New Strategies for the Synthesis of Fluorinated Vinylogous Amidines and β-Enamino Ketones

Santos Fustero,* Marta García de la Torre, Belén Pina, and Antonio Simón Fuentes

Departamento de Química Orgánica, Facultad de Farmacia, Universidad de Valencia, 46100-Burjassot (Valencia), Spain

Received March 4, 1999

Reaction of fluorinated imidoyl chlorides **3** with ketimines **1a** provides fluorinated 1,3-diimines, which were exclusively isolated as vinylogous amidine tautomers **2**β, with good yields. Fluorinated β-enamino ketones **4** are obtained by regioselective hydrolysis of **2**. Complementary methods for the synthesis of regioisomeric β-enamino ketones **4** and **5** are also reported. These methods include the reaction of azaenolates of ketimines with fluorinated esters **6** and reactions of ketone enolates with fluorinated imidoyl chlorides **3**. The behavior of these systems in hydrolysis reactions was also tested.

Introduction

In the past few years organofluorine chemistry has returned as an expanding and productive area of research, as can be seen by the increasing number of recent publications, reviews, topics, and monographs.[1] Furthermore, organofluorine chemicals have found a wide range of applications in medicine and agriculture due, in part, to the unique biological properties imparted by fluorine.[1,2] In addition, 1,2- and 1,3-difunctionalized compounds are useful building blocks for the construction of new and interesting biologically active substrates.[3] Thus, while the direct fluorination of these compounds has emerged as one of the most powerful strategies for synthesizing fluorinated oxygen derivatives,[4] the building block strategy currently represents an attractive alternative for the introduction of fluorine or fluorinated substituents into these acyclic nitrogen compounds.[5]

Fluorine-containing amino compounds such as β-amino alcohols and α- and β-amino acids are important targets due mainly to their synthetic applications as well as to the diverse biological functions exhibited, for example, in the study of biochemical processes.[6] By contrast, much less effort has been focused on the preparation and reactivity of fluorinated 1,3-difunctionalized analogues which contain an enamino moiety in their framework, and which are considered to be precursors of acyclic and heterocyclic compounds of pharmacological interest.[7]

In the context of our ongoing study of the synthesis and reactivity of 1,3-difunctionalized fluorine-containing organocompounds,[5b,8] we have now focused our attention on fluorinated vinylogous amidines and β-enamino ketones. Although nonfluorinated vinylogous amidines are well-known systems,[9] to our knowledge no papers concerning fluorine-containing analogues have yet been published.

In this paper we report for the first time an efficient and simple method of synthesis of fluorinated vinylogous amidines **2** starting from imidoyl chlorides **3** and enolizable ketimines **1a** (X = NR^2). We also describe new and complementary procedures for the synthesis of regioisomeric fluorinated β-enamino ketones **4** and **5** (Scheme 1). In addition, the behavior of these systems in hydrolysis reactions is also reported.

† E-mail: santos.fustero@uv.es.

(1) (a) Resnati, G.; Soloshonok, V. A. Tetrahedron Symposia-in Print no. 58. *Tetrahedron* **1996**, *52*, 1, 319. (b) Banks, R. E.; Tatlow, J. C.; Smart, B. E. *Organofluorine Chemistry: Principles and Commercial Applications*; Plenum Press: New York, 1994. (c) Prakash, G. K. S.; Yudin, A. K. *Chem. Rev.* **1997**, *97*, 757−786.

(2) (a) Kitazume, T.; Lin, J. T.; Yamamoto, T.; Yamazaki, T. *J. Am. Chem. Soc.* **1991**, *113*, 8573. (b) Welch, J. T. *Selective Fluorination in Organic and Bioorganic Chemistry*, ACS Symposium Series 456; American Chemical Society: Whashington, DC, 1991. (c) Filler, R.; Kobayashi, Y.; Yagupolskii, L. M. *Biomedical Aspects of Fluorine Chemistry*; Elsevier: Amsterdam, 1993. (d) Welch, J. T.; Eswarakrishnan, S. *Fluorine in Bioorganic Chemistry*; Wiley: Chichester, 1991.

(3) (a) Beholz, L. G.; Benovsky, P.; Ward, D. L.; Barta, N. S.; Stille, J. R. *J. Org. Chem.* **1997**, *62*, 1033. (b) Fustero, S.; García de la Torre, M.; Jofré, V.; Pérez Carlón, R.; Navarro, A.; Simón Fuentes, A.; Server Carrió, J. *J. Org. Chem.* **1998**, *63*, 8825 and references therein.

(4) See for example: (a) German, L.; Zemskov, S. *New Fluorinating Agents in Organic Synthesis*; Springer-Verlag: Berlin, Heidelberg, 1989. (b) Banks, R. E. *J. Fluorine Chem.* **1998**, *87*, 1−17.

(5) (a) Uneyama, K.; Tamura, K.; Mizukami, H.; Maeda, K.; Watanabe, H. *J. Org. Chem.* **1993**, *58*, 32. (b) Fustero, S.; Navarro, A.; Díaz, D.; de la Torre, M. G.; Asensio, A.; Sanz, F.; Liu González, M. *J. Org. Chem.* **1996**, *61*, 8849. (c) Liu-González, M.; Sanz, F.; Navarro, A.; de la Torre, M. G.; Fustero, S. *Acta Crystallogr.* **1998**, *C54*, 875. (d) Bravo, P.; Farina, A.; Kukhar, V. P.; Markovsky, A. L.; Meille, S. V.; Soloshonok, V. A.; Viani, F.; Sorochinsky, A. E.; Zanda, M.; Zappalá, C. *J. Org. Chem.* **1997**, *62*, 3424. (e) Bravo, P.; Guidetti, M.; Viani, F.; Zanda, M.; Markovsky, A. L.; Sorochinsky, A. E.; Soloshonok, I. V.; Soloshonok, V. A. *Tetrahedron* **1998**, *54*, 12789.

(6) (a) *Fluorine-containing Amino Acids: Synthesis and Properties*; Kukhar, V. P., Soloshonok, V. A., Eds.; Wiley: Chichester, 1994. (b) Bégué, J.-P.; Bonnet-Delpon, D. Trifluoromethylated Amino Alcohols: New Synthetic Approaches and Medicinal Targets. In *Biomedical Frontiers of Fluorine Chemistry*; Ojima, I., McCarthy, J. R., Welch, J. T., Eds.; ACS Books, American Chemical Society: Washington, DC, 1996; pp 59−72. (c) Soloshonok, V. A.; Ono, T.; Soloshonok, I. V. *J. Org. Chem.* **1997**, *62*, 7538. (d) Soloshonok, V. A.; Soloshonok, I. V.; Kuhkar V. P.; Svedas, V. K. *J. Org. Chem.* **1998**, *63*, 1878.

