–7.56 (m, 20H), 7.82 (s, 1H). ^{19}F NMR (282 MHz, $CDCl_3$) δ: −71.2.

4.6.2. (1*E*,3*E*)-1-Ethoxycarbonyl-4-phenyl-3-perfluoroethyl-2-azabuta-1,3-diene (6b). The general procedure was followed using (3*E*)-3-perfluoroethyl-1,1,1,4-tetraphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (0.99 g) **4b** and ethyl glyoxalate (0.20 g) for 2 h at room temperature in $CHCl_3$. The reaction product is unstable to distillation or chromatography and therefore was not isolated and used in situ for the following reactions. Spectroscopic data of crude reaction mixture (**6b**+Ph_3PO): ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.46 (t, *J*=7.2 Hz, 3H), 4.45 (q, *J*=7.2 Hz, 2H), 6.85 (s, 1H), 7.40–7.80 (m, 20H), 7.90 (s, 1H). ^{19}F NMR (282 MHz, $CDCl_3$) δ: −62.0, −93.6.

4.6.3. (1*E*,3*E*)-1-Ethoxycarbonyl-4-phenyl-3-perfluorohepthyl-2-azabuta-1,3-diene (6c). The general procedure was followed using (3*E*)-4-phenyl-3-perfluorohepthyl-1,1,1-triphenyl-2-aza-1λ^5-phosphabuta-1,3-diene (1.50 g) **4c** and ethyl glyoxalate (0.20 g) for 0.5 h at room temperature in $CHCl_3$. The reaction product is unstable to distillation or chromatography and therefore was not isolated and used in situ for the following reactions. Spectroscopic data of crude reaction mixture (**6c**+Ph_3PO): ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.22 (t, *J*=7.2 Hz, 3H), 4.21 (q, *J*=7.2 Hz, 2H), 6.63 (s, 1H),

7.16–7.59 (m, 20H), 7.70 (s, 1H). ^{19}F NMR (282 MHz, $CDCl_3$) δ: −81.1 (t, $^3J_{FF}$=9.2 Hz), −111.3 to −126.5 (m).

4.6.4. (1*E*,3*Z*)-4-Methoxycarbonyl-1-(4-nitrophenyl)-3-trifluoromethyl-2-azabuta-1,3-diene (6d). The general procedure was followed using (3*Z*)-4-methoxycarbonyl-3-trifluoromethyl-1,1,1-trimethyl-2-aza-1λ^5-phosphabuta-1,3-diene **4g** obtained in situ and 4-nitrobenzaldehyde (0.31 g) for 3 h at 110 °C in toluene. The reaction product is unstable to distillation or chromatography and therefore was not isolated and used for the following reactions. Spectroscopic data of crude reaction mixture (**6d**+Me_3PO). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.53 (d, $^2J_{HP}$=12.9 Hz, 9H), 3.71 (s 3H), 5.96 (s, 1H), 8.10 (d, J=8.8 Hz, 2H), 8.36 (d, J=8.8 Hz, 2H), 8.50 (s, 1H). ^{19}F NMR (282 MHz, $CDCl_3$) δ: −70.8.

4.6.5. (1*E*,3*Z*)-1-(2,4-Dinitrophenyl)-4-methoxycarbonyl-3-trifluoromethyl-2-azabuta-1,3-diene (6e). The general procedure was followed using (3*Z*)-4-methoxycarbonyl-3-trifluoromethyl-1,1,1-trimethyl-2-aza-1λ^5-phosphabuta-1,3-diene **4g** obtained in situ and 2,4-dinitrobenzaldehyde (0.39 g) for 3 h at 110 °C in toluene. The reaction product is unstable to distillation or chromatography and therefore was not isolated and used for the following reactions. Spectroscopic data of crude reaction mixture (**6e**+Me_3PO). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.53 (d, $^2J_{HP}$=12.9 Hz, 9H), 3.73 (s, 3H), 5.98 (s, 1H), 8.48 (d, J=8.5 Hz, 1H), 8.61 (dd, J=8.5, 2.1 Hz, 1H), 8.93 (s, 1H), 8.99 (d, J=2.1 Hz, 1H). ^{19}F NMR (282 MHz, $CDCl_3$) δ: −70.6.

4.6.6. (1*E*,3*Z*)-4-Cyano-1-(4-nitrophenyl)-3-trifluoromethyl-2-azabuta-1,3-diene (6f). The general procedure was followed using (3*Z*)-4-cyano-3-trifluoromethyl-1,1,1-trimethyl-2-aza-1λ^5-phosphabuta-1,3-diene **4l** (0.42 g) and 4-nitrobenzaldehyde (0.31 g) for 2 h at 110 °C in toluene. Chromatographic separation (10/1, hexane/ethyl acetate) gave 0.24 g (45%) of **6f** as a yellow oil; R_f=0.50 (1/5, ethyl acetate/hexane). When (3*E*)-4-cyano-3-trifluoromethyl-1,1,1-trimethyl-2-aza-1λ^5-phosphabuta-1,3-diene **4l** (0.42 g) was used the mixture was stirred for 3 h at 110 °C in toluene and chromatographic separation (10/1, hexane/ethyl acetate) gave 0.19 g (35%) of **6f**. IR (KBr) ν 2204, 1708 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.56 (s, 1H), 8.14 (d, J=8.8 Hz, 2H), 8.37 (d, J=8.8 Hz, 2H), 8.68 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 87.7, 113.5, 119.5 (q, $^1J_{CF}$=276 Hz), 124.2, 130.9, 138.5, 150.7, 155.7 (q, $^2J_{CF}$=33 Hz), 165.3. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −69.8. MS (EI) m/z 269 (M^+, 100).

