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New 5-Alkoxypyrimidine Derivatives from β-Alkoxy β-Keto Enamides and Ammonium Salts

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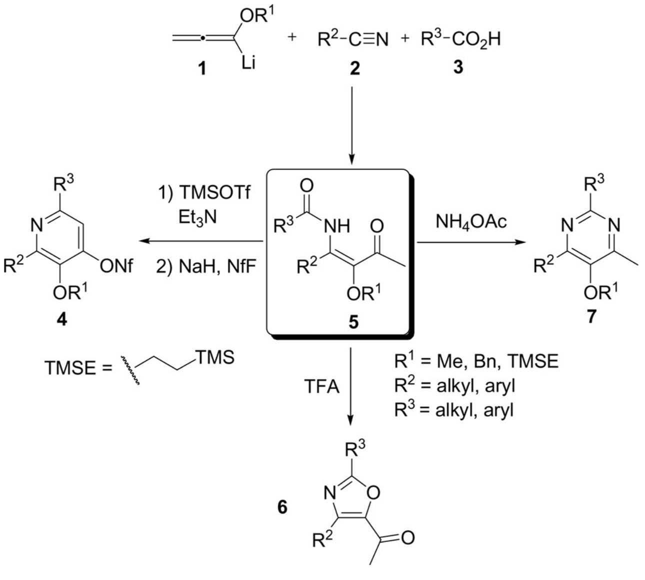
A series of highly substituted β-alkoxy β-keto enamides were prepared by a multi-component reaction combining lithiated alkoxyallenes, nitriles and carboxylic acids. Apt conditions were developed for their conversion into 5-alkoxypyrimidine derivatives. This synthesis is highly flexible with respect to the substitution pattern at C-2 and C-4 of the pyrimidine core. The corresponding pyrimidin-5-yl nonaflates allowed subsequent transformations at C-5 by palladium-catalyzed couplings such as Sonogashira and Suzuki reactions. The Sonogashira coupling of a pyrimidinyl alkyne with a pyridinyl nonaflate and a subsequent cyclization led to an efficient access to pyrimidinyl-substituted furo[2,3-*c*]pyridine derivatives. The C-6 methyl group which is present in all of the prepared pyrimidines can easily be converted into formyl, carboxylic or alkynyl moieties which allow the synthesis of additional pyrimidine derivatives.

Introduction

In recent reports we described the remarkable versatility of lithiated alkoxyallenes **1** as crucial C_3-building blocks for the synthesis of several classes of heterocycles.[1] As an entirely unexpected result we discovered the three-component reaction of **1** with nitriles **2** and carboxylic acids **3** to highly substituted β-alkoxy β-keto enamides **5**. The unique mechanism of this transformation has been disclosed in earlier publications.[2] These enamides **5** have so far served as highly flexible precursor for the cyclization to heteroaromatic compounds such as 3-alkoxypyridinols and their nonaflates **4** or 5-acetyloxazoles **6** (Scheme 1).[2–3] Moreover, preliminary results have shown that enamides **5** can also be employed for the synthesis of highly substituted 5-alkoxypyrimidines **7** when appropriate ammonia sources are used.[4] Due to the permanent interest in highly substituted pyrimidine derivatives[5] for applications in medicinal chemistry and material science we investigated the preparation of this class of heterocycles more closely. In this article, we describe in full detail our efforts aimed at the synthesis of 5-alkoxypyrimidine derivatives **7** by cyclization of β-alkoxy β-keto enamides **5**.[6] We also demonstrate the high flexibility with respect to the substitution pattern at the pyrimidine core and show that subsequent functionalizations such as palladium-catalyzed couplings at C-5 and oxidation reactions of the methyl group at C-6 are easily achieved leading to a broad range of new pyrimidine derivatives.



Scheme 1. Three-component reaction of lithiated alkoxyallenes **1**, nitriles **2** and carboxylic acids **3** leading to enamides **5** and their subsequent conversion into highly substituted 3-alkoxy-4-pyridinyl nonaflates **4**, 5-acetyloxazoles **6** and 5-alkoxypyrimidines **7**.

Results and Discussion

Three-Component Reaction to Enamides and Investigation of the Pyrimidine Formation

The required β-alkoxy β-keto enamides were prepared by the previously described three-component reaction starting with the lithiation of the corresponding alkoxyallene by *n*-butyllithium at –40 °C. Then, the required nitrile was added at –78 °C, followed by quenching with an excess of the carb-

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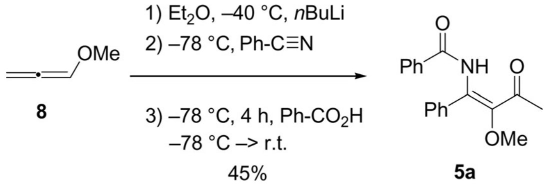
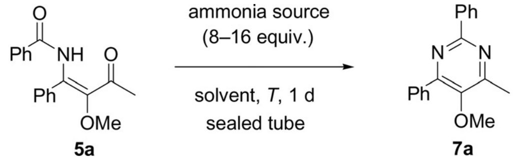
oxylic acid. As depicted in Scheme 2 enamide **5a** is a first example that has been synthesized from methoxyallene **8**, benzonitrile and benzoic acid in 45% yield.



Scheme 2. Synthesis of enamide **5a** starting from methoxyallene **8**, benzonitrile and benzoic acid.

Compound **5a** was chosen as a model substrate for the subsequent optimization of the pyrimidine preparation since the phenyl substituents should not interfere with any of the involved steps. Two methods A and B with different ammonia sources have been developed. For the cyclization of **5a** to pyrimidine derivative **7a** we first applied modified conditions as described by Taddei for the synthesis of 2,4-disubstituted quinazolines (Table 1).[7] Initially, 16 equiv. of ammonium bicarbonate were necessary for a complete conversion and different solvents like toluene, 1,2-dichloroethane, water or methanol have been tested (Entries 1–5, Table 1). In entries 1–4 only traces or low amounts of pyrimidine **7a** were observed, whereas the use of methanol strongly increased the efficacy providing a yield of 65% (Entry 5, method A). A change of the ammonia source to ammonium acetate (8.0 equiv.) led to a slight increase to 73% (Entry 6, method B). Experiments with ammonium chloride or microwave reactions to shorten the reaction time failed to provide the product in good yield (Entries 7–8).

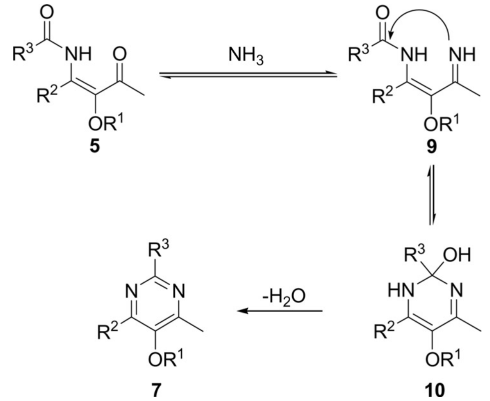
Table 1. Optimization of the conversion of enamide **5a** into pyrimidine derivative **7a**.



Entry	Solvent	T [°C]	Ammonia source	**7a**, % yield (method)
1	PhMe	90	NH_4HCO_3[a]	6
2	$C_2H_4Cl_2$	80	NH_4HCO_3[a]	traces
3	H_2O	80	NH_4HCO_3[a]	traces
4	H_2O	90	NH_3 (25%)	26
5	MeOH	65	NH_4HCO_3[a]	65 (A)
6	MeOH	65	NH_4OAc[b]	73 (B)
7	MeOH	65	NH_4Cl[a]	traces
8	MeOH	60	NH_4OAc[b,c]	60% conv.

[a] Method A: 16 equiv. of NH_4HCO_3. [b] Method B: 8.0 equiv. NH_4OAc. [c] Reaction was carried out in a microwave reactor for 5 h.

The reaction of enamide **5** with an ammonium salt to pyrimidine derivative **7** is supposed to proceed by the simple mechanism depicted in Scheme 3. Initially, imine **9** is formed by condensation of the carbonyl group with ammonia, which is then converted by cyclization to intermediate **10** followed by dehydration to the corresponding product **7**. It is likely that all steps are proton catalyzed.



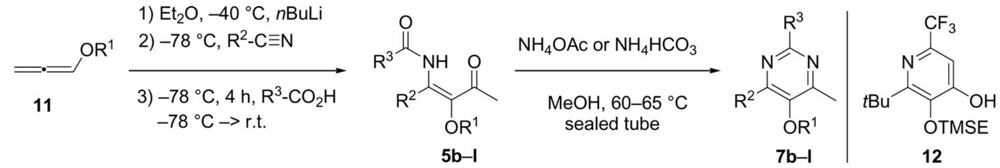
Scheme 3. Proposed mechanism of the formation of pyrimidines **7** from enamides **5** and ammonia.

Conversion of Enamides into 5-Alkoxypyrimidine Derivatives – Scope and Limitations

A variety of differently substituted enamides **5** have been prepared (Table 2) in order to examine the applicability of methods A and B for the synthesis of pyrimidines. In general, enamides **5b–l** could be obtained by following the procedure as briefly described above in fair to good yields. The three-component reaction allows the use of a vast number of nitriles (aliphatic, functionalized aliphatic, aromatic or heteroaromatic) as well as carboxylic acids. The aromatic and heteroaromatic carboxylic acids had to be dissolved in diethyl ether, THF or DMF prior addition to the reaction mixture. With respect to the alkoxyallenes **11**, methoxy-, benzyloxy- or even the acid labile 2-(trimethylsilyl)ethoxy-substituted allenes were successfully employed in the first step. In principle, the reaction can be performed either with 2.7 equiv. of allene and 1.0 equiv. of nitrile (method C in Table 2) or with an excess of nitrile (method D) with comparable yields. However, it should be noted that for α-acidic nitriles only method C furnishes no side products.[2f] In case of a perfluorinated carboxylic acid such as TFA, pyridinol derivatives like **12** were isolated as main product (Entry 9). This subsequent reaction proceeds via a rapid intramolecular acid catalyzed aldol condensation, which has already been discussed in detail in our previous publications describing the route to pyridine derivatives.[2]

By means of methods A and B enamides **5b–l** were then cyclized to furnish 5-alkoxypyrimidine derivatives **7b–l** in 38–86% yield hence demonstrating the impressive flexibility with respect to substituents at C-2, C-4 and C-5 of the pyrimidine core. According to our experience the initial three-component reaction to enamides **5** is the bottle neck of the

Table 2. Synthesis of β-alkoxy β-keto enamides **5b**–**l** starting from alkoxyallenes **11**, nitriles and carboxylic acids followed by their conversion into 5-alkoxypyrimidines **7b**–**l**.

