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Stereoselective and Catalytic Access to β-Enaminones: An Entry to Pyrimidines

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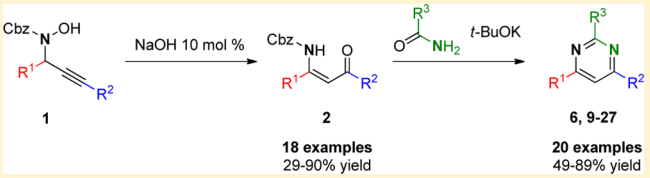
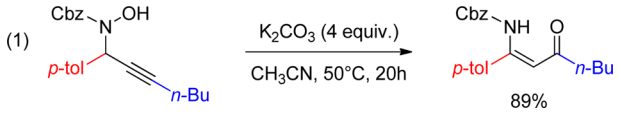
Supporting Information

ABSTRACT: We describe herein a highly stereoselective access to Cbz-protected β-enaminones **2** based on the NaOH catalyzed rearrangement of propargylic hydroxylamines **1**. The synthetic potential of these β-enaminones is illustrated in an original synthesis of pyrimidines.



INTRODUCTION

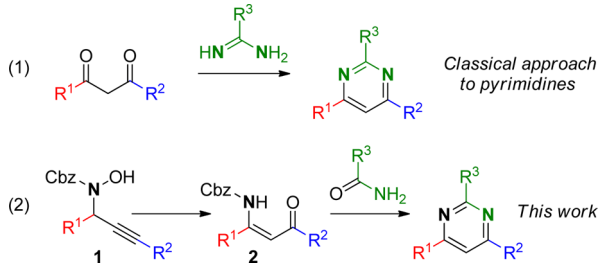
β-Enaminones (vinylogous amides) are versatile compounds,[1] used for their pharmacological properties[2] and as building blocks for heterocyclic[3] and natural product[4] syntheses. Since their biological and chemical properties depend on the alkene stereochemistry, stereoselective syntheses of β-enaminones are thus highly desirable.[5] During initial experiments aimed at developing an interrupted access to trisubstituted isoxazoles,[6] we observed that a propargylic hydroxylamine (Ar = *p*-tol, R = *n*-Bu) was able, under basic conditions, to rearrange to give the Cbz-protected enaminone as a single (*Z*) diastereomer (eq 1, see below for theoretical justification):



Puzzled by this stereoselective isomerization, we were keen to investigate this transformation and to use the enaminones **2** as building blocks for the synthesis of heterocyclic structures such as pyrimidines. Pyrimidines are ubiquitous heterocyclic moieties present in natural products, drugs and in functional materials.[7] Efficient strategies have been developed mainly on the basis of N−C−N condensations, i.e., the addition of guanidines or presynthetized amidines salts to 1,3-diketones or derivatives thereof (such as ynones[7e]) (Scheme 1, eq 1). The presence of a nitrogen atom on enaminones **2** could be advantageous to develop alternative synthetic strategies since it allows for differentiation of the 2 nitrogen groups (which could, for example, be useful for isotopic labeling strategies). Moreover, such a cyclocondensation would use the readily commercially available and stable class of carboxamides, which grants a more convenient access to these heterocycles.[8]

Herein, we describe the catalytic isomerization of readily available propargylic hydroxylamines **1**[9,10] to (*Z*)-β-enaminones **2** and we propose a reaction pathway based on DFT calculations for this unanticipated isomerization. The further transformation of **2** into 2,4,6-trisubstituted pyrimidines is also reported (Scheme 1, eq 2).

Scheme 1. Synthesis of Pyrimidines



RESULTS AND DISCUSSION

The starting propargylic hydroxylamines **1** are easily obtained by $FeCl_3$-catalyzed direct nucleophilic substitution of the propargylic hydroxyl group by the commercially available Cbz-NHOH under reaction conditions developed by Zhan ($FeCl_3$ 5 mol %, DCM, 60 °C, 1 h).[10] First, **1a** was chosen as model substrate and its isomerization under various basic conditions was investigated (Table 1).

Starting from the previously described conditions (4.0 equiv of K_2CO_3 in acetonitrile at 50 °C for 20 h),[6] the influence of the base was first tested: whereas no reaction is observed with NEt_3 (entry 2), the conversion is complete after 1 h using sodium hydroxide (4 equiv), leading to **2a** in 28% isolated yield along with unidentified byproduct (entry 3). The (*Z*) geometry of the double bond was assigned by ^{1}H NMR chemical shift correlation. Indeed, the ^{1}H NMR shift of the proton attached to the nitrogen atom of our enaminones **2** is in good agreement with previously described (*Z*)-β-enaminones (δ_{N-H}: ca. 11 ppm).[11] In sharp contrast, in enecarbamates, which can be seen as analogs where

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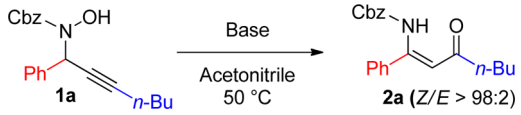
Table 1. Isomerization of Propargylic Hydroxylamine 1a under Various Basic Conditions



	base	equiv	reaction time (h)	**2a** isolated yield (%)
1	K_2CO_3	4	20	71
2	NEt_3	4	20	NR
3	NaOH	4	1	28
4	NaOH	1	1	75
5	**NaOH**	**0.1**	**1**	**86**
6	K_2CO_3	0.1	8	59

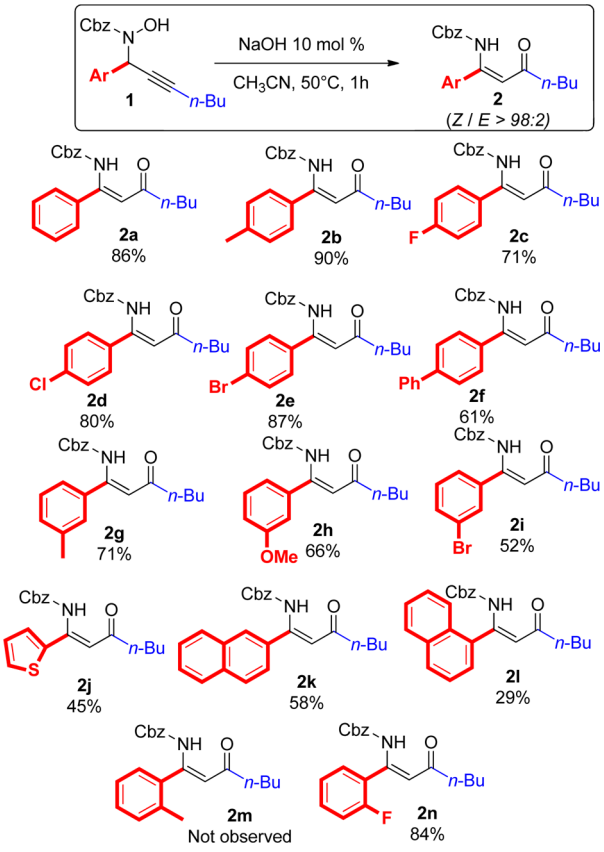
the carbonyl is not present, a lower shift is observed (δ_{N-H}: ca. 6 ppm).[12] This shielding effect observed in the case of enaminones is characteristic of the existence of a H bonding, which is in good agreement with the proposed (*Z*) geometry. Moreover, the structure of **2** was further confirmed by nOesy experiments (see Supporting Information for details).

Anticipating that an excess of base might be problematic, the reaction was carried out with only 1 equiv of NaOH. Indeed, **2a** was isolated in 75% as a single (*Z*) isomer (entry 4). Considering that the isomerization process should lead to an anionic product, we assumed that a catalytic amount of base might be sufficient. Thus, the use of 10 mol % of NaOH was finally attempted and, gratifyingly, **2a** was isolated in an improved 86% yield (entry 5). In a control experiment (0.1 equiv of K_2CO_3 in acetonitrile at 50 °C), compound **2a** was isolated in 59% yield and the reaction required 8 h for completion (entry 6). It is worth noting that the presence of water is required to ensure good conversions (see the mechanistic study for explanations and in particular about the role of water). Consequently, our reactions are run in nondistilled acetonitrile[13] and in an open-air flask, which makes this methodology quite practical.

We next studied the scope and limitations of this isomerization. Using our optimized conditions (Scheme 2), the influence of the aryl substituents at the propargylic position was first investigated. Starting from propargylic hydroxylamines bearing electron-withdrawing or electron-donating groups, at the *para* or *meta* position, Cbz-protected enaminones **2a–i** were obtained in good to excellent yields. Heteroaromatics, such as thiophene, are also well tolerated in this reaction (**2j**). Some limitations appear when using more hindered substrates: compare for example 1-naphtyl vs 2-naphthyl moieties (**2k** and **2l**) or *o*-Me vs *o*-F substituents (**2m** and **2n**). Taken together, these results show that the presence of a sterically hindered group close to the propargylic position has a detrimental effect on the yield. Mechanistic implications of this observation are discussed thereafter.

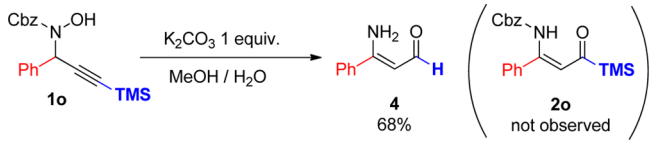
Moving to a TMS group, and under classical conditions, the attempted enaminone **2o** could not be observed. After some optimization, and using 1 equiv of K_2CO_3 at room temperature in a methanol/water mixture, compound **4** could finally be isolated in 68% yield (Scheme 3). Of note, this product is isolated as a single Z isomer and results from a one-pot transformation including three elemental steps: isomerization, desilylation and Cbz deprotection. It is not clear when the Cbz deprotection occurs in this sequence; nevertheless, knowing the stability of acylsilane under hydrolysis conditions,[14] the formation of a formyl group in the final product indicates that the isomerization step takes place after the TMS removal. Clearly, the presence of a

Scheme 2. Scope of the Isomerization of Propargylic Hydroxylamines: Influence of the Aryl Group at the Propargylic Position[a,b]



[a]General conditions: Propargylic hydroxylamine (0.2 mmol), NaOH (0.02 mmol, 10 mol %), CH_3CN (2 mL, 0.1 M), 50 °C, 1 h. [b]Isolated yields.

Scheme 3. Isomerization of a Propargylic Hydroxylamine Substituted by a TMS Group at the Acetylenic Position



TMS at the acetylenic position inhibits the isomerization, whereas terminal alkynes are suitable reagents for this transformation.

Next, substrates bearing different alkyl or aryl substituents on the acetylenic position were tested. With Me and *i*-Pr alkyl groups, the corresponding enaminones **2p,q** were isolated in 75 and 63% yields, respectively (Scheme 4, eq 1 and 2). In contrast, the expected enaminone **2r** could only be observed as traces in the crude material when a bulkier *t*-Butyl group stands at the acetylenic position. Along with unreacted starting material **1r** (recovered in 46% yield), the major product was the imine **3r** isolated in 41% yield (Scheme 4, eq 3). With aryl groups (Ph and *p*-Tol), the expected enaminones were obtained in 51% (**2s**) and 53% (**2t**) yields along with the corresponding imines **3s** and **3t** in 18 and 14% yields, respectively (Scheme 4, eq 4).

The detection of imines **3r–t** provides some insight on the reaction mechanism, which thus appears to be initiated by the β-elimination of the OH group. This transformation is rare in

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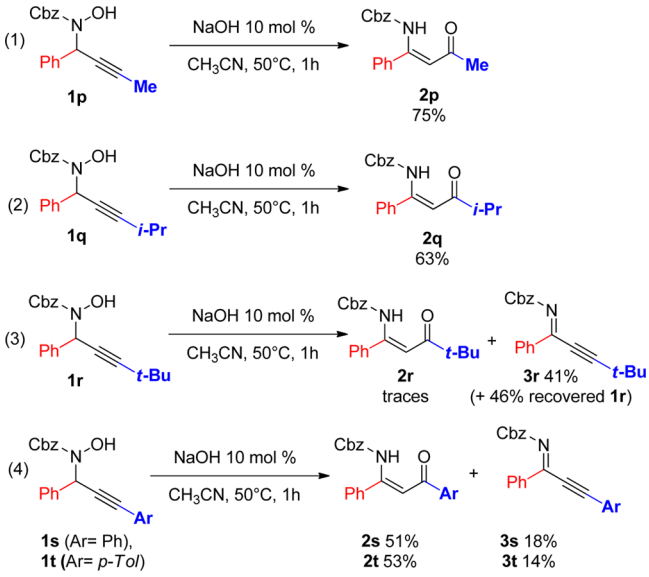
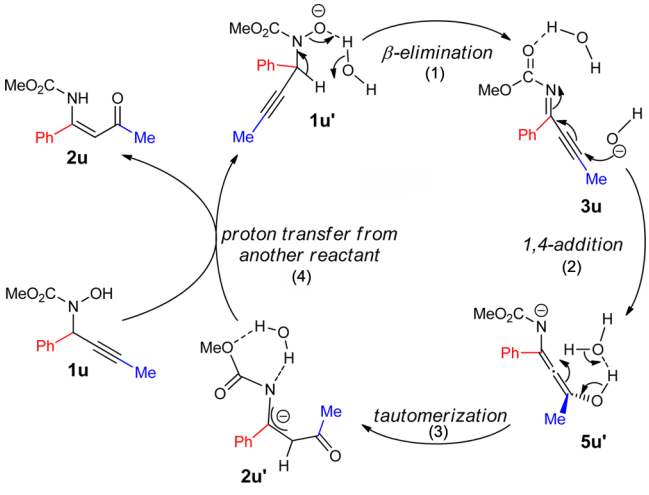
Scheme 4. Isomerization of Propargylic Hydroxylamines: Influence of Alkyl or Phenyl Substituent at the Acetylenic Position



literature,[15] and we were particularly puzzled that it could proceed at relatively low temperature in basic conditions. Moreover, the synthesis of β-enaminones from imines was not documented. We thus decided to elucidate the mechanism of this isomerization, and starting from the observation that imines were formed in the reaction mixture, a mechanism model was sought using a computational approach (DFT based; see Theoretical Section for details). A complete catalytic path was found, including the succession of steps described in Scheme 5.

Scheme 5. Computed Mechanism for the Isomerization Process



The full reaction sequence was found to take place in the anionic, deprotonated form, in the presence of water. It is starting from the deprotonated aminol **1u′** that is readily formed upon geometry optimization when HO^- is associated to **1u** (no cation is considered since ion pairs are supposed to exclusively exist as solvent separated ion pairs (SSIP) in such a polar solvent; see Theoretical Section). The following steps are observed, where the deprotonated forms are noted with prime:

(1) HO^- elimination triggered by deprotonation at the propargylic position to form the transient conjugated imine **3u**.
(2) Addition of HO^- to **3u** yielding an allenol **5u′**.
(3) Keto−enol tautomerization of **5u′** to conduct to deprotonated enaminone **2u′**.
(4) Proton exchange between the reactant **1u** and the anionic product **2u′**.

Step one was found to be a *syn* elimination as, even though the *anti* mechanism exhibits a low energy barrier (less than 0.5 kcal mol^{-1}), it cannot take place in the deprotonated aminol form **1u′**, which is found to be preferred by 22.0 kcal mol^{-1} over the structure leading to the anti process. Step two is associated with the addition of the HO^- at the position 4 of the imine **3u** to yield allenol **5u′**, but no reprotonation of the amide is observed. As for the starting aminol **1u**, when including an explicit water molecule in the modeled system, the most stable form is associated to a delocalized organic anion and a water molecule. An anionic structure is also predominant after the tautomerization, step 3, as the protonation at the central carbon of allenol **5u′** and the deprotonation of the OH group are simultaneous and mediated through an H-bonded water molecule. Even though the proposed reaction step already leads to the right *Z*/*E* isomer of **2u′**, isomerization within this structure is easy, as rotation between the *Z* and *E* isomers exhibit an energy barrier of only 5.7 kcal mol^{-1}. The last step of the reaction mechanism is a reprotonation of **2u′** by the starting material (**1u** in Scheme 5) to yield the final product **2u**, which is found to be exothermic by 1.3 kcal/mol^{-1} and thus fully equilibrated. The overall energy profile is reported in Figure 1.

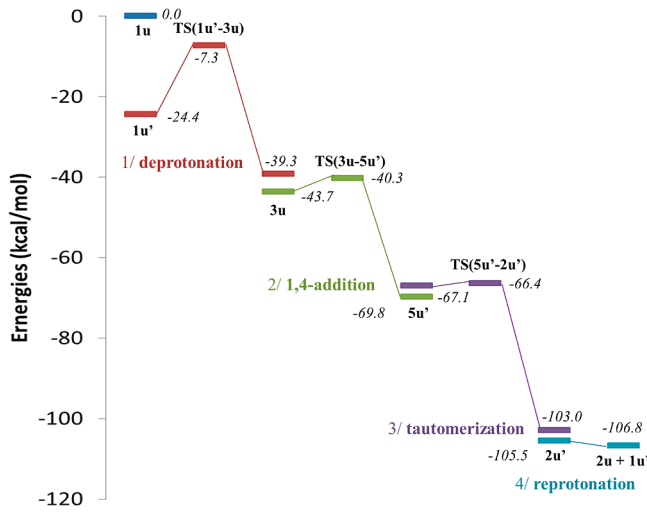


Figure 1. Energy profile (energies in italics are given in kcal/mol) of the HO^- catalyzed isomerization process. Numbers are introduced in Scheme 5.

This reaction profile is found to be in complete agreement with experimental observations. The first step of this reaction path is supported by the lack of reactivity when a weak base such as NEt_3 (pK_a < 10) is used (see Table 1, entry 2). We also observed a drastic drop of the conversion when the reaction is conducted in strictly anhydrous conditions under argon atmosphere, which confirms the crucial role of water in the catalytic process.[13] In two additional control experiments, we confirmed this hypothesis by submitting propargylic hydroxylamines **1v,w** to our standard conditions (Scheme 6, eq 1). As expected, no reaction occurs,

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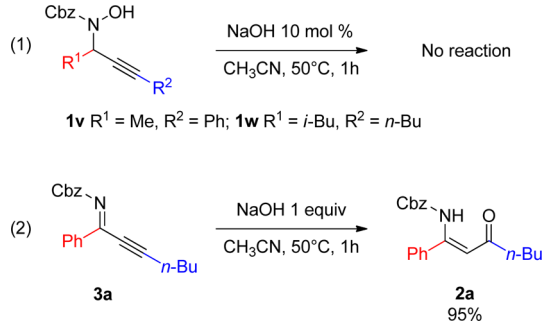
Scheme 6. Complementary Experiments Performed to Support the Mechanistic Model



and the starting material is fully recovered. In this case, because of the replacement of the aryl by an alkyl group in the propargylic position, the propargylic proton is not acidic enough to allow the first deprotonation step. As evidence for the second step of our proposed mechanism, the formation of imines is observed when a sterically hindered *t*-Bu substituent stands in the acetylenic position (Scheme 4, eq 3) or when the intermediate imine is fully conjugated (Scheme 4, eq 4), i.e., when the 1,4 addition step is disfavored. Moreover, when imine **3a**[16] was subjected to a stoichiometric amount of NaOH, the corresponding enaminone **2a** was obtained in almost quantitative yield, which shows that imine is a reaction intermediate (Scheme 6, eq 2).