4.6.7. (1*E*,3*Z*)-4-Cyano-1-(2,4-dinitrophenyl)-3-trifluoromethyl-2-azabuta-1,3-diene (6g). The general procedure was followed using a mixture 80/20 of (3*E*/3*Z*)-4-cyano-3-trifluoromethyl-1,1,1-trimethyl-2-aza-1λ^5-phosphabuta-1,3-diene **4l** (0.42 g) and 2,4-dinitrobenzaldehyde (0.39 g) for 12 h at 61 °C in $CHCl_3$. Chromatographic separation (10/1, hexane/ethyl acetate) gave 0.29 g (45%) of **6g** as an orange oil; R_f=0.48 (1/5, ethyl acetate/hexane). When (3*E*)-4-cyano-3-trifluoromethyl-1,1,1-trimethyl-2-aza-1λ^5-phosphabuta-1,3-diene **4l** (0.42 g) was used the mixture was stirred for 6 h at 110 °C in toluene and chromatographic separation (10/1, hexane/ethyl acetate) gave 0.19 g (30%) of **6g**. IR (KBr) ν 2210, 1708 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.67 (s, 1H), 8.47 (d, J=8.5 Hz, 1H), 8.61 (dd, J=8.5, 2.1 Hz, 1H), 9.01 (d, J=2.1 Hz, 1H), 9.19 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 90.0, 112.9, 119.3 (q, $^1J_{CF}$=277 Hz), 120.6, 128.2, 132.1, 133.4, 149.3, 149.9, 154.6 (q, $^2J_{CF}$=34 Hz), 162.5. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −69.5. M/S (EI) m/z 314 (M^+, 4).

4.6.8. (1*E*,3*Z*)-4-Cyano-1-(4-nitrophenyl)-3-perfluoroethyl-2-azabuta-1,3-diene (6h). The general procedure was followed using a mixture 75/25 of (3*E*/3*Z*)-4-cyano-3-perfluoroethyl-1,1,1-trimethyl-2-aza-1λ^5-phosphabuta-1,3-diene **4m** (0.52 g) and 4-nitrobenzaldehyde (0.31 g) for 120 h at 120 °C in toluene. The reaction product is unstable to distillation or chromatography and therefore was not isolated and used for the following reactions. Spectroscopic data of crude reaction mixture (**6h**+Me_3PO): ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.53 (d, $^2J_{HP}$=12.9 Hz, 9H), 5.50 (s, 1H), 8.10 (d, $^3J_{HH}$=8.6 Hz, 2H), 8.37 (d, $^3J_{HH}$=8.8 Hz, 2H), 8.65 (s, 1H).^{19}F NMR (282 MHz, $CDCl_3$) δ: −82.4, −114.3.

4.6.9. (1*E*,3*Z*)-4-Cyano-1-(4-nitrophenyl)-3-perfluoroheptyl-2-azabuta-1,3-diene (6i). The general procedure was followed using (3*Z*)-4-cyano-3-perfluoroepthyl-1,1,1-trimethyl-2-aza-1λ^5-phosphabuta-1,3-diene **4n** (1.02 g) and 4-nitrobenzaldehyde (0.31 g) for 120 h at 110 °C in toluene. When (3*E*)-4-cyano-3-perfluoroepthyl-1,1,1-trimethyl-2-aza-1λ^5-phosphabuta-1,3-diene **4n** (1.02 g) was used the mixture was stirred for 138 h at 110 °C in toluene. The reaction product is unstable to distillation or chromatography and therefore was not isolated and used for the following reactions. Spectroscopic data of crude reaction mixture (**6i**+Me_3PO): ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.53 (d, $^2J_{HP}$=12.9 Hz, 9H), 5.47 (s, 1H), 8.10 (d, J=8.7 Hz, 2H), 8.36 (d, J=8.7 Hz, 2H), 8.66 (s, 1H). ^{19}F NMR (282 MHz, $CDCl_3$) δ: −81.1, −115.4 to −126.4 (m).

4.6.10. (1*E*,3*Z*)-4-Cyano-1-(2,4-dinitrophenyl)-3-perfluorohepthyl-2-azabuta-1,3-diene (6j). The general procedure was followed using (3*E*)-4-cyano-3-perfluoroheptyl-1,1,1-trimethyl-2-aza-1λ^5-phosphabuta-1,3-diene **4n** (1.02 g) and 2,4-dinitrobenzaldehyde (0.39 g) for 192 h at 120 °C in toluene. The reaction product is unstable to distillation or chromatography and therefore was not isolated and used for the following reactions. Spectroscopic data of crude reaction mixture (**6j**+Me_3PO): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.53 (d, $^2J_{HP}$=12.9 Hz, 9H), 5.56 (s, 1H), 8.39 (d, J=8.4 Hz, 1H), 8.63 (dd, J=8.3, 1.4 Hz, 1H), 9.04 (d, J=1.5 Hz, 1H), 9.17 (s, 1H). ^{19}F NMR (282 MHz, $CDCl_3$) δ: −81.0, −118.1 to −126.3 (m).

4.7. General procedure for reactions of 2-azadienes (6) with enamines (9)

Enamine (5 mmol) was added to a 0–10 °C solution of azadiene **6** (5 mmol) in $CHCl_3$ or toluene (15 mL) under N_2, and the mixture was stirred to adequate temperature, until TLC indicated the disappearance of azadiene.