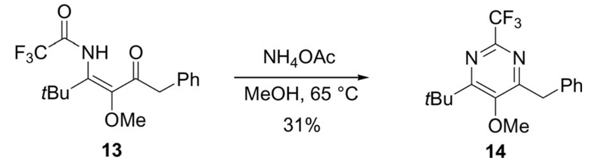


Entry	R^1	R^2	R^3	5	% yield (method[a])	7	% yield (method[b])
1	Me	Me	Ph[c]	**5b**	13 (C)[3b]	**7b**	40 (B)
2	Me	*i*Pr	Ph[c]	**5c**	53 (D)[3b]	**7c**	54 (B)
3	Me	*c*Pr	*c*Pr	**5d**	79 (C)[3b]	**7d**	56 (B)
4	Me	*t*Bu	C≡CH	**5e**	72 (D)[3b]	**7e**	55 (B)
5	Me	Ph	2-thienyl[c]	**5f**	43 (C)[3b]	**7f**	65 (A)
6	Me	Ph	2-Py[d]	**5g**	42 (C)	**7g**	38 (B)
7	Bn	Ph	Ph[c]	**5h**	54 (C)[3b]	**7h**	75 (A)
8	Bn	2-thienyl	2-thienyl[c]	**5i**	32 (D)[3b]	**7i**	68 (B)
9	TMSE	*t*Bu	CF_3	**5j**	14 (D)[e]	**7j**	66 (A)
10	TMSE	Ph	Ph[c]	**5k**	36 (D)	**7k**	86 (B)
11	TMSE	2-thienyl	Ph[c]	**5l**	74 (C)[3b]	**7l**	75 (A)

[a] Method C: 2.7 equiv. lithiated alkoxyallene, 1.0 equiv. nitrile, 5.4 equiv. carboxylic acid; Method D: 1.0 equiv. lithiated alkoxyallene, 1.5–3.0 equiv. nitrile, 3.0–6.0 equiv. carboxylic acid. [b] Method A: 16 equiv. NH_4HCO_3, MeOH, sealed tube, 65 °C, 1 d; Method B: 8.0 equiv. NH_4OAc, MeOH, sealed tube, 60–65 °C, 1 d. [c] Dissolved in Et_2O or THF. [d] Dissolved in DMF. [e] 28% of pyridinol **12**[2f] was isolated.

two stage preparation of pyrimidines **7**, whereas the condensation with ammonia did never make trouble in one of the examples investigated.

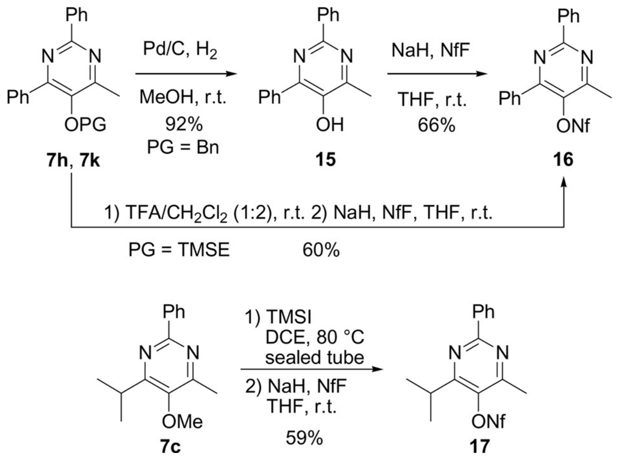
The methyl group at C-6, which is present in all pyrimidines synthesized above, could be replaced by other substituents when suitable precursors of γ-substituted alkoxyallenes are employed in the first step of the sequence.[2f] Enamide **13** shows a benzyl group in this position (Scheme 4) and its cyclization to pyrimidine **14** was achieved in 31% yield applying method B.



Scheme 4. Cyclization of enamide **13** to 6-benzyl-substituted pyrimidine derivative **14**.

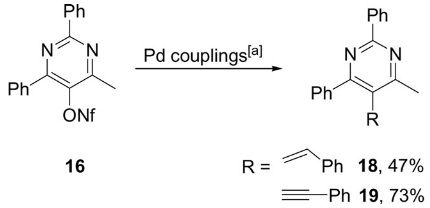
Synthesis of Pyrimidin-5-yl Nonaflates, Subsequent Palladium-Catalyzed Coupling Reactions and other Transformations

The cleavage of the benzyloxy group at C-5 of compound **7h** could be achieved under very mild conditions. The reaction was performed with catalytic amounts of palladium on charcoal under a hydrogen atmosphere and 5-hydroxypyrimidine **15** was obtained in very good yield (Scheme 5). The hydroxy group was then easily converted into a nonaflate group by use of a suspension of sodium hydride in THF and nonafluorobutanesulfonyl fluoride (NfF) as reagent that provided pyrimidin-5-yl nonaflate **16**. 2-(Trimethylsilyl)ethyl protected pyrimidine **7k** was subjected to a mixture of TFA and dichloromethane followed by the nonaflation reaction. Without purification of the intermediate product **16** was isolated in 60% yield after two steps. On the other hand, methyl ether **7c** could only be cleaved under fairly harsh conditions (Scheme 5). Deprotection with trimethylsilyl iodide as reagent and subsequent nonaflation afforded the desired product **17** in 59% yield after two steps.



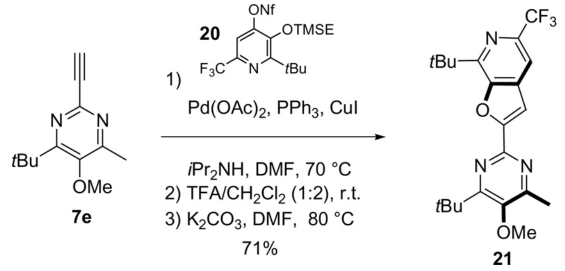
Scheme 5. Cleavage and nonaflation of different alkoxypyrimidines leading to pyrimidin-5-yl nonaflates **16** and **17**.

Alkenyl, aryl and heteroaryl nonaflates have been proven to be excellent substrates in palladium-catalyzed coupling reactions.[2,8–9] We therefore expected that pyrimidin-5-yl nonaflates will also behave well in C–C couplings. The reaction of **16** with *trans*-2-styrylboronic acid under Suzuki conditions led to the desired product **18** in moderate yield whereas the Sonogashira reaction with phenylacetylene as coupling partner furnished alkyne **19** in 73% yield (Scheme 6).



Scheme 6. Palladium-catalyzed couplings. [a] Suzuki reaction conditions: 5 mol-% $Pd(OAc)_2$, 20 mol-% PPh_3, 2.0 equiv. K_2CO_3, 1.2 equiv. *trans*-2-styrylboronic acid, 70 °C; Sonogashira reaction conditions: 5 mol-% $Pd(OAc)_2$, 20 mol-% PPh_3, 5 mol-% CuI, DMF, 1.2 equiv. phenylacetylene, 70 °C.

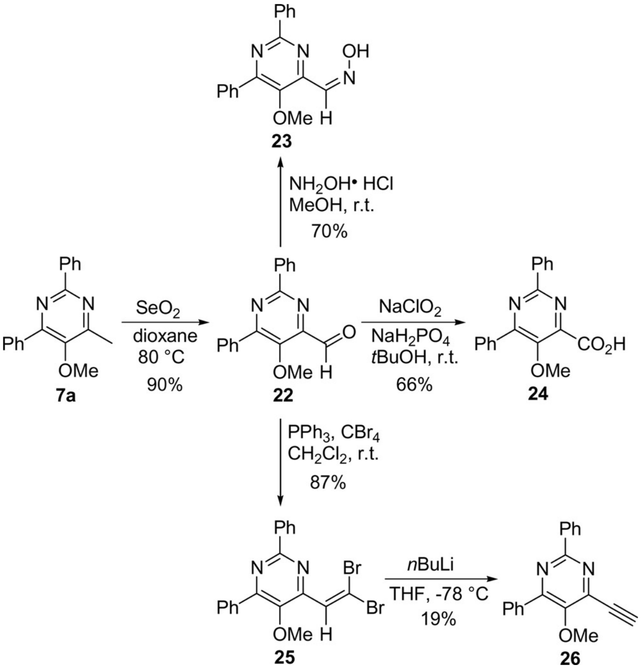
Furo-pyridine derivatives have remarkable photophysical features[2d,3b] that might be useful for the development of novel organic light emitting materials or optoelectronics.[10–12] Thus, a three-step method[2d] to a highly substituted furo[2,3-*c*]pyridine derivative was achieved by a Sonogashira reaction of pyrimidinyl alkyne **7e** with pyridinyl nonaflate **20**[2f] as coupling partner (Scheme 7). The deprotection of the 2-(trimethylsilyl)ethyl ether function at C-5 and a subsequent treatment with potassium carbonate provided the cyclized product **21** in good overall yield (71% after three steps).



Scheme 7. Three-step conversion of pyrimidine derivative **7e** and pyridinyl nonaflate **20** into the highly substituted furo-pyridine **21**.

It should be noted here that compound **21** nicely demonstrates the high versatility of alkoxyallenes as C-3 building blocks for the synthesis of various functionalized heterocycles. In this example two alkoxyallene units are incorporated into the heterocyclic cores and hence we have highlighted the two allene-derived units in Scheme 7 to emphasize this fact.

The methyl group at C-6 of the pyrimidine derivatives prepared by our route might be regarded as limitation of the method (for an exception see Scheme 4). However, this substituent also offers interesting options to install new functional groups at C-6. As an example, the oxidation of the methyl group of pyrimidine **7a** to a formyl substituent was smoothly achieved by using the Riley method. An excess of selenium dioxide as oxidizing agent provided aldehyde **22** in very good yield, which was converted under standard conditions into the corresponding aldoxime **23** as a singular isomer (Scheme 8). Aldehyde **22** could also be oxidized (Pinnick protocol) to furnish the corresponding carboxylic acid **24** in 66% yield. The Corey–Fuchs reaction converted **22** into dibromoolefin **25** in 87% yield, whereas the subsequent (not optimized) *n*-butyllithium promoted elimination yielded only 19% of the expected alkyne **26**. These examples clearly demonstrate the potential of compounds **7** to rapidly lead to a variety of other functionalized pyrimidine derivatives.



Scheme 8. Use of the C-6 methyl group of pyrimidine **7a** for functionalizations leading to aldehyde **22**, oxime **23**, carboxylic acid **24**, dibromoalkene **25**, and alkyne **26**.

Conclusions

We demonstrated that enamides of type **5** are ideal substrates for the synthesis of highly substituted 5-alkoxypyrimidine derivatives **7**. Simple reaction conditions with ammonia sources allow this transformation with good efficacy and all compounds **5** examined could be converted into **7**. This new method allows high flexibility with respect to substituents at C-2, C-4 and C-5 of the pyrimidine core. Conversion of the alkoxy group at C-5 of the prepared pyrimidine derivatives into nonaflates provided the option to perform palladium-catalyzed C–C cross couplings at this position. Furthermore, an alkynyl-substituted pyrimidine could be easily coupled with a pyridin-4-yl nonaflate and cyclized to a furo-pyridine derivative. Several functionalizations at C-6 of pyrimidines also show the broad variability at this position opening further options to many new heterocycles.