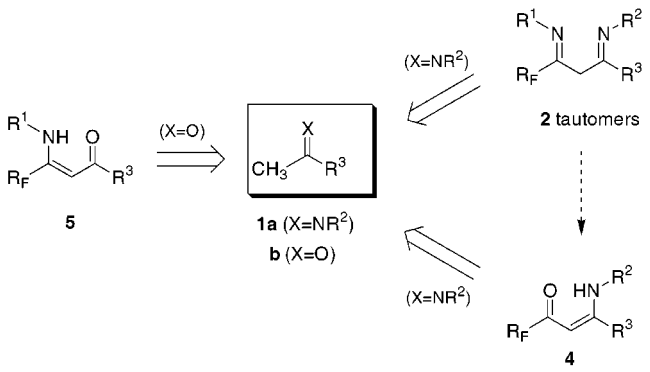
(7) (a) Uneyama, K.; Kobayashi, M. *J. Org. Chem.* **1994**, *59*, 3003. (b) Uneyama, K.; Kobayashi, M. *Tetrahedron Lett.* **1991**, *32*, 5981. (c) Uneyama, K.; Morimoto, O.; Yamashita, F. *Tetrahedron Lett.* **1989**, *30*, 4821. (d) Arnone, A.; Bravo, P.; Capelli, S.; Fronza, G.; Meille, S. V.; Zanda, M.; Cavicchio, G.; Crucianelli, M. *J. Org. Chem.* **1996**, *61*, 3375. Corrigenda: *J. Org. Chem.* **1996**, *61*, 9635.

(8) (a) Fustero, S.; Navarro, A.; Asensio, A. *Tetrahedron Lett.* **1997**, *38*, 4891. Corrigenda: *Tetrahedron Lett.* **1997**, *38*, 6477. (b) Fustero, S.; Navarro, A.; Pina, B.; Asensio, A.; Bravo, P.; Crucianelli, M.; Volonterio, A.; Zanda, M. *J. Org. Chem.* **1998**, *63*, 6210. (c) Fustero, S.; Pina, B.; Simón Fuentes, A. *Tetrahedron Lett.* **1997**, *38*, 6771.

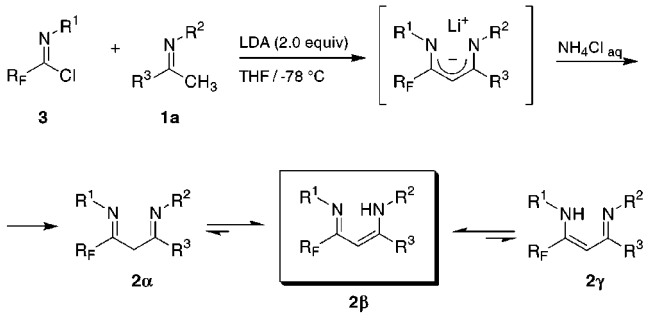
(9) (a) Knorr, R.; Weiss, A. *Chem. Ber.* **1982**, *115*, 139. (b) Barluenga, J. Tomás, M. In *Advances in Heterocyclic Chemistry* **1993**, *57*, 1 and references therein.

10.1021/jo990392w CCC: $18.00
Published on Web 07/09/1999

Scheme 1



Scheme 2



Results and Discussion

In a general experiment, reaction of equimolecular amounts of *N*-substituted fluorinated imidoyl chlorides **3**[5a] and ketimines **1a** (X = NR^2) in THF solution at −78 °C led to a unique mono-*C*-acylated product **2** with good yields as measured by ^{1}H NMR spectroscopy of the crude reaction mixture (Scheme 2). Two equivalents of LDA were necessary for the success of the reaction. [10] Table 1 summarizes the fluorinated vinylogous amidines **2** obtained.

The results reported in Table 1 suggest that the method works well and can be used for both cyclic and acyclic ketimines as well as for aromatic and aliphatic amines (R^1 and R^2). Moreover, it allows easy introduction of chiral substituents at one or both nitrogen atoms (Table 1, entries 11−16). No regioisomers corresponding to *N*-acylation or other competing processes such as polyacylation reactions were observed.[9a]

However, it is also noteworthy that even though several tautomeric **2**α-*γ* and geometric (*Z* or *E*) structures are possible,[9,11] products **2** were always isolated as *single* tautomers. NMR analyses (^{1}H, ^{13}C, and ^{19}F) were in agreement only with enamino structures of type **2***β*. For example, the analysis of the ^{1}H NMR spectra for compounds **2** revealed several interesting features. Specifically, the signals corresponding to the $C_6H_5(Me)CH$ group (R^1 substituent) of compounds **2n** and **2o** (Table 1, entries 14 and 15) appeared as a quartet at *δ* 4.65 and 4.87 ppm, respectively. In contrast, the signals of the $C_6H_5(Me)CH$ group (R^2 substituent) for **2k** (*δ* 4.72 ppm) and **2l** (*δ* 4.76 ppm) (Table 1, entries 11 and 12) appeared as a multiplet due to the additional coupling with the NH of the enaminic form.[12] In addition, the stereochemical assignment of the *Z* configuration for the enamino tautomer **2***β* was based on 2D HOESY NMR ^{1}H−^{19}F experiments using ^{1}H−^{19}F long correlations. Thus, for example, for **2a** (Table 1, entry 1) the vinylic hydrogen at *δ* 5.19 ppm (^{1}H NMR) has an intense cross-peak with the fluorine atoms at *δ* −62.7 ppm (^{19}F NMR). Additionally, the cross-peaks connecting the CF_3 group with the hydrogens of the *p*-anisidine ring unequivocally corroborate the *Z* configuration of the enamino tautomer **2***β*. These findings support the assigned structure.

Also worth emphasizing is the difficulty in preparing derivatives **2** by using other strategies, for example, through condensation reactions starting from the corresponding 1,3-dicarbonyl compounds, a typical procedure for nonfluorinated derivatives.[13] The reaction of fluorine-containing *β*-diketones with amines, for instance, generally yields a complex mixture of products[14] or *β*-enamino ketones resulting from a regioselective monocondensation.[15] These results could explain the lack of general methods for the preparation of fluorinated derivatives **2** in comparison with their nonfluorinated counterparts.[9,13a,b]

The reactivity of these derivatives was explored first in hydrolysis reactions. When 6 N H_2SO_4 was added to a THF solution of **2**, for example **2a**, **2c**, **2j**, and **2p** (Table 1, entries 1, 3, 10, and 16), and the mixture kept at 60 °C for several hours, regioselective hydrolysis occurred and only product **4***β* was detected in the crude reaction mixture (Scheme 3). Spectral data (HRMS and ^{1}H, ^{13}C, and ^{19}F NMR) of each of the reaction products **4a**−**d** revealed that, surprisingly, only the imine group bearing the fluoroalkyl substituent (R_F) had been regioselectively hydrolyzed leading to the corresponding fluorinated *β*-enamino ketones **4***β* in moderate to good yields (see Table 2, entries 1−4, method A). This reactivity was somewhat unexpected in light of that observed in related systems.[16] In fact, in just one case (Table 2, entry 2) and only after prolonged heating (6 N H_2SO_4 60 °C, overnight) was an approximately 1:1 mixture of **4b** and the corresponding 1,3-diketone obtained.

