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Novel Synthesis, Reactivity, and Stereochemistry of Substituted 3-Trifluoromethyl- and 3-Perfluoroalkyl-3-phenoxyprop-2-enal

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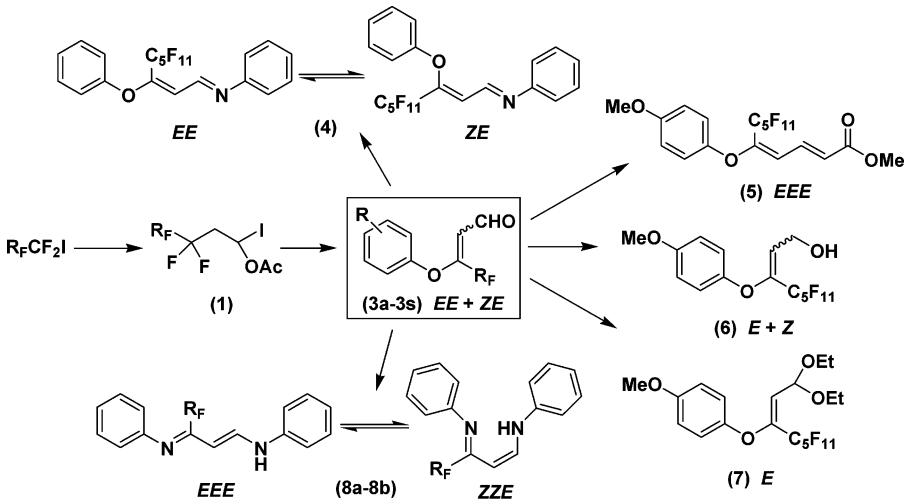
Received April 11, 2006



R_F = CF_3, C_3F_7, C_5F_{11}

R = H, *p*-OMe, *o*-OMe, *p*-Me, *m*-Me, *o*-Me, *p*-Cl, *p*-CN, *p*-NO_2, Ph.

Substituted 3-phenoxy-3-perfluoroalkylprop-2-enals **3a**−**s** are synthesized in high yields starting from a *gem*-iodoacetoxy derivative **1** and phenoxides **2**. Then efficient syntheses of push−pull derivatives **4**, **5**, **8a**,**b**, and nonconjugated analogues **6** and **7** illustrate the synthetic potentialities of **3**. Stereochemical studies of these perfluoroalkyl-containing trisubstituted olefinic derivatives **3**−**8b** revealed that the $^4J_{CF}$ coupling constant observed in the ^{13}C NMR spectra was crucial in the determination of their configurations and conformations in solution. The solvent polarity effect on the stereochemistry of push−pull compounds **3**−**5** and **8a**,**b** was studied. Unusual significant medium polarity effect on the stereochemistry of imino enol ether derivative **4** was observed.

Introduction

α,β-Unsaturated carbonyl derivatives substituted in the β-position with good leaving groups (chloro or alkoxy) serve as convenient building blocks for synthesis of different classes of acyclic, carbocyclic, and heterocyclic compounds.[1,2] In recent years, considerable attention has been given to the development of new procedures for the synthesis of fluorine-containing synthons, for example, trifluoromethylated β-chloroenones (ClCH═C(Ar)$COCF_3$ and $ClC(CF_3)$═CHCOAr)[3,4] or the β-alkoxyvinyl

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10.1021/jo060764i CCC: $33.50
Published on Web 08/10/2006

trifluoromethyl ketones ($ROCH{=}CHCOCF_3$).[5,6] Generally, nucleophiles attack the β-carbon atom with elimination of the alkoxy group[7,8] or chloride anion;[3,4] therefore, those enones are fluorinated keto aldehyde chemical analogues and are extensively used for the synthesis of various trifluoromethylated compounds which are often used in both medicine and agricultural chemistry.[9,10]

In connection with our interest in the synthesis of perfluoroalkylated reactive intermediates,[11−13] we report a convenient synthesis of substituted 3-perfluoroalkyl-3-phenoxyprop-2-enal **3a**−**s** starting from 1-iodo-2-perfluoroalkylethyl acetate **1**.[12,14] It must be remarked that compounds **1** are activated chemical equivalents of aldehydes. Then we prepared compounds **4**−**8**, which were isolated in the course of our exploration of the chemistry of **3**. Because of the difficulties establishing the stereochemistry of derivatives, such as **3**−**8**, we were interested in developing a general easy method for the determination of the configuration of these new compounds by measurement of coupling constants observed by NMR spectroscopy.

Until now, most spectroscopic investigations of the relationship between spatial structure and spectral parameters of unsaturated conjugated compounds have been carried out by comparison of chemical shifts[15] or by absorption spectroscopy.[16,17]

Fluorine−fluorine and fluorine−proton NMR spin−spin coupling constants (J_{FF} and J_{HF}) have become powerful probes for structural and stereochemical analysis of molecules in the fields of chemistry and biology.[18a] The through-space transmission of a spin−spin coupling between spatially proximate nuclei has been studied both experimentally[18b] and theoretically.[18c] Unusually large long-range couplings between carbon and fluorine atoms ($^nJ_{CF}$) connected by more than three chemical bonds have been reported in some aromatic molecules,[19] for example, 5-fluorophenanthrene and tetrafluoronaphthoxepin derivatives.[18b,19,20]

Introduction of a trifluoromethyl or perfluoroalkyl group may be accompanied by changes in spatial and electronic structure and may consequently affect the spectral parameters.[9,21,22] Often during the synthesis of trifluoromethyl- or perfluoroalkyl-containing vinyl compounds, both configurational isomers *Z* and *E* are produced simultaneously. In the case of olefinic compounds bearing a vinylic trifluoromethyl group, determination of the *Z* or *E* configuration is based on the comparison between the coupling constant of fluorine atoms and a vicinal vinylic proton ($^4J_{HF}$ (*Z*) > $^4J_{HF}$ (*E*)) or the coupling observed between fluorine atoms and the olefinic carbon ($^3J_{CF}$ (*Z*) > $^3J_{CF}$ (*E*)).[23−26]

However, the comparison between these coupling constants ($^4J_{HF}$ and $^3J_{CF}$) is not sufficient to attribute the right configurations because they are often hardly observable, especially in the case of substituted trifluoromethylated olefins.[27] Therefore,

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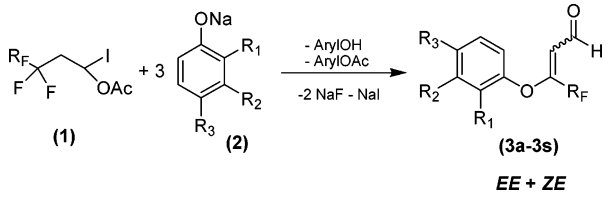
SCHEME 1. Synthesis of 3-(R_1-R_2-R_3-Phenoxy)-3-perfluoroalkylprop-2-enal 3a−s



it is desirable to develop a new method based on NMR coupling constants which has a more general applicability to the wide range of perfluoroalkyl-containing vinyl compounds.

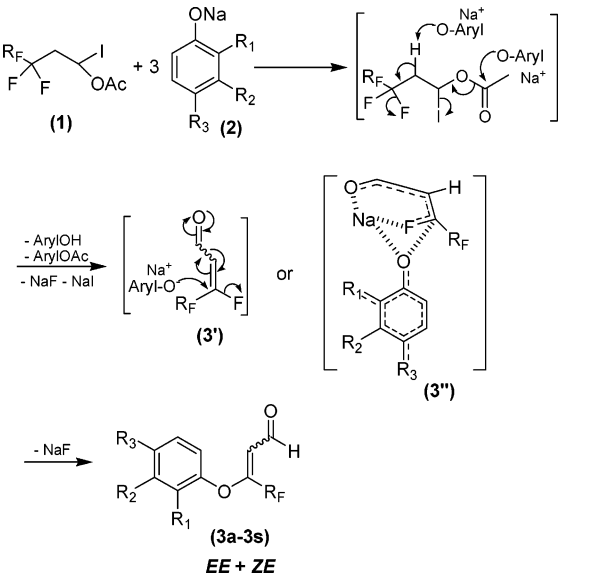
Synthesis of Substituted 3-Phenoxy-3-perfluoroalkylprop-2-enal 3

The reaction of **1** with phenoxides **2** was studied, and the optimum conditions to obtain **3a**−**s** were 1:3 molar mixtures of **1** and **2** in alkane solvents, such as hexane or petroleum ether (Scheme 1).

Under such conditions, enals **3** were the major fluorinated product in the crude mixture (the reaction was monitored by ^{19}F NMR spectroscopy). At the end of the reaction, a simple work up procedure (washing with 1% sodium hydroxide aqueous solution) eliminated the excess of phenols. Final products **3** were easily purified by silica gel column chromatography and were obtained as a mixture of *EE* and *ZE* stereoisomers, which turned out to be not separable except in the case of **3o** and **3p** (see Supporting Information). In the case of **3f**, the *E* isomer precipitates in hexane at −10 °C to yield pure *E*-propenal. All propenals **3a**−**k** and **3s** were obtained in high yields at room temperature. Longer reaction times or higher temperature (40−80 °C) were sometimes required in the presence of a strong electron-withdrawing substituent on the aromatic rings of **3n**−**p**. In the case of compounds **3q** and **3r**, no reaction occurred under our conditions; this could be explained by the steric bulk of the corresponding aryl or heteroaryloxides.