4.7.1. Reaction of 2-azadiene (6a) with enamine (9a).

4.7.1.1. 1-Ethoxycarbonyl-3-trifluoromethyl-4-phenyl-4a-pyrrolidyl-1,4,5,6,7,8-hexahydroisoquinoline (10). The general procedure was followed using (1*E*,3*E*)-1-

ethoxycarbonyl-4-phenyl-3-trifluoromethyl-2-azabuta-1,3-diene **6a** obtained in situ and 1-cyclohex-1-enylpyrrolidine **9a** (0.23 g) at room temperature in $CHCl_3$ for 15 h. Chromatographic separation (15/1, hexane/ethyl acetate) gave 0.51 g (80%) of **10** as a yellow oil; R_f=0.42 (1/5, ethyl acetate/hexane). IR (KBr) ν 1733, 1193 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.09–1.72 (m, 16H), 2.41 (s, 1H), 2.53–2.56 (m, 1H), 2.86–2.88 (m, 1H), 3.06–3.09 (m, 1H), 3.84 (s, 1H), 4.30–4.36 (m, 2H), 4.79 (d, J=9.8 Hz, 1H), 7.23–7.37 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 19.3, 20.6, 22.5, 24.8, 25.2, 32.3, 32.5, 43.2, 43.7, 49.2, 56.6, 61.7, 65.2, 119.3 (q, $^1J_{CF}$=280.8 Hz), 127.7–135.7 (m), 161.4 (q, $^2J_{CF}$=32.0 Hz), 171.6. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −71.3. MS (EI) m/z 422 (M^+, 2). Anal. Calcd for $C_{23}H_{29}F_3N_2O_2$ (422): C, 65.39; H, 6.92; N, 6.63. Found C, 65.41; H, 6.90; N, 6.68.

4.7.1.2. 1-Ethoxycarbonyl-3-trifluoromethyl-4-phenyl-5,6,7,8-tetrahydroisoquinoline (12). The general procedure was followed using (1*E*,3*E*)-1-ethoxycarbonyl-4-phenyl-3-trifluoromethyl-2-azabuta-1,3-diene **6a** obtained in situ and 1-cyclohex-1-enylpyrrolidine **9a** (0.23 g) in refluxing toluene (110 °C) for 48 h. Chromatographic separation (10/1, hexane/ethyl acetate) gave 0.70 g (40%) of **12** as a yellow oil; R_f=0.25 (1/10, ethyl acetate/hexane). IR (KBr) ν 1738, 1210 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 0.94 (t, J=7.1 Hz, 3H), 1.88–2.00 (m, 4H), 2.82 (t, J=6.2 Hz, 2H), 3.08 (t, J=6.4 Hz 2H), 4.00 (q, J=7.1 Hz, 2H) 7.26–7.40 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.6, 22.0, 22.3, 26.1, 32.7, 61.6, 122.0 (q, $^1J_{FC}$=33.0 Hz), 123.2–157.3 (m), 166.4. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −61.3. MS (70 eV) m/z 349 (M^+, 5). Anal. Calcd for $C_{19}H_{18}F_3NO_2$ (349): C, 65.32; H, 5.19; N, 4.01. Found C, 65.29; H, 5.23; N, 3.98.

4.7.2. Reaction of 2-azadiene (6f) with enamine (9a).

4.7.2.1. 4-Cyano-1-(4-nitrophenyl)-3-trifluoromethyl-1,2,6,7,8,8a-hexahydroisoquinoline (13a) and 4-cyano-1-(4-nitrophenyl)-3-trifluoromethyl-5,6,7,8-tetrahydroisoquinoline (14a). The general procedure was followed using (1*E*,3*Z*)-4-cyano-1-(4-nitrophenyl)-3-trifluoromethyl-2-azabuta-1,3-diene **6f** obtained in situ and 1-cyclohex-1-enylpyrrolidine **9a** (0.23 g) at room temperature in $CHCl_3$ for 2 h. Chromatographic separation (10/1, hexane/ethyl acetate) gave 0.20 g (29%) of **13a** as a brown solid mp 156–157 °C (CH_2Cl_2/hexane) and 0.20 g (29%) of **14a** as a brown oil R_f=0.42 (1/5, ethyl acetate/hexane). *Data for* **13a**: IR (KBr) ν 3296, 2211, 1522 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.06–2.44 (m, 7H), 4.00 (d, J=10.7 Hz, 1H), 4.76 (s, 1H), 6.21 (s, 1H), 7.52 (d, J=8.7 Hz, 2H), 8.30 (d, J=8.8 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 21.5, 25.4, 29.6, 39.6, 61.1, 85.3, 114.7, 119.9 (q, $^1J_{CF}$=276 Hz), 124.3, 126.2, 127.3, 128.7, 140.0 (q, $^2J_{CF}$=33 Hz), 145.5, 148.2. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −66.6. MS (EI) m/z 349 (M^+, 5). Anal. Calcd for $C_{17}H_{14}F_3N_3O_2$ (349): C, 58.45; H, 4.04; N, 12.03. Found C, 58.91; H, 3.93; N, 12.13. *Data for* **14a**: IR (KBr) ν 2234, 1522 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.84 (m, 2H), 1.97 (m, 2H), 2.79 (t, J=6.4 Hz, 2H), 3.16 (t, J=6.1 Hz, 2H), 7.74 (d, J=8.8 Hz, 2H), 8.36 (d, J=8.8 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 21.0, 21.7, 107.4, 112.6, 120.3 (q, $^1J_{CF}$=276 Hz), 123.6, 130.1, 135.2, 143.9, 146.8 (q, $^2J_{CF}$=35 Hz), 148.2, 153.9, 158.5. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −65.9. MS (EI) m/z 347 (M^+, 100). Anal. Calcd for $C_{17}H_{12}F_3N_3O_2$ (347): C, 58.79; H, 3.48; N, 12.10. Found C, 58.81; H, 3.53; N, 12.07.