To complete the theoretical study, the stereoselectivity of the final product was examined computationally through the relative stability of the final product **2u**: indeed, the low isomerization barrier between *Z* and *E* forms found in **2u′** associated with the equilibrium of reprotonation of **2u′** to **2u** let us conclude that both isomers are in thermodynamic equilibrium in the final product. Geometry optimization was thus carried out on the products, using increasing size models (see Figure 2): model A, where only H-bond can stabilize the structure, model B where Ph and Me substituent effects are taken into account, and **2u**, which adds the C(O)OMe group at the nitrogen atom, with or without the effect of a continuous representation of the solvent. An anionic model **2u′** deprotonated at the nitrogen and thus unable to stabilize through H-bonding is also examined. Results are given in Table 2. Whatever the model, a *Z* stereoisomer is systematically favored over the *E* one and is evaluated to 6.8 kcal mol^{-1} in the case of the model **2u** (4.1 kcal/mol^{-1} in presence of a continuum model of the solvent). In absence of substituent effects, and thus when only the H-bond is at stake, the preference is only 4.0 kcal mol^{-1}, in good agreement with the results published for similar species.[17] In absence of H-bonding, in the anionic form, the preference for the *Z* form is maintained, with a 3.0 kcal mol^{-1} value. It is thus found that the preference for the *Z* isomer is due both to substituent effects (about 3 kcal/mol^{-1}, steric hindrance of the Ph and Me in the *E* isomer, see Figure 2,

Table 2. Energies of the Various Stereoisomers Relative to the Most Stable One for Each Model[a]

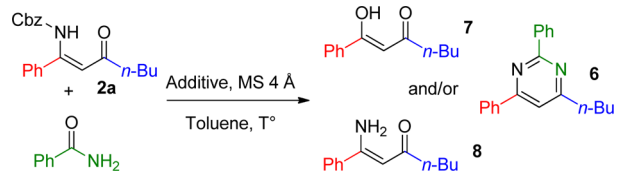
	E-trans	*E*-cis	*Z*-trans	*Z*-cis
model A	4.0	5.1	6.8	0.0
model B	9.5	9.9	8.3	0.0
2u	6.9	6.8	7.2	0.0
$\mathbf{2u}_{solv}$	4.1	5.3	4.4	0.0
2u′	3.0	3.5	0.0	5.6

[a]In kcal/mol^{-1}. The subscript "solv" stands for results in a continuum model for the solvent.

model B) and stabilization by an H-bond (about 4 kcal/mol^{-1}), the latest being weakened (by about 2.7 kcal/mol^{-1}) in presence of a polar solvent. This double effect sheds a new light on the commonly accepted picture of stabilization by intramolecular H-bonding.[17]

In the first part of our work, we explored the isomerization of propargylic hydroxylamine into *β*-enaminones and built a plausible mechanism for this original transformation. We next decided to explore the synthetic potential of the Cbz-protected enaminones **2**. We reasoned that enaminone could represent interesting building block for the synthesis of heterocyclic compounds such as pyrimidines. Indeed, the presence of a geometrically defined double bond as well as a nucleophilic nitrogen and an electrophilic carbonyl groups should allow the development of an alternative synthesis based on the use of a complementary electrophile/nucleophile partner such as carboxamide, in a classical ionic cyclocondensation process. To test this hypothesis, the reactivity of enaminone **2a** with benzamide was screened under various conditions (Table 3).

Table 3. Formation of Pyrimidine 6 from Enaminone 2a and Benzamide: Optimization Study



	additives (equiv)	conditions	product (isolated yield)
1	PTSA (0.1)	Dean−Stark, reflux, 3 d	complex reaction mixture containing **6** and **7** in a 1:1 ratio
2	MeONa (1)	sealed vial, 130 °C, 1 h	**6** (30%) (**6**:**8** in a 1:1 ratio is observed in the crude material)
3	DBU (1)	"	**6** (14%) (**7** is observed as the major compound)
4	*t*BuOK (1)	"	**6** (51%) (**2a** is recovered in 35% yield)
5	*t*BuOK (1.5)	"	**6** (76%)
6	***t*BuOK (2)**	"	**6** (**80%**)

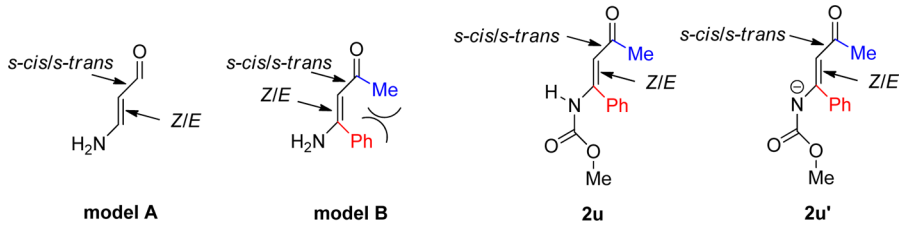


Figure 2. Models examined for relative stability of the *Z* and *E* isomers.

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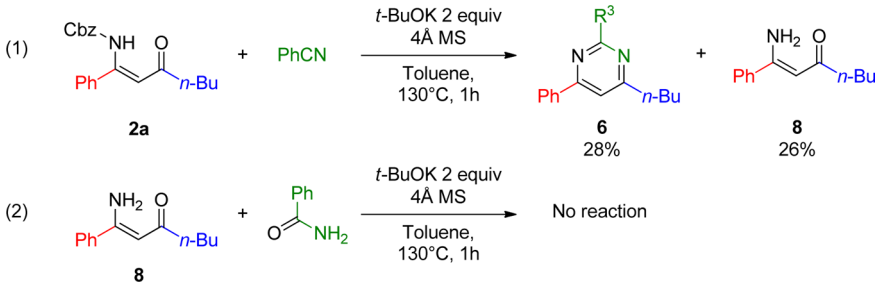
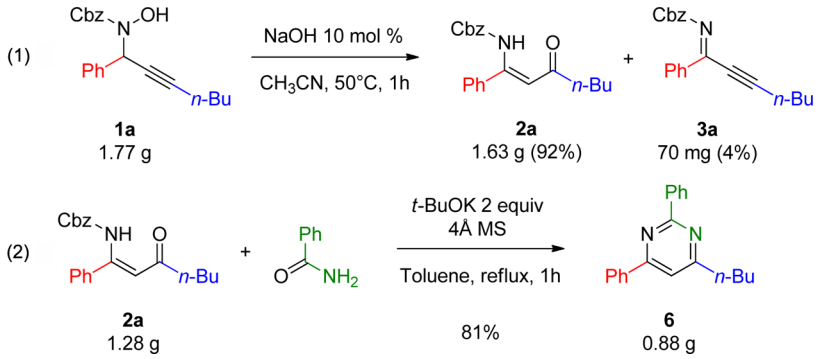
Scheme 7. Attempts of Cyclocondensation Starting from Benzonitrile or Cbz-Deprotected 8



Scheme 8. Gram Scale Synthesis of Pyrimidine 6 from Propargylic Hydroxylamine 1a



Under acidic conditions (entry 1), the expected pyrimidine **6** was observed along with the hydrolysis product **7** (1:1 ratio along with unidentified products). In contrast, in the presence of MeONa (entry 2), pyrimidine **6** could be isolated in 30% yield. This low yield results from the competitive formation of the Cbz deprotected enaminone **8** (**6** and **8** are in a 1:1 ratio in the crude mixture). To avoid the competitive Cbz deprotection, the use of bulkier bases such as DBU or *t*-BuOK was investigated. Whereas deceptive results were observed with DBU (entry 3), the use of 1 equiv of *t*-BuOK led to **6** in 51% yield, along with unreacted starting material **2a** (35%) (entry 4). The amount of base is crucial, and 2 equiv of *t*-BuOK appeared to be necessary to gain full conversion and produce pyrimidine **6** in 80% yield (see entries 5 and 6). Unfortunately, all tries to set up an efficient one-pot two-step access to pyrimidines from *N*-hydroxypropargylamines **1** failed.[18] Indeed, the isolated yield was lowered compared to the stepwise process due to the presence of deprotected enaminone.

Attempt to use a nitrile as coupling partner gave unsatisfying results: when enaminone **2a** and benzonitrile were engaged in the previously optimized reaction conditions, pyrimidine **6** and deprotected enaminone **8** were obtained in 28 and 26% yield, respectively (Scheme 7, eq 1). Of note, when **8** was treated with benzamide, no trace of pyrimidine could be observed in the crude mixture, which highlights (i) that **8** is not an intermediate in the formation of **6** and (ii) the crucial role of the Cbz protecting group for the reaction process (Scheme 7, eq 2). Consequently, some insights into the mechanistic pathway can be brought forward. These two remarks give some insights to the mechanistic pathway of this transformation. If the exact course of the nucleophilic attack steps remains unclear, it seems reasonable to assume that the removal of the Cbz group should occur during the aromatization step, as recently proposed by Kuninobu and Takai for the formation of multisubstituted pyridines.[19]

For practical reasons, these optimization studies have been carried out on small scale (0.2 mmol), using sealed vials. Consequently, these optimized conditions were next tried on a larger scale, using classical glassware, and gratifyingly, pyrimidine **6** was isolated in 81% yield (3.05 mmol, 880 mg, Scheme 8).

With our optimized conditions (2.0 equiv of *t*BuOK in refluxing toluene), the scope and limitations of this pyrimidine synthesis were surveyed. As illustrated in Scheme 9, differently substituted enaminones lead, in the presence of carboxamides, to the corresponding pyrimidines **6**, **9**−**22** in moderate to good yields. Starting from benzamide, pyrimidines **6**, **9**−**16** were obtained in 52−89% yields. Interestingly, the presence of electron-donating groups at the meta or para position has a positive influence on the yield. Nevertheless, halogen substituents are tolerated, and notably, the presence of a bromine atom in compound **13** allows for further functionalization. The nature of the alkyl substituent (primary or secondary) at the carbonyl group (R^2) has little influence (compounds **17**, **18**), whereas a slight decrease in yield is observed when R^2 is a phenyl group (54%, compound **19**). The scope has been successfully extended to heteroaromatic (**20**) and *para*-nitro and -bromo substituted arenes (**21** and **22**, respectively).

2-Vinyl substituted pyrimidines are particularly interesting substrates,[20] usually obtained via cross-coupling reaction from the corresponding 2-chloro pyrimidines. Starting from acrylamide, pyrimidines **23**−**25** have been obtained in 55, 51, and 46% yields, respectively (Scheme 10). Anticipating that these pyrimidines could be sensitive to polymerization, the same reactions were carried out in the presence of TEMPO (1 equiv) as a radical inhibitor. Under these conditions, pyrimidines **23**−**25** were obtained in improved 72, 69, and 68% yields, respectively. Finally, simple alkyl carboxamides, such as acetamide, can be used as partners for this reaction, leading to **26** with a satisfying 72% isolated yield. Starting from formamide, the use of molecular sieves proved to be detrimental, but in its absence, 4,6-disubstituted pyrimidine **19** was finally obtained in 49% yield.

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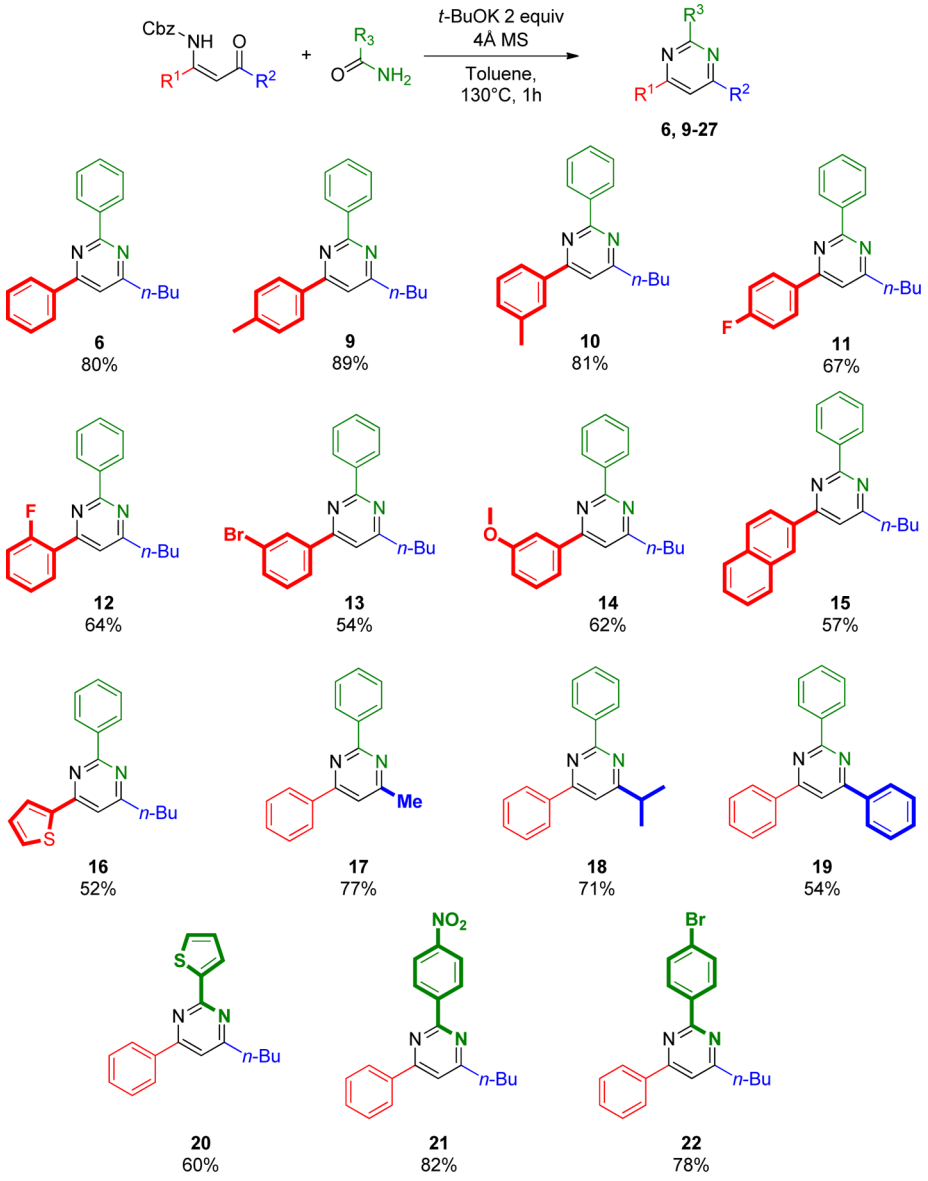
Scheme 9. Synthesis of Pyrimidines from Aromatic and Heteroaromatic Carboxamides: Scope and Limitations[a]



[a]General conditions: vinylogous amide (0.2 mmol), amide (0.3 mmol, 1.5 equiv), *t*-BuOK (0.4 mmol, 2 equiv), 4 Å MS (70 mg), $PhCH_3$ (2 mL, 0.1 M), 130 °C, 1 h.

CONCLUSIONS

In conclusion, we described a catalytic and stereoselective isomerization of readily available propargylic hydroxylamines **1** leading *β*-enaminones **2** under simple and efficient conditions (NaOH 10 mol %, 1 h). This unanticipated transformation was rationalized with the help of an intertwined theoretical/experimental study that allows determining each step of the catalytic pathway, i.e., *β*-elimination, 1,4-addition and tautomerization. The first *β*-elimination step, which leads to the N−O bond breaking, is of particular interest since it occurs via an original water-assisted six-membered *syn* elimination process. Moreover, the model generally admitted to explain the preference for *Z* form of *β*-enaminone has been revisited, and besides the internal stabilizing H-bonding, the substituents effect has been highlighted. The synthetic potential of Cbz-protected *β*-enaminones **2** was illustrated through the development of a novel access to pyrimidines with stable, commercially available and inexpensive carboxylic amides.

THEORETICAL SECTION

Full geometry optimizations were systematically conducted with no symmetry restraints using the Gaussian 09 program[21] within the framework of the Density Functional Theory (DFT) using the dispersion corrected B97D[22] exchange-correlation functional (which was shown to give good results on similar questions[23]) and the 6-31+G** basis set for all atoms. Frequencies were evaluated within the harmonic approximation and the nature of all minima was ensured by confirming the presence of no imaginary frequency. A model system **1u** was examined, derived from **1i** by replacing the Cbz $C(O)OCH_2Ph$ group by a simple C(O)OMe one, which is proposed to be a minor modification as (i) no major electronic effect as conjugation is supposed to be altered as non is expected for this group and (ii) the benzyl group is flexible enough to behave sterically like a methyl in this kind of compound. Solvation was taken into account using an implicit solvation model, and all geometry were fully optimized in presence of the

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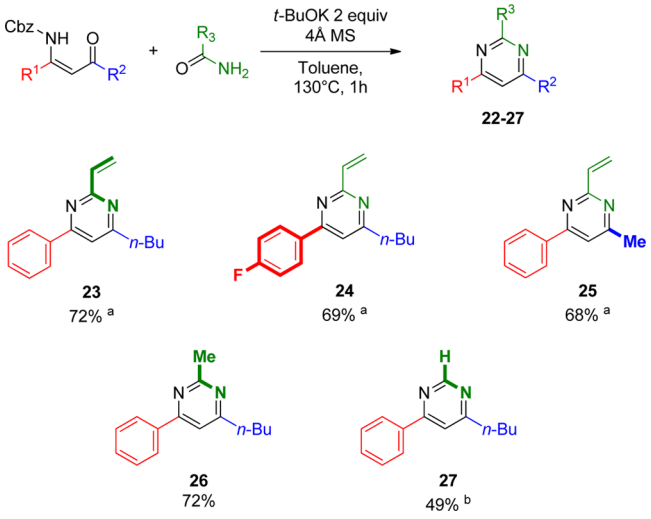
Scheme 10. Synthesis of Pyrimidines from Various Carboxamide Derivatives[c]



[a]Reaction conducted with addition of TEMPO (0.2 mmol, 1 equiv). [b]Reaction carried out without 4 Å MS, and starting enaminone **2a** was recovered in 26% yield. [c]General conditions: vinylogous amide (0.2 mmol), amide (0.3 mmol, 1.5 equiv), *t*-BuOK (0.4 mmol, 2 equiv), 4 Å MS (70 mg), $PhCH_3$ (2 mL, 0.1 M), 130 °C, 1 h.

continuum. For these computations, the PCM model was used within the default framework implemented in Gaussian 09,[24] except for atomic radii where the UFF values are used. The dielectric constant implemented for DMSO ($\varepsilon_R = 46.826$) was used, a value slightly higher than that for acetonitrile ($\varepsilon_R = 35.688$), in order to take into account the presence of non-negligible amount of water in the reaction media. The key intermediates were reoptimized in a model of acetonitrile in order to confirm the validity of this approach. Because of the high polarity of the solvent, NaOH is considered as a fully dissociated ion pair, and no Na^+ cation is included in the computational model.