The mechanism of formation of **3** could be explained by a transesterification which occurs between the phenoxide anion and the acetate group, leading to the elimination of the iodine atom and formation of an aryl-OAc, which was isolated and identified. Then elimination of HF yields a fluorinated propenal intermediate, which by an oxa-Michael addition−elimination mechanism **3′** (nucleophilic vinylic substitution)[33−35] or by a six-membered cyclic plane mechanism occurring between the phenolate group, a sodium atom, and propenal intermediate **3″** gives **3** (Scheme 2). Participation of the *ortho*- or *para*-substituent by conjugation could favor this mechanism. Previous reports on the nucleophilic additions to activated olefins describe a concerted mechanism with a six-center transition state stabilized by hydrogen bonds.[34,35] A similar situation was found during the addition of phenolate to double bonds with a great influence on the substituents on the *para*-position.[35]

SCHEME 2. Mechanisms of Formation of 3a−s



These reactions (Table 1) were found to be stereoselective; a higher degree of *EE* stereoselectivity was obtained in most

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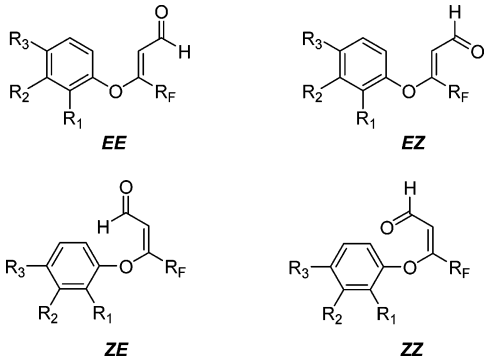
TABLE 1. Synthesis and $^4J_{C1F}$ Coupling Constants Observed for Substituted 3-Phenoxy-3-perfluoroalkylprop-2-enals 3a−s

Compound	R_F	R_1	R_2	R_3	conv[%][a]	*EE*/*ZE*[b]	δ CF_2 or CF_3 (ppm)		$^4J_{CIF}$ (*EE*)[c] (Hz)
							EE	*ZE*	
3a[d]	CF_3	H	H	H	95	64/36	-64.8	-71	9
3b[d]	C_3F_7	H	H	H	95	62/38	-112	-117	8.3
3c[d]	C_5F_{11}	H	H	H	95	64/36	-109	-111	9
3d[d]	CF_3	H	H	OMe	> 95	59/41	-64.9	-71	8.3
3e[d]	C_3F_7	H	H	OMe	> 95	91/9	-111	-117.1	9
3f[d]	C_5F_{11}	H	H	OMe	> 95	92/8	-111	-116	8.4
3g[d]	C_5F_{11}	H	H	Me	92	20/80	-111	-116	9
3h[d]	C_3F_7	H	Me	H	90	58/42	-112.2	-117	8.8
3i[d]	C_3F_7	Me	H	H	92	40/60	-112.1	-116.9	8.6
3j[d]	CF_3	H	OMe	H	93	65/35	-65.2	-71.3	8.8
3k[d]	C_3F_7	OMe	H	H	> 95	46/54	-112	-117	9
3l[e]	C_5F_{11}	H	H	Cl	85	92/8	-111.2	-116.5	8.3
3m[e]	C_5F_{11}	Cl	H	H	65	45/55	-111.5	-117.2	8.3
3n[e]	CF_3	H	H	CN	80	59/41	-65.5	-71.2	9
3o[f]	C_5F_{11}	H	H	NO_2	72	60/40	-111	-116	9
3p[f]	CF_3	H	H	NO_2	70	81/19	-66.2	-73	8.3
3q[f]	C_3F_7			H	0	-	-	-	-
3r[f]	C_5F_{11}			H	0	-	-	-	-
3s[d]	C_5F_{11}	H			86	100/0	-111	-	8.6

[a] Stereoisomeric ratio determined by ^{19}F NMR directly at the end of the reactions. [b] Determined by ^{19}F NMR analysis; NMR yield based on consumed **1** and formed **3**. [c] $^4J_{C1F}$ (*ZE*) = 0 Hz. [d] Reaction conditions: 4 h at 20 °C. [e] Reaction conditions: 24 h at 40 °C. [f] Reaction conditions: 48 h at 80 °C.

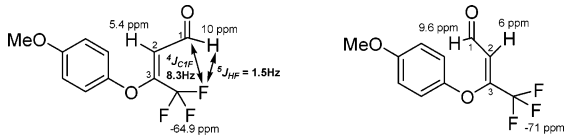
SCHEME 3. Possible Stereoisomers of Phenoxypropenals 3a−s



of the reactions reported, although steric hindrance favors exclusively the *EE* isomer (2-naphthoxy, **3s**). The role of the electronic effect of substituents on the phenyl group appears also to be important (compare **3o** and **3p** with **3d** and **3f** and **3g**, **3h**, and **3i**). Finally, the prevalence of the *ZE* stereoisomer could be explained by the occurrence of **3″** transition state (Scheme 2).

According to the literature, compounds **3a−s** can be characterized as push−pull ethylene derivatives.[28−30] Push−pull alkenes are substituted alkenes with one or two electron-donating

SCHEME 4. Stereochemical Assignment of 3d *EE* and *ZE* Using Coupling Constants



3d, *EE* **3d, *ZE***

substituents on one end of a C═C double bond and with one or two electron-accepting substituents at the other end. Allowance for electron delocalization leads to the central C═C bond becoming more polarized and with a lower barrier to rotation.[28,29] The push−pull effect is of decisive influence on both the dynamic behavior and the chemical reactivity of this class of compounds.[30] These olefins are often involved in isomeric equilibrium, which can be driven by heat,[29a] light,[29] medium polarity,[28,31] or concentration.[28,29] It is expected that each isomer **3a−s** can be described in term of *Z*/*E* isomerism for the C_2═C_3 double bond and around the C_1−C_2 geometry (Scheme 3 and 4).

The change of solvent did not affect the *EE*/*ZE* ratio; however, we observed a thermal isomerization of the stereoisomeric mixture in solution, and the percentage of the thermodynamically favored *EE* isomer increased.[28b]

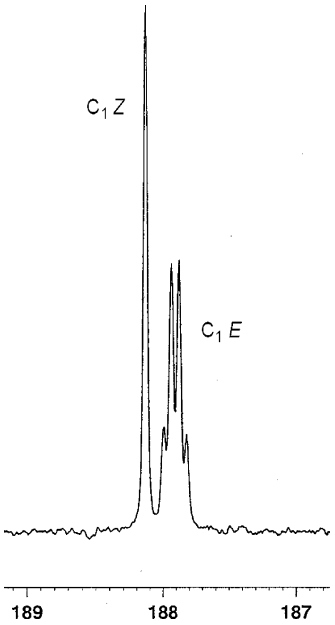


FIGURE 1. ^{1}H-Decoupled ^{13}C NMR spectra of a mixture of *EE* and *ZE* isomers of **3d** showing the aldehydic carbons.

To establish the *Z*/*E* configurations of the double bond of **3a**−**s**, we compared the $^{5}J_{HF}$ coupling constant (0.5−1.5 Hz for the *E* isomer and 0 Hz for the *Z* isomer) between the aldehydic proton and the vinylic CF_2 or CF_3 group and the $^{3}J_{CF}$ coupling constant between the carbon 2 and the fluorine atom of the perfluoroalkyl group.[26,27] These couplings were not observed in all cases and are therefore not general.

Then we focused our attention on the measurement of the $^{4}J_{CF}$ coupling constant between the aldehydic carbon atom and the fluorine atom of the CF_3 or the CF_2 groups. We observed that in all cases (**3a**−**s**), for the *EE* isomer, the $^{4}J_{CF}$ was about 8.3−9 Hz, and no coupling was obtained for the *ZE* isomer (Table 1). Concerning the conformation around C_1-C_2, the measured $^{3}J_{H1H2}$ (around 8 Hz)[15] proved the *E* geometry for every compound **3a**−**s**.

Some reports describe the determination of configuration of α,β-unsaturated carbonyl compounds bearing a vinylic perfluoroalkyl group by comparison of the ^{19}F NMR chemical shifts. Authors found that chemical shifts of *E* isomers are higher than those of *Z* isomers.[7] We reached the same conclusions for **3a**−**s** (Table 1).

Enals **3** are stable compounds compared to their alkoxy or chloro trifluoromethylated analogues, which decompose easily.[32] To our knowledge, no examples of such fluorinated β-phenoxyenals have been mentioned in the literature.