Experimental Section

General Methods: Reactions were generally performed under argon in flame-dried flasks. Solvents and reagents were added by syringes. Solvents were dried using standard procedures. Reagents were purchased and were used as received without further purification unless otherwise stated. Unless otherwise stated, products were purified by flash chromatography on silica gel (230–400 mesh, Merck or Fluka) or HPLC (Nucleosil 50–5). Unless otherwise stated, yields refer to analytically pure samples. NMR spectra were recorded on Bruker (AC 500) and JOEL (Eclipse 500 and ECX 400) instruments. Chemical shifts are reported relative to TMS (^{1}H: δ = 0.00 ppm), $CDCl_3$ (^{1}H: δ = 7.25 ppm, ^{13}C: δ = 77.0 ppm). Integrals are in accordance with assignments; coupling constants are given in Hz. All ^{13}C-NMR spectra are proton-decoupled. Multiplicity is indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), hept (heptet), m (multiplet), m_c (centered multiplet), dd (doublet of doublet), br. s (broad singlet). For detailed peak assignments 2D spectra were measured (COSY, HMBC and HMQC). IR spectra were measured with an FT-IRD spectrometer Nicolet 5 SXC. MS and HRMS analyses were performed with Finnigan MAT 711 (EI, 80 eV, 8 kV), MAT CH7A (EI, 80 eV, 3 kV), CH5DF (FAB, 3 kV), Varian Ionspec QFT-7 (ESI-FT ICRMS) and Agilent 6210 (ESI-TOF) instruments. Elemental analyses were carried out with Perkin–Elmer CHN-Analyzer 2400 or Vario EL Elemental Analyzer. Melting points were measured with a Reichert apparatus Thermovar and are uncorrected. The preparations of enamide derivatives **5b–f**, **5h–i**, **5l**,[3b] **13**[2f] and pyridinol **12**[2f] were published in previous reports.

Typical Procedure for the Enamide Synthesis (Method C): Methoxyallene **8** (1.65 mL, 19.8 mmol) was dissolved in Et_2O (40 mL) and *n*-butyllithium (6.60 mL, 16.5 mmol, 2.5 M in hexanes) was added at –40 °C. After 25 min at –50 to –40 °C the solution was cooled to –78 °C and benzonitrile (0.61 mL, 5.97 mmol) was added. After stirring for 4 h at this temperature picolinic acid (4.80 g, 39.0 mmol, dissolved in 20 mL of DMF) was added and the mixture was warmed up to room temperature overnight. The reaction mixture was quenched with satd. aq. $NaHCO_3$ solution (60 mL) and extracted with Et_2O (3 × 50 mL). The combined organic phases were dried with Na_2SO_4 and then evaporated. The residue was purified by chromatography on silica gel (hexane/ethyl acetate, 2:1) to afford 743 mg (42%) of **(*E*)-*N*-(2-methoxy-3-oxo-1-phenylbut-1-enyl)picolinamide (5g)** as a colourless solid; m.p. 139–140 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.40 (s, 3 H, CH_3), 3.22 (s, 3 H, OMe), 7.40–7.43, 7.49–7.79 (m, 5 H, Ph), 7.44 (ddd, *J* = 7.6, 4.8, 1.1 Hz, 1 H, 5′-H), 7.79 (td, *J* = 7.8, 1.6 Hz, 1 H, 4′-H), 8.04 (dt, *J* = 7.8, 0.7 Hz, 1 H, 3′-H), 8.74 (ddd, *J* = 4.8, 1.6, 1.1 Hz, 1 H, 6′-H), 10.03 (br. s, 1 H, NH) ppm. ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 27.5 (q, Me), 60.7 (q, OMe), 123.0, 126.7 (2d, C-3′, C-5′), 128.0, 128.5, 128.9, 132.6 (3d, s, Ph), 137.4 (s, C-1), 139.6 (d, C-4′), 141.1, (s, C-2), 148.7 (d, C-6′), 149.9 (s, C-2′), 163.3 (s, C-1′′), 201.5 (s, C-3) ppm. IR (KBr): $\tilde{\nu}$ = 3460 (N–H), 3060–2030 (=C–H), 2930–2830 (C–H), 1700–1580 (C=O, C=C) cm^{-1}. MS (EI): *m*/*z* (%) = 296 (10) $[M]^+$, 253 (100) $[M - C_2H_3O]^+$, 107 (23) $[C_6H_6NO]^+$, 78 (48) $[C_5H_5N]^+$, 43 (29) $[C_2H_3O]^+$. HRMS (EI): calcd. for $C_{17}H_{16}N_2O_3$: 296.1161; found 296.1153. $C_{17}H_{16}N_2O_3$ (296.3): calcd. C 68.91, H 5.44, N 9.45; found C 69.00, H 4.95, N 9.69.

Typical Procedure for the Enamide Synthesis (Method D): [2-(Trimethylsilyl)ethoxy]allene (2.45 g, 15.7 mmol) was dissolved in Et_2O (32 mL) and *n*-butyllithium (6.91 mL, 17.3 mmol, 2.5 M in hexanes) was added at –40 °C. After 25 min at –50 to –40 °C the solution was cooled to –78 °C and benzonitrile (2.40 mL, 23.6 mmol) was added. After stirring for 4 h at this temperature benzoic acid (5.74 g, 47.1 mmol, dissolved in 15 mL of Et_2O) was added and the mixture was warmed up overnight to room temperature. Then the reaction mixture was quenched with satd. aq. $NaHCO_3$ solution (30 mL) and extracted with Et_2O (3 × 25 mL). The combined organic phases were dried with Na_2SO_4 and then evaporated. The residue was purified by chromatography on silica gel (hexane/ethyl acetate, 10:1) to afford 2.14 g (36%) of **(*E*)-*N*-{3-oxo-1-phenyl-2-[2-(trimethylsilyl)ethoxy]but-1-enyl}benzamide (5k)** as a colourless solid; m.p. 65 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = –0.15 (s, 9 H, $SiMe_3$), 0.69 (m_c, 2 H, CH_2Si), 2.40 (s, 3 H, Me), 3.36 (m_c, 2 H, OCH_2), 7.36–7.55, 7.95–7.98 (2m, 8 H, 2 H, Ph), 12.40 (br. s, 1 H, NH) ppm. ^{13}C NMR ($CDCl_3$, 101 MHz): δ = –1.7 (q, $SiMe_3$), 18.6 (t, CH_2Si), 27.5 (q, C-4), 71.5 (t, OCH_2), 127.8, 128.4, 128.68, 128.73, 132.3, 132.6, 133.7 (5d, 2s, Ph)*, 137.6, 143.4 (2s, C-1, C-2), 165.2 (s, C-1′′), 202.9 (s, C-3) ppm; * overlap of Ph signals. IR (KBr): $\tilde{\nu}$ = 3400 (N–H), 3110–2995 (=C–H), 2960–2895 (C–H), 1730–1580 (C=O, C=C) cm^{-1}. $C_{22}H_{27}NO_3Si$ (381.5): calcd. C 69.25, H 7.13, N 3.67; found C 69.05, H 7.08, N 3.69.

(*E*)-*N*-{1-*tert*-Butyl-3-oxo-2-[2-(trimethylsilyl)ethoxy]-1-butenyl}-2,2,2-trifluoroacetamide (5j): According to typical procedure (method D), [2-(trimethylsilyl)ethoxy]allene (501 mg, 3.21 mmol) in Et_2O (7.0 mL), *n*-butyllithium (1.41 mL, 3.53 mmol, 2.5 M in hexanes), pivalonitrile (1.06 mL, 9.63 mmol) and TFA (1.48 mL, 19.3 mmol) provided the crude product. The residue was purified by chromatography on silica gel (hexane/ethyl acetate, 10:1) to afford 159 mg (14%) of **5j** as a colourless solid and 302 mg (28%) of **2-*tert*-butyl-6-(trifluoromethyl)-3-[2-(trimethylsilyl)ethoxy]-4-pyridinol (12)** as a pale yellow oil. Characterization of enamide **5j**: M.p. 147–149 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.04 (s, 9 H, $SiMe_3$), 1.11 (m_c, 2 H, CH_2Si), 1.23 (s, 9 H, *t*Bu), 2.28 (s, 3 H, Me), 3.67 (m_c, 2 H, OCH_2), 7.56 (br. s, 1 H, NH) ppm. ^{13}C NMR ($CDCl_3$, 126 MHz): δ = –1.5 (q, $SiMe_3$), 18.7 (t, CH_2Si), 27.4 (q, Me), 28.4, 26.3 (q, s, *t*Bu) 69.9 (t, OCH_2), 115.9 (q, $^1J_{CF}$ = 288 Hz, CF_3), 129.1, 151.2 (2s, C-1, C-2), 156.7 (q, $^2J_{CF}$ = 36.5 Hz, C-1′), 200.7 (s, C-3) ppm. IR (KBr): $\tilde{\nu}$ = 3280 (N–H), 3050–2880 (C–H), 1725–1630 (C=O, C=C) cm^{-1}. $C_{15}H_{26}F_3NO_3Si$ (353.5): calcd. C 50.97, H 7.41, N 3.96; found C 51.02, H 7.31, N 3.87.

Characterization of **12** has been reported previously.[2f]

Typical Procedure for the Pyrimidine Synthesis (Method A): Enamide **5f** (211 mg, 0.700 mmol) and NH_4HCO_3 (885 mg, 11.2 mmol) were placed in an ACE-sealed tube. The mixture was dissolved in MeOH (7.0 mL) and stirred for 1 d at 65 °C. After addition of water and CH_2Cl_2 (7 mL) the layers were separated and the aqueous layer was extracted twice with CH_2Cl_2 (7 mL). The combined organic layers were dried with Na_2SO_4, filtered and concentrated. Column chromatography (silica gel, hexane/ethyl acetate = 10:1) provided 129 mg (65%) **5-methoxy-4-methyl-6-phenyl-2-(thiophen-2-yl)pyrimidine (7f)** as a colourless solid; m.p. 39 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.59 (s, 3 H, Me), 3.54 (s, 3 H, OMe), 7.12 (dd, *J* = 5.0, 3.7 Hz, 1 H, 4′-H), 7.45–7.52, 8.15–8.17 (2 m, 3 H, 2 H, Ph), 7.42 (dd, *J* = 5.0, 1.3 Hz, 1 H, 3′-H), 7.77 (dd, *J* = 3.7, 1.3 Hz, 1 H, 5′-H) ppm. ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 19.1 (q, Me), 60.3 (q, OMe), 128.0, 128.2, 128.5, 129.0, 129.2, 130.0, 135.6 (6d, s, Ph, C-3′, C-4′, C-5′), 143.5 (s, C-2′), 148.9 (s, C-5), 156.18, 156.20, 162.4 (3s, C-2, C-4, C-6) ppm. IR (KBr): $\tilde{\nu}$ = 3095–3025 (=C–H), 3000–2845 (C–H), 1715–1580 (C=C, C=N) cm^{-1}. $C_{16}H_{14}N_2OS$ (282.4): calcd. C 68.06, H 5.00, N 9.92; found C 68.02, H 4.91, N 9.87.