EXPERIMENTAL SECTION

General Considerations. Unless otherwise stated, all commercial materials were used without further purification. Spherical 4 Å MS is used when needed. Chromatography was carried out on silica gel 60 A (35−70 mm). PMA stands for phosphomolybdic acid (ethanolic solution) and is used as TLC stain. Solvents (acetonitrile, toluene and methanol) were used without further purification. ^1H and ^{13}C NMR spectra were obtained on a 400 MHz NMR spectrometer and referenced to $CDCl_3$. ^{19}F NMR spectra are calibrated using C_6F_6 as an external standard. High resolution mass spectra (HRMS) were measured using electrospray ionization and were acquired using a Q-TOF analyzer. Propargylic alcohols have already been described and were easily obtained by the addition of the corresponding alkynyl lithium reagent (in anhydrous THF) to the corresponding aldehyde.[9c,25]

General Procedure A for the Preparation of Propargylic Hydroxylamines (1a−t). To a solution of the corresponding propargylic alcohol (1 equiv) in dichloromethane (C = 0.1 M) was added *N*-hydroxybenzenesulfonamide (1 equiv) and $FeCl_3$ (5 mol %, 0.05 equiv), and the mixture was refluxed for 90 min. After reaction completion (TLC monitoring), the mixture was concentrated under vacuum, and the crude material was purified by flash chromatography on silica gel to give the corresponding *N*-propargylic hydroxylamine.

General Procedure B for the Preparation of β-Enaminones (2a−t). In a 5-mL Wheaton reactor, equipped with a magnetic stirrer bar, the corresponding *N*-propargylic hydroxylamine (0.2 mmol, 1 equiv), and NaOH powder (0.02 mmol, 0.1 equiv) were added in acetonitrile (2 mL) by turn, and the mixture was heated at 50 °C for 1 h. Thus, the reaction mixture was filtered off through a silica gel pad and eluted with ethyl acetate, the filtrate was concentrated, and the residue was purified by flash chromatography on silica gel to give the corresponding *β*-enaminone.

Gram-Scale Procedure for the Obtention of (*Z*)-Benzyl (3-oxo-1-phenylhept-1-en-1-yl)carbamate (2a). In a 250 mL-round-bottom flask equipped with a magnetic stirrer bar and a condenser, the benzyl hydroxy(1-phenylhept-2-yn-1-yl)hept-2-yn-1-yl)carbamate **1a** (1770 mg, 5.25 mmol, 1 equiv), NaOH powder (22 mg, 0.55 mmol, 0.1 equiv) were added in acetonitrile (50 mL), and the mixture was heated at 50 °C for 1 h. The reaction mixture was cooled and then filtered off through a silica gel pad and eluted with ethyl acetate, and the filtrate was concentrated. 1630 mg of the title compound **2a** (4.83 mmol, 92% yield) and 70 mg of (*E*)-benzyl (1-phenylhept-2-yn-1-ylidene)-carbamate **3a** (0.21 mmol, 4% yield) were obtained after purification by flash chromatography on silica gel (pentane/Et_2O 92/8).

General Procedure C for the Preparation of Pyrimidines (6, 9−22, 26, 27). In a 5 mL Wheaton reactor (screw top V-Vials with open-top cap) equipped with a magnetic stirrer bar, the corresponding vinylogous amide (0.2 mmol, 1 equiv), the corresponding amide (0.3 mmol, 1.5 equiv), 4 Å MS (70 mg) and potassium *tert*-butoxide (0.4 mmol, 2 equiv) were introduced by turn in toluene (2 mL), and the mixture was heated at 130 °C for 1 h. The reaction mixture was then filtered off through a silica gel pad and eluted with ethyl acetate. The filtrate was concentrated, and the residue was purified by flash chromatography on silica gel to give the corresponding pyrimidine.

Gram-Scale Procedure for the Obtention of 4-Butyl-2,6-diphenylpyrimidine (6). In an oven-dried 100 mL-round-bottom flask equipped with a magnetic stirrer bar and a condenser, the (*Z*)-benzyl (3-oxo-1-phenylhept-1-en-1-yl)carbamate **2a** (1280 mg, 3.80 mmol, 1 equiv), benzamide (740 mg, 6.10 mmol, 1.6 equiv), 4 Å MS (1300 mg) and potassium *tert*-butoxide (908 mg, 8.mmol, 2.6 equiv) toluene were introduced by turn, and the mixture was heated at reflux for 1 h under argon. The reaction mixture was cooled and then filtered through a silica gel pad and eluted with ethyl acetate, and the filtrate was concentrated. 880 mg of the title compound **6** (3.05 mmol, 81% yield) were obtained after purification by flash chromatography on silica gel (pentane/Et_2O 98/2).

General Procedure D for the Preparation of 2-Vinyl-Substituted Pyrimidines (23−25). In a 5 mL Wheaton reactor (screw top V-Vials with open-top cap) equipped with a magnetic stirrer bar, the corresponding vinylogous amide (0.2 mmol, 1 equiv), the corresponding amide (0.3 mmol, 1.5 equiv), 4 Å MS (70 mg), TEMPO (0.2 mmol, 1 equiv) and potassium *tert*-butoxide (0.4 mmol, 2 equiv) were introduced by turn in toluene (2 mL), and the mixture was heated at 130 °C for 1 h. The reaction mixture was then filtered off through a silica gel pad and eluted with ethyl acetate. The filtrate was concentrated, and the residue was purified by flash chromatography on silica gel to give the corresponding pyrimidine.

Benzyl hydroxy(1-phenylhept-2-yn-1-yl)carbamate (1a). According to general procedure A (on 2 mmol scale) and starting from 1-phenylhept-2-yn-1-ol and benzyl hydroxycarbamate, 626.0 mg of compound **1a** (1.855 mmol, 93% yield) were obtained as a pale yellow solid after purification by flash chromatography on silica gel (pentane/ethyl acetate 88/12): R_f (silica, pentane/ethyl acetate 9/1 = 0.25, UV/PMA); mp 58−59 °C (Et_2O/pentane); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.92 (t, J = 7.3 Hz, 3H), 1.39−1.59 (m, 4H), 2.29 (dt, J = 2.2 Hz and J = 7.1 Hz, 2H), 5.26 (s, 2H), 5.59 (brs, 1H), 6.13 (t, J = 2.1 Hz, 1H), 7.29−7.42 (m, 8H), 7.50−7.56 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.6, 18.5, 22.0, 30.6, 55.9, 68.4, 74.5, 87.1, 127.9, 128.1, 128.2, 128.4, 128.6, 135.6, 136.2, 157.1; IR (ATR, neat) ν (cm^{-1}) 3225, 2957, 2928, 2872, 2859, 2222, 1959, 1704, 1495, 1481, 1453, 1443, 1394, 1346, 1290, 1097, 1030, 959, 763, 743, 713, 694, 636, 608; MS (ESI+) m/z 675 (15, $[2M + H]^+$), 508 (45), 464 (100), 338 (50, $[M + H]^+$), 320 (15), 261 (20); HRMS (ESI+) m/z 338.1742 calcd for $C_{21}H_{23}NO_3 + H^+$ 338.1756.

Benzyl hydroxy(1-(*p*-tolyl)hept-2-yn-1-yl)carbamate (1b). According to general procedure A (on 2 mmol scale) and starting from 1-*p*-tolylhept-2-yn-1-ol and benzyl hydroxycarbamate, 659.5 mg of compound **1b** (1.876 mmol, 94% yield) were obtained as a viscous pale yellow oil after purification by flash chromatography on silica gel (pentane/ethyl acetate 88/12): R_f (silica, pentane/ethyl acetate 9/1 =

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0.25, UV/PMA); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.92 (t, J = 7.2 Hz, 3H), 1.38−1.58 (m, 4H), 2.28 (dt, J = 2.1 Hz and J = 7.0 Hz, 2H), 2.34 (s, 3H), 5.25 (s, 2H), 5.55 (brs, 1H), 6.09 (t, J = 2.1 Hz, 1H), 7.15 (∼d, J = 8.0 Hz, 2H), 7.31−7.44 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.6, 18.5, 21.1, 22.0, 30.6, 55.6, 68.3, 74.7, 87.3, 127.9, 128.2, 128.4, 128.5, 129.1, 133.2, 135.6, 138.0, 157.1; IR (ATR, neat) ν (cm^{-1}) 3314, 3032, 2956, 2931, 2871, 2233, 1702, 1513, 1497, 1455, 1409, 1350, 1328, 1282, 1214, 1180, 1093, 797, 771, 751, 734, 695; MS (ESI+) m/z 536 (15), 492 (15), 352 (10, $[M + H]^+$), 334 (55), 216 (10), 185 (100); HRMS (ESI+) m/z 352.1910 calcd for $C_{22}H_{25}NO_3 + H^+$ 352.1913.

Benzyl (1-(4-fluorophenyl)hept-2-yn-1-yl)(hydroxy)-carbamate (1c). According to general procedure A (on 0.5 mmol scale) and starting from 1-(4-fluorophenyl)hept-2-yn-1-ol and benzyl hydroxycarbamate, 594.0 mg of compound **1c** (1.671 mmol, 84% yield) were obtained as a pale yellow oil after purification by flash chromatography on silica gel (pentane/ethyl acetate 88/12): R_f (silica, pentane/ethyl acetate 9/1 = 0.25, UV/PMA); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.92 (t, J = 7.3 Hz, 3H), 1.39−1.58 (m, 4H), 2.28 (dt, J = 2.1 Hz and J = 7.1 Hz, 2H), 5.23 (s, 2H), 6.03 (brs, 1H), 6.07 (brs, 1H), 7.01 (∼t, J = 8.7 Hz, 2H), 7.31−7.40 (m, 5H), 7.49 (∼dd, J = 5.4 Hz and J = 8.5 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −114.0; ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.6, 18.4, 22.0, 30.6, 55.1, 68.4, 74.5, 87.7, 115.2 (d, $J_{ortho(C-F)}$ = 21.7 Hz), 128.2, 128.4, 128.6, 129.8 (d, $J_{meta(C-F)}$ = 8.3 Hz), 132.1 (d, $J_{para(C-F)}$ = 3.0 Hz), 135.5, 157.1, 162.5 (d, $J_{ipso(C-F)}$ = 246.7 Hz); IR (ATR, neat) ν (cm^{-1}) 3300, 2956, 2932, 2233, 1955, 1699, 1455, 1397, 1345, 1295, 1277, 1252, 1092, 1030, 797, 790, 777, 753, 734, 695, 634; MS (ESI+) m/z 523 (15), 356 (20, $[M + H]^+$), 338 (100), 294 (25), 288 (10), 220 (40), 189 (90); HRMS (ESI+) m/z 356.1660 calcd for $C_{21}H_{22}FNO_3 + H^+$ 356.1662.

Benzyl (1-(4-chlorophenyl)hept-2-yn-1-yl)(hydroxy)-carbamate (1d). According to general procedure A (on 4 mmol scale) and starting from 1-(4-chlorophenyl)hept-2-yn-1-ol and benzyl hydroxycarbamate, 1.290 g of compound **1d** (3.469 mmol, 87% yield) were obtained as a viscous colorless oil after purification by flash chromatography on silica gel (pentane/ethyl acetate 88/12): R_f (silica, pentane/ethyl acetate 9/1 = 0.25, UV/PMA); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.92 (t, J = 7.3 Hz, 3H), 1.37−1.58 (m, 4H), 2.28 (dt, J = 2.1 Hz and J = 7.1 Hz, 2H), 5.23 (s, 2H), 5.97 (brs, 1H), 6.06 (brs, 1H), 7.30 (∼d, J = 8.5 Hz, 2H), 7.32−7.39 (m, 5H), 7.45 (∼d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.6, 18.4, 22.0, 30.6, 55.2, 68.5, 74.2, 87.9, 128.2, 128.4, 128.5, 128.6, 129.4, 134.1, 134.9, 135.5, 157.2; IR (ATR, neat) ν (cm^{-1}) 3297, 2929, 1706, 1491, 1455, 1407, 1292, 1091, 1016, 797, 749, 697; MS (ESI+) m/z 532 (10), 372 (20, $[M + H]^+$), 295 (10), 205 (100), 189 (20); HRMS (ESI+) m/z 372.1377 calcd for $C_{21}H_{22}ClNO_3 + H^+$ 372.1366.

Benzyl (1-(4-bromophenyl)hept-2-yn-1-yl)(hydroxy)-carbamate (1e). According to general procedure A (on 0.5 mmol scale) and starting from 1-(4-bromophenyl)hept-2-yn-1-ol and benzyl hydroxycarbamate, 177.9 mg of compound **1e** (0.427 mmol, 86% yield) were obtained as a viscous colorless oil after purification by flash chromatography on silica gel (pentane/ethyl acetate 88/12): R_f (silica, pentane/ethyl acetate 9/1 = 0.25, UV/PMA); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.92 (t, J = 7.3 Hz, 3H), 1.37−1.57 (m, 4H), 2.28 (dt, J = 2.2 Hz and J = 7.1 Hz, 2H), 5.24 (s, 2H), 5.75 (brs, 1H), 6.04 (brs, 1H),7.31−7.41 (m, 7H), 7.46 (∼d, J = 8.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.6, 18.4, 22.0, 30.6, 55.3, 68.5, 74.1, 88.0, 122.3, 128.2, 128.5, 128.6, 129.7, 131.5, 135.3, 135.4, 157.2; IR (ATR, neat) ν (cm^{-1}) 3220, 2956, 2930, 2871, 2236, 1705, 1486, 1442, 1394, 1346, 1298, 1282, 1261, 1100, 1069, 1011, 954, 788, 745, 693, 672, 608; MS (ESI+) m/z 418 (90, $[M + H]^+$,^{81}Br), 416 (90, $[M + H]^+$,^{79}Br), 400 (98, ^{81}Br), 398 (100, ^{79}Br), 374 (35, ^{81}Br), 372 (35, ^{79}Br), 341 (30, ^{81}Br), 339 (30, ^{79}Br); HRMS (ESI+) m/z 416.0852 calcd for $C_{21}H_{22}BrNO_3 + H^+$ 416.0861.

Benzyl (1-([1,1′-biphenyl]-4-yl)hept-2-yn-1-yl)(hydroxy)-carbamate (1f). According to general procedure A (on 1 mmol scale) and starting from 1-(biphenyl-4-yl)hept-2-yn-1-ol and benzyl hydroxycarbamate, 288.0 mg of compound **1f** (0.696 mmol, 70% yield) were obtained as a viscous pale yellow oil after purification by flash chromatography on silica gel (pentane/ethyl acetate 9/1): R_f (silica, pentane/ethyl acetate 9/1 = 0.3, UV/PMA); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.99 (t, J = 7.2 Hz, 3H), 1.45−1.67 (m, 4H), 2.36 (dt, J = 2.0 Hz and J = 7.0 Hz, 2H), 5.26 (s, 2H), 6.23 (brs, 1H), 6.68 (brs, 1H), 7.31−7.52 (m, 8H), 7.58−7.70 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.5, 18.4, 21.9, 30.5, 55.4, 68.2, 74.7, 87.3, 126.9, 127.0, 127.3, 128.0, 128.2, 128.3, 128.4, 128.6, 135.4, 135.5, 140.5, 140.9, 157.2; IR (ATR, neat) ν (cm^{-1}) 3300, 2956, 2932, 2871, 1955, 1699, 1455, 1397, 1345, 1295, 1277, 1092, 1030, 797, 790, 777, 734, 695, 634; MS (ESI+) m/z 414 (10, $[M + H]^+$), 396 (25), 288 (15), 247 (100), 216 (10); HRMS (ESI+) m/z 414.2054 calcd for $C_{27}H_{27}NO_3 + H^+$ 414.2069.

Benzyl hydroxy(1-(*m*-tolyl)hept-2-yn-1-yl)carbamate (1g). According to general procedure A (on 1 mmol scale) and starting from 1-*m*-tolylhept-2-yn-1-ol and benzyl hydroxycarbamate, 291.3 mg of compound **1g** (0.829 mmol, 83% yield) were obtained as a yellow oil after purification by flash chromatography on silica gel (pentane/ethyl acetate 88/12): R_f (silica, pentane/ethyl acetate 85/15 = 0.4, UV/PMA); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.94 (t, J = 7.2 Hz, 3H), 1.39−1.60 (m, 4H), 2.30 (dt, J = 2.1 Hz and J = 7.0 Hz, 2H), 2.35 (s, 3H), 5.25 (s, 2H), 5.92 (brs, 1H), 6.10 (brs, 1H), 7.13 (∼d, J = 7.3 Hz, 1H), 7.21−7.25 (m, 1H), 7.31−7.43 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.6, 18.5, 21.5, 22.0, 30.7, 55.8, 68.4, 74.8, 87.5, 125.1, 128.2, 128.3, 128.4, 128.6, 128.7, 129.0, 135.7, 136.3, 138.1, 157.2; IR (ATR, neat) ν (cm^{-1}) 3302, 3033, 2956, 2931, 2871, 1702, 1455, 1404, 1350, 1281, 1092, 1029, 961, 753, 736, 719, 695; MS (ESI+) m/z 703 (5, $[2M + H]^+$), 536 (100), 519 (75), 492 (60), 459 (25), 369 (25), 352 (75, $[M + H]^+$), 334 (80), 308 (60), 275 (75), 216 (25); HRMS (ESI+) m/z 352.1909 calcd for $C_{22}H_{25}NO_3 + H^+$ 352.1913.

