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Flexible Synthesis of Pyrimidines with Chiral Monofluorinated and Difluoromethyl Side Chains

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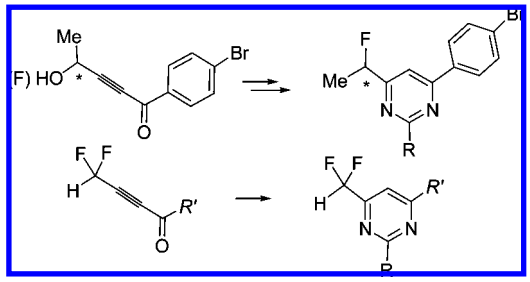
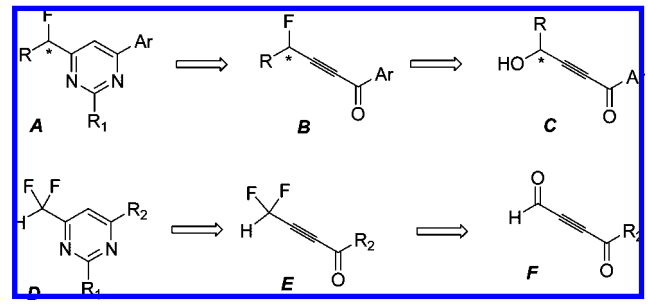
Received March 31, 2009



Chiral pyrimidines with a fluorine atom in the benzylic position are easily accessible in high enantiomeric excesses from optically active propargylic intermediates by two complementary routes. Both the use of optically active propargylic fluorides and the fluorination of the chiral pyrimidine in the final stage give excellent results in terms of enantiocontrol. On the other hand, original pyrimidines with a difluoromethyl side chain are also obtained in a few steps from new propargylic ketones bearing a CHF_2 substituent on the triple bond.

Pyrimidines are widely recognized as important heterocycles in bioorganic and medicinal chemistry.[1] On the other hand, it is well-known that the introduction of fluorine in organic molecules strongly modifies their physical, chemical, and biological activities, and this has also been of much use in fluorobiorganic chemistry.[2] Therefore, pyrimidines bearing one or several fluorine atom(s) on the side chains appear to be particularly attractive target molecules. Several years ago, we started a research program on new strategies for the synthesis of fluorinated molecules, based on the use of easily accessible propargylic fluorides.[3] In particular, we have demonstrated that these derivatives are highly versatile intermediates for the synthesis of linear compounds,[4] as well as carbo-[5] and heterocycles.[6] Now we have become interested in the preparation of novel pyrimidines with fluorine atoms in the benzylic position, and more specifically in this paper, we will develop two aspects:

SCHEME 1. Retrosynthetic Analysis for the Preparation of Type A and D Pyrimidines



(i) In the first part, we will describe a versatile synthesis of type **A** optically active pyrimidines monofluorinated on the side chain, taking advantage of the easy access to type **B** propargylic fluorides. Furthermore, two different routes to highly enantio-enriched pyrimidines **A** will be reported and compared.

(ii) In the second part, we will extend our propargylic strategy to difluoromethyl compounds and we will report the synthesis of type **D** pyrimidines. In this part, we will take advantage of the new versatile, albeit labile, **E** and **F** propargylic derivatives.

All of these pyrimidines have two to three points of molecular diversity, and therefore this strategy could be of interest in the preparation of chemical libraries.

As a model for studying the preparation of pyrimidines from propargylic ketones, we have selected fluoride **3** because it is easily prepared in good yield from butyn-3-ol (**1**), in both racemic and highly enantio-enriched forms. Furthermore, the *p*-bromo substituent can be used for the preparation of chemical libraries.[6] Upon reaction with the appropriate amidines and guanidines in the presence of Na_2CO_3, this ketone (±)-**3** afforded in fair to excellent yields the target racemic pyrimidines (±)-**4a**−**4d** (Scheme 2). All of these derivatives have been fully characterized by their spectral and analytical data.

The next step was the preparation of the corresponding pyrimidines, in optically active form. Toward this goal, the derivative (−)-**4a** was selected as a model and the synthesis

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(1) For a recent review on the synthesis of pyrimidines, see: (a) Hill, M. D.; Movassaghi, M. *Chem.—Eur. J.* **2008**, *14*, 6836–6844, and references cited therein.