Typical Procedure for the Pyrimidine Synthesis (Method B): Enamide **5k** (350 mg, 0.917 mmol) and NH_4OAc (566 mg, 7.34 mmol) were placed in an ACE-sealed tube. The mixture was dissolved in MeOH (5.0 mL) and stirred for 1 d at 65 °C. After addition of water and CH_2Cl_2 (5 mL) the layers were separated and the aqueous layer was extracted twice with CH_2Cl_2 (5 mL). The combined organic layers were dried with Na_2SO_4, filtered and concentrated. Column chromatography (silica gel, hexane/ethyl acetate = 10:1) provided 285 mg (86%) **4-methyl-2,6-diphenyl-5-[2-(trimethylsilyl)-**

ethoxy]pyrimidine (**7k**) as a colourless oil. ^{1}H NMR (CDCl$_3$, 500 MHz): δ = –0.08 (s, 9 H, SiMe$_3$), 1.04 (m$_c$, 2 H, CH$_2$Si), 2.64 (s, 3 H, Me), 3.70 (m$_c$, 2 H, OCH$_2$), 7.41–7.53, 8.16–8.19, 8.47–8.50 (3m, 10 H, Ph) ppm. ^{13}C NMR (CDCl$_3$, 101 MHz): δ = –1.6 (q, SiMe$_3$), 18.9 (t, CH$_2$Si), 19.6 (q, Me), 71.1 (t, OCH$_2$), 128.0, 128.3, 128.4, 129.1, 129.77, 129.84, 136.4, 137.8 (6d, 2s, Ph), 148.2 (s, C-5), 156.6, 158.7, 162.4 (3s, C-2, C-4, C-6) ppm. IR (film): $\tilde{\nu}$ = 3090–2870 (=C–H, C–H), 1680–1540 (C=C, C=N) cm^{-1}. C$_{22}$H$_{26}$N$_2$OSi (362.5): calcd. C 72.88, H 7.23, N 7.73; found C 72.63, H 7.12, N 7.78.

5-Methoxy-4-methyl-2,6-diphenylpyrimidine (7a): According to typical procedure (method B), enamide **5a** (1.17 g, 3.97 mmol) and NH$_4$OAc (2.45 g, 31.8 mmol) in MeOH (5.0 mL) provided the crude product. The residue was purified by chromatography on silica gel (hexane/ethyl acetate, 12:1) to afford 795 mg (73%) of **7a** as a colourless solid; m.p. 91–92 °C. ^{1}H NMR (CDCl$_3$, 500 MHz): δ = 2.64 (s, 3 H, Me), 3.57 (s, 3 H, OMe), 7.41–7.53, 8.18–8.21, 8.46–8.50 (3m, 6 H, 2 H, 2 H, Ph) ppm. ^{13}C NMR (CDCl$_3$, 101 MHz): δ = 19.3 (q, Me), 60.3 (q, OMe), 128.1, 128.4, 128.5, 129.2, 129.9, 136.1, 137.8 (5d, 2s, Ph)*, 149.4 (s, C-5), 156.2, 159.0, 162.2 (3s, C-2, C-4, C-6) ppm; * overlap of Ph signals. IR (KBr): $\tilde{\nu}$ = 3090–3010 (=C–H), 2900–2800 (C–H), 1640–1545 (C=C, C=N) cm^{-1}. HRMS (ESI-TOF): calcd. for C$_{18}$H$_{17}$N$_2$O [M + H]$^+$: 277.1335; found 277.1315.

5-Methoxy-4,6-dimethyl-2-phenylpyrimidine (7b): According to typical procedure (method B), enamide **5b** (80 mg, 0.343 mmol) and NH$_4$OAc (423 mg, 5.49 mmol) in MeOH (2.0 mL) provided the crude product. The residue was purified by chromatography on silica gel (hexane/ethyl acetate, 10:1) to afford 29 mg (40%) of **7b** as a colourless solid; m.p. 53 °C. ^{1}H NMR (CDCl$_3$, 500 MHz): δ = 2.54 (s, 6 H, Me), 3.78 (s, 3 H, OMe), 7.39–7.46, 8.33–8.36 (2m, 3 H, 2 H, Ph) ppm. ^{13}C NMR (CDCl$_3$, 101 MHz): δ = 19.0 (q, Me), 60.4 (q, OMe), 127.9, 128.4, 130.0, 137.7 (3d, s, Ph), 150.1 (s, C-2), 159.0, 159.8 (2s, C-5, C-4) ppm. IR (KBr): $\tilde{\nu}$ = 3065–2765 (=C–H, C–H), 1625–1555 (C=C, C=N) cm^{-1}. HRMS (ESI-TOF): calcd. for C$_{13}$H$_{15}$N$_2$O [M + H]$^+$: 215.1179; found 215.1182. C$_{13}$H$_{14}$N$_2$O (214.3): calcd. C 72.87, H 6.59, N 13.07; found C 72.75, H 6.51, N 12.61.

4-Isopropyl-5-methoxy-6-methyl-2-phenylpyrimidine (7c): According to typical procedure (method B), enamide **5c** (100 mg, 0.383 mmol) and NH$_4$OAc (471 mg, 6.12 mmol) in MeOH (2.0 mL) provided the crude product. The residue was purified by chromatography on silica gel (hexane/ethyl acetate, 10:1) to afford 50 mg (54%) of **7c** as a colourless oil. ^{1}H NMR (CDCl$_3$, 400 MHz): δ = 1.32 (d, J = 6.8 Hz, 6 H, *i*Pr), 2.55 (s, 3 H, Me), 3.43 (hept, J = 6.8 Hz, 1 H, *i*Pr), 3.78 (s, 3 H, OMe), 7.39–7.47, 8.40–8.44 (2m, 3 H, 2 H, Ph) ppm. ^{13}C NMR (CDCl$_3$, 101 MHz): δ = 19.2 (q, Me), 21.6, 28.7 (q, d, *i*Pr), 61.3 (q, OMe), 128.0, 128.3, 129.7, 138.1 (3d, s, Ph), 148.7 (s, C-5), 159.0, 159.9, 167.4 (3s, C-2, C-4, C-6) ppm. IR (film): $\tilde{\nu}$ = 3095–3850 (=C–H, C–H), 1590–1550 (C=C, C=N) cm^{-1}. HRMS (ESI-TOF): calcd. for C$_{15}$H$_{19}$N$_2$O [M + H]$^+$: 243.1492; found 243.1506.

2,4-Dicyclopropyl-5-methoxy-6-methylpyrimidine (7d): According to typical procedure (method B), enamide **5d** (450 mg, 2.02 mmol) and NH$_4$OAc (1.25 mg, 16.2 mmol) in MeOH (8.0 mL) provided the crude product. The residue was purified by chromatography on silica gel (hexane/ethyl acetate, 10:1) to afford 232 mg (56%) of **7d** as a colourless oil. ^{1}H NMR (CDCl$_3$, 500 MHz): δ = 0.82–1.09 (m, 8 H, *c*Pr), 2.03 (m$_c$, 1 H, *c*Pr), 2.25 (m$_c$, 1 H, *c*Pr), 2.38 (s, 3 H, Me), 3.74 (s, 3 H, OMe) ppm. ^{13}C NMR (CDCl$_3$, 126 MHz): δ = 9.8, 10.1 (2t, *c*Pr), 10.3 (d, *c*Pr), 17.4 (d, *c*Pr), 18.4 (q, Me), 60.9 (q, OMe), 148.8 (s, C-5), 157.8, 163.2, 165.7 (3s, C-6, C-2, C-4) ppm. IR (film): $\tilde{\nu}$ = 3050–2830 (C–H), 1720–1560 (C=C, C=N) cm^{-1}. HRMS (ESI-TOF): calcd. for C$_{12}$H$_{17}$N$_2$O [M + H]$^+$: 205.1335; found 205.1351.

4-*tert*-Butyl-2-ethynyl-5-methoxy-6-methylpyrimidine (7e): According to typical procedure (method B), enamide **5e** (600 mg, 2.69 mmol) and NH$_4$OAc (1.66 g, 21.5 mmol) in MeOH (6.0 mL) provided the crude product. The residue was purified by chromatography on silica gel (hexane/ethyl acetate, 10:1) to afford 302 mg (55%) of **7e** as a colourless solid; m.p. 103 °C. ^{1}H NMR (CDCl$_3$, 500 MHz): δ = 1.37 (s, 9 H, *t*Bu), 2.48 (s, 3 H, Me), 2.98 (s, 1 H, ≡C-H), 3.78 (s, 3 H, OMe) ppm. ^{13}C NMR (CDCl$_3$, 126 MHz): δ = 9.7 (q, Me), 29.0, 37.9 (q, s, *t*Bu), 61.1 (q, OMe), 73.6, 82.3 (s, d, C≡C), 144.9 (s, C-2), 152.0 (s, C-5), 160.7 (s, C-6), 169.0 (s, C-4) ppm. IR (KBr): $\tilde{\nu}$ = 3190 (≡C–H), 3020–2860 (C–H), 2110 (C≡C), 1545–1525 (C=C, C=N) cm^{-1}. C$_{12}$H$_{16}$N$_2$O (204.3): calcd. C 70.56, H 7.90, N 13.71; found C 70.38, H 7.96, N 13.63.