Fluorinated *β*-enamino ketones such as **4** have attracted the attention of several authors mainly due to the possibility of using them as building blocks of pharmacologically important CF_3-containing heterocycles.[17] Some of the methods developed for their synthesis have included 1,4-additions of aniline derivatives to trifluoroacetyl (TFA) acetylenes,[17] exchange reactions between *β*-TFA enol ethers and amines,[18] regioselective condensation reactions of fluoroalkyl-*β*-diketones with

(10) For related processes, see: (a) Bartoli, G.; Cimarelli, C.; Dalpozzo, R.; Palmieri, G. *Tetrahedron* **1995**, *51*, 8613. (b) Huang, W. S.; Yuan, C. I. *J. Chem. Soc., Perkin Trans. 1* **1995**, 741. (c) See also ref 5b.

(11) Barluenga, J.; Cuervo, H.; Olano, B.; Fustero, S.; Gotor, V. *Synthesis* **1986**, 469.

(12) In other examples due to overlapping peaks or broads signals, this assignment was more complex.

(13) (a) Knorr, R.; Weiss, A. *Chem. Ber.* **1981**, *114*, 2104. (b) Armesto, D.; Bosch, P.; Gallego, M. G.; Martín, J. F.; Ortíz, M. J.; Pérez Osorio, R.; Ramos, A. *Org. Prep. Proced. Int.* **1987**, *19*, 181. For related systems, see: (c) Kloek, J. A.; Leschinsky, K. L. *J. Org. Chem.* **1978**, *43*, 1460. (d) Ferraz, H. M. C.; Oliveira, E. O.; Payret-Arrua, M. E.; Brandt, C. A. *J. Org. Chem.* **1995**, *60*, 7357. (e) Soloshonok, V. A.; Kukhar, V. *Tetrahedron* **1996**, *52*, 6953.

(14) Ono, T.; Kuhkar, V. P.; Soloshonok, V. A. *J. Org. Chem.* **1996**, *61*, 6563.

(15) (a) Butler, A. R. George, S. D. *Tetrahedron* **1993**, *49*, 7017. (b) Filyakova, V. I.; Ratner, V. G.; Karpenko, N. S.; Paskevich, K. I. *Russ. Chem. Bull.* **1996**, *45*, 2163.

(16) Barluenga, J.; Jardón, J.; Gotor, V. *J. Org. Chem.* **1985**, *50*, 802.

(17) (a) Lang, R. W.; Wenk, P. F. *Helv. Chim. Acta* **1988**, *71*, 596. (b) Linderman, R.; Kirollos, S. *Tetrahedron Lett.* **1990**, *31*, 2689.

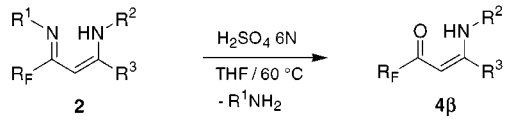
(18) Hojo, M.; Masuda, R.; Okada, E.; Sakaguchi, S.; Narumiya, H.; Morimoto, K. *Tetrahedron Lett.* **1989**, *30*, 6173.

Table 1. Fluorinated Vinylogous Amidines 2 Obtained

entry	R^1	R_F	R^2	R^3	product	yield[a,b] (%)	mp (°C)[c]
1	*p*-$MeOC_6H_4$	CF_3	$(CH_2)_3$		**2a**	80	oil
2	*p*-$MeOC_6H_4$	CF_2Cl	$(CH_2)_3$		**2b**	79	88−90
3	*p*-$MeOC_6H_4$	CF_3CF_2	$(CH_2)_3$		**2c**	80	72−4
4	*p*-$MeOC_6H_4$	$CF_3(CF_2)_7$	$(CH_2)_3$		**2d**	60	90−2
5	*p*-$MeOC_6H_4$	CF_3	*n*-Bu	*i*-Pr	**2e**	40	oil
6	*p*-$MeOC_6H_4$	CF_3	*n*-Bu	Ph	**2f**	93	oil
7	*p*-$MeOC_6H_4$	CF_2Cl	*n*-Bu	Ph	**2g**	82	oil
8	*p*-$MeOC_6H_4$	CF_{2Cl}	*c*-C_6H_{11}	C_2H_5	**2h**	70	oil
9	*p*-$MeOC_6H_4$	CF_3	Ph	Ph	**2i**	81	110−2
10	*p*-$MeOC_6H_4$	CF_2Cl	Ph	Ph	**2j**	77	oil
11	*p*-$MeOC_6H_4$	CF_2Cl	(±)-C_6H_5(Me)CH	*i*-Pr	**2k**	65	89−91
12	*p*-$MeOC_6H_4$	CF_3	(±)-C_6H_5(Me)CH	*i*-Pr	**2l**	48	45−7
13	*p*-$MeOC_6H_4$	CF_2Cl	(*R*)-(+)-C_6H_5(Me)CH	*i*-Pr	**2m**	85	90−2
14	(*R*)-(+)-C_6H_5(Me)CH	CF_3	$(CH_2)_3$		**2n**	75	oil
15	(*R*)-(+)-C_6H_5(Me)CH	CF_3	*n*-Bu	Ph	**2o**	68	oil
16	(*R*)-(+)-C_6H_5(Me)CH	CF_3	(*R*)-(+)-C_6H_5(Me)CH	*i*-Pr	**2p**	83	oil

[a] Isolated yields. [b] Purified by flash chromatography. [c] Melting points are uncorrected.

Scheme 3



amines,[15] and, more recently, *C*-trifluoroacetylation of enamines.[19] However, most of these methods appear to be either limited by the difficulty in obtaining the starting materials or restricted to trifluoromethyl derivatives, including the Hojo approach,[18] which has apparently been the most general strategy for producing derivatives **4**.[20]

The following alternative procedure for the synthesis of fluorinated β-enamino ketones **4** from simple ketimines **1a** and commercially available fluorinated esters **6** (Scheme 4) overcomes both of these limitations. By allowing a THF solution of ketimine **1a** (1.0 equiv) at −78 °C and containing 2 equiv of LDA[10] to react with a THF solution of a fluorinated ester **6** (1.1 equiv) and then stirring the mixture for 30 min, compounds **4** were obtained in good to moderate yields after standard workup (Table 2, entries 5−9, method B). These results indicate that the method also runs smoothly regardless of the nature of the starting ketimine and fluorinated ester (Table 2, entries 5−9).[21]

In a further experiment, we extended this methodology for the preparation of regioisomeric fluorinated β-enamino ketones **5** (Scheme 1), following the same strategy as for the construction of vinylogous amidines **2** but using ketones **1b** (the reaction temperature in this case was 25 °C) instead of ketimines **1a** as the starting material (Scheme 5). The β-enamino ketones **5** synthesized are shown in Table 2 (entries 10−12, method C).