(2) (a) Ojima, I.; McCarthy, J. R.; Welch, J. T. *Biomedical Frontiers in Fluorine Chemistry*; ACS Symposium Series 639; American Chemical Society: Washington, DC, 1996. (b) Welch, J. T.; Eswarakrishnan, S. *Fluorine in Bioorganic Chemistry*; Wiley Interscience: New York, 1991. (c) Welch, J. T. *Tetrahedron* **1987**, *43*, 3123–3197. (d) Isanbor, C.; O'Hagan, D. *J. Fluorine Chem.* **2006**, *127*, 303–319. (e) Bégué, J.-P.; Bonnet-Delpon, D. *J. Fluorine Chem.* **2006**, *127*, 992–1012. (f) Kirk, K. L. *J. Fluorine Chem.* **2006**, *127*, 1013–1029, and references cited therein.

(3) Prakesch, M.; Grée, D.; Grée, R. *Acc. Chem. Res.* **2002**, *35*, 175–181. For a recent review on the chemistry of propargylic and allylic fluorides, see: (a) Pacheco, M. C.; Purser, S.; Gouverneur, V. *Chem. Rev.* **2008**, *108*, 1943–1981, and references cited therein.

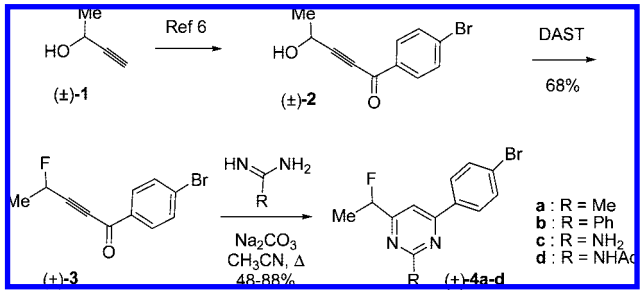
(4) (a) Manthati, V.; Grée, D.; Grée, R. *Eur. J. Org. Chem.* **2005**, 3825–3829. (b) Manthati, V. L.; Murthy, A. S. K.; Caijo, F.; Drouin, D.; Lesot, P.; Grée, D.; Grée, R. *Tetrahedron: Asymm.* **2006**, *17*, 2306–2310, and references cited therein.

(5) (a) Grée, D.; Grée, R. *Tetrahedron Lett.* **2007**, *48*, 5435–5438. (b) Pujari, S. A.; Kaliappan, K. P.; Valleix, A.; Grée, D.; Grée, R. *Synlett* **2008**, 2503–2507.

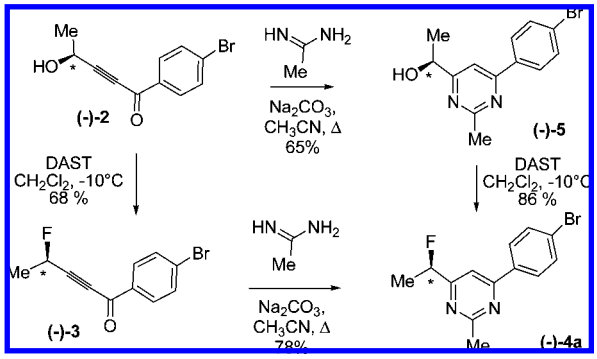
(6) Blayo, A.-L.; Le Meur, S.; Grée, D.; Grée, R. *Adv. Synth. Catal.* **2008**, *350*, 471–476.

10.1021/jo900674u CCC: $40.75
Published on Web 05/19/2009

SCHEME 2. Synthesis of Monofluorinated Pyrimidines (±)-4a−4d



SCHEME 3. Enantioselective Synthesis of Fluorinated Pyrimidine (−)-4a



was studied following two different routes (Scheme 3). In the first pathway, the optically active fluoride (−)-**3** was prepared from (*S*)-butynol, as previously described,[6] and used for the synthesis of pyrimidine (−)-**4a** by condensation with acetamidine. In the second route, the pyrimidine (−)-**5**, with an alcohol on the side chain, was first prepared from acetylenic intermediate (−)-**2**. Then, (diethylamino)sulfur trifluoride (DAST)-mediated fluorination was performed on (−)-**5** to access (−)-**4a**. This allows for the first time a full comparison between the two reaction pathways. The analysis of the enantiomeric excess (ee) could be performed by chiral high-performance liquid chromatography on pyrimidines (−)-**5** and (−)-**4a**, and the results are the following:

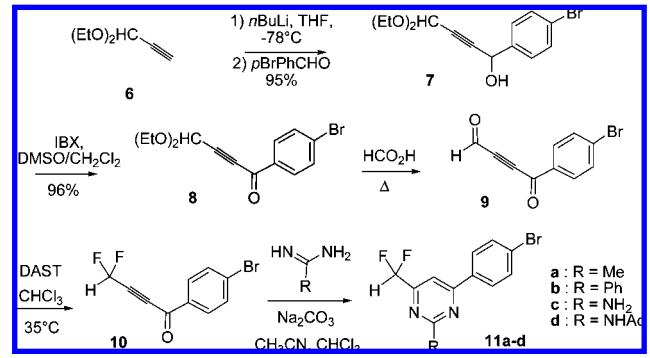
(a) The pyrimidine (−)-**5**, with an alcohol side chain, had an ee = 99%, thus establishing clearly that propargylic precursor (−)-**2** had an ee ≥ 99%.

(b) The ee of pyrimidine (−)-**4a**, obtained from (−)-**3** through the propargylic fluoride route, was 97.2%. This result is fully consistent with our previous results in the synthesis of pyridines, where excellent stereocontrol was also observed during the heterocyclization process.[6]

(c) The pyrimidine (−)-**4a**, obtained by direct fluorination of alcohol (−)-**5**, had an ee = 96.4%.

These data demonstrate that, for this heterocycle, there is very little erosion of stereochemistry during the DAST-mediated fluorination reaction. This result is interesting because it had been clearly established earlier that fluorination in the benzylic position is strongly dependent upon the nature of the substituents on the aromatic system: the electron-withdrawing groups, which destabilize benzylic carbonium ions, favor stereocontrol by the S_N2 process, while the electron-donating substituents favor racemization.[7] The very high stereocontrol during the fluorination of (−)-**5** is likely related to the fact that the pyrimidine nucleus is known as a "π-deficient" heteroaromatic system.[8] Therefore, it is not stabilizing a potential carbenium ion during the DAST-mediated fluorination, and it allows excellent stereocontrol by the S_N2 process. In conclusion, for this type of heterocycle, both routes are possible to access the desired optically active target molecule (−)-**4a** in similar overall yields and ee's.

SCHEME 4. Synthesis of Pyrimidines 11a−11d



Several examples of heteroaromatic derivatives with a CHF_2 chain have already been reported, and they demonstrated some interesting biological properties.[9] Furthermore, pyrimidines with such a chain, and designed to treat CNS disorders, have been reported in a recent patent.[10] Therefore, we decided to extend our propargylic fluoride synthetic strategy to the preparation of pyrimidines with a difluoromethyl side chain. It was checked first with the same *p*-bromophenyl substituent, and the key intermediates were the propargylic derivatives **9** and **10** (Scheme 4). The ketone **8** was prepared from acetal **6** in two steps and in excellent overall yield (91%). Removal of the acetal group was performed using pure formic acid[11] under controlled reaction conditions to afford labile electrophilic alkyne **9**, which was characterized only by NMR. To the best of our knowledge, very few compounds of this type have been described up to now, and some have been proposed as intermediates in the synthesis of (*E*)-3-acylprop-2-enoic acids.[12] The crude aldehyde **9** was submitted directly to a DAST-mediated reaction to yield the fluorinated propargylic ketone **10**, which is also a highly reactive and labile intermediate. Therefore, it has been characterized by NMR and used directly for the preparation of target pyrimidines **11a−11d** under the same reaction conditions as those described previously. These heterocycles, obtained in 24−45% overall yield from **8**, have been fully characterized by their spectral and analytical data.

Then we extended our synthesis to the preparation of pyrimidines **16a−16d** bearing a C_5 alkyl chain. The route

(7) (a) Fritz-Langhals, E. *Tetrahedron Lett.* **1994**, *35*, 1581–1854. (b) Fritz-Langhals, E. *Tetrahedron: Asymm.* **1994**, *5*, 981–986.