Benzyl hydroxy(1-(3-methoxyphenyl)hept-2-yn-1-yl)-carbamate (1h). According to general procedure A (on 2 mmol scale) and starting from 1-(3-methoxyphenyl)hept-2-yn-1-ol and benzyl hydroxycarbamate, 570.0 mg of compound **1h** (1.551 mmol, 78% yield) were obtained as an orange oil after purification by flash chromatography on silica gel (pentane/ethyl acetate 85/15): R_f (silica, pentane/ethyl acetate 85/15 = 0.3, UV/PMA); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.93 (t, J = 7.3 Hz, 3H), 1.39−1.60 (m, 4H), 2.29 (dt, J = 2.2 Hz and J = 7.0 Hz, 2H), 3.76 (s, 3H), 5.23 (s, 2H), 6.11 (t, J = 2.1 Hz, 1H), 6.33 (brs, 1H), 6.84 (ddd, J = 0.7 Hz, J = 2.4 Hz and J = 8.1 Hz, 1H), 7.10−7.15 (m, 2H), 7.25 (t, J = 8.1 Hz, 1H), 7.30−7.41 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.5, 18.4, 21.9, 30.6, 55.1, 55.6, 68.3, 74.7, 87.3, 113.5, 113.8, 120.2, 128.1, 128.2, 128.5, 129.3, 135.6, 137.9, 157.1, 159.5; IR (ATR, neat) ν (cm^{-1}) 3305, 2957, 2933, 2872, 1703, 1601, 1586, 1489, 1454, 1433, 1404, 1350, 1279, 1223, 1159, 1093, 1043, 755, 737, 719, 695, 639; MS (ESI+) m/z 568 (50), 401 (100), 368 (15, $[M + H]^+$), 350 (20), 291 (80), 201 (50); HRMS (ESI +) m/z 368.1854 calcd for $C_{22}H_{25}NO_4 + H^+$ 368.1862.

Benzyl (1-(3-bromophenyl)hept-2-yn-1-yl)(hydroxy)-carbamate (1i). According to general procedure A (on 2 mmol scale) and starting from 1-(3-bromophenyl)hept-2-yn-1-ol and benzyl hydroxycarbamate, 526.5 mg of compound **1i** (1.264 mmol, 64% yield) were obtained as an colorless oil after purification by flash chromatography on silica gel (pentane/ethyl acetate 9/1 → 85/15): R_f (silica, pentane/ethyl acetate 85/15 = 0.4, UV/PMA); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.93 (t, J = 7.3 Hz, 3H), 1.38−1.60 (m, 4H), 2.29 (dt, J = 2.2 Hz and J = 7.0 Hz, 2H), 5.26 (s, 2H), 5.67 (brs, 1H), 6.07 (t, J = 2.1 Hz, 1H), 7.19 (t, J = 7.9 Hz, 1H), 7.31−7.41 (m, 5H), 7.42−7.47 (m, 2H), 7.70 (t, J = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.6, 18.4, 22.0, 30.6, 55.4, 68.6, 73.9, 88.3, 122.5, 126.6, 128.2, 128.5, 128.6, 129.9, 131.1, 131.3, 135.5, 138.6, 157.1; IR (ATR, neat) ν (cm^{-1}) 3291, 3065, 2956, 2932, 2871, 1703, 1593, 1571, 1455, 1423, 1350, 1281, 1093, 745, 730, 695, 673, 633; MS (ESI+) m/z 418 (30, $[M + H]^+$,^{81}Br), 416 (30, $[M + H]^+$,^{79}Br), 251 (98, ^{81}Br), 249 (100, ^{79}Br); HRMS (ESI+) m/z 416.0852 calcd for $C_{21}H_{22}BrNO_3 + H^+$ 416.0861.

Benzyl hydroxy(1-(thiophen-2-yl)hept-2-yn-1-yl)carbamate (1j). According to general procedure A (on 3 mmol scale) and starting from 1-(thiophen-2-yl)hept-2-yn-1-ol and benzyl hydroxycarbamate, 886.0 mg of compound **1j** (2.580 mmol, 86% yield) were obtained as a yellow oil after purification by flash chromatography on silica gel (pentane/ethyl acetate 9/1): R_f (silica, pentane/ethyl acetate 85/15 = 0.45, UV/PMA); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.92 (t, J = 7.2

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Hz, 3H), 1.38−1.58 (m, 4H), 2.27 (dt, J = 2.2 Hz and J = 7.0 Hz, 2H), 5.24 (s, 2H), 6.00 (brs, 1H), 6.28 (brs, 1H), 6.95 (dd, J = 3.5 Hz and J = 5.1 Hz, 1H), 7.16 (td, J = 1.1 Hz and J = 3.5 Hz, 1H), 7.26 (td, J = 1.2 Hz and J = 5.2 Hz, 1H), 7.31−7.41 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.6, 18.4, 21.9, 30.5, 51.7, 68.5, 74.7, 86.7, 126.0, 126.6, 127.0, 128.2, 128.4, 128.5, 135.4, 139.8, 156.9; IR (ATR, neat) ν (cm^{-1}) 3307, 2955, 2928, 2869, 1646, 1444, 1395, 1345, 1296, 1254, 1092, 932, 912, 820, 756, 695; MS (ESI+) m/z 344 (10, $[M + H]^+$), 319 (25), 295 (15), 214 (15), 177 (100); HRMS (ESI+) m/z 344.1339 calcd for $C_{19}H_{21}NO_3S + H^+$ 344.1320.

Benzyl hydroxy(1-(naphthalen-2-yl)hept-2-yn-1-yl)-carbamate (1k). According to general procedure A (on 2 mmol scale) and starting from 1-(naphthalen-2-yl)hept-2-yn-1-ol and benzyl hydroxycarbamate, 706.0 mg of compound **1k** (1.822 mmol, 91% yield) were obtained as an orange oil after purification by flash chromatography on silica gel (pentane/ethyl acetate 9/1 → 85/15): R_f (silica, pentane/ethyl acetate 85/15 = 0.4, UV/PMA); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.95 (t, J = 7.3 Hz, 3H), 1.42−1.63 (m, 4H), 2.35 (dt, J = 2.2 Hz and J = 7.0 Hz, 2H), 5.28 (s, 2H), 5.62 (brs, 1H), 6.28 (brs, 1H), 7.31−7.44 (m, 5H), 7.46−7.52 (m, 2H), 7.59 (dd, J = 1.8 Hz and J = 8.5 Hz, 1H), 7.80−7.86 (m, 3H), 8.03 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.6, 18.5, 22.0, 30.7, 56.0, 68.5, 74.6, 87.9, 125.5, 126.2, 126.3, 127.3, 127.6, 128.1, 128.2, 128.4, 128.6, 133.1, 133.2, 133.7, 135.6, 157.2; IR (ATR, neat) ν (cm^{-1}) 3290, 3059, 2957, 2932, 2871, 1700, 1455, 1402, 1349, 1288, 1093, 808, 782, 739, 695; MS (ESI+) m/z 608 (90), 564 (50), 388 (10, $[M + H]^+$), 370 (30), 311 (100); HRMS (ESI+) m/z 388.1919 calcd for $C_{25}H_{25}NO_3 + H^+$ 388.1913.

Benzyl hydroxy(1-(naphthalen-1-yl)hept-2-yn-1-yl)-carbamate (1l). According to general procedure A (on 1 mmol scale) and starting from 1-(naphthalen-2-yl)hept-2-yn-1-ol and benzyl hydroxycarbamate, 237.0 mg of compound **1l** (0.613 mmol, 62% yield) were obtained as a brown oil after purification by flash chromatography on silica gel (pentane/ethyl acetate 9/1): R_f (silica, pentane/ethyl acetate 9/1 = 0.3, UV/PMA); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.95 (t, J = 7.3 Hz, 3H), 1.42−1.52 (m, 2H), 1.54−1.63 (m, 2H), 2.34 (dt, J = 2.0 Hz and J = 7.1 Hz, 2H), 5.23 (s, 2H), 5.73 (brs, 1H), 6.83 (brs, 1H), 7.32−7.43 (m, 5H), 7.44−7.52 (m, 3H), 7.81−7.87 (m, 2H), 8.02−8.08 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.6, 18.5, 22.0, 30.6, 53.3, 68.3, 74.7, 88.0, 123.0, 125.0, 125.7, 126.5, 127.9, 128.1, 128.3, 128.5, 128.7, 129.3, 130.6, 131.2, 133.7, 135.7, 157.0; IR (ATR, neat) ν (cm^{-1}) 3297, 2956, 2931, 2871, 1948, 1703, 1455, 1398, 1347, 1296, 1278, 1095, 797, 790, 778, 754, 737, 696; MS (ESI+) m/z 608 (10), 388 (5, $[M + H]^+$), 311 (20), 221 (100); HRMS (ESI+) m/z 388.1920 calcd for $C_{25}H_{25}NO_3 + H^+$ 388.1913.

Benzyl hydroxy(1-(*o*-tolyl)hept-2-yn-1-yl)carbamate (1m). According to general procedure A (on 1 mmol scale) and starting from 1-*o*-tolylhept-2-yn-1-ol and benzyl hydroxycarbamate, 243.5 mg of compound **1m** (0.692 mmol, 70% yield) were obtained as a viscous orange oil after purification by flash chromatography on silica gel (pentane/ethyl acetate 88/12): R_f (silica, pentane/ethyl acetate 85/15 = 0.4, UV/PMA); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.95 (t, J = 7.3 Hz, 3H), 1.40−1.60 (m, 4H), 2.30 (dt, J = 2.4 Hz and J = 7.2 Hz, 2H), 2.31 (s, 3H), 5.22 (s, 2H), 6.11 (brs, 1H), 6.22 (t, J = 2.0 Hz, 1H), 7.12−7.16 (m, 1H), 7.20−7.25 (m, 2H), 7.33−7.41 (m, 5H), 7.81−7.85 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.5, 18.4, 18.8, 21.9, 30.6, 53.3, 68.1, 74.9, 87.2, 125.7, 128.0, 128.2, 128.3, 128.4, 129.6, 130.2, 134.1, 135.7, 136.3, 157.1; IR (ATR, neat) ν (cm^{-1}) 3263, 3034, 2960, 2868, 1675, 1655, 1487, 1463, 1455, 1410, 1346, 1296, 1259, 1093, 1079, 1016, 946, 797, 744, 729, 695, 629; MS (ESI+) m/z 536 (70), 519 (25), 492 (45), 459 (15), 369 (25), 352 (75, $[M + H]^+$), 334 (20), 308 (50), 275 (100), 216 (30), 203 (30); HRMS (ESI+) m/z 352.1909 calcd for $C_{22}H_{25}NO_3 + H^+$ 352.1913.

Benzyl (1-(2-fluorophenyl)hept-2-yn-1-yl)(hydroxy)-carbamate (1n). According to general procedure A (on 2 mmol scale) and starting from 1-(2-fluorophenyl)hept-2-yn-1-ol and benzyl hydroxycarbamate, 495.0 mg of compound **1n** (1.393 mmol, 70% yield) were obtained as a white semisolid after purification by flash chromatography on silica gel (pentane/ethyl acetate 9/1 → 85/15): R_f (silica, pentane/ethyl acetate 85/15 = 0.4, UV/PMA); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.91 (t, J = 7.3 Hz, 3H, H_1), 1.36−1.58 (m, 4H, H_2 and H_3), 2.27 (dt, J = 2.1 Hz and J = 7.1 Hz, 2H, H_4), 5.22 (brs, 2H, H_{15}), 6.39 (brs, J = 2.1 Hz, 1H, H_7), 6.99−7.06 (m, 1H, H_{Ar}), 7.16 (dt, J = 1.0 Hz and J = 7.6 Hz, 1H, H_{Ar}), 7.28−7.42 (m, 6H, H_{Ar}), 7.78 (dt, J = 1.8 Hz and J = 7.6 Hz, 1H, H_{Ar}). ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −117.4; ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.5, 18.4, 21.9, 30.6, 49.8 (d, $^3J_{(C-F)}$ = 4.3 Hz), 68.4, 74.0, 87.4, 115.3 (d, $J_{ortho(C-F)}$ = 21.3 Hz), 123.6 (d, $^2J_{(C-F)}$ = 13.2 Hz), 123.8 (d, J = 3.6 Hz), 128.0, 128.2, 128.5, 130.2 (d, J = 8.4 Hz), 131.1 (d, $J_{para(C-F)}$ = 2.9 Hz), 135.7, 157.1, 160.1 (d, $J_{ipso(C-F)}$ = 249.4 Hz); IR (ATR, neat) ν (cm^{-1}) 3347, 2958, 2930, 2873, 1667, 1615, 1589, 1490, 1458, 1403, 1343, 1289, 1271, 1231, 1101, 1078, 952, 883, 753, 746, 698, 684, 626, 610; MS (ESI+) m/z 711 (35, $[2M + H]^+$), 544 (25), 500 (90), 356 (50, $[M + H]^+$), 189 (100); HRMS (ESI+) m/z 356.1645 calcd for $C_{21}H_{22}FNO_3 + H^+$ 356.1662.

Benzyl hydroxy(1-phenyl-3-(trimethylsilyl)prop-2-yn-1-yl)-carbamate (1o). According to general procedure A (on 4 mmol scale) and starting from 1-phenyl-3-(trimethylsilyl)prop-2-yn-1-ol and benzyl hydroxycarbamate, 1.230 g of compound **1o** (3.479 mmol, 87% yield) were obtained as a colorless oil after purification by flash chromatography on silica gel (pentane/ethyl acetate 85/15): R_f (silica, pentane/ethyl acetate 85/15 = 0.3, UV/PMA); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.22 (s, 9H), 5.25 (s, 2H), 5.73 (brs, 1H), 6.15 (s, 1H), 7.30−7.42 (m, 8H), 7.50−7.55 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) −0.1, 56.1, 68.5, 91.9, 99.7, 128.0, 128.2, 128.3, 128.4, 128.5, 128.6, 135.4, 135.5, 156.9; IR (ATR, neat) ν (cm^{-1}) 3276, 3063, 3032, 2959, 1704, 1494, 1455, 1388, 1346, 1286, 1249, 1093, 1046, 1025, 838, 760, 751, 741, 693, 662, 604; MS (ESI+) m/z 707 (15, $[2M + H]^+$), 540 (25), 354 (65, $[M + H]^+$), 187 (100); HRMS (ESI+) m/z 354.1528 calcd for $C_{20}H_{23}NO_3Si + H^+$ 354.1525.

Benzyl hydroxy(1-phenylbut-2-yn-1-yl)carbamate (1p). According to general procedure A (on 1 mmol scale) and starting from 1-phenylbut-2-yn-1-ol and benzyl hydroxycarbamate, 232.2 mg of compound **1p** (0.786 mmol, 79% yield) were obtained as a pale yellow oil after purification by flash chromatography on silica gel (pentane/ethyl acetate 9/1 → 88/12): R_f (silica, pentane/ethyl acetate 8/2 = 0.4, UV/PMA); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.92 (d, J = 2.4 Hz, 3H), 5.24 (s, 2H), 5.99 (brs, 1H), 6.10 (q, J = 2.0 Hz, 1H), 7.28−7.41 (m, 8H), 7.50 − 7.55 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 3.7, 55.6, 68.4, 73.9, 82.9, 127.9, 128.1, 128.2, 128.4, 128.5, 135.6, 136.2, 157.1; IR (ATR, neat) ν (cm^{-1}) 3297, 3065, 3033, 2921, 2251, 1955, 1699, 1496, 1452, 1403, 1350, 1283, 1093, 907, 727, 707, 695; MS (ESI+) m/z 591 (15, $[2M + H]^+$), 424 (10), 380 (100), 296 (70, $[M + H]^+$), 278 (90), 252 (15), 234 (50), 219 (40), 129 (20); HRMS (ESI+) m/z 296.1282 calcd for $C_{18}H_{17}NO_3 + H^+$ 296.1287.

Benzyl hydroxy(4-methyl-1-phenylpent-2-yn-1-yl)-carbamate (1q). According to general procedure A (on 0.5 mmol scale) and starting from 4-methyl-1-phenylpent-2-yn-1-ol and benzyl hydroxycarbamate, 140.8 mg of compound **1q** (0.436 mmol, 88% yield) were obtained as a pale yellow solid after purification by flash chromatography on silica gel (pentane/ethyl acetate 9/1 → 88/12): R_f (silica, pentane/ethyl acetate 9/1 = 0.25, UV/PMA); mp 78−79 °C (Et_2O/pentane); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.21 (d, J = 6.9 Hz, 3H), 1.22 (d, J = 6.9 Hz, 3H), 2.66 (septd, J = 2.0 Hz and J = 6.8 Hz, 1H), 5.26 (s, 2H), 5.60 (brs, 1H), 6.13 (d, J = 1.8 Hz, 1H), 7.28−7.42 (m, 8H), 7.50−7.55 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 20.6, 22.9, 55.7, 68.4, 73.7, 93.0, 127.9, 128.1, 128.2, 128.4, 128.5, 135.6, 136.2, 157.1; IR (ATR, neat) ν (cm^{-1}) 3300, 2967, 2927, 2877, 2255, 1967, 1888, 1754, 1655, 1495, 1448, 1415, 1349, 1288, 1099, 1030, 956, 883, 752, 739, 698, 634; MS (ESI+) m/z 647 (10, $[2M + H]^+$), 491 (10), 480 (20), 436 (100), 324 (98, $[M + H]^+$), 306 (25), 247 (25), 157 (20); HRMS (ESI+) m/z 324.1592 calcd for $C_{20}H_{21}NO_3 + H^+$ 324.1600.

Benzyl hydroxy(4,4-dimethyl-1-phenylpent-2-yn-1-yl)-carbamate (1r). According to general procedure A (on 0.5 mmol scale) and starting from 4,4-dimethyl-1-phenylpent-2-yn-1-ol and benzyl hydroxycarbamate, 148.7 mg of compound **1r** (0.441 mmol, 89% yield) were obtained as a pale yellow solid after purification by flash chromatography on silica gel (pentane/ethyl acetate 88/12): R_f (silica, pentane/ethyl acetate 9/1 = 0.25, UV/PMA); mp 100−102 °C (Et_2O/pentane); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.27 (s, 9H), 5.26 (s, 2H), 5.59 (brs, 1H), 6.12 (s, 1H), 7.28−7.42 (m, 8H), 7.50−7.54 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 27.6, 30.9, 55.7, 68.3, 72.9,

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95.9, 127.9, 128.1, 128.2, 128.4, 128.6, 135.6, 136.3, 157.1; IR (ATR, neat) ν (cm^{-1}) 3268, 2965, 2925, 2250, 1950, 1798, 1697, 1455, 1388, 1348, 1291, 1267, 1213, 1093, 1026, 910, 825, 741, 761, 693, 676, 627; MS (ESI+) m/z 675 (5, $[2M + H]^+$), 508 (35), 464 (20), 338 (100, $[M + H]^+$), 320 (20), 261 (25), 171 (15); HRMS (ESI+) m/z 338.1741 calcd for $C_{21}H_{23}NO_3 + H^+$ 338.1756.