The NMR spectra of **3d** (R_3 = OMe and R_F = CF_3) are typical and will be commented upon in detail. The ^{13}C NMR signals at 187.9 and 188.1 ppm correspond, respectively, to the aldehydic carbons of *E* and *Z* isomers. The difference is due to the coupling with fluorine atoms of the adjacent trifluoromethyl group in the case of isomer *EE* (quartet, $^{4}J_{C1F}$ = 8.3 Hz) (Scheme 4 and Figure 1). Moreover, the ^{1}H NMR signals at 5.4 and 10 ppm represent, respectively, the vinylic and the aldehydic protons of isomer *EE*, and the signals at 6 and 9.6 ppm are due to the other isomer (Scheme 4). The assignments of signals at 9.6 and 10 ppm are evident: the *EE* isomer, which has the signals for its aldehyde proton at lower field than those

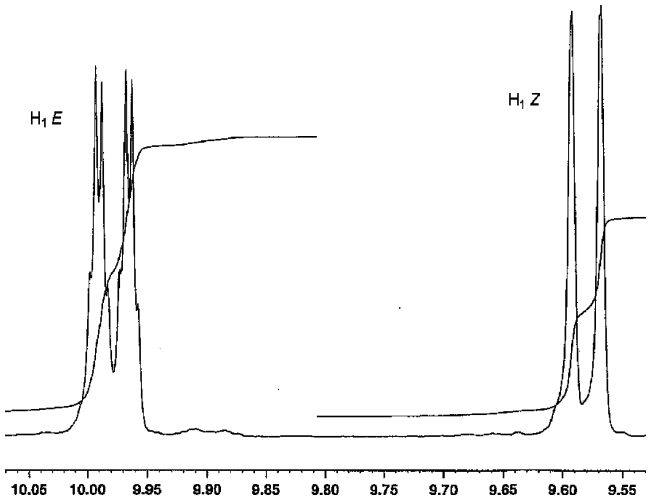
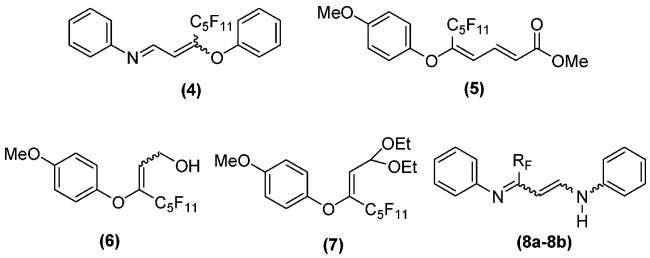


FIGURE 2. ^{1}H NMR spectra of a mixture of *EE* and *ZE* isomers of **3d** showing the aldehydic protons.

SCHEME 5. Synthesized Derivatives 4−8b



of the *ZE* isomer, the difference being due to the interaction of the adjacent CF_3 group (quartet, $^{5}J_{HF}$ = 1.5 Hz for the *E* isomer)[5] (Figure 2).

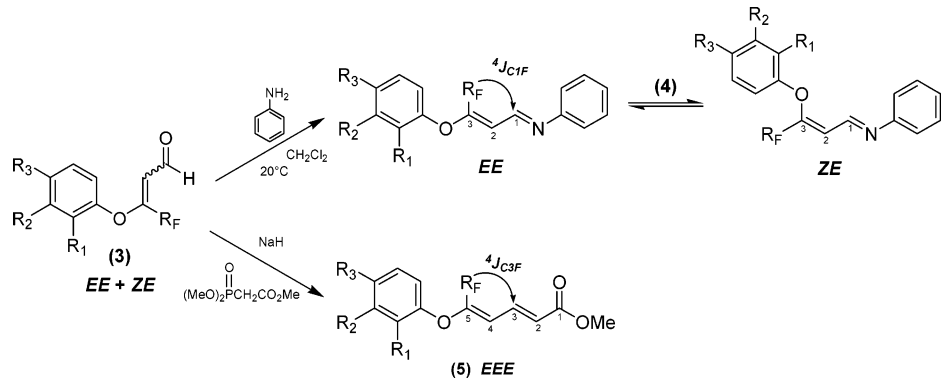
In the course of our studies on the reactivity of compounds **3** and the applications of the $^{4}J_{CF}$ coupling constant for total stereochemical assignments, we prepared compounds **4**−**8b**, which are obtained in high yields and are isolated after simple work up procedures without further purification (Schemes 5−8).

For example, we found that enal **3c** reacts easily with aniline and forms imine derivative **4** with good yields (94%) (Scheme 6). Previously, the reaction of aniline with alkoxy vinyl ketones was studied, precluding a mechanism that involves a Michael addition of aniline with subsequent elimination of the alkoxy group and led to the corresponding enamino enone.[28b,32] In such enol ethers, the nucleophilic replacement of the alkoxy group is the predominant reaction.[7,8] In our case, only 1,2-addition product was observed probably because of steric hindrance of the perfluoroalkyl group and the high conjugation of compound **4**. To our knowledge, imino enol ether compounds have not been described yet in the literature.

Concerning the push−pull olefinic derivative **4**, the ^{1}H NMR spectra showed clearly the presence of a single isomer in nonpolar solvent, such as benzene. In more polar solvent, such as chloroform or acetonitrile, the NMR data are consistent with the compound existing as an equilibrium mixture of two stereoisomers (Table 2).

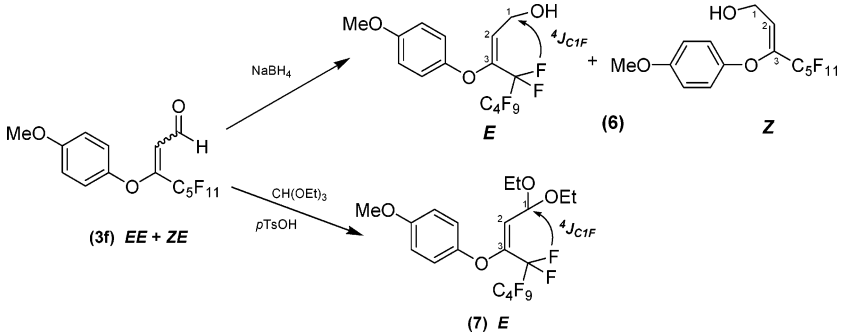
The stereochemistry of the trisubstituted double bond of **4** was established by ^{13}C and ^{19}F NMR spectroscopy using $^{4}J_{C1F}$ coupling constant observed between carbon 1 and fluorine atoms. In nonpolar media (benzene), the coupling constant observed between carbon 1 and fluorine atoms of the perfluoroalkyl chain ($^{4}J_{C1F}$ = 5.9 Hz) suggests a *cis* relationship between

SCHEME 6. Synthesis and Determination of Stereochemistry of Compounds 4 and 5[a]

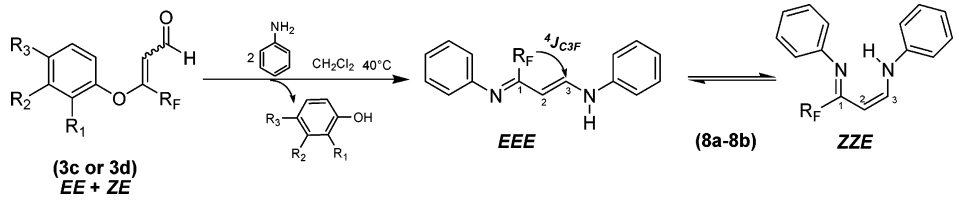


[a] **4**: $R_1 = R_2 = R_3 = H$, $R_F = C_5F_{11}$; **5**: $R_1 = R_2 = H$, $R_3 = OMe$, $R_F = C_5F_{11}$.

SCHEME 7. Synthesis and Stereochemical Assignments of Nonconjugated Derivatives 6 and 7



SCHEME 8. Synthesis and Assignments of Stereochemical Isomers of 2-Trifluoromethyl- and 2-Perfluoropentyl-*N*,*N*′-diphenyl-1,5-diazapentadienes 8a and 8b[a]



[a] **8a**: starting from **3d**, $R_1 = R_2 = H$, $R_3 = OMe$, $R_F = CF_3$; **8b**: starting from **3c**, $R_1 = R_2 = R_3 = H$, $R_F = C_5F_{11}$.

these two groups and indicates an *E* configuration (Table 2). Moreover, the coupling constant obtained between proton 1 and proton 2, $^3J_{H1H2} = 9$ Hz, indicates a *trans* disposition of these two protons and therefore an *E* conformation around the N═C−C═C single bond.[15]

In polar media (acetonitrile), a mixture of *EE* and *ZE* forms is obtained with strong prevalence of the *ZE* stereoisomer. The absence of coupling between carbon 1 and fluorine atoms of the perfluoroalkyl chain, $^4J_{C1F} = 0$ Hz, on one hand and the coupling observed between proton 1 and proton 2, $^3J_{H1H2} = 9.1$ Hz, permitted us to establish the configuration of the C_2═C_3 double bond as *Z* and to completely assign without ambiguity the stereochemistry of the preponderant isomer of **4** (Table 2).

The medium effect on the stereochemistry of compound **4** is very significant and could be explained by the influence of the solvent polarity on the C═C barrier to rotation. Very few works deal with the solvent polarity effect on the stereochemistry of such derivatives.[31] However, according to literature, the more polar the solvent, the lower the corresponding barrier to rotation, which favors isomerizations of push−pull ethylene compounds.[28,31] In comparison with that of **3**, the electronic conjugation on the phenyl group relative to the imine function and probably the interaction between the two phenyl groups could favor the very fast and highly pronounced ratio change of the solvent-dependent *EE*/*ZE* equilibrium of **4**. Finally, the absence of the s-*cis* or *Z* conformation in the stereoisomeric forms of compounds **3** and **4** suggests that the presence of s-*cis* conformers is mainly governed by the tendency of formation of an intramolecular hydrogen bond apparent in nonpolar solvents[15,29,30] (e.g., compounds **8a**,**b**).