(8) (a) Katritzky, A. R. *Handbook of Heterocyclic Chemistry*, 1st ed.; Pergamon: New York, 1985. (b) Eicher, T.; Hauptmann, S.; Speicher, A. *The Chemistry of Heterocycles*, 2nd ed.; Wiley-VCH: New York, 2003; Chapter 6 and references cited therein.

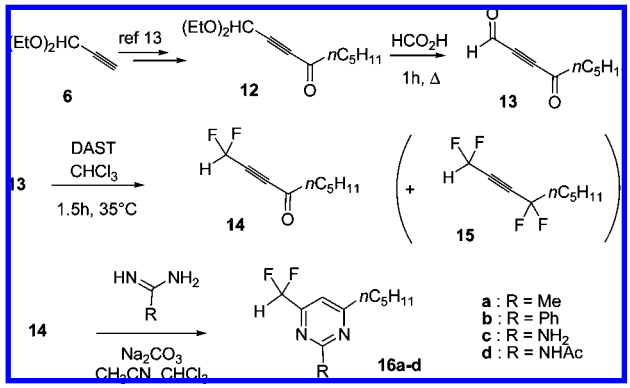
(9) For triazoles with antitubercular activity, see: (a) Costa, M. S.; Boechat, N.; Rangel, E. A.; Da Silva, F. de C.; De Souza, A. M. T.; Rodrigues, C. R.; Castro, H. C.; Junior, I. N.; Lourenço, M. C. S.; Wardwell, S. M. S. V.; Ferreira, V. F. *Biorg. Med. Chem.* **2006**, *14*, 8644–8653. For examples of difluoromethylimidazoles as antileishmanial agents, see: (b) Ferreira, S. B.; Costa, M. S.; Boechat, N.; Bezerra, R. J. S.; Genestra, M. S.; Canto-Cavalheiro, M. M.; Kover, W. B.; Ferreira, V. F. *Eur. J. Med. Chem.* **2007**, *42*, 1388–1395. However, it has to be mentioned also that difluoromethylimidazoles are unstable under basic conditions. (c) Tuan, E.; Kirk, K. L. *J. Fluorine Chem.* **2006**, *127*, 980–982.

(10) For a recent patent on pyrimidines with a CHF_2 side chain, designed for treating CNS disorders, see: (a) Gatti McArthur, S.; Wichmann, J.; Woltering, T. PCT WO2007110337, 2007.

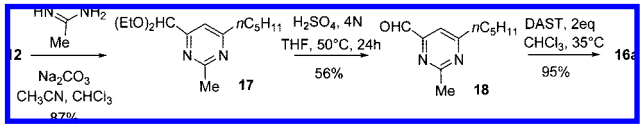
(11) Gorgues, A. *Bull. Soc. Chim. Fr.* **1974**, 529–530.

(12) Obrecht, D.; Weiss, B. *Helv. Chim. Acta* **1989**, *72*, 117–122.

SCHEME 5. Synthesis of Pyrimidines 16a−16d



SCHEME 6. Alternative Synthesis of Pyrimidine 16a



followed was the same as that for **11** and involved as key intermediates the new propargylic derivatives **13** and **14** (Scheme 5). The propargylic ketone **12** was prepared from acetal **6** in two steps, following previously described reactions.[13] Removal of the acetal group was performed using pure formic acid[11] to afford labile electrophilic alkyne **13**, which was submitted directly to fluorination to yield **14**. This DAST-mediated reaction had to be performed under carefully controlled reaction conditions (dilution and temperature); otherwise, the corresponding tetrafluoropropargylic derivative **15** was obtained. This second fluorination has not been observed in the case of **10**. This indicates a higher reactivity, in fluorination, of the propargylic ketone with the alkyl chain as compared to the aryl-type derivative. Both **13** and **14** were also very reactive and labile compounds characterized only by NMR and used directly for the next steps. Condensation of **14** with the required amidines or guanidines afforded the target pyrimidines **16a−16d** in 5.5−19% overall yields from **12**. The lower yields obtained in the case of this C_5 alkyl chain are probably due, at least in part, to the well-known volatility of small fluorinated molecules such as **14**, which makes isolation difficult. On the other hand, ynones such as **13** and **14** are highly reactive and probably much more prone to decomposition than derivatives with the *p*-bromo substituent.