The obtained yields for **5** were only moderate compared with those of compounds **2,** but the method can be also applied to cyclic ketones such as cyclopentanone (Table 2, entry 12). The process is completely regioselective, as compounds **5** are the only isolated products. The structural assignment of β-enamino ketones **4** and **5** is based on the analysis of NMR (^1H, ^{13}C, and ^{19}F) spectra and HRMS (see Experimental Section), from which it can be deduced that derivatives **5** exist as a mixture of enamino−imino tautomers **5**γ and **5**β (Scheme 5), while β-enamino ketones **4** were exclusively isolated as enamino tautomer **4**β (Schemes 3 and 4).

Finally, for the sake of comparison we tested the behavior of β-enamino ketones **4** and **5** in hydrolysis reactions. First, we studied the hydrolysis of β-enamino ketones **4** in different reaction conditions using 6 N H_2SO_4 in THF or 1 M HCl in Et_2O at reflux for several hours. In almost all instances the starting β-enamino ketones **4** were recovered unchanged (Scheme 6).[22] This result contrasts with previous findings[19] which indicated that *N,N′*-disubstituted β-enamino ketones such as **4** are easily hydrolyzed with diluted HCl in THF at 50 °C to the corresponding 1,3-dicarbonyl derivatives. This apparently unusual behavior of **4** in comparison with that described in the literature[19] can be attributed to a strong stabilization of β-enamino ketones **4** due to the additional intramolecular hydrogen bond (R_F) O····H−N.

Additionally, the hydrolysis of fluorinated β-enamino ketones **5** was tested. The reaction was accomplished using the same reaction conditions as for β-enamino ketones **4** (see above). In sharp contrast to the above-mentioned results, β-enamino ketones **5** were hydrolyzed, leading to the corresponding 1,3-dicarbonyl derivatives **7** isolated in the enol form. The results, including those corresponding to the hydrolysis of vinylogous amidines **2** (see, Scheme 3), are summarized in Scheme 6.

In summary, the fact that no 1,3-dicarbonyl products were observed in the hydrolysis of fluorinated vinylogous amidines **2** or β-enamino ketones **4** suggests a higher and regioselective reactivity of the fluorinated imino group (R_FC═N) in comparison to the nonfluorinated one (R^3C═N). Not only can this difference in reactivity be exploited in other processes, such as in selective reduction reactions, but it also further supports (a) the less stable nature of the intramolecular hydrogen bond (R_F) N····H−O or (R_F) N−H····O of **5** with respect to (R_F) O····H−N, postulated for derivatives **4** and (b) the different behavior of these systems in relation to the nonfluorinated analogues, which usually undergo a mild acid hydrolysis to the corresponding β-keto derivatives.

In conclusion, we have reported a new, efficient, and simple method of synthesis of fluorinated vinylogous amidines **2**. In addition, complementary procedures for

(19) Simchem, G.; Schmidt, A. *Synthesis* **1997**, 117.

(20) In fact, Hojo methodology does not allow the synthesis of fluorinated cyclic β-enamino ketones such as **4a**, **4d**, and **4g** (see Table 2, entries 1, 4−5, and 8).

(21) For a similar reaction, see: Bartoli, G.; Cimarelli, C. Palmieri, G.; Rosco, M.; Dalpozzo R. *Synthesis* **1990**, 895.

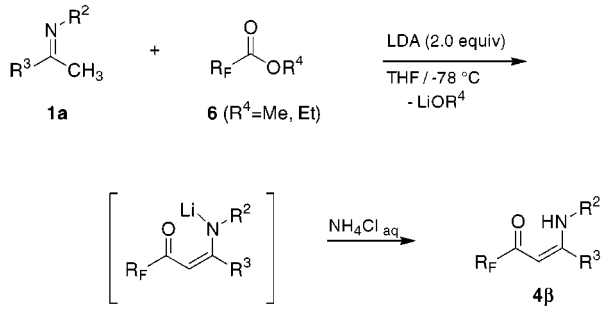
(22) In some occasions, and only after prolonged heating, a complex mixture of products along with starting material was identified in the crude reaction mixture.

Table 2. Fluorinated β-Enamino Ketones 4 and 5

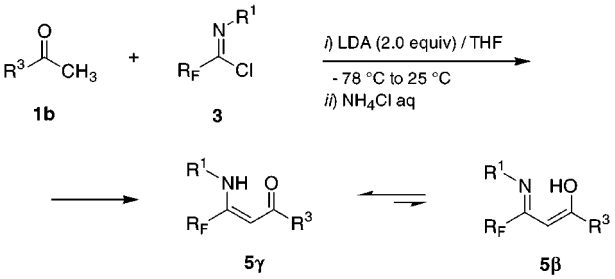
entry	R^1	R_F	R^2	R^3	product	method[a]	yield[b,c] (%)	mp (°C)[d]
1		CF_3CF_2	$(CH_2)_3$		**4a**	A	60	90−2
2		CF_2Cl	Ph	Ph	**4b**	A	60	oil
3		CF_3	(*R*)-(+)-C_6H_5(Me)CH	*i*-Pr	**4c**	A	58	oil
4		CF_3	$(CH_2)_3$		**4d**	A	75	88−90
5						B	67	
6		CF_3	*n*-Bu	*i*-Pr	**4e**	B	50	oil
7		CF_3	*n*-Bu	*t*-Bu	**4f**	B	58	oil
8		CH_2F	$(CH_2)_3$		**4g**	B	76	84−6
9		CF_3	(*S*)-(−)-C_6H_5(Me)CH	*i*-Pr	**4c**	B	61	oil
10	*p*-$MeOC_6H_4$	CF_3CF_2		*i*-Pr	**5a**	C	41	oil
11	*p*-$MeOC_6H_4$	$CF_3(CF_2)_7$		*i*-Pr	**5b**	C	40	51−3
12	*p*-$MeOC_6H_4$	CF_2Cl		e	**5c**	C	48	oil

[a] Method A: vinylogous amidines **2**, 6 N H_2SO_4, THF, Δ. Method B: ketimine **1a** (1.0 equiv), fluorinated ester **6** (1.1 equiv), LDA (2.0 equiv), THF, −78 to 25 °C.; Method C: ketone **1b** (1.0 equiv), imidoyl chloride **3** (1.0 equiv), LDA (2.0 equiv), THF, −78 to 25 °C. [b] Isolated yields. [c] Purified by flash chromatography. [d] Melting points are uncorrected. [e] Cyclopentanone was used as starting ketone.