Benzyl (1,3-diphenylprop-2-yn-1-yl)(hydroxy)carbamate (1s). According to general procedure A (on 1 mmol scale) and starting from 1,3-diphenylprop-2-yn-1-ol and benzyl hydroxycarbamate, 259.7 mg of compound **1s** (0.727 mmol, 73% yield) were obtained as a white solid after purification by flash chromatography on silica gel (pentane/ethyl acetate 88/12): R_f (silica, pentane/ethyl acetate 9/1 = 0.3, UV/PMA); mp 115−117 °C (Et_2O/Pentane); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 5.28 (s, 2H), 5.73 (brs, 1H), 6.37 (s, 1H), 7.29−7.43 (m, 11H), 7.47−7.51 (m, 2H), 7.58−7.63 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 56.1, 68.5, 83.9, 86.6, 122.2, 128.0, 128.2, 128.3, 128.4, 128.5, 128.55, 128.6, 128.7, 131.9, 135.5, 135.7, 157.1; IR (ATR, neat) ν (cm^{-1}) 3298, 3063, 3033, 2949, 2233, 1955, 1702, 1490, 1454, 1443, 1406, 1351, 1285, 1268, 1098, 1028, 756, 707, 692; MS (ESI+) m/z 732 (15), 548 (10), 504 (10), 375 (20), 358 (20, $[M + H]^+$), 296 (10), 214 (10), 191 (100), 171 (15), 102 (25); HRMS (ESI+) m/z 358.1432 calcd for $C_{23}H_{19}NO_3 + H^+$ 358.1443.

Benzyl hydroxy(1-phenyl-3-(*p*-tolyl)prop-2-yn-1-yl)-carbamate (1t). According to general procedure A (on 4 mmol scale) and starting from 1-phenyl-3-(*p*-tolyl)prop-2-yn-1-ol and benzyl hydroxycarbamate, 1.080 g of compound **1t** (2.907 mmol, 73% yield) were obtained as a yellow oil after purification by flash chromatography on silica gel (pentane/ethyl acetate 85/15): R_f (silica, pentane/ethyl acetate 85/15 = 0.3, UV/PMA); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 2.36 (s, 3H) 5.27 (s, 2H), 5.88 (brs, 1H), 6.36 (s, 1H), 7.13 (d, J = 7.6 Hz, 2H), 7.31−7.43 (m, 10H), 7.13 (d, J = 6.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 21.5, 56.1, 68.5, 83.2, 86.7, 119.1, 128.0, 128.2, 128.4, 128.5, 128.6, 129.0, 131.8, 135.6, 135.9, 138.8, 157.1; IR (ATR, neat) ν (cm^{-1}) 3287, 2921, 1698, 1509, 1452, 1404, 1265, 1094, 816, 731, 695; MS (ESI+) m/z 576 (25), 532 (10), 372 (50, $[M + H]^+$), 354 (35), 288 (25), 221 (15), 209 (30), 205 (100); HRMS (ESI+) m/z 372.1609 calcd for $C_{24}H_{21}NO_3 + H^+$ 372.1600.

Benzyl hydroxy(4-phenylbut-3-yn-2-yl)carbamate (1v). A 100 mL round-bottom flask charged with benzyl (*tert*-butyldimethylsilyl)-oxycarbamate[26] (1.27 g, 4.52 mmol, 1.1 equiv), THF (20 mL), PPh_3 (1.19 g, 4.52 mmol, 1.1 equiv) and DIAD (1.02 mL, 5.15 mmol, 1.25 equiv) was cooled to 0 °C, and a solution of 4-phenylbut-3-yn-2-ol (603 mg, 4.12 mmol, 1 equiv) in THF (15 mL) was added dropwise. Then, the reaction was allowed to warm to ambient temperature and stirred for 2 h. Upon completion, the reaction was concentrated in vacuo and purified by flash chromatography on silica gel (Pentane/Et_2O 98/2), which afforded 1.01 g of benzyl (*tert*-butyldimethylsilyl)oxy(4-phenylbut-3-yn-2-yl)carbamate with the unseparable DIAD excess (~20% by ^1H NMR). The product was used as such in the next step: R_f (silica, Pentane/Et_2O 9/1 = 0.8, UV/PMA/$KMnO_4$).

To a solution of benzyl (*tert*-butyldimethylsilyl)oxy(4-phenylbut-3-yn-2-yl)carbamate (1.01 g, 2.47 mmol) in dry THF (12.5 mL) was added TBAF (1 M in THF, 2.5 mL, 2.5 mmol, 1.01 equiv) at 0 °C. After 5 min the mixture was quenched with saturated NH_4Cl solution (10 mL) and diluted with ether (20 mL). The organic layer was washed with water (20 mL) and brine (20 mL), dried over $MgSO_4$, and evaporated, and the crude was further purified by column chromatography on silica (Pentane/Ethyl acetate 8/2) to give 619 mg of the title compound **1v** (2.09 mmol, 51% yield over 2 steps) as a white solid after purification by flash chromatography on silica gel (pentane/ethyl acetate 85/15): R_f (silica, pentane/ethyl acetate 8/2 = 0.3, UV/PMA); mp 90−91 °C (Et_2O/pentane); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.57 (d, J = 7.2 Hz, 3H, H_1), 5.15−5.25 (m, 3H, H_2 and H_{11}), 6.82 (brs, 1H, H_3), 7.25−7.44 (m, 10H, H_{Ar}); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 18.8, 48.2, 68.3, 83.5, 86.7, 122.4, 128.1, 128.0, 128.1, 128.2, 128.3, 128.5, 131.8, 135.6, 157.2; IR (ATR, neat) ν (cm^{-1}) 3279, 2985, 2939, 1954, 1698, 1489, 1454, 1443, 1402, 1353, 1289, 1114, 1068, 753, 690; MS (ESI+) m/z 591 (30, $[2M + H]^+$), 419 (25), 296 (100, $[M + H]^+$), 252 (25), 234 (40), 193 (40); HRMS (ESI+) m/z 296.1276 calcd for $C_{18}H_{17}NO_3 + H^+$ 296.1287.

Benzyl hydroxy(2-methyldec-5-yn-4-yl)carbamate (1w). An anhydrous and purged with N_2 10 mL round-bottom flask equipped with a magnetic stirrer bar was charged with dry THF (1 mL) and 1-hexyne (0.23 mL, 2 mmol, 4 equiv), and the resulting solution was cooled at −78 °C. *n*-Butyllithium (1.6 M in hexanes, 1.25 mL, 2 mmol, 4 equiv) was then added dropwise, and after 10 min, a solution of benzyl hydroxy(3-methyl-1-(phenylsulfonyl)butyl)carbamate (189 mg, 0.5 mmol, 1 equiv) in dry THF (1 mL) was added via syringe. The resulting mixture was stirred 30 min at −78 °C and then allowed to run at 0 °C for 2 h. A saturated aqueous NH_4Cl (2 mL) was then added, and the solution was allowed to reach room temperature. The reaction mixture was then extracted with ethyl acetate (2 × 10 mL), and the combined organic layers were washed with brine (5 mL), dried over anhydrous $MgSO_4$ and filtered. After the removal of the solvent, the crude mixture was purified by column chromatography (Pentane/Ethyl acetate 95/5) to give 4 mg of the title compound **1w** (0.013 mmol, 3% yield) as a white solid after purification by flash chromatography on silica gel (pentane/ethyl acetate 95/5): R_f (silica, pentane/ethyl acetate 85/15 = 0.7, UV/PMA); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.86−0.94 (m, 9H), 1.32−1.77 (m, 7H), 2.17 (dt, J = 2.0 Hz and J = 7.0 Hz, 2H), 4.87 (tt, J = 2.0 Hz and J = 7.6 Hz, 1H), 5.22 (s, 2H), 5.59 (brs, 1H), 7.30−7.42 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.6, 18.3, 21.9, 22.2, 22.3, 24.8, 30.7, 41.5, 50.9, 68.2, 73.4, 85.2, 128.1, 128.3, 128.5, 135.7, 157.3; IR (ATR, neat) ν (cm^{-1}) 3254, 2959, 2932, 2871, 1970, 1704, 1456, 1305, 1260, 1091, 1021, 798; MS (ESI+) m/z 635 (25, $[2M + H]^+$), 608 (25), 410 (25), 359 (15), 324 (15), 318 (100, $[M + H]^+$), 288 (65), 241 (20), 210 (35), 209 (25); HRMS (ESI+) m/z 318.2064 calcd for $C_{19}H_{27}NO_3 + H^+$ 318.2069.

(*Z*)-Benzyl (3-oxo-1-phenylhept-1-en-1-yl)carbamate (2a). According to general procedure B (on 0.2 mmol scale) and starting from benzyl hydroxy(1-phenylhept-2-yn-1-yl)carbamate **1a**, 57.3 mg of compound **2a** (0.170 mmol, 86% yield) were obtained as a pale yellow oil after purification by flash chromatography on silica gel (pentane/Et_2O 92/8): R_f (silica, pentane/Et_2O 9/1 = 0.35, UV/Vanillin); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.92 (t, J = 7.2 Hz, 3H), 1.29−1.41 (m, 2H), 1.55−1.67 (m, 2H), 2.47 (t, J = 7.0 Hz, 2H), 5.07 (s, 2H), 5.57 (s, 1H), 7.28−7.46 (m, 10H), 11.58 (brs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.9, 22.4, 26.9, 43.5, 67.4, 107.2, 127.5, 128.0, 128.3, 128.4, 128.5, 129.8, 135.5, 135.6, 152.8, 154.5, 202.6; IR (ATR, neat) ν (cm^{-1}) 2958, 2928, 2870, 1750, 1642, 1589, 1573, 1495, 1473, 1280, 1195, 1119, 1047, 765, 750, 694; MS (ESI+) m/z 675 (5, $[2M + H]^+$), 505 (10), 338 (100, $[M + H]^+$), 320 (15), 294 (10); HRMS (ESI+) m/z 338.1747 calcd for $C_{21}H_{23}NO_3 + H^+$ 338.1756.

(*E*)-Benzyl (1-phenylhept-2-yn-1-ylidene)carbamate (3a). According to the gram-scale procedure for the preparation of (*Z*)-benzyl (3-oxo-1-phenylhept-1-en-1-yl)carbamate **2a**, 70 mg of compound **3a** (0.21 mmol, 4% yield) were isolated as a minor product: R_f (silica, Pentane/Et_2O 9/1 = 0.45, UV/PMA); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.93 (t, J= 7.2 Hz, 3H), 1.38−1.60 (m, 4H), 2.36 (t, J= 7.2 Hz, 2H), 5.33 (s, 2H), 7.30−7.55 (m, 8H), 8.08 (~d, J = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.5, 19.0, 21.9, 29.8, 68.2, 74.1, 103.4, 128.3, 128.4, 128.5, 132.4, 135.0, 135.6, 153.6, 163.1; IR (ATR, neat) ν (cm^{-1}) 3066, 3033, 2972, 2929, 2868, 2218, 1724, 1597, 1571, 1450, 1318, 1295, 1258, 1203, 1176, 906, 690; MS (ESI+) m/z 320 (100, $[M + H]^+$), 276 (30), 187 (15); HRMS (ESI+) m/z 320.1649 calcd for $C_{21}H_{21}NO_2 + H^+$ 320.1651.

(*Z*)-Benzyl (3-oxo-1-(*p*-tolyl)hept-1-en-1-yl)carbamate (2b). According to general procedure B (on 0.1 mmol scale) and starting from benzyl (1-(*p*-tolyl)hept-2-yn-1-yl)(hydroxy)carbamate **1b**, 27.7 mg of compound **2b** (0.0788 mmol, 90% yield) were obtained as a pale yellow oil after purification by flash chromatography on silica gel (pentane/Et_2O 92/8): R_f (silica, pentane/Et_2O 9/1 = 0.35, UV/Vanillin); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.92 (t, J = 7.2 Hz, 3H), 1.30−1.41 (m, 2H), 1.56−1.66 (m, 2H), 2.38 (s, 3H), 2.46 (t, J = 7.0 Hz, 2H), 5.08 (s, 2H), 5.57 (s, 1H), 7.19 (~d, J = 8 Hz, 2H), 7.28−7.37 (m, 7H), 11.58 (brs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.9, 21.4, 22.4, 26.8, 43.4, 67.3, 106.8, 127.4, 128.2, 128.4, 128.7, 132.6, 135.5, 140.0, 152.8, 154.5, 202.4; IR (ATR, neat) ν (cm^{-1}) 3032, 2957, 2930, 2871, 1956, 1905, 1750, 1641, 1589, 1567, 1474, 1455,

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1286, 1195, 1136, 1047, 810, 764, 754, 696; MS (ESI+) m/z 703 (5, [2M + H]$^+$), 352 (100, [M + H]$^+$), 334 (55), 308 (10), 210 (10), 154 (10); HRMS (ESI+) m/z 352.1913 calcd for $C_{22}H_{25}NO_3$ + H$^+$ 352.1913.

(*Z*)-Benzyl (1-(4-fluorophenyl)-3-oxohept-1-en-1-yl)-carbamate (2c). According to general procedure B (on 0.2 mmol scale) and starting from benzyl (1-(4-fluorophenyl)hept-2-yn-1-yl)-(hydroxy)carbamate **1c**, 48.0 mg of compound **2c** (0.135 mmol, 71% yield) were obtained as a red oil after purification by flash chromatography on silica gel (pentane/Et_2O 92/8): R_f (silica, pentane/Et_2O 9/1 = 0.4, UV/Vanillin); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.93 (t, J = 7.2 Hz, 3H), 1.31−1.41 (m, 2H), 1.58−1.66 (m, 2H), 2.47 (t, J = 7.6 Hz, 2H), 5.08 (s, 2H), 5.54 (s, 1H), 7.19 (∼t, J = 8.4 Hz, 2H), 7.29−7.42 (m, 7H), 11.58 (brs, 1H, NH). ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −110.6; ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.9, 22.4, 26.8, 43.5, 67.3, 107.2, 115.2 (d, $J_{ortho(C-F)}$ = 22.0 Hz), 128.3, 128.4, 128.6, 129.5 (d, $J_{meta(C-F)}$ = 8.4 Hz), 131.5 (d, $J_{para(C-F)}$ = 3.4 Hz), 135.4, 152.9, 153.3, 163.6 (d, $J_{ipso(C-F)}$ = 249.9 Hz), 202.5; IR (ATR, neat) ν (cm^{-1}) 2958, 2930, 2872, 1748, 1644, 1604, 1582, 1507, 1473, 1455, 1286, 1192, 1157, 1134, 1074, 1044, 839, 763, 731, 695; MS (ESI+) m/z 356 (100, [M + H]$^+$), 338 (15), 312 (20); HRMS (ESI+) m/z 356.1669 calcd for $C_{21}H_{22}FNO_3$ + H$^+$ 356.1662.

(*Z*)-Benzyl (1-(4-chlorophenyl)-3-oxohept-1-en-1-yl)-carbamate (2d). According to general procedure B (on 0.1 mmol scale) and starting from benzyl (1-(4-chlorophenyl)hept-2-yn-1-yl)-(hydroxy)carbamate **1d**, 29.5 mg of compound **2d** (0.794 mmol, 80% yield) were obtained as a yellow oil after purification by flash chromatography on silica gel (pentane/Et_2O 92/8): R_f (silica, pentane/Et_2O 9/1 = 0.4, UV/Vanillin); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.92 (t, J = 7.3 Hz, 3H), 1.30−1.40 (m, 2H), 1.56−1.66 (m, 2H), 2.47 (t, J = 7.2 Hz, 2H), 5.07 (s, 2H), 5.54 (s, 1H), 7.28−7.38 (m, 9H), 11.54 (brs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.9, 22.4, 26.7, 43.5, 67.5, 107.2, 128.3, 128.4, 128.5, 128.8, 134.0, 135.3, 135.8, 152.8, 153.0, 202.5; IR (ATR, neat) ν (cm^{-1}) 3066, 3034, 2957, 2930, 2872, 1748, 1644, 1598, 1585, 1490, 1471, 1281, 1193, 1135, 1073, 1045, 1013, 908, 815, 729, 695; MS (ESI+) m/z 743 (5, [2M + H]$^+$), 372 (100, [M + H]$^+$), 328 (15); HRMS (ESI+) m/z 372.1364 calcd for $C_{21}H_{22}ClNO_3$ + H$^+$ 372.1366.

(*Z*)-Benzyl (1-(4-bromophenyl)-3-oxohept-1-en-1-yl)-carbamate (2e). According to general procedure B (on 0.1 mmol scale) and starting from benzyl (1-(4-bromophenyl)hept-2-yn-1-yl)(hydroxy)carbamate **1e**, 36.1 mg of compound **2e** (0.867 mmol, 87% yield) were obtained as a red oil after purification by flash chromatography on silica gel (pentane/Et_2O 92/8): R_f (silica, Pentane/Et_2O 9/1 = 0.4, UV/Vanillin); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.92 (t, J = 7.3 Hz, 3H), 1.29−1.40 (m, 2H), 1.54−1.65 (m, 2H), 2.47 (t, J = 7.6 Hz, 2H), 5.07 (s, 2H), 5.53 (s, 1H), 7.26 (∼d, J = 8.4 Hz, 2H), 7.28−7.37 (m, 5H), 7.50 (∼d, J = 8.4 Hz, 2H), 11.53 (brs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.9, 22.4, 26.8, 43.5, 67.6, 107.3, 124.2, 128.3, 128.4, 128.6, 129.1, 131.3, 134.5, 135.3, 152.8, 153.1, 202.5; IR (ATR, neat) ν (cm^{-1}) 3020, 2958, 2930, 2872, 1746, 1596, 1582, 1561, 1489, 1472, 1281, 1194, 1137, 1067, 1047, 1010, 746, 695, 666; MS (ESI+) m/z 418 (97, [M + H]$^+$,^{81}Br), 416 (100, [M + H]$^+$,^{79}Br); HRMS (ESI+) m/z 416.0844 calcd for $C_{21}H_{22}BrNO_3$ + H$^+$ 416.0861.

(*Z*)-Benzyl (1-([1,1′-biphenyl]-4-yl)-3-oxohept-1-en-1-yl)-carbamate (2f). According to general procedure B (on 0.2 mmol scale) and starting from benzyl (1-([1,1′-biphenyl]-4-yl)hept-2-yn-1-yl)(hydroxy)carbamate **1f**, 49.8 mg of compound **2f** (0.120 mmol, 61% yield) were obtained as a pale yellow oil after purification by flash chromatography on silica gel (pentane/Et_2O 92/8): R_f (silica, pentane/Et_2O 9/1 = 0.4, UV/Vanillin); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.95 (t, J = 7.2 Hz, 3H), 1.32−1.44 (m, 2H), 1.58−1.70 (m, 2H), 2.50 (t, J = 7.2 Hz, 2H), 5.11 (s, 2H), 5.65 (s, 1H), 7.30−7.41 (m, 6H), 7.44−7.52 (m, 4H), 7.60−7.65 (m, 4H), 11.62 (brs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.9, 22.4, 26.8, 43.4, 67.4, 107.2, 126.7, 127.1, 127.6, 128.0, 128.2, 128.3, 128.5, 128.8, 134.4, 135.4, 140.3, 142.6, 152.9, 154.0, 202.4; IR (ATR, neat) ν (cm^{-1}) 3062, 3032, 2956, 2930, 2871, 1748, 1587, 1578, 1472, 1280, 1192, 1134, 1075, 1047, 908, 763, 752, 730, 694; MS (ESI+) m/z 414 (100, [M + H]$^+$), 288 (10), 252 (10), 216 (25), 203 (5); HRMS (ESI+) m/z 414.2065 calcd for $C_{27}H_{27}NO_3$ + H$^+$ 414.2069.