Moreover, enals **3** react with phosphonate carbanions. For example, condensation of triethylphosphonoacetate with a mixture *EE* and *ZE* of **3f** was conducted in methanol, and the phosphonate carbanion was generated by sodium hydride in situ. The Wadsworth−Emmons product is obtained, and the conjugated ester derivative **5** is isolated as a single stereoisomer in very high yields (>98%) (Scheme 6). There has been interest in conjugated unsaturated systems, such as polyenes, as a consequence of the physiological behavior exhibited by representatives of these systems.[2c,36] They have also been shown in

(36) (a) Ogawa, Y.; Maruno, M.; Wakamatsu, T. *Heterocycles* **1995**, *4*, 2587. (b) Baeckstrom, P.; Jacobsson, U.; Norin, T.; Unelius, C. R. *Tetrahedron* **1988**, *44*, 2541.

TABLE 2. Determination of the Content of Isomeric Forms and Stereochemistry in Solutions of 4−7 by NMR Coupling Constant ($^4J_{C1F}$ and $^3J_{H1H2}$)

		C_6D_6			$CDCl_3$			CD_3CN		
compound	isomers	%	$^4J_{CIF}$ (Hz)	$^3J_{H1H2}$ (Hz)	%	$^4J_{CIF}$ (Hz)	$^3J_{H1H2}$(Hz)	%	$^4J_{CIF}$ (Hz)	$^3J_{H1H2}$ (Hz)
4	*EE*	99	5.7	9	85	5.9	9	8	5.7	9.2
	ZE	1	0	8.8	15	0	8.9	92	0	8.8

		C_6D_6 or CD_3CN			
		%	$^4J_{C3F}$ (Hz)	$^3J_{H2H3}$ (Hz)	$^3J_{H3H4}$ (Hz)
5	*EEE*	100	6.4	15.1	12

		C_6D_6 or $CDCl_3$		
		%	$^4J_{C1F}$ (Hz)	$^3J_{H1H2}$ (Hz)
6	*Z*	5	0	6.1
	E	95	6.6	6.8

		C_6D_6 or $CDCl_3$		
		%	$^4J_{C3F}$ (Hz)	$^3J_{H1H2}$ (Hz)
7	*E*	100	8	7.5

many cases to serve as effective synthons in the construction of a wide variety of interesting molecules, such as retinoid analogues.[37]

The stereochemistry of the Wadsworth−Emmons product **5** is shown to be *EEE* based on the coupling constants observed ($^3J_{H2H3}$, $^3J_{H3H4}$, and $^4J_{C3F}$) (Table 2). The configuration of the C_2═C_3 double bond of **5** was established as *E* by ^{1}H NMR coupling constants ($^3J_{H2H3}$ = 15.1 Hz). On the other hand, the coupling observed between C_3 and fluorine atoms of the perfluoroalkyl group in the ^{13}C NMR spectrum ($^4J_{C3F}$ = 6.4 Hz) suggest a *cis* relationship between these two groups and allowed us to assign without ambiguity the configuration of the trisubstituted olefin C_4═C_5 as *E* (Table 2). Finally the *E* or s-*trans* conformation of the C═CH−CH═C moiety is proved by the coupling constant of the H_3−H_4 atoms ($^3J_{H3H4}$ = 12 Hz).

The stereochemistry of **5** was unaffected when the solvent was changed from benzene to chloroform or acetonitrile. Our results are in accord with reported works for similar systems.[26,38]

Compounds **3**, **4**, and **5** are all trisubstituted conjugated olefinic derivatives. The coupling constants $^4J_{C1F}$ and $^4J_{C3F}$ observed for **3**, **4**, and **5** are mainly transmitted through chemical bonds. Previous results have shown that coupling between carbon or proton and fluorine atoms occurs with significant contribution of the through-bond components when strong π-conjugation intervenes between coupled centers.[39] Likewise, other molecular systems might exhibit exclusive through-space coupling via the contribution of fluorine lone pairs and fluorine core orbitals.[40]

To investigate whether the $^4J_{CF}$ correlation established for conjugated derivatives **3**, **4**, and **5** is still reliable for nonconjugated perfluoroalkyl chain-containing vinylic systems, we synthesized compounds **6** and **7** starting from propenals **3**.

Reduction of perfluoroalkyl enal **3f** by sodium borohydride in methanol afforded, after usual treatment, the corresponding alcohol **6** as a mixture of stereoisomers (Scheme 7). This reaction was run with complete conversion. The two stereoisomers of **6** were differentiated using the four-bond carbon−fluorine coupling $^4J_{C1F}$; the difference observed between the coupling constants of the sp^3 carbon 1 and the fluorine atoms ($^4J_{C1F}$ = 6.6 Hz for the *E* isomer and 0 for the *Z* isomer) allowed us to clearly assign the configuration of the double bond of **6** (Table 2).

Interestingly, the allylic alcohol obtained **6** is very stable in acidic media even in concentrated acids. This proves that the fluorinated groups provide greater stability to such molecules since enol ethers of nonfluorinated 1,3-dicarbonyl analogues undergo, after reduction, an allylic rearrangement when treated with aqueous acids and give mainly unsaturated ketones.[41]

On heating in ethanol in the presence of *p*-toluenesulfonic acid, triethyl orthoformate reacts with enal **3f** to give (*E*)-acetal **7** in 86% yield (Scheme 7). The coupling constants observed between the sp^3 carbon 1 and fluorine atoms permitted us to establish the stereochemistry of the double bond of this compound ($^4J_{C1F}$ = 8 Hz for the *E* isomer) (Table 2). This coupling constant relationship can be used to determine the configurational assignments not only in the mixture of two stereoisomers but also in the case where only one isomer is obtained. In contrast, the use of other coupling constant ($^nJ_{CF}$, $n < 4$) needs the presence of a mixture of stereoisomers identified by comparison of the obtained values.

This compound **7**, which is less sensitive to moisture than its nonfluorinated analogues,[42] was isolated and could be used further in synthesis. In contrast, the other β-dicarbonyl derivatives give under similar conditions regioisomers which are difficult to separate.[43]

Because derivatives **6** and **7** are unconjugated, there must be a contribution of the through-space transmission of the coupling. This behavior can be attributed to structural features, such as changes in the bond angles, hybridization due to steric hindrance, and through-space orbital interactions.[18]

Besides the configurational assignments of perfluoroalkyl-containing vinyl compounds and to verify if the through-space

(37) (a) Anastasia, L.; Xu, C.; Negishi, E. *Tetrahedron Lett.* **2002**, *43*, 5673. (b) Bellina, F.; Biagetti, M.; Carpita, A.; Rossi, R. *Tetrahedron* **2001**, *57*, 2857.

(38) Segre, A.; Zetta, L.; Di Corato, A. *J. Mol. Spectrosc.* **1969**, *32*, 296.

(39) Peralta, J. E.; Barone, V.; Ruiz de Azua, M. C.; Contreras, R. H. *Mol. Phys.* **2001**, *99*, 655.

(40) (a) Peralta, J. E.; Contreras, R. H.; Snyder, J. P. *Chem Commun.* **2000**, 2025. (b) Bryce, D. L.; Wasylishen, R. E. *J. Am. Chem. Soc.* **2000**, *122*, 11236.

(41) (a) Gannon, W. F.; House, H. O. *Org. Synth.* **1960**, *40*, 14. (b) Stiles, M.; Longroy, A. *Tetrahedron Lett.* **1961**, *10*, 337.

(42) Pohland, A. E.; Benson, W. R. *Chem. Rev.* **1964**, *64*, 161.

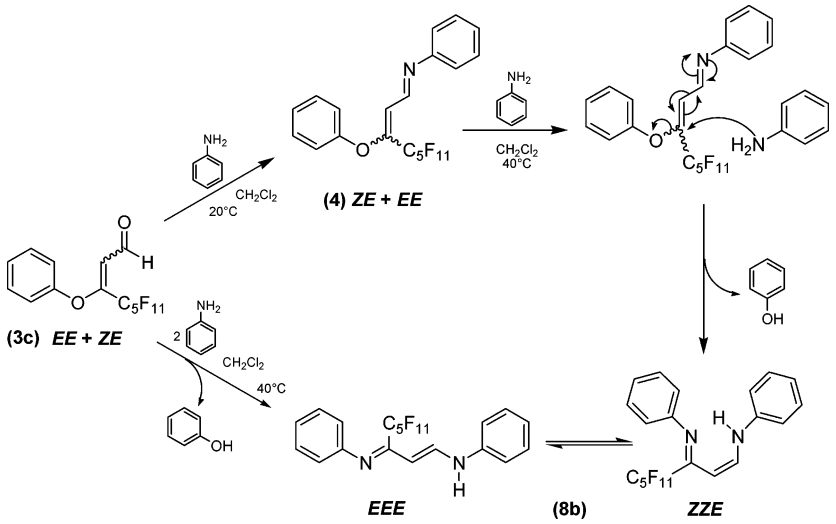
(43) Pashkevich, K. I.; Saloutin, V. I.; Postovskii, I. Ya. *Russ. Chem. Rev.* **1981**, *50*, 180.