5-Methoxy-4-methyl-6-phenyl-2-(pyridin-2-yl)pyrimidine (7 g): According to typical procedure (method B), enamide **5g** (175 mg, 0.591 mmol) and NH$_4$OAc (729 mg, 9.46 mmol) in MeOH (3.0 mL) provided the crude product. The residue was purified by chromatography on silica gel (hexane/ethyl acetate, 2:1) to afford 62 mg (38%) of **7g** as a colourless solid; m.p. 101 °C. ^{1}H NMR (CDCl$_3$, 500 MHz): δ = 2.69 (s, 3 H, Me), 3.55 (s, 3 H, OMe), 7.31 (ddt, J = 7.4, 4.9, 0.5 Hz, 1 H, 5′-H), 7.43–7.49, 8.14–8.16 (2m, 3 H, 2 H, Ph), 7.79 (tdd, J = 7.4, 1.8, 0.5 Hz, 1 H, 4′-H), 8.52 (dt, J = 7.4, 1.8 Hz, 1 H, 3′-H), 8.80 (dt, J = 4.9, 0.5 Hz, 1 H, 6′-H) ppm. ^{13}C NMR (CDCl$_3$, 101 MHz): δ = 19.4 (q, Me), 60.2 (q, OMe), 123.5 (d, C-5′), 124.1 (d, C-3′), 128.4, 129.1, 130.0, 135.6 (3d, s, Ph), 136.6 (d, C-4′), 149.9 (d, C-6′), 150.3 (s, C-5), 154.9 (s, C-2′), 156.4, 158.0, 163.1 (3s, C-2, C-4, C-6) ppm. IR (KBr): $\tilde{\nu}$ = 3090–3005 (=C–H), 2945–2850 (C–H), 1595–1545 (C=C, C=N) cm^{-1}. C$_{17}$H$_{15}$N$_3$O (277.3): calcd. C 73.63, H 5.45, N 15.15; found C 73.30, H 5.56, N 14.94.

5-(Benzyloxy)-4-methyl-2,6-diphenylpyrimidine (7h): According to typical procedure (method A), enamide **5h** (210 mg, 0.565 mmol) and NH$_4$HCO$_3$ (536 mg, 6.78 mmol) in MeOH (6.0 mL) provided the crude product. The residue was purified by chromatography on silica gel (hexane/ethyl acetate, 10:1) to afford 149 mg (75%) of **7h** as a colourless oil. ^{1}H NMR (CDCl$_3$, 500 MHz): δ = 2.58 (s, 3 H, Me), 4.62 (s, 2 H, CH$_2$Ph), 7.23–7.55, 8.19–8.22, 8.49–8.52 (3m, 11 H, 2 H, 2 H, Ph) ppm. ^{13}C NMR (CDCl$_3$, 126 MHz): δ = 19.6 (q, Me), 75.0 (t, CH$_2$Ph), 128.11, 128.13, 128.39, 128.44, 128.5, 129.3, 130.0, 136.1, 137.7 (6d, 3s, Ph)*, 147.9 (s, C-5), 156.8, 159.1, 162.6 (3s, C-2, C-4, C-6) ppm; * overlap of Ph signals. IR (film): $\tilde{\nu}$ = 3090–3030 (=C–H), 2955–2845 (C–H), 1720–1550 (C=C, C=N) cm^{-1}. HRMS (ESI-TOF): calcd. for C$_{24}$H$_{21}$N$_2$O [M + H]$^+$: 353.1648; found 353.1665.

5-(Benzyloxy)-4-methyl-2,6-bis(thiophen-2-yl)pyrimidine (7i): According to typical procedure (method B), enamide **5i** (100 mg, 0.261 mmol) and NH$_4$OAc (322 mg, 4.18 mmol) in MeOH (2.0 mL) provided the crude product. The residue was purified by chromatography on silica gel (hexane/ethyl acetate, 10:1) to afford 65 mg (68%) of **7i** as a colourless oil. ^{1}H NMR (CDCl$_3$, 500 MHz): δ = 2.53 (s, 3 H, Me), 4.90 (s, 2 H, CH$_2$Ph), 7.13, 7.15 (2dd, J = 5.0, 3.7 Hz, 1 H each, 4′-H, 4′′-H), 7.37–7.48 (m, 5 H, Ph), 7.44, 7.54 (2dd, J = 5.0, 1.0 Hz, 1 H each, 3′-H, 3′′-H), 7.98, 8.15 (2dd, J = 3.7, 1.0 Hz, 1 H each, 5′-H, 5′′-H) ppm. ^{13}C NMR (CDCl$_3$, 101 MHz): δ = 19.4 (q, Me), 76.7 (t, CH$_2$Ph), 128.1, 128.2, 128.4, 128.5, 128.7, 129.2, 130.5, 130.7, 136.1 (9d, s, C-3′, C-4′, C-5′, C-3′′, C-4′′, C-5′′, Ph)*, 139.1, 143.2, (2s, C-2′, C-2′′), 144.9 (s, C-5), 151.2 (s, C-6), 156.1, 162.6 (2s, C-2, C-4) ppm; * overlap of Ph signals. IR (film): $\tilde{\nu}$ = 3090–3030 (=C–H), 3000–2865 (C–H), 1710–1610 (C=C, C=N) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{20}H_{17}N_2OS_2$ [M + H]$^+$: 365.0777; found 365.0796.

4-*tert*-Butyl-6-methyl-2-(trifluoromethyl)-5-[2-(trimethylsilyl)ethoxy]pyrimidine (7j): According to typical procedure (method A), enamide **5j** (156 mg, 0.441 mmol) and NH_4HCO_3 (558 mg, 7.06 mmol) in MeOH (4.0 mL) provided the crude product. The residue was purified by chromatography on silica gel (hexane/ethyl acetate, 20:1) to afford 97 mg (66%) of **7j** as a colourless oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.06 (s, 9 H, $SiMe_3$), 1.25 (m$_c$, 2 H, CH_2Si), 1.40 (s, 9 H, *t*Bu), 2.54 (s, 3 H, Me), 3.92 (m$_c$, 2 H, OCH_2) ppm. ^{13}C NMR ($CDCl_3$, 101 MHz): δ = –1.5 (q, $SiMe_3$), 18.6 (t, CH_2Si), 20.0 (q, Me), 29.0, 38.3 (q, s, *t*Bu), 71.8 (t, OCH_2), 119.8 (q, $^1J_{CF}$ = 276 Hz, CF_3), 152.4 (s, C-5), 149.2 (q, $^2J_{CF}$ = 36.1 Hz, C-2), 161.9, 169.7 (2s, C-4, C-6) ppm. ^{19}F NMR ($CDCl_3$, 470 MHz): δ = –69.4 (s, CF_3) ppm. IR (film): $\tilde{\nu}$ = 2960–2870 (C–H), 1740–1570 (C=C, C=N) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{15}H_{26}F_3N_2OSi$ [M + H]$^+$: 335.1761; found 335.1772.

4-Methyl-2-phenyl-6-(thiophen-2-yl)-5-[2-(trimethylsilyl)ethoxy]pyrimidine (7l): According to typical procedure (method A), enamide **5l** (200 mg, 0.511 mmol) and NH_4HCO_3 (333 mg, 4.22 mmol) in MeOH (4.0 mL) provided the crude product. The residue was purified by chromatography on silica gel (hexane/ethyl acetate, 8:1) to afford 141 mg (75%) of **7l** as a colourless oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.06 (s, 9 H, $SiMe_3$), 1.31 (m$_c$, 2 H, CH_2Si), 2.62 (s, 3 H, Me), 3.99 (m$_c$, 2 H, OCH_2), 7.20 (dd, *J* = 5.1, 3.7 Hz, 1 H, 4′-H), 7.55 (dd, *J* = 5.1, 1.1 Hz, 1 H, 5′-H), 8.23 (dd, *J* = 3.7, 1.1 Hz, 1 H, 3′-H), 7.43–7.52, 8.48–8.51 (2m, 3 H, 2 H, Ph) ppm. ^{13}C NMR ($CDCl_3$, 101 MHz): δ = –1.5 (q, $SiMe_3$), 19.2 (t, CH_2Si), 19.6 (q, Me), 70.9 (t, OCH_2), 127.97, 128.0, 128.4, 129.9, 130.08, 130.12, 137.5 (6d, s, Ph, C-3′, C-4′, C-5′), 139.7 (s, C-2′), 145.5 (s, C-5), 151.1 (s, C-6), 158.6 (s, C-2), 162.2 (s, C-4) ppm. IR (film): $\tilde{\nu}$ = 3090–3030 (=C–H), 2955–2895 (C–H), 1590–1545 (C=C, C=N) cm^{-1}. $C_{20}H_{24}N_2OSSi$ (368.6): calcd. C 65.17, H 6.56, N 7.60; found C 64.95, H 6.84, N 7.42.

4-Benzyl-6-*tert*-butyl-5-methoxy-2-(trifluoromethyl)pyrimidine (14): According to typical procedure (method B), enamide **13** (442 mg, 1.29 mmol) and NH_4OAc (794 mg, 10.3 mmol) in MeOH (6.0 mL) provided the crude product. The residue was purified by chromatography on silica gel (hexane/ethyl acetate, 10:1) to afford 128 mg (31%) of **14** as a colourless oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.41 (s, 9 H, *t*Bu), 3.78 (s, 3 H, OMe), 4.22 (s, 2 H, CH_2Ph), 7.20–7.33 (m, 5 H, Ph) ppm. ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 29.0, 38.5 (q, s, *t*Bu), 38.3 (t, CH_2Ph), 62.7 (q, OMe), 119.8 (q, $^1J_{CF}$ = 276 Hz, CF_3), 126.8, 128.6, 129.8, 137.1 (3d, s, Ph), 149.7 (q, $^2J_{CF}$ = 36.2 Hz, C-2), 153.3, (s, C-4), 163.2 (s, C-5), 170.8 (s, C-6) ppm. ^{19}F NMR ($CDCl_3$, 470 MHz): δ = –69.4 (s, CF_3) ppm. IR (film): $\tilde{\nu}$ = 3110–2870 (=C–H, C–H), 1605–1560 (C=C, C=N) cm^{-1}. $C_{17}H_{19}F_3N_2O$ (324.3): calcd. C 62.95, H 5.90, N 8.64; found C 63.32, H 5.99, N 8.48.

4-Methyl-2,6-diphenylpyrimidin-5-ol (15): A mixture of pyrimidine **7h** (212 mg, 0.602 mmol) and palladium (61 mg, 10% on charcoal) in MeOH (2.0 mL) was stirred for one day under an atmosphere of hydrogen. Filtration of the reaction mixture through celite with MeOH afforded 145 mg (92%) of **15** as a colourless solid; m.p. 142–144 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.60 (s, 3 H, Me), 5.44 (br. s, 1 H, OH), 7.38–7.56, 7.84–7.87, 8.38–8.41 (3m, 6 H, 2 H, 2 H, Ph) ppm. ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 19.1 (q, Me), 127.7, 128.4, 128.6, 129.3, 129.5, 129.9, 135.0, 137.8 (6d, 2s, Ph), 144.4 (s, C-5), 150.1, 155.5, 156.8 (3s, C-2, C-4, C-6) ppm. IR (KBr): $\tilde{\nu}$ = 3170 (O–H), 3090–3030 (=C–H), 2965–2900 (C–H), 1605–1550 (C=C, C=N) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{17}H_{15}N_2O$ [M + H]$^+$: 263.1179; found 263.1184.