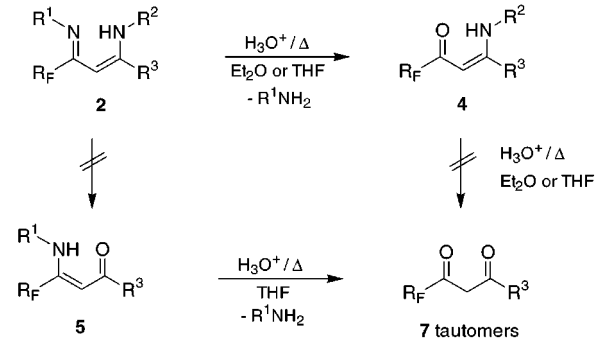
Scheme 4



Scheme 5



Scheme 6



obtaining fluorinated β-enamino ketones **4** and **5** have been developed. The approaches described here to synthesize derivatives **4** and **5** are regioselective and particularly attractive as useful alternatives to existing methods. Further work on the synthetic utilization of **2** and **4**(**5**) for the stereoselective synthesis of biologically important fluoro−amino compounds is in progress.[23]

(23) The synthetic utility of related nonfluorinated derivatives has been successfully studied by Barluenga's group (see refs 9, 11, and 16).

Experimental Section

General Methods. All reactions were carried out in anhydrous solvents, under an argon atmosphere and in oven-dried glassware. Imidoyl chlorides were prepared according to the methods described in the literature.[5a] Ketimines were prepared from ketones by conventional procedures.[24] Complete descriptions of the equipment and analytical methods used for the synthesis and characterization of the described compounds have been previously reported.[3b,8b]

Fluorinated 1,3-Diimines 2. General Procedure. *n*-Butyllithium (2.5 M in hexane, 2.8 mL, 7 mmol) was added dropwise to a solution of diisopropylamine (1 mL, 7 mmol) in THF (10 mL) at 0 °C under argon. After being stirred for 10 min, ketimine **1a** (3.5 mmol) in THF (7 mL) was added. The resulting mixture was stirred at 0 °C for 30 min and then cooled to −78 °C. Imidoyl chloride **3** (3.5 mmol) in 7 mL of THF was added and stirred at −78 °C. When TLC analysis indicated the disappearance of the starting material, after approximately 1 h in all cases, the reaction was quenched by addition of a saturated ammonium chloride solution. The aqueous layer was extracted with dichloromethane (3 × 25 mL). The combined organic extracts were washed with brine and then dried (Na_2SO_4) and evaporated under reduced pressure to furnish the crude product. Purification was carried out as indicated in each case.

***N*2-(4-Methoxyphenyl)-3-(2-pyrrolidinylidene)-1,1,1-trifluoro-2-propanimine (2a).** Flash chromatography (*n*-hexane−EtOAc (5:1)) on silica gel gave a yellow oil (80%): ^{1}H NMR (250 MHz) 1.93 (m, 2H), 2.64 (t, J = 7.8, 2H), 3.66 (t, J = 7.0, 2H), 3.72 (s, 3H), 5.19 (s, 1H), 6.73−6.84 (m, 4H), 10.43 (br s, 1H); ^{13}C NMR (62.8 MHz) 21.8 (t), 34.6 (t), 52.2 (t), 55.1 (q), 84.9 (q, $^3J_{CF}$ = 3.96), 113.6 (d), 116.4 (q, $^1J_{CF}$ = 310.8), 123.4 (d), 140.2 (s), 151.3 (q, $^2J_{CF}$ = 26.6), 157.0 (s), 168.3 (s); ^{19}F NMR (235 MHz) −62.67; HRMS calcd for (M^+ + 1) $C_{14}H_{16}F_3N_2O$ 285.1214, found 285.1205. Anal. Calcd for $C_{14}H_{15}F_3N_2O$: C, 59.15; H, 5.32; N, 9.85. Found: C, 59.02; H, 5.36; N, 9.79.

***N*2-(4-Methoxyphenyl)-1-(2-pyrrolidinylidene)perfluorooctyl-2-decanimine (2d).** Flash chromatography (*n*-hexane−EtOAc (9:1)) on silica gel gave a yellow solid (60%): mp 90−2 °C; ^{1}H NMR (250 MHz) 1.89 (m, 2H), 2.63 (t, J = 7.8, 2H), 3.62 (t, J = 6.8, 2H), 3.73 (s, 3H), 5.10 (s, 1H), 6.70−6.73 (m, 4H), 10.1 (br s, 1H); ^{13}C NMR (62.8 MHz) 21.8 (t), 34.7 (t), 52.0 (t), 55.4 (q), 88.2 (d), 109.0−120.2 (C_8F_{17}), 113.4 (d), 122.3 (s), 122.6 (d), 139.9 (s), 155.8 (br s), 166.6 (s); ^{19}F NMR (235 MHz) −80.97 (3F), −107.89 (2F), −120.44 (2F), −122.11 (4F), −123.02 (2F), −126.41 (4F); HRMS (FAB) calcd for (M^+) $C_{21}H_{15}F_{17}N_2O$ 634.0912, found 634.0932.

***N*3-Butyl-(*Z*)-6,6,6-trifluoro-5-(4-methoxyphenylimino)-2-methyl-3-hexen -3-amine (2e).** Flash chromatography (*n*-hexane−EtOAc (30:1)) on silica gel gave an orange oil (40%): ^{1}H NMR (250 MHz) 0.83 (t, J = 7.2, 3H), 1.13 (d, J = 6.8, 6H),

(24) (a) Smith, J. K.; Bergbreiter, D. E.; Newcomb, M. *J. Am. Chem. Soc.* **1983**, *105*, 4396.

1.29 (m, 2H), 1.48 (m, 2H), 2.74 (m, 1H), 3.23 (m, 2H), 3.71 (s, 3H), 5.00 (s, 1H), 6.69−6.77 (m, 4H), 11.23 (br s, 1H); ^{13}C NMR (62.8 MHz) 13.5 (q), 19.9 (t), 21.3 (q), 28.7 (d), 32.2 (t), 42.0 (t), 55.1 (q), 81.8 (q, $^{3}J_{CF}$ = 3.9), 113.4 (d), 116.8 (q, $^{1}J_{CF}$ = 305.0), 121.4 (d), 142.7 (s), 152.6 (q, $^{2}J_{CF}$ = 25.0), 155.3 (s), 169.6 (s); ^{19}F NMR (235 MHz) −62.23; HRMS calcd for (M^+) $C_{18}H_{25}F_3N_2O$ 342.1918, found 342.1909.