(*Z*)-Benzyl (3-oxo-1-(*m*-tolyl)hept-1-en-1-yl)carbamate (2g). According to general procedure B (on 0.4 mmol scale) and starting from benzyl (1-(*m*-tolyl)hept-2-yn-1-yl)(hydroxy)carbamate **1g**, 103.5 mg of compound **2g** (0.295 mmol, 74% yield) were obtained as a yellow oil after purification by flash chromatography on silica gel (pentane/Et_2O 92/8): R_f (silica, pentane/Et_2O 9/1 = 0.4, UV/Vanillin); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.91 (t, J = 7.3 Hz, 3H), 1.29−1.39 (m, 2H), 1.56−1.65 (m, 2H), 2.36 (s, 3H), 2.45 (t, J = 7.2 Hz, 2H), 5.06 (s, 2H), 5.55 (s, 1H), 7.16−7.36 (m, 9H), 11.56 (brs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.8, 21.3, 22.3, 26.7, 43.3, 67.3, 107.0, 124.6, 127.8, 127.9, 128.1, 128.2, 128.4, 130.5, 135.4, 135.5, 137.6, 152.7, 154.5, 202.4; IR (ATR, neat) ν (cm^{-1}) 3033, 2957, 2929, 2871, 1750, 1642, 1576, 1472, 1455, 1288, 1204, 1188, 1135, 1049, 786, 763, 754, 733, 695; MS (ESI+) m/z 352 (100, [M + H]$^+$), 308 (10); HRMS (ESI+) m/z 352.1929 calcd for $C_{22}H_{25}NO_3$ + H$^+$ 352.1913.

(*Z*)-Benzyl (1-(3-methoxyphenyl)-3-oxohept-1-en-1-yl)-carbamate (2h). According to general procedure B (on 0.4 mmol scale) and starting from benzyl (1-(3-methoxyphenyl)hept-2-yn-1-yl)(hydroxy)carbamate **1h**, 96.5 mg of compound **2h** (0.263 mmol, 66% yield) were obtained as a pale yellow oil after purification by flash chromatography on silica gel (pentane/Et_2O 92/8): R_f (silica, pentane/Et_2O 9/1 = 0.3, UV/Vanillin); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.94 (t, J = 7.2 Hz, 3H), 1.32−1.43 (m, 2H), 1.58−1.68 (m, 2H), 2.48 (t, J = 7.2 Hz, 2H), 3.81 (s, 3H), 5.09 (s, 2H), 5.60 (s, 1H), 6.92−7.46 (m, 3H), 7.28−7.39 (m, 6H), 11.55 (brs, 1H, NH). ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −114.1; ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.8, 22.3, 26.7, 43.4, 55.2, 67.3, 107.0, 113.1, 115.1, 119.8, 128.2, 128.4, 128.9, 135.4, 136.9, 152.6, 154.0, 159.1, 202.4; IR (ATR, neat) ν (cm^{-1}) 3066, 3033, 2957, 2932, 1749, 1644, 1574, 1464, 1287, 1223, 1191, 1134, 1039, 880, 785, 755, 733, 695; MS (ESI+) m/z 368 (100, [M + H]$^+$), 324 (20); HRMS (ESI+) m/z 368.1855 calcd for $C_{22}H_{25}NO_4$ + H$^+$ 368.1862.

(*Z*)-Benzyl (1-(3-bromophenyl)-3-oxohept-1-en-1-yl)-carbamate (2i). According to general procedure B (on 0.4 mmol scale) and starting from benzyl (1-(3-bromophenyl)hept-2-yn-1-yl)(hydroxy)carbamate **1i**, 86.0 mg of compound **2i** (0.206 mmol, 52% yield) were obtained as a pale yellow oil after purification by flash chromatography on silica gel (petroleum ether/Et_2O 92/8): R_f (silica, pentane/Et_2O 9/1 = 0.4, UV/Vanillin); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.93 (t, J = 7.3 Hz, 3H), 1.31−1.42 (m, 2H), 1.57−1.68 (m, 2H), 2.48 (t, J = 7.2 Hz, 2H), 5.08 (s, 2H), 5.54 (s, 1H), 7.21−7.27 (m, 1H), 7.28−7.49 (m, 6H), 7.52−7.56 (m, 2H), 11.51 (brs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.8, 22.3, 26.6, 43.4, 67.5, 107.4, 122.0, 126.2, 128.2, 128.3, 128.4, 129.3, 130.2, 132.5, 135.3, 137.6, 152.4, 152.6, 202.4; IR (ATR, neat) ν (cm^{-1}) 3065, 3034, 2957, 2930, 2871, 1748, 1582, 1600, 1558, 1479, 1463, 1280, 1192, 1131, 1046, 909, 785, 729, 694; MS (ESI+) m/z 418 (97, [M + H]$^+$,^{81}Br), 416 (100, [M + H]$^+$,^{79}Br), 148 (45); HRMS (ESI+) m/z 416.0860 calcd for $C_{21}H_{22}BrNO_3$ + H$^+$ 416.0861.

(*Z*)-Benzyl (3-oxo-1-(thiophen-2-yl)hept-1-en-1-yl)-carbamate (2j). According to general procedure B (on 1 mmol scale) and starting from benzyl hydroxy(1-(thiophen-2-yl)hept-2-yn-1-yl)carbamate **1j**, 155.0 mg of compound **2j** (0.451 mmol, 45% yield) were obtained as a red oil after purification by flash chromatography on silica gel (petroleum ether/Et_2O 92/8): R_f (silica, Pentane/Et_2O 9/1 = 0.4, UV/Vanillin); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.94 (t, J = 7.3 Hz, 3H), 1.32−1.42 (m, 2H), 1.58−1.67 (m, 2H), 2.48 (t, J = 7.6 Hz, 2H), 5.13 (s, 2H), 5.78 (s, 1H), 7.06 (dd, J = 3.7 Hz and J = 5.0 Hz, 1H), 7.33 (td, J = 1.2 Hz and J = 3.7 Hz, 1H), 7.34−7.38 (m, 5H), 7.42 (dd, J = 1.2 Hz and J = 5.0 Hz, 1H), 11.45 (brs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.8, 22.3, 26.7, 43.4, 67.4, 107.2, 127.2, 128.0, 128.2, 128.3, 128.4, 129.2, 135.4, 136.5, 146.9, 152.8, 202.2; IR (ATR, neat) ν (cm^{-1}) 2957, 2930, 1749, 1639, 1582, 1464, 1455, 1191, 1267, 1191, 1134, 1109, 694; MS (ESI+) m/z 344 (100, [M + H]$^+$), 300 (30); HRMS (ESI+) m/z 344.1313 calcd for $C_{19}H_{21}NO_3S$ + H$^+$ 344.1320.

(*Z*)-Benzyl (1-(naphthalen-2-yl)-3-oxohept-1-en-1-yl)-carbamate (2k). According to general procedure B (on 0.4 mmol scale) and starting from benzyl (1-(naphthalen-2-yl)hept-2-yn-1-

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yl)(hydroxy)carbamate **1k**, 87.1 mg of compound **2k** (0.225 mmol, 58% yield) were obtained as a pale yellow oil after purification by flash chromatography on silica gel (petroleum ether/Et_2O 92/8): R_f (silica, Pentane/Et_2O 9/1 = 0.4, UV/PMA/Vanillin); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.98 (t, J = 7.6 Hz, 3H, H_1), 1.36−1.47 (m, 2H, H_2), 1.64−1.73 (m, 2H, H_3), 2.53 (t, J = 7.2 Hz, 2H, H_4), 5.11 (s, 2H, H_{18}), 5.72 (s, 1H, H_6), 7.28−7.36 (m, 5H, H_{Ar}), 7.48−7.58 (m, 3H, H_{Ar}), 7.81−7.95 (m, 4H, H_{Ar}), 11.71 (brs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.8 (C_1), 22.3 (C_2), 26.7 (C_3), 43.4 (C_4), 67.4 (C_{18}), 107.4 (C_6), 125.1 (C_{Ar}), 126.4 (C_{Ar}), 126.7 (C_{Ar}), 126.9 (C_{Ar}), 127.3 (C_{Ar}), 127.7 (C_{Ar}), 128.1 (C_{Ar}), 128.2 (C_{Ar}), 128.3 (2C, C_{Ar}), 128.4 (2C, C_{Ar}), 132.7 (C_q, C_{Ar}), 133.2 (C_q, C_{Ar}), 133.8 (C_q, C_{Ar}), 135.4 (C_q, C_{Ar}), 152.8 (C_q, C_{Ar}), 154.3 (C_q, C_{Ar}), 202.4 (C_5); IR (ATR, neat) ν (cm^{-1}) 3060, 2958, 2931, 2872, 1747, 1641, 1584, 1478, 1463, 1361, 1284, 1191, 1135, 1109, 1047, 906, 814, 726, 695, 646; MS (ESI+) m/z 388 (100, $[M + H]^+$), 370 (20), 148 (20); HRMS (ESI+) m/z 388.1920 calcd for $C_{25}H_{25}NO_3 + H^+$ 388.1913.

(*Z*)-Benzyl (1-(naphthalen-1-yl)-3-oxohept-1-en-1-yl)-carbamate (2l). According to general procedure B (on 0.2 mmol scale) and starting from benzyl (1-(naphthalen-1-yl)hept-2-yn-1-yl)(hydroxy)carbamate **1l**, 18.5 mg of compound **2l** (0.048 mmol, 29% yield) were obtained as a pale yellow oil after purification by flash chromatography on silica gel (pentane/Et_2O 92/8): R_f (silica, Pentane/Et_2O 9/1 = 0.4, UV/PMA/Vanillin); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.93 (t, J = 7.2 Hz, 3H), 1.32−1.44 (m, 2H), 1.60−1.68 (m, 2H), 2.48 (t, J = 7.2 Hz, 2H), 4.92 (s, 2H), 5.59 (s, 1H), 7.15−7.21 (m, 2H), 7.27−7.32 (m, 3H), 7.40 (dd, J = 1.1 Hz and J = 7.1 Hz, 1H), 7.45−7.54 (m, 3H), 7.81−7.94 (m, 3H), 12.05 (brs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.9, 22.4, 26.8, 43.4, 67.3, 107.0, 124.4, 124.9, 125.3, 126.0, 126.7, 128.1, 128.2, 128.4, 128.5, 129.4, 131.0, 132.9, 133.7, 135.3, 152.0, 153.4, 202.9; IR (ATR, neat) ν (cm^{-1}) 3062, 2957, 2930, 2871, 1754, 1642, 1591, 1575, 1477, 1286, 1200, 1179, 1140, 1092, 801, 776, 697; MS (ESI+) m/z 388 (100, $[M + H]^+$), 344 (10), 320 (15), 288 (25), 214 (10), 187 (10); HRMS (ESI+) m/z 388.1920 calcd for $C_{25}H_{25}NO_3 + H^+$ 388.1913.

(*Z*)-Benzyl (1-(2-fluorophenyl)-3-oxohept-1-en-1-yl)-carbamate (2n). According to general procedure B (on 0.4 mmol scale) and starting from benzyl (1-(2-fluorophenyl)hept-2-yn-1-yl)-(hydroxy)carbamate **1n**, 119.9 mg of compound **2n** (0.337 mmol, 84% yield) were obtained as a yellow oil after purification by flash chromatography on silica gel (pentane/Et_2O 92/8): R_f (silica, Pentane/Et_2O 9/1 = 0.4, UV/PMA/Vanillin); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.93 (t, J = 7.3 Hz, 3H), 1.31−1.42 (m, 2H), 1.57−1.67 (m, 2H), 2.47 (t, J = 7.2 Hz, 2H), 5.09 (s, 2H), 5.50 (s, 1H), 7.08 (∼t, J = 9.6 Hz, 1H), 7.18 (∼t, J = 7.5 Hz, 1H), 7.27−7.46 (m, 7H), 11.77 (brs, 1H, NH). ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −114.1; ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.8, 22.3, 26.7, 43.4, 67.4, 106.9, 115.1 (d, $J_{ortho(C-F)}$ = 22.0 Hz), 123.7 (d, $J_{meta(C-F)}$ = 14.7 Hz), 123.9 (d, $J_{para(C-F)}$ = 3.5 Hz), 128.1, 128.2, 128.4, 129.3 (d, $J_{(C-F)}$ = 2.9 Hz), 131.2 (d, $J_{meta(C-F)}$ = 8.3 Hz), 135.4, 149.0, 152.4, 159.7 (d, $J_{ipso(C-F)}$ = 249.9 Hz), 202.5; IR (ATR, neat) ν (cm^{-1}) 3067, 3034, 2958, 2929, 2872, 1749, 1589, 1575, 1453, 1261, 1220, 1187, 113, 1100, 1046, 909, 752, 731, 695; MS (ESI+) m/z 356 (100, $[M + H]^+$), 336 (20), 312 (30), 288 (10); HRMS (ESI+) m/z 356.1665 calcd for $C_{21}H_{22}FNO_3 + H^+$ 356.1662.

(*Z*)-3-Amino-3-phenylacrylaldehyde (4). In 10 mL round-bottom flask equipped with a magnetic stirrer bar was added benzyl hydroxy(1-phenyl-3-(trimethylsilyl)prop-2-yn-1-yl)carbamate **1o** (178.6 mg, 0.5 mmol, 1 equiv), methanol (3 mL), water (0.25 mL) and potassium carbonate (69 mg, 0.5 mmol, 1 equiv), and the resulting mixture was stirred at room temperature for 3 h. The reaction mixture was then filtered through a silica gel pad and eluted with ethyl acetate. The filtrate was concentrated, and the residue was purified by flash chromatography on silica gel (pentane/ethyl acetate 8/2 → 7/3, R_f (silica, pentane/ethyl acetate 8/2 = 0.3, UV/Vanillin), to give 51.8 mg (0.35 mmol, 68% yield) of the title compound **4** as a yellow semisolid: ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 5.40 (s, 1H), 5.78 (brs, 1H), 7.39−7.50 (m, 3H), 7.53−7.59 (m, 2H), 10.00 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 95.5, 126.2, 128.9, 130.9, 136.2, 162.3, 188.1; IR (ATR, neat) ν (cm^{-1}) 3315, 3165, 3061, 2806, 2728, 1636, 1611, 1576, 1531, 1486, 1449, 1412, 1365, 1298, 1141, 1119, 1075, 996, 918, 773, 729, 692, 623, 611; MS (ESI+) m/z 260 (10), 148 (100, $[M + H]^+$); HRMS (ESI+) m/z 148.0746 calcd for $C_9H_9NO + H^+$ 148.0762.

(*Z*)-Benzyl (3-oxo-1-phenylbut-1-en-1-yl)carbamate (2p). According to general procedure B (on 0.2 mmol scale) and starting from benzyl (1-phenylbut-2-yn-1-yl)(hydroxy)carbamate **1p**, 44.1 mg of compound **2p** (0.149 mmol, 75% yield) were obtained as a pale yellow solid after purification by flash chromatography on silica gel (pentane/Et_2O 92/8): R_f (silica, Pentane/Et_2O 9/1 = 0.35, UV/PMA/Vanillin); mp 62−64 °C (Et_2O/pentane); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 2.23 (s, 3H), 5.08 (s, 2H), 5.59 (s, 1H), 7.27−7.48 (m, 10H), 11.54 (brs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 30.8, 67.4, 107.4, 127.4, 127.9, 128.2, 128.3, 128.4, 129.8, 135.3, 135.4, 152.7, 154.5, 199.5; IR (ATR, neat) ν (cm^{-1}) 3033, 2949, 1752, 1639, 1605, 1587, 1570, 1494, 1467, 1454, 1357, 1290, 1206, 1170, 1114, 1046, 766, 747, 694; MS (ESI+) m/z 296 (100, $[M + H]^+$), 252 (50), 162 (20); HRMS (ESI+) m/z 296.1286 calcd for $C_{18}H_{17}NO_3 + H^+$ 296.1287.

(*Z*)-Benzyl (4-methyl-3-oxo-1-phenylpent-1-en-1-yl)-carbamate (2q). According to general procedure B (on 0.1 mmol scale) and starting from benzyl (4-methyl-1-phenylpent-2-yn-1-yl)-(hydroxy)carbamate **1q**, 20.8 mg of compound **2q** (0.064 mmol, 63% yield) were obtained as a pale yellow oil after purification by flash chromatography on silica gel (pentane/Et_2O 92/8): R_f (silica, Pentane/Et_2O 9/1 = 0.4, UV/PMA/Vanillin); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.15 (d, J = 7.2 Hz, 6H), 2.65 (sept., J = 7.2 Hz, 1H), 5.08 (s, 2H), 5.61 (s, 1H), 7.27−7.48 (m, 10H), 11.61 (brs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 17.7, 40.3, 66.4, 104.9, 126.5, 127.0, 127.2, 127.3, 127.5, 128.7, 135.5, 135.7, 151.8, 154.1, 205.1; IR (ATR, neat) ν (cm^{-1}) 3065, 3034, 2969, 2872, 1749, 1639, 1604, 1587, 1573, 1495, 1462, 1286, 1194, 1174, 1129, 1069, 1048, 906, 726, 694; MS (ESI+) m/z 647 (5, $[2M + H]^+$), 324 (100, $[M + H]^+$), 306 (50), 280 (45), 262 (10); HRMS (ESI+) m/z 324.1599 calcd for $C_{20}H_{21}NO_3 + H^+$ 324.1600.

(*E*)-Benzyl (4,4-dimethyl-1-phenylpent-2-yn-1-ylidene)-carbamate (3r). According to general procedure B (on 0.2 mmol scale) and starting from benzyl (4,4-dimethyl-1-phenylpent-2-yn-1-yl)(hydroxy)carbamate **1r**, 25.3 mg of compound **3r** (0.079 mmol, 41% yield) were obtained as a yellow oil after purification by flash chromatography on silica gel (pentane/Et_2O 95/5): R_f (silica, Pentane/Et_2O 9/1 = 0.45, UV/PMA); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.28 (s, 9H), 5.31 (s, 2H), 7.30−7.55 (m, 8H), 8.06 (∼d, J = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 28.3, 30.1, 68.3, 72.8, 110.7, 128.3, 128.35, 128.4, 128.5, 128.6, 132.4, 135.0, 135.5, 153.6, 163.0; IR (ATR, neat) ν (cm^{-1}) 3065, 3033, 2970, 2929, 2868, 2218, 1722, 1595, 1573, 1450, 1318, 1295, 1256, 1201, 1176, 905, 690.MS (ESI+) m/z 320 (100, $[M + H]^+$), 276 (5), 228 (10); HRMS (ESI+) m/z 320.1638 calcd for $C_{21}H_{21}NO_2 + H^+$ 320.1651.