TABLE 3. Conformational and Configurational Assignments of Compounds 8a and 8b Using Coupling Constants $^4J_{C3F}$, $^3J_{H2H3}$, and $^3J_{H3NH}$

		C_6D_6					DMSO-d_6				
compound	isomer	%	$\delta_{CF2,CF3}$ (ppm)	$^4J_{C3F}$ (Hz)	$^3J_{H2H3}$ (Hz)	$^3J_{H3NH}$ (Hz)	%	$\delta_{CF2,CF3}$ (ppm)	$^4J_{C3F}$ (Hz)	$^3J_{H2H3}$ (Hz)	$^3J_{H3NH}$ (Hz)
8a	*ZZE*	64	−62.3	0	7.9	10*	0				
	EEE	36	−66.6	3.5	14	14	100	−65.8	3	13.7	12.3
8b	*ZZE*	28.5	−107.8	0	8.2	10[a]	0				
	EEE	71.5	−109.5	5.2	13.9	14	100	−109.6	5.5	13.7	12.4

[a] Broad doublet.

SCHEME 9. Mechanism of Formation of 2-Perfluoropentyl-*N*,*N*′-diphenyl-1,5-diazapentadiene 8b



$^4J_{CF}$ coupling constant could be used for the determination of conformational preferences, we synthesized the dissymmetric imino enamine derivatives **8a**,**b**.

The reaction of **3c** or **3d** with 2 equiv of aniline in refluxing dichloromethane gives the corresponding *N*,*N*′-diphenyl-1,5-diazapentadienes **8a** and **8b** with elimination of their phenoxy groups in 94 and 96% yields, respectively (Scheme 8).

To reveal the mechanism of formation of **8a**,**b**, we monitored the reaction of **3c** with 2 equiv of aniline by ^{19}F NMR spectroscopy and TLC. We observed that NMR signals which were assigned to **4** (Scheme 9) appear quite quickly during the reaction and after 1 h disappear to give new peaks corresponding to **8b** (Scheme 9). This observation leads us to the conclusion that compound **4** is the intermediate of the synthesis of diazapentadiene **8b**.

To verify the assumption that the synthesis of **8a** and **8b** proceeds through intermediates of type **4** and to reveal the reaction route as a whole, we decided to test after its isolation the reactivity of **4** toward 1 molar equiv of aniline in dichloromethane at 40 °C, and in these conditions, diazapentadiene **8b** was formed with elimination of the phenoxy group in high yield (conversion of **4** to **8b** = 90%) (Scheme 9).

Such processes are analogous to nucleophilic addition at the β-carbon of the α,β-unsaturated carbonyl compounds and could be explained by an aza-Michael addition−elimination mechanism[28,29] such as in the case of intermediate **3′** (Schemes 2 and 9).

It has been shown that the salts of *N*,*N*′-diaryl-1,5-diazapentadienes (Ar−NH═CH−CH═CHNH−Ar) exist as conjugated amino imines, generally as a mixture of the all-*trans* (or *EE*), all-*cis* (or *ZZ*), and *cis-trans* (*ZE* or *EZ*) isomers with slow exchange between them at room temperature.[44] The stereochemistry of these compounds was determined by comparison of the vicinal $^3J_{HH}$ couplings constants observed in their ^{1}H NMR spectra: in nonpolar media, open chain diazapentadienes have a NH group existing predominantly in the *ZZ* form, wherein they are stabilized by intramolecular hydrogen bonding.[39,44] In contrast, their salts take up the *EE* configuration in polar solvents.[44] The NMR spectra have been investigated by several workers, with results agreeing with those obtained from IR studies and excluding the presence of tautomeric forms.[45,46] However, the application of this method to the stereochemical assignments of such derivatives is limited by the substitution pattern of the propene moiety: in the case of substituent occurring on the propene bridge, structure of the corresponding diazapentadienes could not be established completely.[47]

In our case, the NMR spectra of diaryl-1,5-diazapentadienes **8a**,**b** in polar solvent (DMSO) show that the compounds exist solely in the *EEE* form as deduced from the $^3J_{H2H3}$, $^3J_{H3NH}$, and $^4J_{C3F}$ couplings, whereas in nonpolar solvent (benzene), an equilibrium is established between this form and the intramolecularly bonded *ZZE* form (Table 3).

(44) (a) Richards, C. P.; Webb, G. A. *Org. Magn. Reson.* **1975**, *7*, 401. (b) Lloyd, D.; McNab, H. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 459. (c) Barry, W. J.; Finar, I. L.; Mooney, E. F. *Spectrochim. Acta* **1965**, *21*, 1095. (d) Limbach, H. H.; Seiffert, W. *Tetrahedron Lett.* **1972**, 371.

(45) (a) Nair, V.; Vietti, D. E.; Cooper, C. S. *J. Am. Chem. Soc.* **1981**, *103*, 3030. (b) Kikugawa, K.; Maruyama, T.; Machida, Y.; Kurechi, T. *Chem. Pharm. Bull.* **1981**, *29*, 1423.

(46) (a) McNab, H. *J. Chem. Soc., Perkin Trans. 2* **1981**, 1283. (b) Radeglia, R. *J. Prakt. Chem.* **1973**, *315*, 1121.

(47) (a) Honeybourne, C. L.; Webb, G. A. *Spectrochim. Acta* **1969**, *25A*, 1075. (b) Bayer, E. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 325.

In the case of the *EEE* isomer, the configuration of the C_2═C_3 double bond was determined as *E* by the coupling constant of proton 2 and proton 3 ($^3J_{H2H3}$ = 13.7−14 Hz), then the coupling observed between proton 3 and the proton of the NH group ($^3J_{H3NH}$ = 12.3−14 Hz) is consistent with the *E* geometry around the ═C_3−NH single bond.[5,15] Finally, the coupling observed between carbon 3 and fluorine atoms ($^4J_{C3F}$ = 3−5.5 Hz) suggests that this carbon is spatially proximate (or in a *cis*-position) to the perfluoroalkyl group and permitted us to attribute an *E* conformation around the N═C_1−C_2═C_3 single bond (Scheme 8 and Table 3).

In benzene solution, the coupling constants of proton 2 and proton 3 ($^3J_{H2H3}$ = 7.9−8.2 Hz) and proton 3 and a NH proton ($^3J_{H3NH}$ = 10 Hz) permitted us to establish the *ZE* stereochemistry of the CH═CH−NH moiety. Moreover, the absence of coupling between carbon 3 and fluorine atoms ($^4J_{C3F}$ = 0 Hz) allowed us to attribute a *Z* conformation around the N═C−C═C single bond and to assign unequivocally the *ZZE* isomer of **8a** and **8b**.

In the case of **8a**, the resonance-assisted hydrogen bonding (RAHB) occurring in nonpolar solvent (benzene) governs the stereoisomeric equilibrium,[28,30] and the *ZZE* isomer prevails (64%). However, the results observed for **8b** suggest that the length of the perfluoroalkyl group plays a crucial role; the *EEE* isomer is considerably more stable and comprises more than 71% of the equilibrium of **8b** in benzene solution (Table 3). The more polar solvent (DMSO) totally shifts the equilibrium of **8a** and **8b** to the *EEE* isomer, stabilized by intermolecular hydrogen bonds, strong electrostatic interactions, and minimal steric hindrance.[30,44]

In a previous publication,[11] we reported that 2-trifluoromethyl-1,5-diazapentadiene **8a** exists as a single stereochemically pure tautomer. Other works describe that the two nitrogen atoms in this imino enamine compound are not entirely equivalent.[44] The signals in the ^{13}C NMR spectrum obtained for **8a** and **8b** confirmed these results (for both isomers, the imine carbon showed coupling with fluorine atoms ($^1J_{C1F}$), and in both cases, a coupling between proton 3 and a NH proton is obtained ($^3J_{H3NH}$)).

The case of substituted imino enamine derivatives **8a**,**8** indicates that the use of the $^4J_{CF}$ coupling constant to determine the relative conformations of its C_1−C_2 bond is reliable and permits one to attribute unambiguously conformational preferences of such compounds having an F-alkyl substituent on the propene moiety. The $^nJ_{CF}$ basically decreases with the increase in the spatial distance of the two nuclei;[18,19] therefore, the configuration or the conformation of a compound considerably influences the value of $^nJ_{CF}$ through the change in the internuclear distance. The observed $^4J_{CF}$ (for compounds **3**−**8**) confirmed that the more spatially proximate carbon−fluorine assumes coupling. Therefore, $^4J_{CF}$ could be used as a criterion for the determination of configurational and conformational isomerism of F-alkyl-containing olefins. To our knowledge, such a description of the use of $^nJ_{CF}$ coupling constants for the determination of conformations has not been reported in the literature until now.