***N*1-Butyl-(*Z*)-4-chloro-4,4-difluoro-3-(4-methoxyphenylimino)-1-phenyl-1-buten-1-amine (2g).** Flash chromatography (*n*-hexane−EtOAc (10:1)) on silica gel gave an orange oil (82%): ^{1}H NMR (250 MHz) 0.74 (t, *J* = 7.2, 3H), 1.16−1.25 (m, 2H), 1.32−1.41 (m, 2H), 3.08 (q, *J* = 6.4, 2H), 3.72 (s, 3H), 5.01 (s, 1H), 6.74−6.83 (m, 4H), 7.30−7.34 (m, 5H), 10.73 (br s, 1H); ^{13}C NMR (62.8 MHz) 13.6 (q), 19.8 (t), 32.9 (t), 44.5 (t), 55.3 (q), 88.2 (t, $^{3}J_{CF}$ = 4.7), 113.5 (d), 121.2 (t, $^{1}J_{CF}$ = 295.6), 121.35 (d), 127.9 (d), 128.3 (d), 129.1 (d), 136.3 (s), 142.3 (s), 155.3 (s), 155.5 (t, $^{2}J_{CF}$ = 21.5), 162.4 (s); ^{19}F NMR (235 MHz) −51.71; HRMS calcd for (M^+ + 1) $C_{21}H_{24}ClF_2N_2O$ 393.1545, found 393.1547.

Phenyl[(*Z*)-4,4,4-trifluoro-3-(4-methoxyphenylimino)-1-phenyl-1-butenyl] amine(2i). Flash chromatography (*n*-hexane−EtOAc (30:1)) on silica gel. Recrystallization (*n*-hexane) gave an orange solid (81%): mp 110−2 °C; ^{1}H NMR (250 MHz) 3.81 (s, 3H), 5.52 (s, 1H), 6.69−7.36 (m, 14H), 11.37 (br s, 1H); ^{13}C NMR (62.8 MHz) 55.4 (q), 93.7 (q, $^{3}J_{CF}$ = 3.7), 113.7 (d), 119.0 (q, $^{1}J_{CF}$ = 286.7), 122.18 (d), 122.7 (d), 123.6 (d), 128.3 (d), 128.4 (d), 128.6 (d), 129.2 (d), 136.4 (s), 140.2(s), 141.2(s), 151.7 (q, $^{2}J_{CF}$ = 26.7), 156.5 (s), 158.6 (s); ^{19}F NMR (235 MHz) −62.7; HRMS calcd for (M^+) $C_{23}H_{19}F_3N_2O$ 396.1449, found 396.1441. Anal. Calcd for $C_{23}H_{19}F_3N_2O$: C, 69.70; H, 4.80; N, 7.07. Found: C, 69.56; H, 4.69; N, 7.15.

***N*3-[(1*R*)-1-Phenylethyl]-(*Z*)-6-chloro-6,6-difluoro-5-(4-methoxyphenyl imino)-2-methyl-3-hexen-3-amine (2m).** Flash chromatography (*n*-hexane−EtOAc (3:1)) on silica gel gave an orange solid (85%): mp 90−2 °C; $[\alpha]^{25}_D$ −6.15° (*c* 0.011, $CHCl_3$); ^{1}H NMR (250 MHz) 0.83 (d, *J* = 6.8, 3H), 1.10 (d, *J* = 6.8, 3H), 1.41 (d, *J* = 6.8, 3H), 2.65 (m, 1H), 3.71 (s, 3H), 4.72 (m, 1H), 4.99 (s, 1H), 6.78−6.79 (m, 4H), 7.18−7.25 (m, 5H), 11.50 (br s, 1H); ^{13}C NMR (62.8 MHz) 21.1 (q), 22.3 (q), 25.3 (q), 29.1 (d), 52.5 (d), 55.3 (q), 82.3 (t, $^{3}J_{CF}$ = 4.9), 113.5 (d), 121.5 (d), 121.6 (t, $^{1}J_{CF}$ = 300.5), 125.4 (d), 127.1 (d), 128.7 (d), 142.2 (s), 144.9 (s), 155.2 (s), 155.8 (t, $^{2}J_{CF}$ = 20.7), 169.2 (s); ^{19}F NMR (235 MHz) −50.88 (d, J_{FF} = 157.2), −51.60 (d, J_{FF} = 157.2); HRMS (FAB) calcd for (M^+) $C_{22}H_{25}ClF_2N_2O$ 406.1623, found 406.1645. Anal. Calcd for $C_{22}H_{25}ClF_2N_2O$: C, 64.94; H, 6.19; N, 6.88. Found: C, 64.71; H, 6.05; N, 6.71.

***N*2-[(1*R*)-1-Phenylethyl]-3-(2-pyrrolidinylidene)-1,1,1-trifluoro-2-propanimine (2n).** Flash chromatography (*n*-hexane−EtOAc (30:1)) on silica gel gave an orange oil (75%): $[\alpha]^{25}_D$ −559.9° (*c* 0.014, $CHCl_3$); ^{1}H NMR (250 MHz) 1.41 (d, *J* = 6.7, 3H), 1.73 (m, 2H), 2.49 (t, *J* = 7.9, 2H), 3.88 (t, *J* = 7.1, 2H), 4.65 (q, 1H), 5.19 (s, 1H), 7.09−7.29 (m, 5H), 10.24 (br s, 1H); ^{13}C NMR (62.8 MHz) 21.8 (t), 25.6 (t), 37.9 (q), 54.2 (d), 60.0 (d), 89.3 (q, $^{3}J_{CF}$ = 6.2), 120.9 (q, $^{1}J_{CF}$ = 275.3), 125.4 (d), 126.9 (d), 128.4 (d),141.7 (q, $^{2}J_{CF}$ = 29.77), 145.3 (s), 172.7 (s); ^{19}F NMR (235 MHz) −65.31; HRMS calcd for (M^+ + 1) $C_{15}H_{18}F_3N_2$ 283.1422, found 283.1417.

***N*1-Butyl-(*Z*)-4,4,4-trifluoro-1-phenyl-3-[(1*R*)-1-phenylethylimino]-1-buten-1-amine (2o).** Flash chromatography (*n*-hexane−EtOAc (30:1)) on silica gel gave a yellow oil (68%): $[\alpha]^{25}_D$ −309.9° (*c* 0.010, $CHCl_3$); ^{1}H NMR (250 MHz) 0.75 (t, *J* = 7.2, 3H), 1.21 (m, 2H), 1.36 (m, 2H), 1.47 (d, *J* = 6.4, 3H), 3.07 (m, 2H), 4.87 (q, 1H), 4.94 (s, 1H), 7.09−7.32 (m, 10H), 11.23 (br s, 1H); ^{13}C NMR (62.8 MHz) 13.7 (q), 20.0 (t), 25.8 (q), 33.1 (t), 45.9 (t), 58.6 (d), 89.1 (q, $^{3}J_{CF}$ = 4.7), 119.1 (q, $^{1}J_{CF}$ = 286.2), 126.1 (d), 126.6 (d), 127.7 (d), 128.2 (d), 128.3 (d), 128.6 (d), 137.1 (s), 146.0 (s), 149.9 (q, $^{2}J_{CF}$ = 25.9), 162.8 (s); ^{19}F NMR (235 MHz) −64.40; HRMS calcd for (M^+ + 1) $C_{22}H_{26}F_3N_2$ 375.2048, found 375.2050.