4-Methyl-2,6-diphenylpyrimidin-5-yl Nonaflate (16): Pyrimidine **15** was dissolved in THF (5.0 mL) and NaH (87 mg, 2.17 mmol) was added. After 5 min NfF (0.39 mL, 2.36 mmol) was added and the reaction mixture was stirred overnight at room temperature. After slow addition of water and ethyl acetate (5 mL) the layers were separated and the aqueous layer was extracted with EtOAc (2 × 8 mL). The combined organic layers were dried with Na_2SO_4, filtered and concentrated. Column chromatography (silica gel, hexane/ethyl acetate = 40:1) provided 260 mg (66%) of **16** as a colourless oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.77 (s, 3 H, Me), 7.49–7.56, 7.89–7.91, 8.52–8.55 (3m, 10 H, Ph) ppm. ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 20.5 (q, Me), 128.56, 128.58, 128.7, 129.5, 130.8, 129.9, 134.3, 136.3 (6d, 2s, Ph), 140.7 (s, C-5), 159.0, 162.0, 162.3 (3s, C-2, C-4, C-6) ppm. ^{19}F NMR ($CDCl_3$, 470 MHz): δ = –80.6, –109.8, –120.6, –125.8 (4 m$_c$, ONf) ppm. IR (film): $\tilde{\nu}$ = 3095–2855 (=C–H, C–H), 1605–1560 (C=C, C=N) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{21}H_{14}F_9N_2O_3S$ [M + H]$^+$: 545.0576; found 545.0607. $C_{21}H_{13}F_9N_2O_3S$ (544.4): calcd. C 46.33, H 2.41, N 5.15; found C 46.93, H 2.18, N 5.06.

Synthesis of 4-Methyl-2,6-diphenylpyrimidin-5-yl Nonaflate (16) Starting from 7k: Pyrimidine **7k** (285 mg, 0.786 mmol) was dissolved in a 1:2 mixture of TFA and CH_2Cl_2 (3.0 mL) and stirred for 30 min at room temperature. After addition of water and CH_2Cl_2 (5 mL) the layers were separated and the aqueous layer was extracted twice with CH_2Cl_2 (8 mL). The combined organic layers were dried with Na_2SO_4, filtered and concentrated. The crude product was dissolved in THF (5.0 mL) and NaH (94 mg, 2.36 mmol) was added. After 5 min NfF (0.42 mL, 2.36 mmol) was added and the reaction mixture was stirred overnight at room temperature. After slow addition of water and ethyl acetate (5 mL) the layers were separated and the aqueous layer was extracted with ethyl acetate (2 × 8 mL). The combined organic layers were dried with Na_2SO_4, filtered and concentrated. Column chromatography (silica gel, hexane/ethyl acetate = 40:1) provided 257 mg (60%) of **16**.

Synthesis of 4-Isopropyl-6-methyl-2-phenylpyrimidin-5-yl Nonaflate (17) Starting from 7c: Pyrimidine **7c** (200 mg, 0.825 mmol) and trimethylsilyl iodide (2.4 mL, 2.40 mmol, 1 M in CH_2Cl_2) were placed in an ACE-sealed tube. The mixture was dissolved in 1,2-dichloroethane (4.0 mL) and stirred for 1 d at 80 °C. The mixture was allowed to cool to room temperature, diluted with satd. aq. $Na_2S_2O_3$ solution (8 mL) and extracted with CH_2Cl_2 (3 × 8 mL). The combined organic layers were dried with Na_2SO_4, filtered and concentrated. The crude product was dissolved in THF (10 mL) and NaH (99 mg, 2.48 mmol) was added. After 5 min NfF (0.45 mL, 2.48 mmol) was added and the reaction mixture was stirred overnight at room temperature. After slow addition of water and ethyl acetate (10 mL) the layers were separated and the aqueous layer was extracted twice with ethyl acetate (10 mL). The combined organic phases were dried with Na_2SO_4 and concentrated to dryness. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 10:1) to give 249 mg (59%) of **17** as a colourless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.35 (d, *J* = 6.7 Hz, 6 H, *i*Pr), 2.65 (s, 3 H, Me), 3.44 (hept, *J* = 6.7 Hz, 1 H, *i*Pr), 7.47–7.49, 8.46–8.48 (2m, 3 H, 2 H, Ph) ppm. ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 20.4, 21.3 (q, d, *i*Pr), 29.6 (q, Me), 128.5, 128.6, 131.0, 136.6 (3d, s, Ph), 139.7 (s, C-5), 160.6, 162.4, 168.1 (3s, C-2, C-4, C-6) ppm. ^{19}F NMR ($CDCl_3$, 470 MHz): δ = –80.4, –108.9, –120.4, –125.6 (4 m$_c$, ONf) ppm. IR (film): $\tilde{\nu}$ = 3005–2880 (C–H), 1610–1580 (C=C, C=N) cm^{-1}. $C_{18}H_{15}F_9N_2O_3S$ (510.4): calcd. C 42.36, H 2.96, N 5.49; found C 42.84, H 3.12, N 5.53.

Suzuki Coupling of Pyrimidinyl Nonaflate 16 to (*E*)-4-Methyl-2,6-diphenyl-5-styrylpyrimidine (18): A mixture of pyrimidinyl nonaflate **16** (190 mg, 0.349 mmol), $Pd(OAc)_2$ (3.8 mg, 0.017 mmol), PPh_3 (18 mg, 0.070 mmol), K_2CO_3 (96 mg, 0.689 mmol), *trans*-2-styrylboronic acid (67 mg, 0.454 mmol) in DMF (1.5 mL) was heated to 70 °C for 2 h under an argon atmosphere. The mixture was allowed to cool to room temperature, diluted with brine (5 mL) and extracted with Et_2O (3 × 5 mL). The combined organic phases were dried with Na_2SO_4 and concentrated to dryness. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 20:1) to give 57 mg (47%) of **18** as a colourless solid; m.p. 91–93 °C. ^1H NMR ($CDCl_3$, 500 MHz): δ = 2.79 (s, 3 H, Me), 6.68 (d, *J* = 16.7 Hz, 1 H, C=CH), 7.03 (d, *J* = 16.7 Hz, 1 H, C=CH), 7.27–7.51, 7.78–7.80, 8.53–8.56 (3m, 11 H, 2 H, 2 H, Ph) ppm. ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 24.3 (q, Me), 123.6 (d, C=CH), 126.0 (s, C-5), 126.4, 128.1, 128.16, 128.2, 128.4, 128.8, 129.2, 130.0, 130.4, 136.9, 137.8, 138.9 (9d, 3s, Ph), 135.8 (d, C=CH), 161.5, 163.9, 165.5 (3s, C-2, C-4, C-6) ppm. IR (KBr): $\tilde{\nu}$ = 3100–3025 (=C–H), 2995–2845 (C–H), 1695–1580 (C=C, C=N) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{25}H_{21}N_2$ $[M + H]^+$: 349.1699; found 349.1720.

Sonogashira Coupling of Pyrimidinyl Nonaflate 16 to 4-Methyl-2,6-diphenyl-5-(phenylethynyl)pyrimidine (19): A mixture of pyrimidinyl nonaflate **16** (114 mg, 0.209 mmol), $Pd(OAc)_2$ (2.3 mg, 0.010 mmol), PPh_3 (11 mg, 0.041 mmol), CuI (1.9 mg, 0.011 mmol), phenylacetylene (26 mg, 0.251 mmol) in DMF (1.0 mL) and diisopropylamine (0.5 mL) was heated to 70 °C for 3 h under an argon atmosphere. The mixture was allowed to cool to room temperature, diluted with brine (5 mL) and extracted with Et_2O (3 × 5 mL). The combined organic phases were dried with Na_2SO_4 and concentrated to dryness. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 40:1) to give 53 mg (73%) of **19** as a colourless solid; m.p. 109–110 °C. ^1H NMR ($CDCl_3$, 500 MHz): δ = 2.88 (s, 3 H, Me), 7.34–7.38, 7.43–7.56, 8.25–8.28, 8.57–8.59 (4m, 3 H, 8 H, 2 H, 2 H, Ph) ppm. ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 24.2 (q, Me), 85.2, 100.8 (2s, C≡C), 112.8 (s, C-5), 122.9, 128.0, 128.48, 128.49, 128.51, 128.8, 129.6, 130.1, 130.7, 131.2, 137.5, 137.9 (s, 9d, 2s, Ph), 161.2, 165.1, 170.1 (3s, C-2, C-4, C-6) ppm. IR (KBr): $\tilde{\nu}$ = 3060–3030 (=C–H), 2955–2845 (C–H), 2205 (C≡C), 1600–1565 (C=C, C=N) cm^{-1}. $C_{25}H_{18}N_2$ (346.4): calcd. C 86.68, H 5.24, N 8.09; found C 86.44, H 5.15, N 8.00.

7-*tert*-Butyl-2-(4-*tert*-butyl-5-methoxy-6-methylpyrimidin-2-yl)-5-(trifluoromethyl)furo[2,3-*c*]pyridine (21): A mixture of pyridine-4-yl nonaflate **20** (403 mg, 0.653 mmol), $Pd(OAc)_2$ (7.3 mg, 0.033 mmol), PPh_3 (34 mg, 0.131 mmol), CuI (6.2 mg, 0.033 mmol), pyrimidine **7e** (267 mg, 1.31 mmol) in DMF (2.7 mL) and diisopropylamine (1.3 mL) was heated to 70 °C for 3 h under an argon atmosphere. The mixture was allowed to cool to room temperature, diluted with brine (10 mL) and extracted with Et_2O (3 × 10 mL). The combined organic phases were dried with Na_2SO_4 and concentrated to dryness. The crude product was dissolved in a 1:2 mixture of TFA and CH_2Cl_2 (4 mL). After stirring for 2 h at room temperature the reaction mixture was quenched with H_2O (10 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phases were dried with Na_2SO_4 and concentrated to dryness. The resulting crude product was dissolved in DMF (2.7 mL) and K_2CO_3 (271 mg, 1.96 mmol) was added. After heating for 3 h at 80 °C, the mixture was quenched at room temperature with H_2O (10 mL) and extracted with Et_2O (3 × 10 mL). The combined organic phases were dried with Na_2SO_4 and concentrated to dryness. Column chromatography on silica gel (hexane/ethyl acetate = 10:1) afforded 195 mg (71%) of **21** as a colourless solid; m.p. 92–94 °C. ^1H NMR ($CDCl_3$, 500 MHz): δ = 1.47, 1.62 (2s, 9 H each, *t*Bu), 2.60 (s, 3 H, Me), 3.84 (s, 3 H, OMe), 7.54 (s, 1 H, 3-H), 7.82 (s, 1 H, 4-H) ppm. ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 20.0 (q, Me), 28.8, 29.0, 37.7, 38.2 (2q, 2s, *t*Bu), 61.1 (q, OMe), 106.4 (d, C-3), 112.3 (dq, $^3J_{CF}$ = 3.0 Hz, C-4), 122.3 (q, $^1J_{CF}$ = 273 Hz, CF_3), 135.5 (s, C-2), 140.0 (q, $^2J_{CF}$ = 34.0 Hz, C-5), 150.3 (s, C-2′), 151.0 (q, $^4J_{CF}$ = 1.0 Hz, C-3a), 151.8 (s, C-5′), 154.6, 157.0 (2s, C-7, C-7a), 161.1 (s, C-6′), 168.7 (s, C-4′) ppm. ^{19}F NMR ($CDCl_3$, 470 MHz): δ = –67.1 (s, CF_3) ppm. IR (KBr): $\tilde{\nu}$ = 2965–2870 (=C–H, C–H), 1605–1540 (C=C) cm^{-1}. $C_{22}H_{26}F_3N_3O_2$ (421.5): calcd. C 62.70, H 6.22, N 9.97; found C 62.69, H 6.19, N 9.90.