In conclusion, we provided new trifluoromethyl- and perfluoroalkyl-containing synthons **3a**−**s** in a two-step reaction starting from commercially available R_FI. Then we explored the reactivity of **3** and prepared push−pull derivatives **4**, **5**, **8a**,**b**, and nonconjugated compounds **6** and **7**. The $^4J_{CF}$ coupling constants observed in the ^{13}C NMR spectra allowed us to establish a valuable methodology for the determination of configurations of unsaturated derivatives, such as **3**−**7**, and even the determination of conformational preferences of compounds, such as **8a** and **8b**, in favorable solvents.

Experimental Section

General Procedure for the Preparation of Perfluoroalkylated Propenals 3a−k and 3s. In a typical procedure, to a stirred solution of *gem*-iodoacetoxy compound **1** (1 equiv) in *n*-heptane or petroleum ether (5 mL/1 g of **1**) was added portion wise 3 equiv of the corresponding sodium phenoxides **2** at 0 °C. After 30 min, the resulting brown mixture was stirred at 20 °C until ^{19}F NMR signals disappeared, corresponding to the starting product **1** (1−2 h). At the end of the reaction, the brown precipitate which had formed was eliminated by vacuum filtration and was washed five times with heptane or petroleum ether. The filtrate was concentrated in vacuo to give brown oil. Then it was diluted in dichloromethane, washed five times with 1% aqueous sodium hydroxide solution to eliminate excess of phenols, and concentrated under reduced pressure. The resulting yellow oil was purified by column chromatography on silica gel (EtOAc/petroleum ether, 6/94) to afford **3**. All of these enol ethers are described for the first time. In each case, the corresponding substituted phenylacetate was isolated (1 equiv compared to **1**) and identified. Here we describe only the phenylacetates obtained in reactions of **3a**, **3l**, and **3o**.

3-Phenoxy-3-trifluoromethylprop-2-enal (3a). Sodium phenoxide (15.7 g, 0.135 mol) was added to a solution of 15 g (4.5×10^{-2} mol) of **1** (R_F = CF_3) in 75 mL of dry heptane at 0 °C. The mixture was stirred for 30 min at 0 °C then for 2 h at 20 °C. In this case, no chromatographic purifications were needed (only washing five times with 1% aqueous sodium hydroxide solution to eliminate excess of phenols); 9.3 g of the title product was obtained, with a total yield of 90% (*EE/ZE*: 64:36): ^{1}H NMR (300.13 MHz, $CDCl_3$) δ (*EE*) 5.6 (d, J = 7.3 Hz, 1H), 7−7.5 (m, 5H), 9.9 (d, J = 7.3 Hz, 1H); (*ZE*) 6.2 (d, J = 7.2 Hz, 1H), 7−7.5 (m, 5H), 9.6 (d, J = 7.1 Hz, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 113.5, 115, 117.5, 121, 144.3, 156.5, 157.5, 159 (q, C−CF_3, $^2J_{CF}$ = 28.6 Hz), 186.8 (s, CHO (*Z*)), 187.5 (q, CHO (*E*), $^4J_{CF}$ = 9 Hz); ^{19}F NMR (282.4 MHz, $CDCl_3$) δ −64.8 (s, 3F, (*EE*), 64%), −71 (s, 3F, (*ZE*), 36%). MS (*m*/*z*): 217 (M^+, 100). HRMS calcd for $C_{10}H_8F_3O_2$ 217.0476, found 217.0477. Anal. Calcd for $C_{10}H_7F_3O_2$: C, 55.56; H, 3.26; O, 14.80. Found: C, 55.55; H, 3.26; O, 14.81. Chromatographic purification of the reaction mixture allowed us to isolate 6.1 g (4.49×10^{-2} mol) of phenylacetate: ^{1}H NMR (300.13 MHz, $CDCl_3$) δ 2.1 (s, 3H), 7−7.4 (m, 5H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 20.4, 121.5, 126.6, 125.5, 130.1, 155.2, 170.1. MS (*m*/*z*): 137 (M^+, 100). HRMS calcd for $C_8H_9O_2$ 137.0603, found 137.0610. Anal. Calcd for $C_8H_8O_2$: C, 70.57; H, 5.92; O, 23.50. Found: C, 70.58; H, 5.92; O, 23.49.

General Procedure for the Preparation of Perfluoroalkylated Propenals (3l−n). To a stirred solution of perfluoroalkylated *gem*-iodoacetoxy compound **1** (1 equiv) in dry *n*-heptane or petroleum ether (5 mL/ 1 g of **1**) was added 3 equiv of the corresponding substituted phenoxides **2**. The mixture was stirred at 40 °C (Table 1) for the desired time until complete consumption of the starting material was judged by TLC and ^{19}F NMR spectroscopy. At the end of the reaction, the mixture was filtered and evaporated; the residue was worked up and chromatographed as described previously to afford the desired products **3**.

3-(4-Chlorophenoxy)-3-perfluoropentylprop-2-enal (3l). Sodium 4-chlorophenoxide (12.7 g, 0.084 mol) was added to a stirred solution of 15 g (2.8×10^{-2} mol) of **1** (R_F = C_5F_{11}) in 75 mL of dry heptane or petroleum ether. The mixture was stirred at 40 °C for 12 h, and 10.2 g of the title product was obtained: total yield 80% (*EE/ZE*: 92/8); ^{1}H NMR (300.13 MHz, $CDCl_3$) δ (*EE*) 5.6 (d, J = 7.3 Hz, 1H), 7 (s, 4H), 9.9 (d, J = 7.3 Hz, 1H); (*ZE*) 6 (d, J = 7.3 Hz, 1H), 7 (s, 4H), 9.4 (d, J = 7.3 Hz, 1H); ^{13}C NMR

(75.4 MHz, $CDCl_3$) δ 114.2, 115.5, 118.6, 121.6, 145.2, 158, 159.5 (t, C−CF_3, $^2J_{CF}$ = 27.8 Hz), 187.5 (s, CHO (*ZE*)), 188.2 (t, CHO (*EE*), $^4J_{CF}$ = 8.3 Hz); ^{19}F NMR (282.4 MHz, $CDCl_3$) δ −81 (s, 3F), −111.2 (s, 2F, (*EE*), 92%), −116.5 (s, 2F, (*ZE*), 8%), −123.3 (s, 4F), −127 (s, 2F). MS (*m*/*z*): 451.5 (M^+, 100). HRMS calcd for $C_{14}H_7ClF_{11}O_2$ 450.9959, found 450.9961. Anal. Calcd for $C_{14}H_6ClF_{11}O_2$: C, 37.31; H, 1.34; O, 7.10. Found: C, 37.31; H, 1.33; O, 7.11. Chromatographic purification of the reaction mixture allowed us to isolate 4.75 g (2.79×10^{-2} mol) of 4-chlorophenylacetate: ^{1}H NMR (300.13 MHz, $CDCl_3$) δ 2.2 (s, 3H), 7 (d, J = 7.5 Hz, 2H), 7.3 (d, J = 7.5 Hz, 2H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 20.6, 123.1, 123.2, 129.4, 132.1, 150.5, 170.3. MS (*m*/*z*): 171 (M^+, 100). HRMS calcd for $C_8H_8ClO_2$ 171.0213, found 171.0216. Anal. Calcd for $C_8H_7ClO_2$: C, 56.32; H, 4.14; O, 18.76. Found: C, 56.34; H, 4.14; O, 18.77.

General Procedure for the Preparation of 3-Perfluoroalkyl-3-(4-nitrophenoxy)prop-2-enals (3o,p). To a stirred solution of perfluoroalkylated *gem*-iodoacetoxy compound **1** (1 equiv) in dry *n*-heptane (5 mL/ 1 g of **1**) was added 3 equiv of 4-nitrophenoxide **2**. The mixture was stirred at 80 °C for the desired time (Table 1) until complete consumption of the starting material was judged by TLC and ^{19}F NMR spectroscopy. At the end of the reaction, the mixture was filtered and evaporated; the residue was worked up and chromatographed as described previously to afford the desired products **3o**,**p**.