4.7.3. Reaction of 2-azadiene (6g) with enamine (9a).

4.7.3.1. 4-Cyano-1-(2,4-dinitrophenyl)-3-trifluoromethyl-1,2,6,7,8,8a-hexahydroisoquinoline (13b) and 4-cyano-1-(2,4-dinitrophenyl)-3-trifluoromethyl-5,6,7,8-tetrahydroisoquinoline (14b). The general procedure was followed using (1*E*,3*Z*)-4-cyano-1-(2,4-dinitrophenyl)-3-trifluoromethyl-2-azabuta-1,3-diene (**6g**, 1.57 g) and 1-cyclohex-1-enylpyrrolidine **9a** (0.23 g) at room temperature in $CHCl_3$ for 3 h. After column chromatography (hexane/ethyl acetate 10/1) a mixture (1.348 g) of compounds **13b** and **14b** (6/1) was obtained. Spectroscopic data of mixture **13b** and **14b**: ^1H NMR (300 MHz, $CDCl_3$) δ: 1.11–2.35 (m, 11H), 2.48 (m, 2H), 3.16 (t, J=6.1 Hz, 2H), 4.66 (d, J=10.4 Hz, 1H), 5.38 (s, 1H), 6.21 (s, 1H), 7.64 (d, J=8.4 Hz, 1H), 7.90 (d, J=8.7 Hz, 1H), 8.54 (dd, J=8.7, 2.2 Hz, 1H), 8.62 (dd, J=8.4, 2.3 Hz, 1H), 8.70 (d, J=2.1 Hz, 1H) 9.09 (d, J=2.3 Hz, 1H).^{19}F NMR (282 MHz, $CDCl_3$) δ: −65.8, −71.5. Compound **13b** is unstable and the separation of both products was not possible. Therefore *p*-benzoquinone (0.15 g) was added to a solution of (0.39 g) of **13b** and **14b** mixture in dioxane and was heated at 80 °C for 144 h. Evaporation of solvent and chromatographic separation (10/1, hexane/ethyl acetate) gave 0.27 g (70%) of **14b** as a brown oil; R_f=0.40 (1/5, ethyl acetate/hexane). *Data for* **14b**: IR (KBr) ν 2210. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.85 (m, 2H), 1.96 (m, 2H), 2.48 (m, 2H), 3.16 (t, J=6.1 Hz, 2H), 7.64 (d, J=8.4 Hz, 1H), 8.62 (dd, J=8.4, 2.3 Hz, 1H), 9.09 (d, J=2.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.9, 21.3, 26.7, 28.6, 108.2, 112.3, 118.3 (q, $^1J_{CF}$=269 Hz) 120.7, 128.1, 132.4, 135.2, 139.0, 147.5.(q, $^2J_{CF}$=42 Hz), 148.3, 153.7, 156.7. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −65.8. MS (EI) m/z 392 (M^+, 11).

4.7.4. Reaction of 2-azadiene (6e) with enamine (9b).

4.7.4.1. 5-Isopropyl-6-(2,4-dinitrophenyl)-2-trifluoromethyl-1,2-dihydropiridine-3-carboxylic acid methyl ester (15a) and 5-isopropyl-6-(2,4-dinitrophenyl)-2-trifluoromethylnicotinic acid methyl ester (16a). The general procedure was followed using (1*E*,3*Z*)-1-(2,4-dinitrophenyl)-4-methoxycarbonyl-3-trifluoromethyl-2-azabuta-1,3-diene **6e** obtained in situ and *trans* 3-methyl-1-pyrrolidyl-but-1-ene **9b** (0.67 g) at room temperature in $CHCl_3$ for 3 h. Chromatographic separation (10/1, hexane/ethyl acetate) gave 0.72 g (35%) of **15a** as a brown oil; R_f=0.26 (1/5, ethyl acetate/hexane) and 0.88 g (43%) of **16a** as a brown oil; R_f=0.39 (1/5, ethyl acetate/hexane), 0.09 g of **18a** (7%) and 0.06 g of **19** (9%).[26] *Data for* **15a**: IR (KBr) ν 3362, 2867, 1692 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.88 (d, J=6.8 Hz, 3H), 0.93 (d, J=6.8 Hz, 3H), 1.90 (dq, J=6.8 Hz, 1H), 3.82 (s, 3H), 4.30 (d, J=5.6 Hz, 1H), 5.21 (dq, $^3J_{HF}$=7.3 Hz, J=6.7 Hz, 1H), 7.45 (s, 1H), 7.72 (d, J=8.3 Hz, 1H), 8.53 (dd, J=8.3, 2.1 Hz, 1H), 8.81 (d, J=2.2 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 21.1, 23.3, 28.1, 51.9, 52.1 (q, $^2J_{CF}$=32 Hz), 117.1, 118.3 (q, $^1J_{CF}$=284 Hz), 119.7, 127.5, 134.4, 135.9, 136.2, 136.6, 142.5, 148.1, 148.4, 165.6. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −81.3. MS (EI) m/z 415 (M^+, 3). *Data for* **16a**: IR (KBr) ν 2873, 1744, 1601 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.23 (d, J=6.7 Hz, 6H), 2.76 (m, J=6.8 Hz, 1H), 4.02 (s, 3H), 7.65

(d, J=8.2 Hz, 1H), 8.17 (s, 1H), 8.59 (dd, J=8.3, 2.2 Hz, 1H), 9.05 (d, J=2.1 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 23.2, 30.1, 53.4, 120.1, 120.5, 120.6 (q, $^1J_{CF}$=275 Hz), 127.6, 132.8, 136.9, 139.5, 145.2, 148.1, 153.7–154.1 (m), 154.3, 165.7. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −64.6. MS (EI) m/z 413 (M^+, 5). ^{1}H NMR (300 MHz, $CDCl_3$) for **18a** δ: 1.22 (d, J=6.7 Hz, 6H), 3.02–3.11 (m, 1H), 7.58 (d, J=8.4 Hz, 1H), 7.70 (s, 1H), 8.49 (dq, J=8.4, 2.4 Hz, 1H), 9.06 (d, J=2.4 Hz, 1H), 9.63 (s, 1H).