(*Z*)-Benzyl (3-oxo-1,3-diphenylprop-1-en-1-yl)carbamate (2s) and (*E*)-Benzyl (1,3-diphenylprop-2-yn-1-ylidene)-carbamate (3s). According to general procedure B (on 0.2 mmol scale) and starting from benzyl (1,3-diphenylprop-2-yn-1-yl)(hydroxy)-carbamate **1s**, 36.3 mg of compound **2s** as a viscous yellow oil (0.101 mmol, 51% yield) and 12.0 mg of compound **3s** as a pale yellow oil (0.035 mmol, 18% yield) were obtained. **2s**, R_f (silica, Pentane/Et_2O 9/1) = 0.45, UV/PMA/Vanillin), and **3s**, R_f (silica, Pentane/Et_2O 9/1) = 0.4, UV/PMA), were separated by flash chromatography on silica gel (pentane/Et_2O 95/5). **2s**: ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 5.11 (s, 2H), 6.29 (s, 1H), 7.28−7.58 (m, 13H), 7.93−7.98 (m, 2H), 12.01 (brs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 67.5, 103.8, 127.6, 127.8, 128.1, 128.3, 128.4, 128.5, 128.6, 129.9, 132.6, 135.4, 136.0, 138.6, 152.8, 156.8, 191.3; IR (ATR, neat) ν (cm^{-1}) 3063, 3032, 2923, 2851, 1749, 1722, 1621, 1586, 1567, 1496, 1469, 1319, 1291, 1171, 1126, 1045, 1020, 776, 750, 688; MS (ESI+) m/z 358 (100, $[M + H]^+$), 340 (40), 314 (15), 288 (15); HRMS (ESI+) m/z 358.1447 calcd for $C_{23}H_{19}NO_3 + H^+$ 358.1443. **3s**: ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 5.38 (s, 2H), 7.27−7.34 (m, 2H), 7.34−7.40 (m, 3H), 7.41−7.50 (m, 7H), 7.53−7.58 (m, 1H), 8.16−8.19 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 68.4, 81.7, 100.1, 120.3, 128.3, 128.4, 128.5, 128.7, 130.5, 132.6, 132.7, 134.9, 135.6, 153.3, 163.0; IR (ATR, neat) ν (cm^{-1}) 3083, 3060, 2215, 2192, 1711, 1589, 1566, 1490, 1446, 1330, 1255, 1239, 1195, 1172, 776, 752, 699, 690, 678, 605; MS (ESI+) m/z 679 (20,

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$[2M + H]^+$), 340 (100, $[M + H]^+$), 169 (5); HRMS (ESI+) m/z 340.1333 calcd for $C_{23}H_{17}NO_2 + H^+$ 340.1338.

(*Z*)-Benzyl (3-oxo-1-phenyl-3-(*p*-tolyl)prop-1-en-1-yl)carbamate (2t) and (*E*)-Benzyl (1-phenyl-3-(*p*-tolyl)prop-2-yn-1-ylidene)carbamate (3t). According to general procedure B (on 0.2 mmol scale) and starting from benzyl (1-phenyl-3-(*p*-tolyl)prop-2-yn-1-yl)(hydroxy)carbamate **1t**, 39.2 mg of compound **2t** as a pale yellow oil (0.105 mmol, 53% yield) and 11.8 mg of compound **3t** as a colorless oil (0.033 mmol, 14% yield) were obtained. **2t**, R_f (silica, Pentane/Et_2O 9/1) = 0.45, UV/PMA/Vanillin), and **3t**, R_f (silica, Pentane/Et_2O 9/1) = 0.4, UV/PMA), were separated by flash chromatography on silica gel (pentane/Et_2O 95/5). **2t**: ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 2.41 (s, 3H), 5.11 (s, 2H), 6.28 (s, 1H), 7.26 (d, J = 8.0 Hz, 2H), 7.30−7.38 (m, 5H), 7.40−7.52 (m, 5H), 7.86 (d, J = 8.4 Hz, 2H), 12.03 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 21.6, 67.5, 103.8, 127.6, 127.9, 128.0, 128.3, 128.5, 129.3, 129.8, 135.5, 136.0, 136.1, 143.4, 152.8, 156.3, 191.0; IR (ATR, neat) ν (cm^{-1}) 3061, 3034, 2957, 1748, 1622, 1605, 1585, 1572, 1495, 1472, 1315, 1294, 1190, 1173, 1044, 805, 732, 694; MS (ESI+) m/z 372 (100, $[M + H]^+$), 354 (45); HRMS (ESI+) m/z 372.1599 calcd for $C_{24}H_{21}NO_3 + H^+$ 372.1600. **3t**: ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 2.40 (s, 3H), 5.38 (s, 2H), 7.18(d, J = 8 Hz, 2H), 7.28−7.36 (m, 5H), 7.44−7.50 (m, 4H), 7.52−7.57 (m, 1H), 8.15−8.19 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 21.7, 68.4, 81.5, 100.8, 117.2, 128.3, 128.4, 128.5, 128.6, 128.7, 129.3, 132.6, 135.0, 135.6, 141.2, 153.4, 163.0; IR (ATR, neat) ν (cm^{-1}) 3064, 3032, 2953, 2207, 2189, 1718, 1593, 1569, 1508, 1449, 1324, 1232, 1193, 1171, 1048, 814, 688; MS (ESI+) m/z 354 (100, $[M + H]^+$); HRMS (ESI+) m/z 354.1505 calcd for $C_{24}H_{19}NO_2 + H^+$ 354.1494.

(*Z*)-1-Amino-1-phenylhept-1-en-3-one (7). In 10 mL round-bottom flask equipped with a magnetic stirrer bar was added (*Z*)-benzyl (3-oxo-1-phenylhept-1-en-1-yl)carbamate **2a** (67.5 mg, 0.2 mmol, 1 equiv), methanol (2 mL), palladium on carbon (wt. 10%, 23 mg, 0.02 mmol, 0.1 equiv), and the resulting mixture was stirred at room temperature under hydrogen atmosphere for 30 min. The reaction mixture was then filtered through a silica gel pad and eluted with ethyl acetate. The filtrate was concentrated, and the residue was purified by flash chromatography on silica gel (pentane/ethyl acetate 8/2, R_f (silica, pentane/ethyl acetate 8/2 = 0.25, UV/Ninhydrin)) to give 39.1 mg (0.19 mmol, 97% yield) of the title compound **7** as a pale yellow oil: ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.92 (t, J = 7.6 Hz, 3H), 1.36 (sext, J = 7.6 Hz, 2H), 1.63 (pent, J = 7.6 Hz, 2H), 2.38 (t, J = 7.6 Hz, 2H), 5.25 (brs, 1H), 5.44 (s, 1H), 7.38−7.48 (m, 3H), 7.38−7.48 (m, 2H), 9.95 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.9, 22.6, 28.0, 42.6, 94.7, 126.2, 128.8, 130.4, 137.4, 160.8, 200.7. The spectral data are consistent with those of the literature.[27]

4-Butyl-2,6-diphenylpyrimidine (6). According to general procedure C (on 0.1 mmol scale) and starting from (*Z*)-benzyl (3-oxo-1-phenylhept-1-en-1-yl)carbamate **2a** and benzamide, 23.0 mg of compound **6** (0.797 mmol, 80% yield) were obtained as a white solid after purification by flash chromatography on silica gel (pentane/Et_2O 98/2): R_f (silica, pentane/Et_2O 95/5 = 0.8, UV/Vanillin); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.01 (t, J = 7.4 Hz, 3H), 1.43−1.54 (m, 2H), 1.82−1.91 (m, 2H), 2.90 (t, J = 7.4 Hz, 2H), 7.46 (s, 1H), 7.47−7.57 (m, 6H), 8.21−8.26 (m, 2H), 8.63 (dd, J = 1.8 Hz and J = 7.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 14.0, 22.5, 31.0, 37.9, 113.4, 127.2, 128.3, 128.4, 128.8, 130.4, 130.6, 137.4, 138.1, 163.7, 164.2, 171.6. The spectral data are consistent with those of the literature.[28]

4-Butyl-2-phenyl-6-(*p*-tolyl)pyrimidine (9). According to general procedure C (on 0.2 mmol scale) and starting from (*Z*)-benzyl (3-oxo-1-(*p*-tolyl)hept-1-en-1-yl)carbamate **2b** and benzamide, 53.4 mg of compound **9** (0.177 mmol, 89% yield) were obtained as a pale yellow solid after purification by flash chromatography on silica gel (pentane/Et_2O 98/2): R_f (silica, pentane/Et_2O 95/5 = 0.8, UV/Vanillin); mp 61−63 °C (Et_2O/Pentane); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.01 (t, J = 7.6 Hz, 3H), 1.44−1.54 (m, 2H), 1.82−1.91 (m, 2H), 2.45 (s, 3H), 2.88 (t, J = 7.6 Hz, 2H), 7.34 (d, J = 8 Hz, 2H) 7.43 (s, 1H), 7.47−7.56 (m, 3H), 8.14 (d, J = 8 Hz, 2H), 8.63 (dd, J = 1.7 Hz and J = 7.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.9, 21.4, 22.5, 31.0, 37.9, 113.0, 127.1, 128.3, 129.5, 130.3, 134.6, 138.4, 140.8, 163.6, 164.1, 171.4; IR (ATR, neat) ν (cm^{-1}) 2956, 2929, 1588, 1571, 1528, 1511, 14818, 1360, 820, 752, 695, 661; MS (ESI+) m/z 303 (100, $[M + H]^+$); HRMS (ESI+) m/z 303.1853 calcd for $C_{21}H_{22}N_2 + H^+$ 303.1856.

4-Butyl-2-phenyl-6-(*m*-tolyl)pyrimidine (10). According to general procedure C (on 0.2 mmol scale) and starting from (*Z*)-benzyl (3-oxo-1-(*m*-tolyl)hept-1-en-1-yl)carbamate **2g** and benzamide, 49.0 mg of compound **10** (0.162 mmol, 81% yield) were obtained as a pale yellow oil after purification by flash chromatography on silica gel (pentane/Et_2O 98/2): R_f (silica, pentane/Et_2O 95/5 = 0.9, UV/Vanillin); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.01 (t, J = 7.4 Hz, 3H), 1.43−1.58 (m, 2H), 1.82−1.91 (m, 2H), 2.49 (s, 3H), 2.89 (t, J = 7.6 Hz, 2H), 7.33 (d, J = 7.6 Hz, 1H) 7.42 (t, J = 7.6 Hz, 1H), 7.45 (s, 1H), 7.48−7.56 (m, 3H), 8.00 (d, J = 7.6 Hz, 1H), 8.05 (brs, 1H), 8.62 (dd, J = 1.8 Hz and J = 7.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 14.0, 21.5, 22.5, 31.0, 38.0, 113.5, 124.3, 127.8, 128.4, 128.7, 130.3, 131.3, 137.4, 138.3, 138.5, 163.9, 164.2, 171.5; IR (ATR, neat) ν (cm^{-1}) 2955, 2926, 2870, 2859, 1587, 1569, 1532, 1367, 1173, 1027, 755, 692, 666, 639; MS (ESI+) m/z 303 (100, $[M + H]^+$); HRMS (ESI+) m/z 303.1861 calcd for $C_{21}H_{22}N_2 + H^+$ 303.1861.

4-Butyl-6-(4-fluorophenyl)-2-phenylpyrimidine (11). According to general procedure C (on 0.2 mmol scale) and starting from (*Z*)-benzyl (1-(4-fluorophenyl)-3-oxohept-1-en-1-yl)carbamate **2c** and benzamide, 41.0 mg of compound **11** (0.134 mmol, 67% yield) were obtained as a pale yellow solid after purification by flash chromatography on silica gel (pentane/Et_2O 98/2): R_f (silica, pentane/Et_2O 95/5 = 0.75, UV/Vanillin); mp 78−79 °C (Et_2O/pentane); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.00 (t, J = 7.2 Hz, 3H), 1.42−1.53 (m, 2H), 1.81−1.90 (m, 2H), 2.88 (t, J = 7.6 Hz, 2H), 7.21 (~t, J = 8.8 Hz, 2H), 7.40 (s, 1H), 7.47−7.56 (m, 3H), 8.17−8.29 (m, 2H), 8.60 (dd, J = 2.4 Hz and J = 8.0 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −110.2; ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.9, 22.5, 31.0, 37.9, 113.0, 115.8 (d, $J_{ortho(C-F)}$ = 21.7 Hz), 128.3, 128.4, 129.2 (d, $J_{meta(C-F)}$ = 8.7 Hz), 130.5, 133.5 (d, $J_{para(C-F)}$ = 3.2 Hz), 138.9, 157.1, 162.5, 164.2, 164.4 (d, $J_{ipso(C-F)}$ = 250.9 Hz), 171.2; IR (ATR, neat) ν (cm^{-1}) 2957, 2929, 2870, 1603, 1586, 1573, 1527, 1509, 1416, 1360, 1231, 1219, 1163, 831, 751, 690, 663; MS (ESI+) m/z 307 (100, $[M + H]^+$); HRMS (ESI+) m/z 307.1608 calcd for $C_{20}H_{19}FN_2 + H^+$ 307.1611.

4-Butyl-6-(2-fluorophenyl)-2-phenylpyrimidine (12). According to general procedure C (on 0.2 mmol scale) and starting from (*Z*)-benzyl (1-(2-fluorophenyl)-3-oxohept-1-en-1-yl)carbamate **2n** and benzamide, 39.1 mg of compound **12** (0.128 mmol, 64% yield) were obtained as a viscous colorless oil after purification by flash chromatography on silica gel (pentane/Et_2O 98/2): R_f (silica, pentane/Et_2O 95/5 = 0.8, UV/Vanillin); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.00 (t, J = 7.2 Hz, 3H, H_1), 1.43−1.53 (m, 2H, H_2), 1.81−1.90 (m, 2H, H_3), 2.90 (t, J = 7.6 Hz, 2H, H_4), 7.20 (ddd, J = 1.0 Hz, J = 8.3 Hz, J = 11.7 Hz, 1H, H_{Ar}), 7.34 (dt, J = 1.1 Hz and J = 7.6 Hz, 1H, H_{Ar}), 7.43−7.55 (m, 4H, H_{Ar}), 7.59 (d, J = 2.1 Hz, 1H, H_{Ar}), 8.36 (dt, J = 1.9 Hz and J = 7.8 Hz, 1H, H_{Ar}), 8.57−8.61 (m, 2H, H_{16}). ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −114.8; ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.9, 22.5, 31.0, 37.9, 116.3 (d, $J_{ortho(C-F)}$ = 22.9 Hz), 117.7 (d, $J_{meta(C-F)}$ = 8.7 Hz), 124.6 (d, $^4J_{(C-F)}$= 3.5 Hz), 125.5 (d, $^4J_{(C-F)}$= 11.5 Hz), 128.3, 128.4, 130.4, 131.1 (d, $J_{para(C-F)}$ = 2.5 Hz), 131.8 (d, $J_{meta(C-F)}$ = 8.8 Hz), 138.1, 159.7 (d, $J_{(C-F)}$ = 2.5 Hz), 161.4 (d, $J_{ipso(C-F)}$ = 251.9 Hz), 164.1, 171.6; IR (ATR, neat) ν (cm^{-1}) 3074, 3036, 2959, 2926, 2873, 2857, 1614, 1568, 1527, 1489, 1373, 1358, 1260, 1209, 872, 853, 773, 753, 734, 726, 694, 628; MS (ESI+) m/z 307 (100, $[M + H]^+$); HRMS (ESI+) m/z 307.1606 calcd for $C_{20}H_{19}FN_2 + H^+$ 307.1611.

4-(3-Bromophenyl)-6-butyl-2-phenylpyrimidine (13). According to general procedure C (on 0.2 mmol scale) and starting from (*Z*)-benzyl (1-(3-bromophenyl)-3-oxohept-1-en-1-yl)carbamate **2i** and benzamide, 39.0 mg of compound **13** (0.106 mmol, 54% yield) were obtained as a pale yellow oil after purification by flash chromatography on silica gel (petroleum ether/Et_2O 97/3): R_f (silica, pentane/Et_2O 95/5 = 0.8, UV/Vanillin); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.01 (t, J = 7.6 Hz, 3H), 1.42−1.52 (m, 2H), 1.79−1.89 (m, 2H), 2.89 (t, J = 7.6 Hz, 2H), 7.35−7.66 (m, 6H), 8.09−8.15 (m, 1H), 8.31−8.40 (m, 1H), 8.50−8.75 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.9, 22.5, 30.9, 38.0, 113.4, 123.1, 125.7, 128.3, 128.4, 130.2, 130.3, 130.5, 133.4, 138.0, 139.5, 162.1, 164.3, 172.0; IR (ATR, neat) ν (cm^{-1}) 3066, 2957,

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2928, 2859, 1587, 1563, 1531, 1367, 1115, 1069, 789, 756, 689, 660, 634; MS (ESI+) m/z 369 (98, $[M + H]^+$,^{81}Br), 367 (100, $[M + H]^+$,^{79}Br). 303 (15); HRMS (ESI+) m/z 367.0815 calcd for $C_{20}H_{19}BrN_2 + H^+$ 367.0810.

4-Butyl-6-(3-methoxyphenyl)-2-phenylpyrimidine (14). According to general procedure C (on 0.2 mmol scale) and starting from (*Z*)-benzyl (1-(3-methoxyphenyl)-3-oxohept-1-en-1-yl)-carbamate **2h** and benzamide, 38.9 mg of compound **14** (0.122 mmol, 62% yield) were obtained as a pale yellow oil after purification by flash chromatography on silica gel (petroleum ether/Et_2O 97/3): R_f (silica, pentane/Et_2O 95/5 = 0.6, UV/Vanillin); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.01 (t, J = 7.6 Hz, 3H), 1.43−1.54 (m, 2H), 1.82−1.91 (m, 2H), 2.89 (t, J = 7.6 Hz, 2H), 3.94 (s, 3H), 7.07 (dd, J = 2.5 Hz and J = 8.2 Hz, 1H), 7.42−7.47 (m, 2H), 7.48−7.56 (m, 3H), 7.77 (d, J = 7.7 Hz, 1H), 7.84 (brs, 1H), 8.60−8.65 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.9, 22.5, 30.9, 37.9, 55.4, 112.6, 113.5, 116.1, 119.5, 128.3, 128.4, 129.8, 130.4, 138.2, 138.9, 160.1, 163.4, 164.1, 171.6; IR (ATR, neat) ν (cm^{-1}) 3066, 2955, 2930, 2870, 1587, 1568, 1531, 1463, 1368, 1253, 1045, 858, 756, 691, 673, 636; MS (ESI+) m/z 319 (100, $[M + H]^+$); HRMS (ESI+) m/z 319.1805 calcd for $C_{21}H_{22}N_2O + H^+$ 319.1810.