3-(4-Nitrophenoxy)-3-perfluoropentylprop-2-enal (3o). Sodium 4-nitrophenoxide (9 g, 0.056 mol) was added to a stirred solution of 10 g (1.8×10^{-2} mol) of **1** ($R_F = C_5F_{11}$) in 50 mL of dry *n*-heptane. The mixture was stirred at 80 °C for 48 h, and 5.63 g of the title product was obtained: total yield 65% (*EE*/*ZE*: 60/40). The mixture of both stereoisomers was precipitated in heptane at −20 °C. A white solid of pure *E* isomer was obtained: ^{1}H NMR (300.13 MHz, $CDCl_3$) δ (*EE*) 5.7 (d, J = 7 Hz, 1H), 7.3 (d, J = 7.2 Hz, 2H), 8.5 (d, J = 7.1 Hz, 1H), 10 (d, J = 7 Hz, 1H); (*ZE*) 6.6 (d, J = 6.8 Hz, 1H), 7.3 (d, J = 7.2 Hz, 2H), 8.5 (d, J = 7.1 Hz, 1H), 9.8 (d, J = 6.9 Hz, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 114, 115.5, 119.1, 121.4, 145.3, 151.3, 158.4, 160.2 (t, C−CF_3, $^2J_{CF}$ = 29.1 Hz), 187.1 (s, CHO (*ZE*)), 188.2 (t, CHO (*EE*), $^4J_{CF}$ = 8 Hz); ^{19}F NMR (282.4 MHz, $CDCl_3$) δ −81 (s, 3F), −111 (s, 2F, (*EE*), 60%), −116 (s, 2F, (*ZE*), 40%), −122 (s, 4F), −126 (s, 2F). Spectral data of *EE* isomer: ^{1}H NMR (300.13 MHz, $CDCl_3$) δ 5.6 (d, J = 6.9 Hz, 1H), 7.3 (d, J = 7.2 Hz, 2H), 8.5 (d, J = 7.2 Hz, 2H), 10 (d, J = 6.9 Hz, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 115.2, 121.6, 126.3, 146.2, 156.3, 157.2 (t, C−CF_3, $^2J_{CF}$ = 29.4 Hz), 187.2 (t, CHO (*EE*), $^4J_{CF}$ = 9 Hz); ^{19}F NMR (282.4 MHz, $CDCl_3$) δ −80.6 (s, 3F), −111.2 (s, 2F), −122.5 (s, 4F), −126 (s, 2F). Spectral data of *ZE* isomer: ^{1}H NMR (300.13 MHz, $CDCl_3$) δ 6.6 (d, J = 6.8 Hz, 1H), 7.3 (d, J = 7.3 Hz, 2H), 8.5 (d, J = 7.3 Hz, 1H), 9.8 (d, J = 6.9 Hz, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 116.1, 122.9, 126.5, 144.3, 152.9 (t, C−CF_3, $^2J_{CF}$ = 27 Hz), 161.4, 186.4 (s, CHO (*ZE*)); ^{19}F NMR (282.4 MHz, $CDCl_3$) δ −80.7 (s, 3F), −115.6 (s, 2F), −122.1 (s, 2F), −122.5 (s, 2F), −126.1 (s, 2F). MS (*m*/*z*): 462 (M^+, 100). HRMS calcd for $C_{14}H_7F_{11}NO_4$ 462.0199, found 462.0196. Anal. Calcd for $C_{14}H_6F_{11}NO_4$: C, 36.46; H, 1.31; O, 13.88. Found: C, 36.48; H, 1.33; O, 13.86. Chromatographic purification of the reaction mixture allowed us to isolate 3.23 g (1.78×10^{-2} mol) of 4-nitrophenylacetate: ^{1}H NMR (300.13 MHz, $CDCl_3$) δ 2 (s, 3H), 7.3 (d, J = 7.4 Hz, 2H), 7.9 (d, J = 7.5 Hz, 2H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 20.4, 122.2, 123.5, 146.1, 158.1, 169.9. MS (*m*/*z*): 182 (M^+, 100). HRMS calcd for $C_8H_8NO_4$ 182.0453, found 182.0455. Anal. Calcd for $C_8H_7NO_4$: C, 53.04; H, 3.89; O, 35.33. Found: C, 53.00; H, 3.91; O, 35.34.

Reaction of 3c with Aniline: Synthesis of 1-Phenylimino-3-phenoxy-3-perfluoropentylprop-2-ene 4. To a solution of 4.27 g (1.02×10^{-2} mol) of **3c** in dichloromethane (20 mL) was added 0.95 g (1.02×10^{-2} mol) of aniline. The mixture was stirred at room temperature for 2 h. At the end of the reaction, the solution was diluted with dichloromethane and washed with water. The organic layer was dried over sodium sulfate and concentrated in vacuo. The resulting oil was purified by column chromatography over silica gel to afford **4** (4.72 g, 9.610^{-3} mol, 94%): ^{1}H NMR (300.13 MHz, C_6D_6, *EE* 99%) δ (*EE*) 6.4 (d, $^3J_{H1H2}$ = 9.1 Hz, H_2), 6.8−7.3 (m, 10H), 8.7 (d, $^3J_{H1H2}$ = 9 Hz, H_1); ^{13}C NMR (75.4 MHz) δ (*EE*) 116.8, 117.4, 121.5, 121.7, 127.1, 127.7, 130.3, 131.4, 152.2 (t, C_3−CF_3, $^2J_{CF}$ = 27.3 Hz), 153, 153.9, 154.4 (t, H*C*=N (*EE*), $^4J_{C1F}$ = 5.7 Hz); ^{19}F NMR (282.4 MHz) δ −80.8 (s, 3F), −111.4 (m, 2F, (*EE*), 99%), −115 (s, 2F, (*ZE*), 1%), −122.3 (s, 4F), −125.9 (s, 2F); ^{1}H NMR (300.13 MHz, $CDCl_3$, *ZE*/*EE* 15/85) δ (*EE*) 6.2 (d, $^3J_{H1H2}$ = 9 Hz, 1H), 7−7.5 (m, 10H), 8.5 (d, $^3J_{H1H2}$ = 9 Hz, 1H); (*ZE*) 6.9 (d, $^3J_{H1H2}$ = 8.9 Hz, 1H), 7−7.5 (m, 10H), 8.2 (d, $^3J_{H1H2}$ = 8.9 Hz, 1H); ^{13}C NMR (75.4 MHz) δ 115.1, 115.8, 120.8, 121, 123 (t, $^3J_{C2F}$ = 4.9 Hz, C_2, (*ZE*)), 126.4, 126.7, 127.4, 129.2, 129.3, 130.1, 130.5, 146.8 (t, C_3−CF_3, $^2J_{CF}$ = 25.8 Hz), 150.7, 151.4, 152.2 (t, C_3−CF_3, $^2J_{CF}$ = 27.3 Hz), 152.7, 153.2 (s, H*C*=N (*ZE*)), 154.6 (t, H*C*=N (*EE*), $^4J_{C1F}$ = 5.9 Hz), 157.7; ^{19}F NMR (282.4 MHz) δ −80.8 (s, 3F), −111.7 (m, 2F, (*EE*), 85%), −114.9 (m, 2F, (*ZE*), 15%), −122.5 (m, 4F), −126.1 (s, 2F); ^{1}H NMR (300.13 MHz, CD_3CN, *ZE* 92%) δ (*ZE*) 6.7 (d, $^3J_{H1H2}$ = 9.2 Hz, 1H), 6.8−7.3 (m, 10H), 8.1 (d, $^3J_{H1H2}$ = 9 Hz, 1H); ^{13}C NMR (75.4 MHz) δ (*ZE*) 115.6, 120.6, 122.7 (t, $^3J_{C2F}$ = 4.8 Hz, C_2, (*ZE*)), 123.8, 127, 128.9, 130, 145.9 (t, C_3−CF_3, $^2J_{CF}$ = 25.8 Hz), 150, 152.9, 157.3 (s, H*C*=N (*ZE*)); ^{19}F NMR (282.4 MHz) δ −81.5 (s, 3F), −111.8 (m, 2F, (*EE*), 8%), −115.5 (s, 2F, (*ZE*), 92%), −122.5 (s, 2F), −123 (s, 2F), −126.6 (s, 2F). MS (*m*/*z*): 492 (M^+, 100). HRMS calcd for $C_{20}H_{13}F_{11}NO$ 492.0821, found 492.0822. Anal. Calcd for $C_{20}H_{12}F_{11}NO$: C, 48,89; H, 2.46; O, 3.26. Found: C, 48.90; H, 2.46; O, 3.28.

Synthesis of Methyl (*EEE*)-5-(4-Methoxyphenoxy)-5-perfluoropentyl-2,4-pentadienoate 5. To a solution of 2.25 (1.23×10^{-2} mol) of trimethylphosphonoacetate in methanol (8 mL) was added portion wise 0.35 g (1.47×10^{-2} mol) of sodium hydride. The resulting suspension was stirred at room temperature, and 5.5 g (1.23×10^{-2} mol) of **3f** was added. The mixture was stirred for 2 h, filtered, and concentrated in vacuo. The resulting oil was diluted in ether and washed with water. The organic layer was dried over sodium sulfate and concentrated in vacuo. The resulting oil was precipitated in petroleum ether at 0 °C to give **5** with very high yield as a white solid (6.2 g, 0.0123 mol, 100%): ^{1}H NMR (300.13 MHz, C_6D_6) δ 3.3 (s, 3H), 3.4 (s, 3H), 5.5 (d, $^3J_{H2H3}$ = 15.1 Hz, H_2), 5.8 (d, $^3J_{H3H4}$ = 12 Hz, H_4), 6.7 (d, J = 7.8 Hz, 2H), 6.8 (d, J = 7.8 Hz, 1H), 8 (dd, J = 12.6 and 14.6 Hz, H_3); ^{13}C NMR (75.46 MHz, C_6D_6) δ 51.2, 55, 113.1, 115.5, 121.8, 125.1, 134.8 (t, C_3=C, $^4J_{C3F}$ = 6.4 Hz), 146.7, 149.1 (t, C−CF_3, $^2J_{C5F}$ = 25.8 Hz), 157.8, 165.8; ^{19}F NMR (235.36 MHz, C_6D_6) δ −81 (s, 3F), −113 (s, 2F), −123 (s, 4F), −126 (s, 2F). MS (*m*/*z*): 503 (M^+, 100). HRMS calcd for $C_{18}H_{14}F_{11}O_4$ 503.0716, found 503.0718. Anal. Calcd for $C_{18}H_{13}F_{11}O_4$: C, 43.04; H, 2.61; O, 12.74. Found: C, 43.06; H, 2.60; O, 12.73.