4.7.5. Reaction of 2-azadiene (6d) with enamine (9b).

4.7.5.1. 5-Isopropyl-6-(4-nitrophenyl)-2-trifluoromethyl-1,2-dihydropiridine-3-carboxylic acid methyl ester (15b). The general procedure was followed using (1*E*,3*Z*)-4-methoxycarbonyl-1-(4-nitrophenyl)-3-trifluoromethyl-2-azabuta-1,3-diene **6d** obtained in situ and *trans* 3-methyl-1-pyrrolidylbut-1-ene **9b** (0.67 g) at 120 °C in toluene for 24 h. Chromatographic separation (10/1, hexane/ethyl acetate) gave 1.11 g (60%) of **15b** as an orange solid; mp 155–157 °C (hexane/CH_2Cl_2). IR (KBr) ν 3426, 2852, 1679 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.96 (d, J=6.8 Hz, 3H), 1.19 (d, J=6.9 Hz, 3H), 2.48 (dq, J=6.9, 6.8 Hz, 1H), 3.85 (s, 3H), 4.15 (d, J=5.2 Hz, 1H) 5.20 (q, $^3J_{HF}$=7.5 Hz, $^3J_{HH}$=5.6 Hz, 1H), 7.57 (d, J=8.8 Hz, 2H), 7.58 (s, 1H), 8.30 (d, J=8.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 23.7, 29.7, 52.6–53.2 (m), 53.3, 117.0, 119.4 (q, $^1J_{CF}$=285 Hz), 123.7, 130.2, 137.2, 141.6, 144.5, 145.1, 148.1, 165.9. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −64.8. MS (EI) m/z 370 (M^+, 9). Anal. Calcd for $C_{17}H_{17}F_3N_2O_4$ (370): C, 55.14; H, 4.63; N, 7.56. Found: C, 55.22; H, 4.72; N, 7.61.

4.7.5.2. 5-Isopropyl-6-(4-nitrophenyl)-2-trifluoromethylnicotinic acid methyl ester (16b). *p*-Benzoquinone (0.32 g, 3 mmol) was added to a solution of **15b** (0.74 g, 2 mmol) in dioxane and the mixture was heated at 80 °C for 48 h. Evaporation of solvent and chromatographic separation (10/1, hexane/ethyl acetate) gave 0.53 g (72%) of **16b** as a green solid; mp 145–146 °C (hexane/ethyl acetate). IR (KBr) ν 1727, 1606, 1522 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.26 (d, J=6.9 Hz, 6H), 3.17 (q, J=6.9 Hz, 1H), 4.00 (s, 3H), 7.68 (d, J=8.8 Hz, 2H), 8.15 (s, 1H), 8.35 (d, J=8.8 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 23.7, 29.2, 53.3, 120.9 (q, $^1J_{CF}$=275 Hz), 123.7, 130.1, 137.1, 142.8 (q, $^2J_{CF}$=37 Hz), 144.5, 145.1, 148.1, 156.9, 165.9. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −64.7. MS (EI) m/z 368 (M^+, 47). Anal. Calcd for $C_{17}H_{15}F_3N_2O_4$ (368): C, 55.44; H, 4.11; N, 7.61. Found: C, 55.99; H, 4.23; N, 7.58.

4.7.6. Reaction of 2-azadiene (6f) with enamine (9b).

4.7.6.1. 5-Isopropyl-6-(4-nitrophenyl)-2-trifluoromethyl-3-cyanopiridine (16c). The general procedure was followed using (1*E*,3*Z*)-4-cyano-1-(4-nitrophenyl)-3-trifluoromethyl-2-azabuta-1,3-diene **6f** (1.35 g) and *trans* 3-methyl-1-pyrrolidylbut-1-ene **9b** (0.67 g) at room temperature in $CHCl_3$ for 3 h. Chromatographic separation (10/1, hexane/ethyl acetate) gave 0.87 g (52%) of **16c** as a white solid; mp 143–144 °C (hexane/ethyl acetate). IR (KBr) ν 2234, 1600, 1526 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.28 (d, J=6.8 Hz, 6H), 3.22 (dq, J=6.8 Hz, 1H), 7.69 (d, J=8.9 Hz, 2H), 8.22 (s, 1H), 8.39 (d, J=8.9 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 23.6, 29.3, 107.3, 113.7, 120.1 (q, $^1J_{CF}$=276 Hz), 123.8, 130.1, 141.3, 143.5, 145.7, 146.4 (q, $^2J_{CF}$=36 Hz), 148.4, 158.4. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −65.9. MS (EI) m/z 334 (M^+−1, 35). Anal. Calcd for $C_{16}H_{12}F_3N_3O_2$ (335): C, 57.32; H, 3.61; N, 12.53. Found: C, 57.33; H, 3.65; N, 12.50.

4.7.7. Reaction of 2-azadiene (6g) with enamine (9b).

4.7.7.1. 5-Isopropyl-6-(2,4-dinitrophenyl)-2-trifluoromethyl-3-cyanopiridine (16d). The general procedure was followed using (1*E*,3*Z*)-4-cyano-1-(2,4-dinitrophenyl)-3-trifluoromethyl-2-azabuta-1,3-diene **6g** (1.57 g) and *trans* 3-methyl-1-pyrrolidylbut-1-ene **9b** (0.67 g) at room temperature in $CHCl_3$ for 3 h. Chromatographic separation (10/1, hexane/ethyl acetate) gave 1.22 g (64%) of **16d** as an orange solid; mp 96–97 °C (hexane/ethyl acetate). IR (KBr) ν 2240, 1731, 1602 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.25 (d, J=6.9 Hz, 6H), 2.76 (dq, J=6.9 Hz, 1H), 7.65 (d, J=8.4 Hz, 1H), 8.24 (s, 1H), 8.64 (dd, J=8.3, 2.2 Hz, 1H), 9.10 (d, J=2.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 23.1, 30.2, 108.1, 113.5, 119.9 (q, $^1J_{CF}$=276 Hz), 120.7, 127.9, 132.4, 138.6, 140.9, 145.8, 146.5 (q, $^2J_{CF}$=36 Hz), 147.9, 148.5, 156.2; ^{19}F NMR (282 MHz, $CDCl_3$) δ: −65.9. MS (CI) m/z 381 (M^++1, 100). Anal. Calcd for $C_{16}H_{11}F_3N_3O_4$ (380): C, 50.53; H, 2.92; N, 14.99. Found: C, 50.33; H, 2.94; N, 15.01.