As discussed previously, an alternative strategy could be to first prepare the pyrimidine nucleus bearing the aldehyde group[14] and then perform the fluorination reaction (Scheme 6). Therefore, the pyrimidine **17** was prepared in good yield from intermediate **12**. However, all attempts to remove the acetal group using pure formic acid were unsuccessful, affording mostly degradation products. On the other hand, hydrolysis using sulfuric acid[14] in THF afforded the desired aldehyde **18**, albeit in moderate yield. Then, a reaction with 2 equiv of DAST at 35 °C afforded the desired pyrimidine **16a**. Therefore, for these series of pyrimidines with the difluoromethyl side chain, both routes, through the propargylic fluoride or by fluorination of formylpyrimidine, can be used with success.

In conclusion, this study confirms the versatility of propargylic fluorides in the synthesis of useful building blocks for further applications in organic and medicinal chemistry. The chiral propargylic fluorides are easily accessible in high enantiomeric purity and afford by condensation with amidines or guanidines interesting pyrimidines with several points of molecular diversity. On the other hand, it has been established that direct fluorination of the alcohol on the side chain also affords the target fluorinated pyrimidine in high ee and, therefore, both routes are possible for this π-electron-deficient heterocycle. Furthermore, new electrophilic alkynes, including derivatives bearing a CHF_2 substituent on the triple bond, have been prepared and used in the synthesis of the corresponding pyrimidines. Even if they are sensitive molecules, intermediates such as **9**, **10**, **13**, and **14** could be of much use in the synthesis. The development of this chemistry, as well as the preparation of other heterocycles starting from propargylic fluorides, is under active study in our group and will be reported in due course.

Experimental Section

General Procedure for the Monofluorinated Pyrimidines: To a solution of **3** (0.39 mmol) in acetonitrile (6 mL) were added sodium carbonate (0.94 mmol, 2.4 equiv) and amidine/guanidine derivatives (0.47 mmol, 1.2 equiv). The solution was stirred under reflux for 3 h. After cooling, the mixture was filtered and concentrated in vacuo. The product was purified on a silica gel column with a mixture of pentane/AcOEt as the eluent.

Synthesis of 4-(4-Bromophenyl)-6-(1-fluoroethyl)-2-methylpyrimidine [(±)-4a]: Pyrimidine **4a** was obtained as a pale-yellow solid (89.6 mg, 78% yield); R_f = 0.29 (9/1 pentane/AcOEt). Mp: 45 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.03−7.97 (m, 2H); 7.66 (bs, 1H); 7.65−7.60 (m, 2H); 5.63 (dq, J_{HF} = 48.1 Hz, J = 6.6 Hz, 1H); 2.78 (s, 3H); 1.71 (dd, J_{HF} = 24.5 Hz, J = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.1 (d, J_{CF} = 24.7 Hz); 168.0 (d, J_{CF} = 3.0 Hz); 163.9 (d, J_{CF} = 1.5 Hz); 135.9, 132.2, 128.8, 125.6, 108.2 (d, J_{CF} = 8.3 Hz); 90.5 (d, J_{CF} = 172.1 Hz); 26.1, 21.4 (d, J_{CF} = 26.4 Hz). ^{19}F NMR ($CDCl_3$, 282 MHz): δ −183.61 (dq, J_1 = 48.0 Hz, J_2 = 24.0 Hz). HRMS (EI). Calcd for $C_{13}H_{12}N_2F^{79}Br$ [M^+]: *m/z* 294.0168. Found: *m/z* 294.0172.