***N*3-[(1*R*)-1-Phenylethyl]-(*Z*)-6,6,6-trifluoro-2-methyl-5-[(1*R*)-1-phenyl ethylimino]-3-hexen-3-amine (2p).** Flash chromatography (*n*-hexane−EtOAc (20:1)) on silica gel gave a yellow oil (83%): $[\alpha]^{25}_D$ −925.9° (*c* 0.010, $CHCl_3$); ^{1}H NMR (250 MHz) 0.86 (d, *J* = 6.8, 3H), 1.11 (d, *J* = 6.8, 3H), 1.53 (d, *J* = 6.8, 6H), 2.76 (m, 1H), 4.80−4.83 (m, 2H), 5.04 (s, 1H), 7.20−7.38 (m, 10H), 11.95 (br s, 1H); ^{13}C NMR (62.8 MHz) 20.9 (q), 21.9 (q), 25.5 (q), 26.1 (q), 29.0 (d), 53.8 (d), 57.8 (d), 84.2 (q, $^{3}J_{CF}$ = 5.2), 119.5 (q, $^{1}J_{CF}$ = 284.6), 125.8 (d), 126.1 (d), 126.6 (d), 126.8 (d), 128.3 (d), 128.6 (d), 145.7 (s), 146.1 (s), 149.1 (q, $^{2}J_{CF}$ = 26.1), 169.6 (s); ^{19}F NMR (235 MHz) −64.54; HRMS calcd for (M^++1) $C_{23}H_{28}F_3N_2$ 389.2204, found 389.2201.

Fluorinated *β*-Enamino ketones 4 and 5. Method A. To a solution of **2** (6 mmol) in THF (10 mL) was added 4 mL of 6 N H_2SO_4, and the mixture was allowed to warm to 60 °C. After stirring for several hours (2−5 h), the solution was quenched by addition of a saturated ammonium chloride solution and extracted with dichloromethane. The combined organic layers were washed with brine, dried over anhydrous sodium sulfate, filtered, and evaporated under vacuum to afford flourinated *β*-enamino ketones **4**.

Method B. *n*-Butyllithium (2.5 M in hexane, 2.0 mL, 5 mmol) was added under argon to a solution of freshly distilled diisopropylamine (0.7 mL, 5 mmol) in THF (10 mL) at 0 °C. After being stirred for 10 min, ketimine **1a** (2.5 mmol) in THF (10 mL) was added. The solution was stirred for 30 min at 0 °C and then cooled to −78 °C. Fluorinated ester **6** (2.75 mmol) in THF (10 mL) was added, and the solution was stirred for several hours (2−5 h) at −78 °C. The reaction mixture was poured onto a saturated ammonium chloride solution. Workup of the reaction followed the procedure described in method A.

(*Z*)-4-Anilino-1-chloro-1,1-difluoro-4-phenyl-3-buten-2-one (4b). Starting from **2j** (method A). Flash chromatography (*n*-hexane−EtOAc (3:1)) on silica gel gave a yellow oil (60%): ^{1}H NMR (250 MHz) 5.62 (t, *J* = 1.1, 1H), 6.74−7.34 (m, 10H), 9.50 (br s, 1H); ^{13}C NMR (62.8 MHz) 91.4 (t, $^{3}J_{CF}$ = 4.8), 123.9 (d), 125.8 (d), 126.5 (t, $^{1}J_{CF}$ = 259.7), 128.3 (d), 128.7 (d), 129.0 (d), 130.6 (d), 134.0 (s), 137.9 (s), 166.3 (s), 179.5 (t, $^{2}J_{CF}$ = 20.8); ^{19}F NMR (235 MHz) −64.64; HRMS calcd for (M^+ + 1) $C_{16}H_{13}ClF_2NO$ 308.0653, found 308.0665.

(*Z*)-1,1,1-Trifluoro-5-methyl-4-[(1*S*)-1-phenylethylamino]-3-hexen-2-one (4c) (Entry 9, Table 2). Flash chromatography (*n*-hexane−EtOAc (5:1)) on silica gel gave a yellow oil (61%): $[\alpha]^{25}_D$ +561.1° (*c* 0.015, $CHCl_3$); ^{1}H NMR (250 MHz) 0.79 (d, *J* = 6.8, 3H), 1.11 (d, *J* = 6.8, 3H), 1.53 (d, *J* = 6.8, 3H), 2.68 (m, 1H), 4.79 (m, 1H), 5.32 (s, 1H), 7.16−7.32 (m, 5H), 11.81 (br s, 1H); ^{13}C NMR (62.8 MHz) 20.2 (q), 21.1 (q), 24.4 (q), 29.2 (d), 53.0 (d), 84.3 (q, $^{3}J_{CF}$ = 1.76), 111.7 (q, $^{1}J_{CF}$ = 288.19), 125.9 (d), 127.6 (d), 128.9 (d), 142.7 (s), 175.8 (q, $^{2}J_{CF}$ = 32.28), 178.9 (s); ^{19}F NMR (235 MHz) −76.72; HRMS calcd for (M^+) $C_{15}H_{18}F_3NO$ 285.1340, found 285.1337. Anal. Calcd for $C_{15}H_{18}F_3NO$: C, 63.15; H, 6.36; N, 4.91. Found: C, 63.21; H, 6.25; N, 4.77. (**1*R*)-(*Z*)-4c** (entry 3, Table 2) was obtained by hydrolysis of **2p** in 58% yield (method A); ^{1}H, ^{13}C, and ^{19}F spectra were identical to those of enantiomeric compound (**1*S*)-(*Z*)-4c**.

3-(2-Pyrrolidinylidene)-1,1,1-trifluoroacetone (4d). Starting from **2a** (method A). Recrystallization (*n*-hexane) gave a white solid (75%): mp 88−90 °C; ^{1}H NMR (250 MHz) 2.05 (m, 2H), 2.72 (t, *J* = 7.9, 2H), 3.68 (t, *J* = 7.2, 2H), 5.40 (s, 1H), 10.15 (br s, 1H); ^{13}C NMR (62.8 MHz) 20.8 (t), 33.3 (t), 48.5 (t), 83.6 (q, $^{3}J_{CF}$ = 1.86), 117.7 (q, $^{1}J_{CF}$ = 288.0), 173.4 (q, $^{2}J_{CF}$ = 31.3), 175.6 (s); ^{19}F NMR (235 MHz) −76.89; HRMS calcd for (M^+) $C_7H_8NOF_3$ 179.0557, found 179.0556. Anal. Calcd for $C_7H_8F_3NO$: C, 46.93; H, 4.47; N, 7.82. Found: C, 46.81; H, 4.53; N, 7.69.