4.7.8. Reaction of 2-azadiene (6b) with enamine (9a).

4.7.8.1. 1-Ethoxycarbonyl-3-(1,2,2,2-tetrafluoroethyl)-4-phenyl-5,6,7,8-tetrahydroisoquinoline (20). The general procedure was followed using (1*E*,3*E*)-1-ethoxycarbonyl-4-phenyl-3-pentafluoroethyl-2-azabuta-1,3-diene **6b** in situ and 1-cyclohex-1-enylpyrrolidine **9a** (0.68 g) in refluxing $CHCl_3$ for 60 h. Chromatographic separation (15/1, hexane/ethyl acetate) gave 1.33 g (70%) of **20** as a yellow solid, mp 84–85 °C (ethyl acetate/hexane). IR (KBr) ν 1747, 1173 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.45 (t, J=7.2 Hz, 3H), 1.64–1.85 (m, 4H), 2.35–2.41 (m, 2H), 3.00–3.02 (m, 2H), 4.48 (q, J=7.2 Hz, 2H), 5.45 (dq, $^2J_{HF}$=46 Hz, $^3J_{HF}$=6.0 Hz, 1H), 7.13–7.55 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 21.7, 21.8, 26.1, 28.5, 61.7, 85.0 (dq, $^1J_{CF}$=187.8 Hz, $^2J_{CF}$=34.7 Hz), 122.0 (dq, $^1J_{CF}$=281.0 Hz, $^2J_{CF}$=29.0 Hz), 128.3–160.2 (m), 166.5. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −75.6 (dd, $^3J_{FF}$=14 Hz, $^3J_{HF}$=6 Hz), −190.1 (dq, $^2J_{HF}$=46 Hz, $^3J_{FF}$=14 Hz). MS (EI) m/z 381 (M^+, 73). Anal. Calcd for $C_{20}H_{19}F_4NO_2$ (381): C, 62.99; H, 5.02; N, 3.67. Found C, 63.01; H, 5.00; N, 3.66.

4.7.9. Reaction of 2-azadiene (6b) with enamine (9c).

4.7.9.1. 2-Ethoxycarbonyl-6-(1,2,2,2-tetrafluoroethyl)-3,4-trimethylen-5-phenylpyridine (24a). The general procedure was followed using (1*E*,3*E*)-1-ethoxycarbonyl-4-phenyl-3-pentafluoroethyl-2-azabuta-1,3-diene **6b** obtained in situ and 1-cyclopent-1-enylpyrrolidine **9c** (0.67 g) in $CHCl_3$ at room temperature for 2 h. Chromatographic separation (15/1, hexane/ethyl acetate) gave 0.77 g (42%) of **24a** as a colorless oil; R_f=0.23 (1/10, ethyl acetate/hexane). IR (KBr) ν 1724, 1294 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.46 (t, J=7.1 Hz, 3H), 2.10–2.17 (m, 2H), 2.70–2.76 (m, 2H), 3.41–3.45 (m, 2H), 4.47 (m, 2H), 5.67 (dq, $^2J_{HF}$=45 Hz, $^3J_{HF}$=6.0 Hz, 1H), 7.23–7.51 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 24.4, 32.4, 33.1, 61.6, 85.9 (dq, $^1J_{CF}$=188.6 Hz, $^2J_{CF}$=34.6 Hz), 122.0 (dq, $^1J_{CF}$=282.7 Hz, $^2J_{CF}$=29.1 Hz), 126.4–156.7

(m), 165.3. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −75.2 (dd, $^3J_{FF}$=15 Hz, $^3J_{HF}$=6 Hz), −190.0 (dq, $^2J_{HF}$=45 Hz, $^3J_{FF}$=15 Hz). MS (EI) *m/z* 367 (M^+, 3). Anal. Calcd for $C_{25}H_{19}F_4NO_2$ (367): C, 62.12; H, 4.66; N, 3.81. Found: C, 61.99; H, 4.70; N, 3.83.

4.7.10. Reaction of 2-azadiene (6c) with enamine (9c).

4.7.10.1. 2-Ethoxycarbonyl-6-(1,2,2,3,3,4,4,5,5,6,6,7,7,7-tetradecafluoro-heptyl)-3,4-trimethylen-5-phenyl-pyridine (24b). The general procedure was followed using (1*E*,3*E*)-1-ethoxycarbonyl-4-phenyl-3-perfluorohepthyl-2-azabuta-1,3-diene **6c** obtained in situ and 1-cyclopent-1-enylpyrrolidine **9c** (0.67 g) in $CHCl_3$ at room temperature for 15 h. Chromatographic separation (15/1, hexane/ethyl acetate) gave 1.76 g (56%) of **24b** as a colorless oil; R_f=0.43 (1/5, ethyl acetate/hexane). IR (KBr) ν 1724, 1224 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.46 (t, *J*=7.1 Hz, 3H), 2.08–2.18 (m, 2H), 2.71–2.76 (m, 2H), 3.41–3.48 (m, 2H), 4.44–4.55 (m, 2H), 5.83–5.99 (m, 1H), 7.18–7.51 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 24.3, 32.4, 33.1, 61.6, 82.5–85.0 (m), 107.0–120.2 (m), 128.1–156.6 (m), 165.4. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −81.2, −117.1 to −126.6 (m). MS (EI) *m/z* 617 (M^+, 2). Anal. Calcd for $C_{24}H_{17}F_{14}NO_2$ (617): C, 46.69; H, 2.78; N, 2.27. Found: C, 46.73; H, 2.81; N, 2.25.