Oxidation of 7a to 5-Methoxy-2,6-diphenylpyrimidine-4-carbaldehyde (22): Pyrimidine **7a** (800 mg, 2.90 mmol) and SeO_2 (995 mg, 8.97 mmol) were placed in an ACE-sealed tube. The mixture was dissolved in 1,4-dioxane (22 mL) and stirred for 2 d at 80 °C. The mixture was allowed to cool to room temperature, diluted with satd. aq. $NaHCO_3$ solution (20 mL) and extracted with ethyl acetate (3 × 20 mL). The combined organic phases were dried with Na_2SO_4 and concentrated to dryness. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 6:1) to give 760 mg (90%) of **22** as a colourless solid; m.p. 98 °C. ^1H NMR ($CDCl_3$, 500 MHz): δ = 3.76 (s, 3 H, OMe), 7.48–7.56, 8.22–8.24, 8.54–8.56 (3m, 6 H, 2 H, 2 H, Ph), 10.32 (s, 1 H, CHO) ppm. ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 62.6 (q, OMe), 128.2, 128.6, 129.5, 130.7, 130.8, 134.9, 136.5 (5d, 2s, Ph)*, 150.4, 150.7 (2s, C-5, C-4), 159.7, 161.3 (2s, C-2, C-6), 191.5 (d, CHO) ppm; * overlap of Ph signals. IR (KBr): $\tilde{\nu}$ = 3110–3005 (=C–H), 2955–2830 (C–H), 1710–1580 (C=O, C=C, C=N) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{18}H_{15}N_2O_2$ $[M + H]^+$: 291.1128; found 291.1130.

5-Methoxy-2,6-diphenylpyrimidine-4-carbaldehyde Oxime (23): Aldehyde **22** (160 mg, 0.551 mmol) and $NH_2OH·HCl$ (115 mg, 1.65 mmol) were dissolved in MeOH (3.0 mL). The mixture was stirred for 1 d at room temperature, then diluted with H_2O (5 mL) and extracted with CH_2Cl_2 (3 × 5 mL). The combined organic phases were dried with Na_2SO_4 and concentrated to dryness. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 4:1) to give 117 mg (70%) of **23** as a colourless solid; m.p. 187 °C. ^1H NMR ($CDCl_3$, 500 MHz): δ = 3.64 (s, 3 H, OMe), 7.46–7.56, 8.22–8.25, 8.52–8.55 (3m, 6 H, 2 H, 2 H, Ph), 8.62 (s, 1 H, CHN), 10.50 (br. s, 1 H, OH) ppm. ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 61.7 (q, OMe), 128.3, 128.5, 128.6, 129.3, 130.4, 130.5, 135.5, 137.1 (6d, 2s, Ph), 144.8 (d, CHN), 149.1, 152.1 (2s, C-5, C-4), 159.2, 159.8 (2s, C-2, C-6) ppm. IR (KBr): $\tilde{\nu}$ = 3375 (O–H), 3080–2850 (=C–H, C–H), 1600–1545 (C=C, C=N) cm^{-1}. $C_{18}H_{15}N_3O_2$ (305.3): calcd. C 70.81, H 4.95, N 13.76; found C 70.60, H 4.99, N 13.74.

Oxidation of 22 to 5-Methoxy-2,6-diphenylpyrimidine-4-carboxylic Acid (24): $NaClO_2$ (75 mg, 0.828 mmol) was dissolved in a satd. aq. NaH_2PO_4 solution (2.0 mL) and stirred for 5 min at room temperature. The solution was added to a mixture of aldehyde **22** (185 mg, 0.637 mmol) in *t*BuOH (2.0 mL) and stirred for 1 d at room temperature. The mixture was diluted with HCl (4 mL, 1 M) and extracted with ethyl acetate (3 × 5 mL). The combined organic phases were dried with Na_2SO_4 and concentrated to dryness. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 2:1) to give 128 mg (66%) of **24** as a colourless solid; m.p. 111 °C. ^1H NMR ($CDCl_3$, 500 MHz): δ = 3.82 (s, 3 H, OMe), 7.49–7.58, 8.23–8.26, 8.41–8.46 (3m, 6 H, 2 H, 2 H, Ph) ppm; the CO_2H signal could not be detected. ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 62.5 (q, OMe), 128.1, 128.6, 128.8, 129.7, 131.15, 131.23, 134.6, 135.5 (6d, 2s, Ph), 145.3, 151.1 (2s, C-5, C-4), 158.0, 163.2 (2s, C-2, C-6), 161.7 (s, CO_2H) ppm. IR (KBr): $\tilde{\nu}$ = 3515–

3110 (O–H), 3065–2825 (=C–H, C–H), 1765–1555 (C=O, C=C, C=N) cm^{-1}. $C_{18}H_{14}N_2O_3$ (306.3): calcd. C 70.58, H 4.61, N 9.15; found C 70.20, H 4.76, N 9.18.

4-(2,2-Dibromovinyl)-5-methoxy-2,6-diphenylpyrimidine (25): Aldehyde **22** (151 mg, 0.520 mmol) was dissolved in CH_2Cl_2 (10 mL) and added at 0 °C to a mixture of PPh_3 (542 mg, 2.02 mmol) and CBr_4 (345 mg, 1.04 mmol). After 5 min at this temperature the mixture was warmed up to room temperature and stirred for 2 h. After filtration with pentane the filtrate was concentrated to dryness. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 10:1) to give 201 mg (87%) of **25** as a colourless oil. ^1H NMR ($CDCl_3$, 500 MHz): δ = 3.60 (s, 3 H, OMe), 7.45–7.56, 8.19–8.21, 8.56–8.58 (3m, 6 H, 2 H, 2 H, Ph), 7.91 (s, 1 H, CH=C) ppm. ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 61.5 (q, OMe), 98.3 (s, CH=C), 128.3, 128.4, 128.5, 129.1, 130.30, 130.31, 135.7, 137.4 (6d, 2s, Ph), 129.4 (d, CH=C), 148.2 (s, C-5), 154.9, 158.0, 158.9 (3s, C-2, C-4, C-6) ppm. IR (film): $\tilde{\nu}$ = 3085–3000 (=C–H), 2955–2845 (C–H), 1600–1565 (C=C, C=N) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{19}H_{15}Br_2N_2O$ $[M + H]^+$: 444.9546; found 444.9559. $C_{19}H_{14}Br_2N_2O$ (446.1): calcd. C 51.15, H 3.16, N 6.28; found C 51.49, H 3.58, N 5.95.

4-Ethynyl-5-methoxy-2,6-diphenylpyrimidine (26): The dibromoolefin **25** (338 mg, 0.758 mmol) was dissolved in THF (4.6 mL) and cooled to –78 °C. *n*-Butyllithium (0.64 mL, 1.59 mmol, 2.5 M in hexanes) was slowly added to this solution and stirred for 1 h. The reaction mixture was warmed up to room temperature and stirred for 1 h, then diluted with H_2O (10 mL) and extracted with ethyl acetate (3 × 10 mL). The combined organic phases were dried with Na_2SO_4 and concentrated to dryness. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 20:1) to give 41 mg (19%) of **26** as a colourless oil. ^1H NMR ($CDCl_3$, 400 MHz): δ = 3.59 (s, 1 H, C≡CH), 3.83 (s, 3 H, OMe), 7.44–7.53, 8.21–8.23, 8.47–8.50 (3m, 6 H, 2 H, 2 H, Ph) ppm. ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 61.4 (q, OMe), 78.9, 84.6 (s, d, C≡CH), 128.3, 128.46, 128.53, 129.4, 130.4, 130.5, 135.2, 136.9 (6d, 2s, Ph), 144.6 (s, C-5), 152.3 (s, C-4), 158.0, 159.6 (2s, C-2, C-6) ppm. IR (film): $\tilde{\nu}$ = 3280 (≡C–H), 3095–3000 (=C–H), 2960–2850 (C–H), 2115 (C≡C), 1600–1525 (C=C, C=N) cm^{-1}. MS (EI): *m/z* (%) = 286 (100) $[M]^+$, 77 (21) $[C_6H_5]^+$. HRMS (EI): calcd. for $C_{19}H_{14}N_2O$: 286.1090; found 286.1106.

Supporting Information (see also the footnote on the first page of this article): Copies of all NMR spectra of compounds described here.

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[1] For reviews dealing with the chemistry of alkoxyallenes, see: a) R. Zimmer, *Synthesis* **1993**, 165–178; b) R. Zimmer, F. A. Khan, *J. Prakt. Chem.* **1996**, *338*, 92–94; c) H.-U. Reissig, W. Schade, M. G. Okala Amombo, R. Pulz, A. Hausherr, *Pure Appl. Chem.* **2002**, *74*, 175–180; d) R. Zimmer, H.-U. Reissig, *Donor-Substituted Allenes*, in: *Modern Allene Chemistry* (Eds.: N. Krause, A. S. K. Hashmi), Wiley-VCH, Weinheim, **2004**, p. 425–492; e) H.-U. Reissig, R. Zimmer, *Science of Synthesis*, vol. 44 (Ed.: N. Krause), Thieme, Stuttgart, **2007**, p. 301–352; f) M. Brasholz, H.-U. Reissig, R. Zimmer, *Acc. Chem. Res.* **2009**, *42*, 45–56; g) F. Pfrengle, H.-U. Reissig, *Chem. Soc. Rev.* **2010**, *39*, 549–557; h) T. Lechel, H.-U. Reissig, *Pure Appl. Chem.* **2010**, in press. For most recent applications of alkoxyallenes as building blocks from our group, see: i) M. Brasholz, H.-U. Reissig, *Eur. J. Org. Chem.* **2009**, 3595–3604; j) F. Pfrengle, D. Lentz, H.-U. Reissig, *Angew. Chem.* **2009**, *121*, 3211–3215; *Angew. Chem. Int. Ed.* **2009**, *48*, 3165–3169; k) B. Bressel, H.-U. Reissig, *Org. Lett.* **2009**, *11*, 527–530; l) F. Pfrengle, A. Al-Harrasi, I. Brüdgam, H.-U. Reissig, *Eur. J. Org. Chem.* **2009**, 282–291; m) V. Prisyazhnyuk, M. Jachan, I. Brüdgam, R. Zimmer, H.-U. Reissig, *Collect. Czech. Chem. Commun.* **2009**, *74*, 1069–1080; n) V. Dekaris, H.-U. Reissig, *Synlett* **2010**, 42–46; o) V. Dekaris, B. Bressel, H.-U. Reissig, *Synlett* **2010**, 47–50; p) A. Al-Harrasi, S. Fischer, R. Zimmer, H.-U. Reissig, *Synthesis* **2010**, 304–314.