(*Z*)-4-Butylamino-1,1,1-trifluoro-5,5-dimethyl-3-hexen-2-one (4f). Flash chromatography (*n*-hexane−EtOAc (7:1)) on silica gel gave a yellow oil (58%): ^{1}H NMR (250 MHz) 0.90 (t, *J* = 7.2, 3H), 1.26 (s, 9H), 1.44 (m, 2H), 1.55 (m, 2H), 3.52 (q, *J* = 6.4, 2H), 5.40 (s, 1H), 11.88 (br s, 1H); ^{13}C NMR (62.8 MHz) 13.6 (q), 19.7 (t), 28.5 (q), 32.0 (t), 36.4 (s), 45.9 (t), 85.2 (q, $^{3}J_{CF}$ = 1.90), 117.9 (q, $^{1}J_{CF}$ = 288.0), 175.0 (q, $^{2}J_{CF}$ = 32.09), 179.5 (s); ^{19}F NMR (235 MHz) −76.56; HRMS calcd for (M^+) $C_{12}H_{20}F_3NO$ 251.1497, found 251.1487.

1-(2-Pyrrolidinylidene)-3-fluoroacetone (4g). Recrystallization (*n*-hexane−EtOH) gave a brown solid (76%): mp 84−6 °C; ^{1}H NMR (250 MHz) 1.93 (m, 2H), 2.59 (t, *J* = 7.8, 2H), 3.53 (t, *J* = 7.1, 2H), 4.60 (d, $^{1}J_{FH}$ = 47.8, 2H), 5.32 (d, $^{2}J_{FH}$ = 4.6, 1H), 9.90 (br s, 1H); ^{13}C NMR (62.8 MHz) 21.0 (t),

32.7 (t), 47.8 (t), 83.7 (d, $^1J_{CF}$ = 183.7), 84.5 (d, $^3J_{CF}$ = 3.51), 170.0 (s), 190.9 (d, $^2J_{CF}$ = 17.46); ^{19}F NMR (235 MHz) −54.53 (dt, $^1J_{FH}$ = 47.57, $^4J_{FH}$ = 4.77); HRMS calcd for (M^+) $C_7H_{10}FNO$ 143.0746, found 143.0749. Anal. Calcd for $C_7H_{10}FNO$: C, 58.73; H, 7.04; N, 9.78. Found: C, 58.59; H, 6.86; N, 9.83.

Method C. To a solution of diisopropylamine (1 mL, 7 mmol) in 10 mL of THF at 0 °C was added *n*-butyllithium (2.5 M in hexane, 2.8 mL, 7 mmol) dropwise under argon. After being stirred for 10 min, ketone **1b** (3.5 mmol) in THF (10 mL) was added. The resulting mixture was stirred at 0 °C for 2 h. The solution was cooled to −78 °C, and imidoyl chloride **3** (3.5 mmol) in THF was added. The solution was allowed to warm to room temperature. After several hours (2−5 h), the reaction was quenched by addition of a saturated ammonium chloride solution. The aqueous layer was extracted with dichloromethane. The combined organic extracts were washed with brine and then dried (Na_2SO_4) and evaporated under vacuum to furnish the crude product **5**.

***(Z)*-6,6,7,7,7-Pentafluoro-5-(4-methoxyanilino)-2-methyl-4-hepten-3-one (5a).** Flash chromatography (*n*-hexane−EtOAc (6:1)) on silica gel gave a yellow oil (41%). Major enamino tautomer (ca. 90% of the mixture): ^{1}H NMR (250 MHz) 1.09 (d, *J* = 6.9, 6H), 2.55−2.61 (m, 1H), 3.72 (s, 3H), 5.58 (s, 1H), 6.74 (d, *J* = 8.5, 2H), 7.00 (d, *J* = 8.5, 2H), 11.20 (br s, 1H); ^{13}C NMR (62.8 MHz) 18.9 (q), 40.8 (d), 55.2 (q), 96.0 (t, $^3J_{CF}$ = 6.2), 110.4 (tq, $^1J_{CF}$ = 260.3, $^2J_{CF}$ = 36.7), 113.6 (d), 115.8 (qt, $^1J_{CF}$ = 284.2, $^2J_{CF}$ = 39.5), 119.8 (s), 128.1 (d), 130.7 (s), 141.1 (s), 147.2 (t, $^2J_{CF}$ = 21.7), 158.4 (s); ^{19}F NMR (235 MHz) −83.17, −111.70. Minor enamino tautomer (ca. 10% of the mixture), representative signals: ^{1}H NMR (250 MHz) 1.00 (d, *J* = 6.9, 6H), 2.50 (m, 1H), 3.55 (s, 3H); ^{13}C NMR (62.8 MHz) 17.9 (q), 40.3 (d), 41.4 (t), 113.8 (d), 120.4 (s), 157.7 (s); ^{19}F NMR (235 MHz) − 81.78, −117.62; HRMS (M^++1) calcd for $C_{15}H_{17}F_5NO_2$ 338.1179, found 338.1183.

2-[(*Z*)-2-Chloro-2,2-difluoro-1-(4-methoxyanilino)ethylidene]-1-cyclo pentanone (5c). Flash chromatography (*n*-hexane−EtOAc (40:1)) on silica gel gave a red oil (48%): ^{1}H NMR (250 MHz) 1.87−1.96 (m, 2H), 2.37 (t, *J* = 7.9, 2H), 2.75−2.83 (m, 2H), 3.72 (s, 3H), 7.11 (d, *J* = 6.5, 2H), 6.67 (d, *J* = 6.5, 2H), 11.01 (br s, 1H); ^{13}C NMR (62.8 MHz) 20.4 (d), 26.7 (d), 38.9 (d), 55.2 (q), 86.4 (t, $^3J_{CF}$ = 3.9), 110.4 (d), 111.4 (d), 117.1 (d), 122.4 (t, $^1J_{CF}$ = 296.0), 129.4 (d), 141.1 (s), 145.5 (t, $^2J_{CF}$ = 26.5), 159.9 (s), 209.0 (s); ^{19}F NMR (235 MHz) −49.93; HRMS (EI$^+$) calcd for (M^+) $C_{14}H_{14}ClF_2NO_2$ 301.0681, found 301.0691.

Acknowledgment. We are grateful to the Dirección General de Investigación Científica y Técnica for financial support of this research (DGES PB97-0760-C02-01). A predoctoral fellowship from the Fundación Ramón Areces to M.G.T. and from Generalitat Valenciana to B.P. are also gratefully acknowledged. We also thank Dr. T. Richert (Bruker S.A.) for assistance in HOESY experiments.

Supporting Information Available: Physical, spectroscopic (^{1}H, ^{13}C, and ^{19}F and HRMS), and analytical data for products **2b**, **2c**, **2f**, **2h**, **2j**, **2k**, **2l**, **4a**, **4e**, **5b**, and **7a**. HOESY ^{1}H−^{19}F spectrum for **2a** and general procedure for hydrolysis of **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO990392W