4.7.11. Reaction of 2-azadiene (6h) with enamine (9b).

4.7.11.1. 5-Isopropyl-6-(4-nitrophenyl)-2-perfluoro-ethyl-3-cyanopiridine (25a) and 5-isopropyl-6-(4-nitro-phenyl)-2-(1,2,2,2-tetrafluoroethyl)-3-cyanopiridine (26a). The general procedure was followed using (1*E*,3*Z*)-4-cyano-1-(4-nitrophenyl)-3-perfluoroethyl-2-azabuta-1,3-diene (**6h**) obtained in situ and *trans* 3-methyl-1-pyrro-lidylbut-1-ene **9b** (0.67 g) in $CHCl_3$ at room temperature for 3 h. Chromatographic separation (15/1, hexane/ethyl acetate) gave 0.78 g (40%) of **25a** as a white solid; mp 120–121 °C (ethyl acetate/hexane); 0.33 g (18%) of **26a** as an orange oil, R_f=0.50 (1/5, ethyl acetate/hexane); 0.04 g (4%) of *E*-**18b** as yellow oil, R_f=0.27 (1/5, ethyl acetate/hexane); 0.03 g (3%) of *Z*-**18b** and as a orange oil, R_f=0.45 (1/5, ethyl acetate/hexane) and 0.06 g (6%) of **28a** as an orange solid; mp 69–70 °C (ethyl acetate/hexane). *Data for* **25a**: IR (KBr) ν 2237, 1520 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.30 (d, *J*=6.8 Hz, 6H), 3.26 (dq, *J*=6.8 Hz, 1H), 7.68 (d, *J*=8.7 Hz, 2H), 8.24 (s, 1H), 8.38 (d, *J*=8.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 23.6, 29.2, 108.6, 110.9 (tq, $^1J_{CF}$=258 Hz, $^2J_{CF}$=39 Hz), 113.8, 118.5 (tq, $^1J_{CF}$=287 Hz, $^2J_{CF}$=36 Hz), 123.8, 130.1, 141.7, 143.4, 145.6, 145.8–146.4 (m), 148.5, 158.2. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −82.4, −113.3. MS (EI) *m/z* 385 (M^+, 23). Anal. Calcd for $C_{17}H_{12}F_5N_3O_2$ (385): C, 52.99; H, 3.14; N, 10.91. Found: C, 52.48; H, 3.31; N, 10.81. *Data for* **26a**: IR (KBr) ν 2236, 1522 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.26 (d, *J*=7.1 Hz, 3H), 1.28 (d, *J*=7.0 Hz, 3H), 3.20 (dq, *J*=7.0, 7.1 Hz, 1H), 5.97 (dq, $^2J_{HF}$=44.3 Hz, $^3J_{HF}$=6.0 Hz, 1H), 7.66 (d, *J*=8.8 Hz, 2H), 8.16 (s, 1H), 8.37 (d, *J*=8.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 23.6, 23.7, 29.2, 87.8 (dq, $^1J_{CF}$=194 Hz, $^2J_{CF}$=35 Hz), 109.2, 114.5, 121.5 (dq, $^1J_{CF}$=283 Hz, $^2J_{CF}$=28 Hz), 123.7, 130.0, 140.6, 143.9, 144.2, 148.3, 158.6. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −76.6 (dd, $^3J_{FF}$=12.5 Hz, $^3J_{HF}$=6.0 Hz), −197.9 (dq, $^2J_{HF}$=44.3 Hz, $^3J_{FF}$=12.5 Hz). MS (CI, 80V) *m/z* 368 (M^++1, 100). Anal. Calcd for $C_{17}H_{13}F_4N_3O_2$ (367): C, 55.59; H, 3.57; N, 11.44. Found: C, 55.48; H, 3.38; N, 11.31. ^{1}H NMR (400 MHz, $CDCl_3$) for *E*-isomer of **18b**, δ: 1.28 (d, *J*=7.0 Hz, 6H), 3.02 (dq, *J*=7.0 Hz, 1H), 7.50 (s, 1H), 7.51 (d, *J*=8.8 Hz, 2H), 8.30 (d, *J*=8.8 Hz, 2H), 9.59 (s, 1H). ^{1}H NMR (400 MHz, $CDCl_3$) for *Z*-isomer of **18b**, δ: 1.18 (d, *J*=6.8 Hz, 6H), 3.05 (dq, *J*=6.8 Hz, 1H), 7.46 (d, *J*=8.7 Hz, 2H), 7.50 (s, 1H), 8.26 (d, *J*=8.7 Hz, 2H), 9.82 (s, 1H). ^{1}H NMR (400 MHz, $CDCl_3$) for **28a**, δ: 4.51 (s, 1H), 5.19 (bs, 2H).