[2] a) O. Flögel, J. Dash, I. Brüdgam, H. Hartl, H.-U. Reissig, *Chem. Eur. J.* **2004**, *10*, 4283–4290; b) O. Flögel, H.-U. Reissig, German Patent Nr. 103 36 497.8. A1 (March 03, 2005); c) J. Dash, T. Lechel, H.-U. Reissig, *Org. Lett.* **2007**, *9*, 5541–5544; d) T. Lechel, J. Dash, H.-U. Reissig, *Eur. J. Org. Chem.* **2008**, 3647–3655; e) C. Eidamshaus, H.-U. Reissig, *Adv. Synth. Catal.* **2009**, *351*, 1162–1166; f) T. Lechel, J. Dash, P. Hommes, D. Lentz, H.-U. Reissig, *J. Org. Chem.* **2010**, *75*, 726–732.

[3] For recent applications of β-alkoxy β-keto enamides in the synthesis of highly functionalized oxazoles or pyridines, see: a) T. Lechel, H.-U. Reissig, *Chem. Eur. J.* **2009**, *15*, 5432–5435; b) T. Lechel, J. Dash, C. Eidamshaus, I. Brüdgam, H.-U. Reissig, *Org. Biomol. Chem.* **2010**, in press.

[4] For a preliminary publication, see: T. Lechel, S. Möhl, H.-U. Reissig, *Synlett* **2009**, 1059–1062.

[5] a) D. J. Brown, in: *Comprehensive Heterocyclic Chemistry*, vol. 3 (Eds.: A. R. Katritzky, C. W. Rees), Pergamon-Press, Oxford, **1984**, chapter 2.13; b) T. Eicher, S. Hauptmann, *Chemie der Heterocyclen*; Thieme, Stuttgart, **1994**, p. 398; c) T. L. Gilchrist, *Heterocyclenchemie* (Ed.: H. Neunhoeffer), Wiley-VCH, Weinheim, **1995**, p. 270; d) M. G. Hoffmann, A. Nowak, M. Müller, in: *Houben-Weyl*, *Methoden der organischen Chemie*, vol. E9b, part 1 (Ed.: E. Schaumann), Thieme, Stuttgart, **1996**, p. 1–373; e) S. von Angerer, *Science of Synthesis*, vol. 16 (Ed.: Y. Yamamoto), Thieme, Stuttgart, **2004**, p. 379–572; f) M. Radi, S. Schenone, M. Botta, *Org. Biomol. Chem.* **2009**, *7*, 2841–2847; and references cited therein. Selected recent publications dealing with new methods: g) A. S. Karpov, T. J. J. Müller, *Synthesis* **2003**, 2815–2826; h) D. Bevk, U. Grošelj, A. Meden, J. Svete, B. Stanovnik, *Helv. Chim. Acta* **2007**, *90*, 1737–1743; i) R. Sagar, M.-J. Kim, S. B. Park, *Tetrahedron Lett.* **2008**, *49*, 5080–5083; j) M. Blangetti, A. Deagostino, C. Prandi, C. Zavattaro, P. Venturello, *Chem. Commun.* **2008**, 1689–1691; k) F. Xie, H. Zhao, L. Zhao, L. Lou, L. Hu, *Bioorg. Med. Chem. Lett.* **2009**, *19*, 275–278; l) T. Sasada, F. Kobayashi, N. Sakai, T. Konakahara, *Org. Lett.* **2009**, *11*, 2161–2164; m) C. Shishoo, S. Ananthan, V. Bhadti, G. Ullas, M. Chhabria, J. Bariwal, L. V. G. Nargund, K. Jain, *Heterocycles* **2009**, *78*, 1627–1665; n) E. Merkul, T. Oeser, T. J. J. Müller, *Chem. Eur. J.* **2009**, *15*, 5006–5011.

[6] Recent syntheses of pyrimidine derivatives starting from enamides: a) M. G. Barthakur, M. Borthakur, P. Devi, C. J. Saikia, A. Saikia, U. Bora, A. Chetia, R. C. Boruah, *Synlett* **2007**, 223–226; b) M. D. Hill, M. Movassaghi, *Chem. Eur. J.* **2008**, *14*, 6836–6844; c) O. K. Ahmad, M. D. Hill, M. Movassaghi, *J. Org. Chem.* **2009**, *74*, 8460–8463.

[7] S. Ferrini, F. Ponticelli, M. Taddei, *Org. Lett.* **2007**, *9*, 69–72.

[8] Selected reviews on palladium-catalyzed cross-coupling reactions: a) K. Sonogashira, in: *Handbook of Organopalladium Chemistry for Organic Synthesis* (Eds.: E.-i. Negishi, A. de Meijere), Wiley, New York, **2002**, pp. 493–529; b) K. Sonogashira, *J. Organomet. Chem.* **2002**, *653*, 46–49; c) J. A. Marsden, M. M. Haley, in: *Metal-Catalyzed Cross-Coupling Reactions* (Eds.: A. de Meijere, F. Diederich), Wiley-VCH, Weinheim, **2004**, pp. 317–394; d) E.-i. Negishi, L. Anastasia, *Chem. Rev.* **2003**, *103*,

1979–2017; e) R. Chinchilla, C. Nájera, *Chem. Rev.* **2007**, *107*, 874–922; f) H. Doucet, J.-C. Hierso, *Angew. Chem.* **2007**, *119*, 850–888; *Angew. Chem. Int. Ed.* **2007**, *46*, 834–871.

[9] Recent review about applications of perfluoroalkylsulfonates, see: J. Högermeier, H.-U. Reissig, *Adv. Synth. Catal.* **2009**, *351*, 2447–2463.

[10] For reviews on furo-pyridines and related heterocycles, see: a) W. Friedrichsen, in: *Comprehensive Heterocyclic Chemistry*, vol. 4 (Eds.: A. R. Katritzky, C. W. Rees), Pergamon Press, New York, **1984**, pp. 974–1036; b) S. Shiotani, *Heterocycles* **1997**, *45*, 975–1011; c) S. Cacchi, G. Fabrizi, A. Goggiomani, *Heterocycles* **2002**, *56*, 613–632; d) H. van de Poël, G. Guillaumet, M.-C. Viaud-Massuard, *Heterocycles* **2002**, *57*, 55–71; e) I. Nakamura, Y. Yamamoto, *Chem. Rev.* **2004**, *104*, 2127–2198; f) G. Zeni, R. C. Larock, *Chem. Rev.* **2004**, *104*, 2285–2309; g) R. C. Larock, in: *Acetylene Chemistry* (Eds.: F. Diederich, P. J. Stang, R. R. Tykwinski), Wiley-VCH, New York, **2005**, pp. 55–91.

[11] For recent syntheses of furo-pyridine derivatives, see: a) I. N. Houpis, W. B. Choi, P. J. Reider, A. Molina, H. Churchill, J. Lynch, R. P. Volante, *Tetrahedron Lett.* **1994**, *35*, 9355–9358; b) D. G. Wishka, D. R. Graber, E. P. Seest, L. A. Dolak, F. Han, W. Watt, J. Morris, *J. Org. Chem.* **1998**, *63*, 7851–7859; c) W.-T. Li, F.-C. Lai, G.-H. Lee, S.-M. Peng, R.-S. Liu, *J. Am. Chem. Soc.* **1998**, *120*, 4520–4521; d) A. Arcadi, S. Cacchi, S. D. Giuseppe, G. Fabrizi, F. Marinelli, *Synlett* **2002**, 453–457; e) W. S. Yue, J. J. Li, *Org. Lett.* **2002**, *4*, 2201–2203; f) A. Arcadi, S. Cacchi, S. di Giuseppe, G. Fabrizi, F. Marinelli, *Org. Lett.* **2002**, *4*, 2409–2412; g) A. Fayol, J. Zhu, *Org. Lett.* **2004**, *6*, 115–118; h) P. Cironi, J. Tulla-Puche, G. Barany, F. Albericio, M. Alvarez, *Org. Lett.* **2004**, *6*, 1405–1408; i) I. Aillaud, E. Bossharth, D. Conreaux, P. Desbordes, N. Monteiro, G. Balme, *Org. Lett.* **2006**, *8*, 1113–1116; j) D. Conreaux, S. Belot, P. Desbordes, N. Monteiro, G. Balme, *J. Org. Chem.* **2008**, *73*, 8619–8622.

[12] For a recent thematic issue on organic electronics and optoelectronics: a) S. R. Forrest, M. E. Thompson (Guest Eds.), *Chem. Rev.* **2007**, *107*, 923–1386; also see: b) K. Müllen, U. Scherf, *Organic Light-Emitting Devices: Synthesis Properties and Applications*, Wiley-VCH, Weinheim, **2006**; c) T. J. J. Müller, U. H. F. Bunz, *Functional Organic Materials*, Wiley-VCH, Weinheim, **2007**. For reviews on light-emitting organic materials, see: d) D. Y. Kim, H. N. Cho, C. Y. Kim, *Prog. Polym. Sci.* **2000**, *25*, 1089–1139; e) C.-T. Chen, *Chem. Mater.* **2004**, *16*, 4389–4400; f) C. W. Tang, S. A. VanSlyke, *Appl. Phys. Lett.* **1987**, *51*, 913–915; g) A. Kraft, A. C. Grimsdale, A. B. Holmes, *Angew. Chem.* **1998**, *110*, 416–443; *Angew. Chem. Int. Ed.* **1998**, *37*, 402–428. For reviews on organic field-effect transistors, see: h) C. D. Dimitrakopoulos, P. R. L. Malenfant, *Adv. Mater.* **2002**, *14*, 99–117; i) Y. Qiu, Y. Hu, G. Dong, L. Wang, J. Xie, Y. Ma, *Appl. Phys. Lett.* **2003**, *83*, 1644–1646; j) C. Pannemann, T. Diekmann, U. Hilleringmann, *J. Mater. Res.* **2004**, *19*, 1999–2002; k) S. Achelle, I. Nouira, B. Pfaffinger, Y. Ramondenc, N. Plé, J. Rodríguez-Lopez, *J. Org. Chem.* **2009**, *74*, 3711–3717.

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