Synthesis of 1-(4-Bromophenyl)-4,4-diethoxybut-2-yn-1-ol (7): To a solution of **6** (1.12 mL, 7.54 mmol) in anhydrous THF (10 mL) under argon at −78 °C was added dropwise *n*-BuLi (a 1.6 M solution in hexane, 5.2 mL, 8.32 mmol, 1.1 equiv). The reaction mixture was stirred for 1 h at this temperature, and *p*-bromobenzaldehyde (1.7 g, 9.1 mmol, 1.2 equiv) was added. The reaction mixture was stirred for 3 h with the temperature rising slowly to room temperature before the addition of a saturated NH_4Cl solution. Then water (50 mL) was added, and the aqueous phase was extracted with diethyl ether (3 × 50 mL). The organic layers were washed, dried over $MgSO_4$, and concentrated in vacuo to give a yellow oil. After purification on a silica gel column, compound **7** was obtained as a yellow oil (2.25 g, 95% yield); R_f = 0.27 (75/25 pentane/AcOEt). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.49−7.32 (m, 4H); 5.43 (bd, J = 5.7 Hz, 1H); 5.3 (d, J = 1.3 Hz, 1H); 3.77−3.46 (m, 4H); 1.20 (t, J = 7.3 Hz, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 139.1; 131.6; 128.3; 122.3; 91.22; 84.8; 81.8; 63.5; 61.1; 61.0; 15.0. HRMS (EI). Calcd for $C_{14}H_{17}O_3{}^{79}Br$ [M^+]: *m/z* 312.0361. Found: *m/z* 312.0355.

Synthesis of 1-(4-Bromophenyl)-4,4-diethoxybut-2-yn-1-one (8): 2-Iodoxybenzoic acid (IBX; 3.2 g, 11.5 mmol, 3 equiv) was dissolved in DMSO (20 mL) at 60 °C. A solution of **7** (1.2 g, 3.83 mmol) in CH_2Cl_2 (28 mL) was added, and the mixture was stirred under reflux for 3 h. Ice-cold water was added to quench the reaction, and a white suspension appeared. The reaction mixture

(13) Kerouredan, E.; Prakesch, M.; Grée, D.; Grée, R. *Lett. Org. Chem.* **2004**, *1*, 78–80.

(14) For two recent examples of synthesis and the use of formylpyrimidines, see: (a) Verron, J.; Malherbe, P.; Prinssen, E.; Thomas, A. W.; Nock, N.; Masciadri, R. *Tetrahedron Lett.* **2007**, *48*, 377–380. (b) Choung, W.; Lorsbach, B. A.; Sparks, T. C.; Ruiz, J. M.; Kurth, M. J. *Synlett* **2008**, 3036–3040.

was filtered, and the layers were separated. The organic layer was washed, dried over $MgSO_4$, and concentrated under vacuum to give a yellow oil. After purification on a silica gel column (1:1 pentane/ether), compound **8** was obtained as a yellow oil (1.15 g, 96% yield); $R_f = 0.49$ (9/1 pentane/AcOEt). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.01−7.92 (m, 2H); 7.66−7.57 (m, 2H); 5.49 (s, 1H); 3.87−3.59 (m, 4H); 1.25 (t, $J = 7.3$ Hz, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 176.2; 135.0; 132.1; 131.0; 130.0; 91.2; 88.2; 81.1; 61.7; 15.1. HRMS (EI). Calcd for $C_{12}H_{10}O_2{}^{79}Br$ $[M - C_2H_5O]^+$: *m*/*z* 264.9864. Found: *m*/*z* 264.9853.

Synthesis of 4-(4-Bromophenyl)-4-oxobut-2-ynal (9): To a solution of **8** (1.15 g, 3.7 mmol) in CH_2Cl_2 (25 mL) was added formic acid (25 mL), and it was stirred under reflux for exactly 1 h. Then the excess of formic acid and the ethyl formate formed were removed under vacuum, without water wash, to give **9** as a brown oil, which could not be further purified. It was characterized by NMR and used immediately for the next step. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.67 (s, 1H); 8.00−7.91 (m, 2H); 7.73−7.62 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 175.2; 164.5; 134.2; 132.5; 131.0; 129.0; 86.1; 85.9.

Synthesis of 1-(4-Bromophenyl)-4,4-difluorobut-2-yn-1-one (10): A solution of the previous **9** (crude, 3.7 mmol expected) in $CHCl_3$ (stabilized with amylene, 66 mL) was stirred under argon at 35 °C. Then DAST (0.97 mL, 7.4 mmol, 2 equiv) was added dropwise, and the mixture was stirred at 35 °C for 1.5 h. It was washed with water until neutral pH and dried over $MgSO_4$. The intermediate **10** was highly volatile, and therefore the reaction mixture was not concentrated and was used immediately for the next step. In order to obtain the NMR data of **10**, the reaction was reproduced on a small scale in $CDCl_3$. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.03−7.92 (m, 2H); 7.74−7.62 (m, 2H); 6.43 (t, $J_{HF} = 53.5$ Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 174.9 (t, $J_{CF} = 2.2$ Hz); 134.3, 132.1, 131.1, 129.2, 103.2 (t, $J_{CF} = 235.7$ Hz); 82.51 (t, $J_{CF} = 6.9$ Hz); 80.92 (t, $J_{CF} = 35.1$ Hz). ^{19}F NMR ($CDCl_3$, 282 MHz): δ −109.3 (d, $J = 54.0$ Hz).