Synthesis of 3-(4-Methoxyphenoxy)-3-perfluoropentylprop-2-enol 6. To a solution of 10 g (2.24×10^{-2} mol) of **3f** in 30 mL of dry methanol was added 0.42 g (1.12×10^{-2} mol) of sodium borohydride. The resulting solution was stirred for 6 h at room temperature. At the end of the reaction, the mixture was concentrated in vacuo, diluted with ether, and washed with water. The organic layer was dried over sodium sulfate then concentrated in vacuo. Final alcohol **6** was obtained with total conversion (10 g, 0.0223 mol, 100%): ^{1}H NMR (250.13 MHz, C_6D_6, mixture of *E* and *Z* isomers, 95/5) δ (*E*) 1.6 (br s, 1H), 3.3 (s, 3H), 4.1 (m, 2H), 5.3 (t, J = 6.8 Hz, H_2), 6.6 (d, J = 7.6 Hz, 2H), 6.8 (d, J = 7.7 Hz, 2H); (*Z*) 1.4 (br s, 1H), 3.3 (s, 3H), 3.9 (m, 2H), 6 (t, J = 6.1 Hz, H_2), 6.6 (d, J = 7.6 Hz, 2H), 6.8 (d, J = 7.7 Hz, 2H); ^{13}C NMR (100.61 MHz, C_6D_6) δ 36 (s, *C*H_2OH, (*Z*)), 37.2 (t, *C*H_2OH, (*E*), $^4J_{C1F}$ = 6.6 Hz), 55.1, 55.2, 112.4, 115.4, 115.6, 116.7, 121.9, 122.3, 141.7 (t, C−CF_3, $^2J_{C3F}$ = 25.5 Hz), 146.7 (t, C−CF_3, $^2J_{C3F}$ = 25.7 Hz), 147.1, 150.7, 156.4, 157.8; ^{19}F NMR (235.3 MHz, C_6D_6) δ −81.5 (s, 3F), −113 (s, 2F, (*E*), 95%), −115 (s, 2F, (*Z*), 5%), −123 (s, 4F), −127 (s, 2F). MS (*m*/*z*): 449 (M^+, 100). HRMS calcd for $C_{15}H_{12}F_{11}O_3$ 449.0611, found 449.0614. Anal. Calcd for

$C_{15}H_{11}F_{11}O_3$: C, 40,19; H, 2.47; O, 10.71. Found: C, 40.21; H, 2.45; O, 10.73.

Reaction of 3-(4-Methoxyphenoxy)-3-perfluoropentylprop-2-enal 3f with Triethylorthoformate: Synthesis of Acetals 7. To a solution of 3.6 g (8×10^{-3} mol) of **3f** and 3.6 g (2.4×10^{-2} mol) of triethylorthoformate in 7 mL of dry ethanol was added 1.39 g (8×10^{-3} mol) of *para*-toluenesulfonic acid. The resulting mixture was put under reflux for 6 h. At the end of the reaction, the mixture was concentrated in vacuo, diluted with ether, and washed with a solution of 2% sodium hydrogenocarbonate (until the aqueous layer had pH > 7). The organic layer was then dried over sodium sulfate and concentrated in vacuo to give final product **7** (4 g, 7.7×10^{-3} mol, 96%): ^{1}H NMR (300.13 MHz, $CDCl_3$, (*E*)-**7**) δ 1.1 (t, $J = 7$ Hz, 6H), 3.4 (m, 2H), 3.6 (m, 2H), 3.8 (s, 3H), 5.1 (d, $^3J_{H1H2} = 7.5$ Hz, 1H), 6.1 (d, $^3J_{H1H2} = 7.5$ Hz, 1H), 6.8 (d, $J = 9$ Hz, 2H), 7(d, $J = 9$ Hz, 2H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 15, 55.6, 62, 63.2, 95.8, 114.6, 116.5, 123.6 (t, $C_1-(OEt)_2$, $^4J_{C1F} = 8$ Hz); ^{19}F NMR (282.4 MHz, $CDCl_3$) δ −80.7 (s, 3F), −114.7 (s, 2F), −122.2 (s, 2F), −122.6 (s, 2F), −126.1 (s, 2F). MS (*m*/*z*): 521 (M^+, 100). HRMS calcd for $C_{19}H_{20}F_{11}O_4$ 521.1186, found 521.1189. Anal. Calcd for $C_{19}H_{19}F_{11}O_4$: C, 43,-86; H, 3.68; O, 12.30. Found: C, 43.88; H, 3.68; O, 12.31.

Reaction of 3d with Aniline: Synthesis of 2-Trifluoromethyl-1-phenylamino-3-phenyliminopropene 8a. To a solution of 1 g (4×10^{-3} mol) of **3d** in dichloromethane (5 mL) was added 0.75 g (8.1×10^{-3} mol) of aniline. The mixture was put under reflux for 3 h. At the end of the reaction, the solution was diluted with dichloromethane and washed with water. The organic layer was dried over sodium sulfate and concentrated in vacuo. The resulting powder was recrystallized from petroleum ether at 0 °C to yield diazapentadiene **8a** (1.1 g, 3.8×10^{-3} mol, 94%): ^{1}H NMR (DMSO-d_6, *EEE*) δ 5.5 (d, $^3J_{H2H3} = 13.7$ Hz, H_2), 6.8 (d, $J = 7.5$ Hz, 2H), 7 (m, 3H), 7.15 (t, $J = 7.4$ Hz, 1H), 7.3 (t, $J = 7.8$ Hz, 2H), 7.4 (t, $J = 7.7$ Hz, 2H), 7.6 (t, $J = 13$ Hz, H_3), 9.9 (d, $^3J_{H3NH} = 12.3$ Hz, N*H*); ^{13}C NMR δ 90.8, 115, 119.2, 120.6 (q, CF_3, $^1J_{CF} = 279.2$ Hz), 122.14, 123.6, 129.3, 129.6, 140.64, 140.8 (q, C_3H, $^4J_{C3F} = 3$ Hz), 149.5, 153.3 (q, $C-CF_3$, $^2J_{C1F} = 30.5$ Hz); ^{19}F NMR δ −65.8 (s, 3F); ^{1}H NMR (300.13 MHz, C_6D_6, *EEE*/*ZZE* 36/64) δ (*EEE*) 5.1 (br s, 1H, N*H*), 5.2 (d, $^3J_{H2H3} = 14$ Hz, H_2), 6.4−7.4 (m, 10H), 7.5 (t, $J = 14$ Hz, H_3); (*ZZE*) 5.4 (d, $^3J_{H2H3} = 7.8$ Hz, H_2), 6.4−7.4 (m, 10H), 7 (m, H_3), 12 (br d, $^3J_{H3NH} = 10$ Hz, N*H*); ^{13}C NMR δ 90.4, 93.2, 115.5, 116.6, 119.8, 120.3, 122.8, 123.7, 124, 124.2, 128.9, 129.5, 129.7, 129.8, 139.7 (q, C_3H, $^4J_{C3F} = 3$ Hz, (*EEE*)), 140.4, 141.2, 142.3 (s, C_3H, (*ZZE*)), 148.5, 150.6, 152.8 (q, C_1-CF_3, $^2J_{C1F} = 27$ Hz), 153.8 (q, C_1-CF_3, $^2J_{C1F} = 31.9$ Hz); ^{19}F NMR δ −62.2 (s, 3F, (*ZZE*), 64%), −66.6 (s, 3F, (*EEE*), 36%). MS (*m*/*z*): 291 (M^+, 100). HRMS calcd for $C_{16}H_{14}F_3N_2$ 291.1109, found 291.1087 Anal. Calcd for $C_{16}H_{13}F_3N_2$: C, 66.20; H, 4.51; N, 9.65. Found: C, 66.15; H, 4.31; N, 9.45.

Reaction of 4 with Aniline: Synthesis of 2-Perfluoropentyl-1-phenylamino-3-phenyliminopropene 8b. To a solution of 1 g (2×10^{-3} mole) of **4** in dichloromethane (5 mL) was added 0.19 g (2×10^{-3} mol) of aniline. The mixture was put under reflux for 2 h. At the end of the reaction, the solution was diluted with dichloromethane and washed five times with water. The organic layer was dried over sodium sulfate and concentrated in vacuo. The resulting liquid was recrystallized from petroleum ether at 0 °C to yield diazapentadiene **8b** (0.9 g, 1.81×10^{-3} mol, 90%).

Acknowledgment. We would like to thank Dr. Maryse Bejaud for NMR analyses and interesting discussions.

Supporting Information Available: Experimental procedures and analytical data for compounds **3b**−**k**,**m**,**n**,**p**,**s** and **8b**; copies of ^{1}H, ^{13}C, cosy ^{1}H−^{1}H, ^{13}C−^{1}H, or ^{19}F NMR spectra of **3a**−**s**, **4**−**7**, and **8a**,**b**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO060764I