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# A novel access to pyrido[4,3-*d*]pyrimidine scaffold via Staudinger/intramolecular aza-Wittig reaction of 5-acyl-4-(β-azidoalkyl)-1,2,3,4-tetrahydropyrimidin-2-ones

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ABSTRACT

A general four-step approach to 1,2,3,7,8,8a-hexahydropyrido[4,3-*d*]pyrimidin-2-ones via Staudinger/intramolecular aza-Wittig reaction of 5-acyl-4-(β-azidoalkyl)-1,2,3,4-tetrahydropyrimidin-2-ones promoted by $PPh_3$ was developed. Synthesis of the starting pyrimidinones included preparation of 3-azidoaldehydes by the addition of hydrazoic acid to α,β-unsaturated aldehydes, transformation of 3-azidoaldehydes into *N*-[(3-azido-1-tosyl)alkyl]ureas followed by the reaction with enolates of dibenzoylmethane, benzoylacetone, acetylacetone, or ethyl 2,4-dioxo-4-phenylbutanoate and dehydration of the resulting products under acidic conditions.

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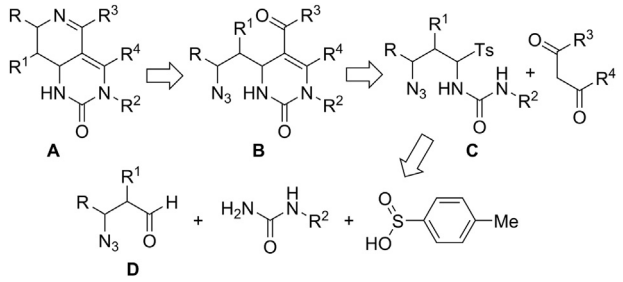
## 1. Introduction

Pyridopyrimidines are of current interest due to their multifaceted pharmacological profiles.[1] Among them, pyrido[4,3-*d*]pyrimidines remain relatively less explored in spite of their interesting applications. For example, they manifest remarkable inhibitory properties against epidermal growth factor receptor tyrosine kinase[2] and dihydrofolate reductase.[3] These compounds possess antioxidant,[4] antitumor,[5] antiulcer,[6] antibacterial,[7] and pesticidal activities.[8] The described syntheses of pyrido[4,3-*d*]pyrimidines mainly start with either pyridine or pyrimidine precursor, which is modified to annulate the other ring.[1] However, to the best of our knowledge, Staudinger/intramolecular aza-Wittig reaction,[9] a powerful strategy for nitrogen heterocycles construction has never been applied to pyrido[4,3-*d*]pyrimidines synthesis.

Previously, we developed a completely general and flexible approach to the synthesis of various 5-functionalized 1,2,3,4-tetrahydropyrimidin-2-ones/thiones, specifically, 5-acyl-substituted ones, based on ureidoalkylation of ketone enolates with α-tosyl-substituted *N*-alkylureas or *N*-alkylthioureas.[10] We have hypothesized that pyrido[4,3-*d*]pyrimidin-2-one scaffold **A** could be assembled from 5-acyl-4-(2-azidoalkyl)pyrimidines **B** using Staudinger/aza-Wittig sequence (Scheme 1). The synthesis of pyrimidines **B** could include ureidoalkylation of enolates of 1,3-diketones with *N*-(3-azido-1-tosylalkyl)ureas **C** followed by dehydration of the resulting products. Azides **C** could be obtained by three-component condensation of 3-azidoaldehydes **D**, *p*-toluenesulfinic acid, and ureas.



**Scheme 1.** Retrosynthesis of pyrido[4,3-*d*]pyrimidin-2-ones via ureidoalkylation/Staudinger/aza-Wittig reactions.

Successful application of this methodology has been reported in our preliminary communication.[11] Here, we describe full details of hexahydropyrido[4,3-*d*]pyrimidines synthesis via Staudinger/aza-Wittig reaction of 5-acyl-4-(β-azidoalkyl)-1,2,3,4-tetrahydropyrimidin-2-ones promoted by $PPh_3$. A three-step preparation of the starting pyrimidines using transformation of 3-