4-Butyl-6-(naphthalen-2-yl)-2-phenylpyrimidine (15). According to general procedure C (on 0.2 mmol scale) and starting from (*Z*)-benzyl (1-(naphthalen-2-yl)-3-oxohept-1-en-1-yl)carbamate **2k** and benzamide, 38.2 mg of compound **15** (0.113 mmol, 57% yield) were obtained as a yellow oil after purification by flash chromatography on silica gel (petroleum ether/Et_2O 98/2): R_f (silica, pentane/Et_2O 95/5 = 0.8, UV/Vanillin); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.04 (t, J = 7.6 Hz, 3H), 1.46−1.57 (m, 2H), 1.85−1.95 (m, 2H), 2.93 (t, J = 8.0 Hz, 2H), 7.50−7.62 (m, 6H), 7.89−8.05 (m, 3H), 8.35 (d, J = 8.4 Hz, 1H), 8.66−8.74 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 14.0, 22.5, 31.0, 38.0, 113.6, 124.2, 126.4, 127.1,127.2, 127.7, 128.3, 128.4, 128.5, 128.9, 130.4, 133.3, 134.5, 134.7, 138.3, 163.5, 164.3, 171.6; IR (ATR, neat) ν (cm^{-1}) 3060, 2954, 2927, 2858, 1587, 1568, 1531, 1373; 1173, 854, 817, 758, 694, 656; MS (ESI+) m/z 339 (100, $[M + H]^+$); HRMS (ESI+) m/z 339.1861 calcd for $C_{24}H_{22}N_2 + H^+$ 339.1861.

4-Butyl-2-phenyl-6-(thiophen-2-yl)pyrimidine (16). According to general procedure C (on 0.2 mmol scale) and starting from (*Z*)-benzyl (3-oxo-1-(thiophen-2-yl)hept-1-en-1-yl)carbamate **2j** and benzamide, 30.5 mg of compound **16** (0.104 mmol, 52% yield) were obtained as a yellow oil after purification by flash chromatography on silica gel (pentane/Et_2O 98/2): R_f (silica, pentane/Et_2O 95/5 = 0.7, UV/Vanillin); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.00 (t, J = 7.2 Hz, 3H), 1.42−1.52 (m, 2H), 1.79−1.88 (m, 2H), 2.85 (t, J = 8 Hz, 2H), 7.17 (dd, J = 3.9 Hz and J = 4.8 Hz, 1H), 7.30 (s, 1H), 7.44−7.56 (m, 4H), 7.82 (d, J = 3.2 Hz, 1H), 8.57 (dd, J = 1.9 Hz and J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.9, 22.5, 30.9, 37.8, 111.5, 126.8, 128.1, 128.3, 128.4, 129.5, 130.4, 137.8, 143.3, 158.7, 164.1, 171.4; IR (ATR, neat) ν (cm^{-1}) 2955, 2927, 2858, 1720, 1588, 1570, 1528, 1432, 1373, 1269, 1235, 1172, 1026, 856, 756, 694; MS (ESI+) m/z 295 (100, $[M + H]^+$); HRMS (ESI+) m/z 295.1261 calcd for $C_{18}H_{18}N_2S + H^+$ 295.1269.

4-Methyl-2,6-diphenylpyrimidine (17). According to general procedure C (on 0.2 mmol scale) and starting from (*Z*)-benzyl (3-oxo-1-phenylbut-1-en-1-yl)carbamate **2p** and benzamide, 32.9 mg of compound **17** (0.134 mmol, 77% yield) were obtained as a pale yellow solid after purification by flash chromatography on silica gel (pentane/Et_2O 96/4): R_f (silica, pentane/Et_2O 95/5 = 0.4, UV/Vanillin); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 2.65 (s, 3H), 7.47 (s, 1H), 7.49−7.57 (m, 6H), 8.20−8.25 (m, 2H), 8.58−8.64 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 24.6, 114.0, 127.1, 128.3, 128.4, 128.8, 130.4, 130.6, 137.2, 138.1, 163.6, 164.2, 167.7. The spectral data are consistent with those of the literature.[29]

4-Isopropyl-2,6-diphenylpyrimidine (18). According to general procedure C (on 0.2 mmol scale) and starting from (*Z*)-benzyl (4-methyl-3-oxo-1-phenylpent-1-en-1-yl)carbamate **2q** and benzamide, 39.2 mg of compound **18** (0.142 mmol, 71% yield) were obtained as a pale yellow oil after purification by flash chromatography on silica gel (pentane/Et_2O 98/2): R_f (silica, pentane/Et_2O 95/5 = 0.8, UV/Vanillin); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.44 (t, J = 6.8 Hz, 6H, H_1 and $H_{1'}$), 3.15 (sept., J = 6.8 Hz, 1H, H_2), 7.48 (s, 1H, H_4), 7.49−7.58 (m, 6H, H_{Ar}), 8.24 (dd, J = 2.0 Hz and J = 8.0 Hz, 2H, H_7), 8.66 (dd, J = 2.0 Hz and J = 8.0 Hz, 2H, H_{12}); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 21.9, 36.3, 111.5, 127.2, 128.4, 128.8, 130.3, 130.5, 137.6, 138.3, 163.9, 164.0, 176.3; IR (ATR, neat) ν (cm^{-1}) 2961, 2924, 2866, 1590, 1568, 1531, 1496, 1373, 756, 692, 633; MS (ESI+) m/z 275 (100, $[M + H]^+$); HRMS (ESI+) m/z 275.1551 calcd for $C_{19}H_{18}N_2 + H^+$ 275.1548.

2,4,6-Triphenylpyrimidine (19). According to general procedure C (on 0.1 mmol scale) and starting from (*Z*)-benzyl (3-oxo-1,3-diphenylprop-1-en-1-yl)carbamate **2s** and benzamide, 16.6 mg of compound **19** (0.054 mmol, 54% yield) were obtained as a white solid after purification by flash chromatography on silica gel (pentane/Et_2O 98/2): R_f (silica, pentane/Et_2O 95/5 = 0.4, UV/Vanillin); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.50−7.62 (m, 9H), 8.06 (s, 1H), 8.28−8.33 (dd, 1H, J = 1.6 Hz and J = 8.0 Hz, 4H), 8.28−8.33 (dd, 1H, J = 2.0 Hz and J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 110.3, 127.3,128.4, 128.9, 130.6, 130.7, 137.5, 138.1, 164.5, 164.7. The spectral data are consistent with those of the literature.[30]

4-Butyl-6-phenyl-2-(thiophen-2-yl)pyrimidine (20). According to general procedure C (on 0.2 mmol scale) and starting from (*Z*)-benzyl (3-oxo-1-phenylhept-1-en-1-yl)carbamate **2a** and 2-thiophenecarboxamide, 36.2 mg of compound **20** (0.122 mmol, 60% yield) were obtained as a pale yellow oil after purification by flash chromatography on silica gel (pentane/Et_2O 98/2): R_f (silica, pentane/Et_2O 95/5 = 0.75, UV/Vanillin); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.00 (t, J = 7.6 Hz, 3H), 1.42−1.52 (m, 2H), 1.78−1.88 (m, 2H), 2.84 (t, J = 7.6 Hz, 2H), 7.17 (dd, J = 3.7 Hz and J = 5.0 Hz, 1H), 7.37 (s, 1H), 7.48 (dd, J = 1.2 Hz and J = 5.0 Hz, 1H), 7.50−7.56 (m, 3H), 8.14 (dd, J = 1.2 Hz and J = 3.6 Hz, 1H), 8.17−8.21 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.9, 22.4, 30.8, 37.7, 112.8, 127.1, 128.0, 128.6, 128.8, 129.3, 130.6, 137.0, 144.2, 161.1, 163.6, 171.7. The spectral data are consistent with those of the literature.[31]

4-Butyl-2-(4-nitrophenyl)-6-phenylpyrimidine (21). According to general procedure C (on 0.2 mmol scale) and starting from (*Z*)-benzyl (3-oxo-1-phenylhept-1-en-1-yl)carbamate **2a** and 4-nitrobenzamide, 54.6 mg of compound **21** (0.164 mmol, 82% yield) were obtained as a yellow solid after purification by flash chromatography on silica gel (pentane/Et_2O 97/3): R_f (silica, pentane/Et_2O 95/5 = 0.5, UV/Vanillin); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.01 (t, J = 7.2 Hz, 3H), 1.43−1.54 (m, 2H), 1.80−1.90 (m, 2H), 2.90 (t, J = 7.6 Hz, 2H), 7.52−7.58 (m, 4H), 8.18 − 8.22 (m, 2H), 8.33 (~d, J = 8.8 Hz, 2H),8.77 (~d, J = 9.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.9, 22.5, 30.9, 37.9, 114.4, 123.5, 127.2, 128.9, 129.2, 131.0, 136.8, 144.0, 149.1, 162.0, 164.0, 172.1; IR (ATR, neat) ν (cm^{-1}) 2953, 2926, 2869, 1577, 1520, 1463, 1420, 1353, 1336, 1223, 867, 857, 829, 773, 743, 690, 646; MS (ESI+) m/z 386 (15), 334 (100, $[M + H]^+$), 288 (10), 213 (10); HRMS (ESI+) m/z 334.1536 calcd for $C_{20}H_{19}N_3O_2 + H^+$ 334.1556.

2-(4-Bromophenyl)-4-butyl-6-phenylpyrimidine (22). According to general procedure C (on 0.2 mmol scale) and starting from (*Z*)-benzyl (3-oxo-1-phenylhept-1-en-1-yl)carbamate **2a** and 4-bromobenzamide, 56.7 mg of compound **22** (0.154 mmol, 78% yield) were obtained as a pale yellow solid after purification by flash chromatography on silica gel (pentane/Et_2O 98/2): R_f (silica, pentane/Et_2O 95/5 = 0.7, UV/Vanillin); mp 88−90 °C (Et_2O/pentane); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.00 (t, J = 7.6 Hz), 1.42−1.53 (m, 2H), 1.79−1.88 (m, 2H), 2.88 (t, J = 7.6 Hz, 2H), 7.46 (s, 1H), 7.50−7.56 (m, 3H), 7.63 (~d, J = 8.8 Hz, 2H), 8.18−8.22 (m, 2H), 8.49 (~d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.9, 22.5, 31.0, 37.9, 113.6, 125.1, 127.2, 128.8, 130.0, 130.7, 131.5, 137.1, 137.2, 163.3, 163.8, 171.7; IR (ATR, neat) ν (cm^{-1}) 2956, 2924, 2857, 1588, 1564, 1530, 1363, 1169, 1069, 1010, 841, 767, 690, 639; MS (ESI+) m/z 369 (97, $[M + H]^+$,^{81}Br), 367 (100, $[M + H]^+$,^{79}Br). 288 (15), 275 (10); HRMS (ESI +) m/z 367.0796 calcd for $C_{20}H_{19}BrN_2 + H^+$ 367.0810.

4-Butyl-6-phenyl-2-vinylpyrimidine (23). According to general procedure D (on 0.1 mmol scale) and starting from (*Z*)-benzyl (3-oxo-1-phenylhept-1-en-1-yl)carbamate **2a** and acrylamide, 17.1 mg of compound **23** (0.072 mmol, 72% yield) were obtained as a yellow oil after purification by flash chromatography on silica gel (pentane/Et_2O 95/5): R_f (silica, pentane/Et_2O 9/1 = 0.6, UV/Vanillin); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.97 (t, J = 7.4 Hz, 3H), 1.38−1.49 (m, 2H),

1.73−1.83 (m, 2H), 2.81 (t, J = 7.6 Hz, 2H), 5.74 (dd, J = 1.9 Hz and J = 10.5 Hz, 1H), 6.75 (dd, J = 1.9 Hz and J = 17.3 Hz, 1H), 6.96 (dd, J = 10.5 Hz and J = 17.3 Hz, 1H), 7.40 (s, 1H), 7.47−7.53 (m, 3H), 8.09−8.14 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.9, 22.5, 31.1, 37.8, 113.6, 123.5, 127.2, 128.8, 130.6, 137.0, 137.2, 163.8, 164.0, 171.3; IR (ATR, neat) ν (cm^{-1}) 2956, 2926, 2857, 1573, 1531, 1420, 1371, 991, 940, 772, 690; MS (ESI+) m/z 239 (100, $[M + H]^+$); HRMS (ESI+) m/z 239.1537 calcd for $C_{16}H_{18}N_2 + H^+$ 239.1548.

4-Butyl-6-(4-fluorophenyl)-2-vinylpyrimidine (24). According to general procedure D (on 0.1 mmol scale) and starting from (*Z*)-benzyl (1-(4-fluorophenyl)-3-oxohept-1-en-1-yl)carbamate **2c** and acrylamide, 17.7 mg of compound **24** (0.069 mmol, 69% yield) were obtained as a yellow oil after purification by flash chromatography on silica gel (pentane/Et_2O 96/4): R_f (silica, pentane/Et_2O 9/1 = 0.7, UV/Vanillin); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.97 (t, J = 7.3 Hz, 3H, H_1), 1.38−1.49 (m, 2H, H_2), 1.72−1.82 (m, 2H, H_3), 2.80 (t, J = 7.6 Hz, 2H, H_4), 5.74 (dd, J = 1.9 Hz and J = 10.4 Hz, 1H, $H_{14'}$), 6.73 (dd, J = 2.0 Hz and J = 17.3 Hz, 1H, H_{14}), 6.94 (dd, J = 10.4 Hz and J = 17.3 Hz, 1H, H_{13}), 7.14−7.21 (m, 2H, H_{10}), 7.34 (s, 1H, H_6), 8.09−8.16 (m, 2H, H_9). ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −110.1; ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.9, 22.5, 31.1, 37.8, 113.2, 115.8 (d, $J_{ortho(C-F)}$ = 21.8 Hz), 123.6, 129.2 (d, $J_{meta(C-F)}$ = 8.7 Hz, 2C), 133.3 (d, $J_{para(C-F)}$ = 2.9 Hz), 136.9, 162.6, 164.0, 164.5 (d, $J_{ipso(C-F)}$ = 250.9 Hz), 171.5; IR (ATR, neat) ν (cm^{-1}) 2957, 2927, 2858, 1731, 1601, 1575, 1532, 1509, 1232, 1156, 837, 819; MS (ESI+) m/z 420 (15), 257 (100, $[M + H]^+$); HRMS (ESI+) m/z 257.1454 calcd for $C_{16}H_{17}FN_2 + H^+$ 257.1454.

4-Methyl-6-phenyl-2-vinylpyrimidine (25). According to general procedure D (on 0.1 mmol scale) and starting from (*Z*)-benzyl (3-oxo-1-phenylbut-1-en-1-yl)carbamate **2p** and acrylamide, 13.3 mg of compound **25** (0.0678 mmol, 68% yield) were obtained as a yellow oil after purification by flash chromatography on silica gel (pentane/Et_2O 88/12): R_f (silica, pentane/Et_2O 9/1 = 0.25, UV/Vanillin); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 2.59 (s, 3H), 5.75 (dd, J = 1.9 Hz and J = 10.5 Hz, 1H), 6.74 (dd, J = 1.9 Hz and J = 17.3 Hz, 1H), 6.95 (dd, J = 10.5 Hz and J = 17.3 Hz, 1H), 7.42 (s, 1H), 7.48−7.53 (m, 3H), 8.09−8.14 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 24.2, 114.3, 123.8, 127.2, 128.9, 130.8, 136.7, 137.0, 163.9, 167.2; IR (ATR, neat) ν (cm^{-1}) 3034, 2924, 2853, 1574, 1535, 1441, 1354, 773, 690; MS (ESI+) m/z 197 (100, $[M + H]^+$), 184 (5); HRMS (ESI+) m/z 197.1074 calcd for $C_{13}H_{12}N_2 + H^+$ 197.1079.

4-Butyl-2-methyl-6-phenylpyrimidine (26). According to general procedure C (on 0.2 mmol scale) and starting from (*Z*)-benzyl (3-oxo-1-phenylhept-1-en-1-yl)carbamate **2a** and acetamide, 31.6 mg of compound **26** (0.142 mmol, 71% yield) were obtained as a pale yellow oil after purification by flash chromatography on silica gel (pentane/Et_2O 85/15): R_f (silica, pentane/Et_2O 85/15 = 0.25, UV/Vanillin); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.96 (t, J = 7.6 Hz, 3H), 1.37−1.48 (m, 2H), 1.70−1.79 (m, 2H), 2.77 (t, J = 7.8 Hz, 2H), 2.78 (s, 3H), 7.35 (s, 1H), 7.46−7.52 (m, 3H), 8.02−8.08 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.9, 22.5, 26.2, 31.4, 37.9, 112.8, 127.2, 128.8, 130.5, 137.3, 164.1, 167.9, 171.3; IR (ATR, neat) ν (cm^{-1}) 2956, 2926, 2858, 1576, 1537, 1394, 1371, 754, 690; MS (ESI+) m/z 227 (100, $[M + H]^+$); HRMS (ESI+) m/z 227.1527 calcd for $C_{15}H_{18}N_2 + H^+$ 227.1548.

4-Butyl-6-phenylpyrimidine (27). According to general procedure C (on 0.2 mmol scale) in the absence of 4 Å MS and starting from (*Z*)-benzyl (4-methyl-3-oxo-1-phenylpent-1-en-1-yl)carbamate **2i** and formamide, 20.7 mg of compound **27** (0.098 mmol, 49% yield) were obtained as a yellow oil after purification by flash chromatography on silica gel (pentane/Et_2O 95/5 → 9/1): R_f (silica, pentane/Et_2O 9/1 = 0.3, UV/Vanillin); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.96 (t, J = 7.2 Hz, 3H), 1.37−1.48 (m, 2H), 1.73−1.82 (m, 2H), 2.82 (t, J = 7.6 Hz, 2H), 7.48−7.53 (m, 3H), 7.50 (s, 1H), 8.04−8.10 (m, 2H), 9.10 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.9, 22.4, 31.1, 37.7, 115.9, 127.1, 128.9, 130.8, 136.8, 158.7, 163.9, 171.3; IR (ATR, neat) ν (cm^{-1}) 2956, 2927, 2859, 1588, 1578, 1526, 1465, 1442, 1374, 752, 690, 637; MS (ESI+) m/z 583 (20, $[2M + H]^+$), 292 (100, $[M + H]^+$), 83 (5); HRMS (ESI+) m/z 213.1377 calcd for $C_{14}H_{16}N_2 + H^+$ 213.1392.

■ ASSOCIATED CONTENT

Supporting Information

Table of atom coordinates and absolute energies, and NMR spectra (^{1}H, ^{13}C, ^{19}F) for all products (**1a−t**, **1v,w**, **2a−l**, **2n**, **2p,q**, **2s,t**, **4**, **6**, **7**, **9−27**). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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