General Procedure for the Synthesis of the Difluoropyrimidines 11a−11d: To a solution of the previous **10** (crude in $CHCl_3$, 0.92 mmol expected) in CH_3CN (15 mL) were added Na_2CO_3 (2.36 mmol, 2.4 equiv) and amidine/guanidine derivatives (1.06 mmol, 1.2 equiv). The solution was stirred overnight under reflux. After cooling, the mixture was filtered and concentrated in vacuo. The crude product was purified on a silica gel column with pentane/AcOEt as the eluent.

Synthesis of 4-(4-Bromophenyl)-6-(difluoromethyl)-2-methylpyrimidine (11a): Pyrimidine **11a** was obtained as a pale-yellow solid (96.0 mg, 35% yield over three steps); $R_f = 0.12$ (98/2 pentane/Et_2O). Mp: 98 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.03−7.92 (m, 2H); 7.73 (s, 1H); 7.67−7.57 (m, 2H); 6.54 (t, $J_{HF} = 55.0$ Hz, 1H); 2.81 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 169.0 (t, $J_{CF} = 1.0$ Hz); 164.7; 161.0 (t, $J_{CF} = 26.0$ Hz); 135.1, 132.3, 128.8, 126.3, 112.7 (t, $J_{CF} = 242.0$ Hz); 109.0 (t, $J_{CF} = 3.3$ Hz); 26.0. ^{19}F NMR ($CDCl_3$, 282 MHz): δ −119.55 (d, $J = 55.0$ Hz). HRMS (EI). Calcd for $C_{12}H_9N_2F_2{}^{79}Br$ $[M^+]$: *m*/*z* 297.9917. Found: *m*/*z* 297.9915.

General Procedure for the Synthesis of the Difluoropyrimidines 16a−16d: To a solution of the previous **14** (crude in $CHCl_3$, 0.88 mmol expected) in CH_3CN (15 mL) were added Na_2CO_3 (2.11 mmol, 2.4 equiv) and amidine/guanidine derivatives (1.06 mmol, 1.2 equiv). The solution was stirred under reflux overnight. After cooling, the mixture was filtered and concentrated under vacuum. The product was purified on a silica gel column with pentane/AcOEt as the eluent.

Synthesis of 4-(Difluoromethyl)-2-methyl-6-pentylpyrimidine (16a): Pyrimidine **16a** was obtained as a pale-yellow oil (36.2 mg, 19% yield over three steps); $R_f = 0.2$ (95/5 pentane/AcOEt). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.24 (s, 1H); 6.47 (t, $J_{HF} = 55.0$ Hz, 1H); 2.77 (t, $J = 7.7$ Hz, 2H); 2.73 (s, 3H); 1.79−1.63 (m, 2H); 1.40−1.29 (m, 4H); 0.89 (t, $J = 6.8$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 173.2; 168.3; 159.9 (t, $J_{CF} = 26.0$ Hz); 112.8 (t, $J_{CF} = 242.0$ Hz); 112.4 (t, $J_{CF} = 3.0$ Hz); 60.4, 38.2, 31.5, 28.7, 25.9, 22.4, 21.0, 14.2, 13.9. ^{19}F NMR ($CDCl_3$, 282 MHz): δ −119.58 (d, $J = 55.0$ Hz). HRMS (EI). Calcd for $C_9H_{11}N_2F_2$ $[M - C_2H_5]^+$: *m*/*z* 185.0890. Found: *m*/*z* 185.0892.

Acknowledgment. We thank CNRS and MESR for financial support and for a research fellowship (to P.B.). We thank Prof. F. Mongin for fruitful discussions.

Supporting Information Available: Complementary experimental procedures, analytical data, and ^{1}H, ^{13}C, and ^{19}F NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

JO900674U