4.7.12. Reaction of 2-azadiene (6i) with enamine (9b).

4.7.12.1. 5-Isopropyl-6-(4-nitrophenyl)-2-perfluoro-hepthyl-3-cyanopiridine (25b), 5-isopropyl-6-(4-nitro-phenyl)-2-(1,2,2,3,3,4,4,5,5,6,6,7,7,7-tetradecafluoro-hepthyl)-3-cyanopiridine (26b) and 3-isopropyl-2-(4-nitrophenyl)-6-perfluorohepthyl-1,2-dihydro-5-cyano-piridine (27b). The general procedure was followed using (1*E*,3*Z*)-4-cyano-1-(4-nitrophenyl)-3-perfluorohepthyl-2-azabuta-1,3-diene (**6i**) obtained in situ and and *trans* 3-methyl-1-pyrrolidylbut-1-ene **9b** (0.67 g) in $CHCl_3$ at room temperature for 5 h. Chromatographic separation (10/1, hexane/ethyl acetate) gave 1.11 g (35%) of **25b** as an orange solid; mp 80–81 °C (CH_2Cl_2/hexane); 0.56 g (18%) of **26b** as a yellow solid; mp 93–94 °C (CH_2Cl_2/hexane); 0.68 g (22%) of **27b** as a yellow solid; mp 90–91 °C (ethyl acetate/hexane) 0.03 g (3%) of **18b** (see reaction of 2-azadiene **6h** with enamine **9b**) and 0.15 g (7%) of **28b** as a white solid mp 127–128 °C (hexane/ethyl acetate). *Data for* **25b**: IR (KBr) ν 2233, 1523 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.30 (d, *J*=6.9 Hz, 6H), 3.25 (dq, *J*=6.9 Hz, 1H), 7.68 (d, *J*=8.8 Hz, 2H), 8.23 (s, 1H), 8.38 (d, *J*=8.8 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 23.6, 29.7, 109.2, 110.2–111.1 (m), 113.9, 123.8, 130.1, 141.6, 143.4, 145.6, 145.7–146.4 (m), 148.5, 158.4. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −81.0, −110.8 to −126.3 (m). MS (EI) *m/z* 635 (M^+, 20). Anal. Calcd for $C_{22}H_{12}F_{15}N_3O_2$ (635): C, 41.59; H, 1.90; N, 6.61. Found: C, 41.31; H, 1.91; N, 6.79. *Data for* **26b**: IR (KBr) ν 2235, 1524 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.29 (d, *J*=6.7 Hz, 3H), 1.30 (d, *J*=6.7 Hz, 3H), 3.21 (dq, *J*=6.7 Hz, 1H), 6.20 (dd, $^1J_{HF}$=24.9 Hz, $^3J_{HF}$=19.1 Hz, 1H), 7.66 (d, *J*=8.8 Hz, 2H), 8.18 (s, 1H), 8.37 (d, *J*=8.8 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 23.6, 29.2, 87.3 (dt, $^1J_{CF}$=195 Hz, $^2J_{CF}$=23 Hz), 109.8, 110.2–111.2 (m), 114.5, 123.7, 123.7, 130.0, 140.7, 143.1–143.6 (m), 144.0, 144.2, 148.3, 158.6. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −81.1, −110.8 (t, $^3J_{FF}$=13.7 Hz), −120.8 to −126.4 (m), −198.6 (d, $^3J_{FF}$=13.7 Hz). MS (CI) *m/z* 618 (M^++1, 100). Anal. Calcd for $C_{22}H_{13}F_{14}N_3O_2$ (617): C, 42.80; H, 2.12; N, 6.81. Found: C, 42.77; H, 2.09; N, 6.85. *Data for* **27b**: IR (KBr) ν 3284, 2214, 1531 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.00 (d, *J*=6.8 Hz, 3H), 1.05 (d, *J*=6.7 Hz, 3H), 2.07 (dq, *J*=6.8, 6.7 Hz, 1H), 5.25 (s, 1H), 5.33 (d, *J*=3.3 Hz, 1H), 6.08 (s, 1H), 7.50 (d, *J*=8.7 Hz, 2H), 8.26 (d, *J*=8.8 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.7, 21.2, 31.6, 57.1, 83.8, 109.8–110.9 (m), 116.0, 116.6, 124.4, 128.0, 137.6, 143.5–144.2 (m), 147.4, 148.3. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −81.1, −112.7 to −126.4 (m). MS (CI) *m/z* 638 (M^++1, 100). Anal. Calcd for $C_{22}H_{14}F_{15}N_3O_2$ (637): C, 41.46; H, 2.21; N, 6.59. Found: C, 41.41; H, 2.26; N, 6.57. ^{1}H NMR (400 MHz, $CDCl_3$) for **28b**, δ: 4.56 (s, 1H), 5.30 (bs, 2H).

4.7.13. Reaction of 2-azadiene (6j) with enamine (9b).

4.7.13.1. 5-Isopropyl-6-(2,4-dinitrophenyl)-2-perfluorohepthyl-3-cyanopiridine (25c) and 5-isopropyl-6-(2,4-dinitrophenyl)-2-(1,2,2,3,3,4,4,5,5,6,6,7,7,7-tetrafluorohepthyl-3-cyanopiridine (26c). The general procedure was followed using (1*E*,3*Z*)-4-cyano-1-(2,4-dinitrophenyl)-3-perfluorohepthyl-2-azabuta-1,3-diene (**6j**) obtained in situ and **9b** (0.23 g) at room temperature in $CHCl_3$ for 5 h. After column chromatography (hexane/ethyl acetate 10/1) 2.0 g of an inseparable mixture of compounds **25c** and **26c** (1/2), 0.05 g (4%) of **18a** (see reaction of 2-azadiene **6e** with enamine **9b**) and 0.18 g (8%) of **28b** (see reaction of 2-azadiene **6g** with enamine **9b**) were obtained. Spectroscopic data of mixture **25c** and **26c**: IR (KBr) ν 2239, 1640, 1547 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.19–1.28 (m, 18H), 2.77–2.86 (m, 2H) for **25c** and **26c**, 6.12 (dq $^2J_{FH}=25.1$ Hz, $^3J_{FH}=2.8$ Hz, 1H) for **26c**, 7.65 (d, $J=8.3$ Hz, 4H) for **25c** and **26c**, 8.21 (s, 1H) for **26c**, 8.27 (s, 1H) for **25c**, 8.64 (d, $J=8.3$ Hz, 2H) for **26c**, 8.66 (d, $J=8.3$ Hz, 2H) for **25c**, 9.07–9.13 (m, 2H) for **25c** and **26c**. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 23.1, 30.1, 87.3 (dt, $^1J_{CF}=167$ Hz, $^2J_{CF}=23$ Hz), 107.0–119.1 (m), 120.8, 127.8, 132.2, 138.5–148.5 (m), 156.2. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −81.1, −111.3 to −126.5 (m), −198.6 to −199.6 (m).

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