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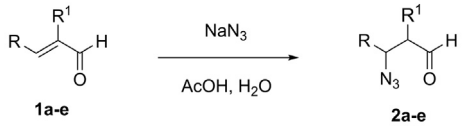
azidoaldehydes into *N*-[(3-azido-1-tosyl)alkyl]ureas followed by reaction with enolates of dibenzoylmethane, benzoylacetone, acetylacetone, or ethyl 2,4-dioxo-4-phenylbutanoate and dehydration of resulting products under acidic conditions is described. The procedure for preparative synthesis of 3-azidoaldehydes by the addition of hydrazoic acid to α,β-unsaturated aldehydes is also reported.

## 2. Results and discussion

### 2.1. Synthesis of 3-azidoaldehydes and *N*-[(3-azido-1-tosyl) alk-1-yl]ureas

3-Azidoaldehydes served as starting compounds for the synthesis of pyrido[4,3-*d*]pyrimidines. The described methods of their preparation include oxidation of 3-azido alkohols,[12] reduction of 3-azido esters,[13] reaction of 3-tosyloxy aldehydes with sodium azide,[14] and addition of hydrazoic acid to α,β-unsaturated aldehydes.[15] However, 3-azidoaldehydes were prepared only on a small scale (<1 g) and usually used in further reactions without purification.[16] Our initial task focused on preparation of pure 3-azidoaldehydes on a multigram scale. We used the method based on the reaction of sodium azide with α,β-unsaturated aldehydes **1a**–**e** in aqueous acetic acid, which seems to be the most promising.

3-Azidopropanal (**2a**) was prepared by the addition of aqueous solution of $NaN_3$ (1.5 equiv) to a cooled (−12 °C) solution of acrolein in acetic acid (Scheme 2). The product was isolated from the reaction mixture as a yellowish oil in 62% yield after extraction with diethyl ether followed by neutralization of the ether extracts with aqueous $Na_2CO_3$, drying, and evaporation of the solvent under reduced pressure. We failed to remove diethyl ether completely and achieve constant mass of the residue due to high volatility of azide **2a**. According to $^1$H NMR data, the crude **2a** always contained a small quantity of diethyl ether. Previously, we described the use of azide **2a** prepared in this way in the synthesis of functionalized pyridine derivatives[17] and two pyrido[4,3-*d*]pyrimidines.[11] In the current work, we attempted to purify the crude **2a** by fast vacuum distillation at 48–59 °C/15–20 mmHg collecting the main fraction in an ice-cooled flask.[18] As a result, azide **2a** was obtained as a colorless transparent liquid (53% yield from acrolein). However, the distilled **2a** was unstable and decomposed in the receiving flask already during distillation. After some time, we observed slow gas evolution (probably $HN_3$) from the main fraction and a minor decrease in vacuum.[19] Therefore, 3-azidopropanal (**2a**) was used immediately after distillation.




**1, 2 a** R = $R^1$ = H; **b** R = Me, $R^1$ = H; **c** R = Et, $R^1$ = H; **d** R = H, $R^1$ = Me; **e** R = H, $R^1$ = Et.

**Scheme 2.** Synthesis of 3-azidoaldehydes **2a**–**e**.

We extended this method to the preparation of other 3-azidoaldehydes **2b**–**e**. In contrast to acrolein, crotonaldehyde (**1b**) reacted with $NaN_3$ (1.5 equiv) in aqueous acetic acid more slowly affording only 72% conversion after 4.25 h at −12 °C according to $^1$H NMR spectroscopic analysis of a sample of the reaction mixture dissolved in $D_2O$. Increase in the reaction temperature improved conversion, which changed to 83% after additional 55 min at 0 °C, and then to 93% after 1.5 h at 25 °C. The work-up of the reaction mixture as described above for **2a** gave practically pure azide **2b** containing only 3% of the starting material. The obtained results prompted us to examine the addition of $HN_3$ to aldehydes **2b**–**e** more thoroughly using $^1$H NMR spectroscopy. The selected data are given in Table 1.

**Table 1**
$^1$H NMR study of the reaction of aldehydes **1b**–**e** with $NaN_3$ in aqueous AcOH at 25 °C

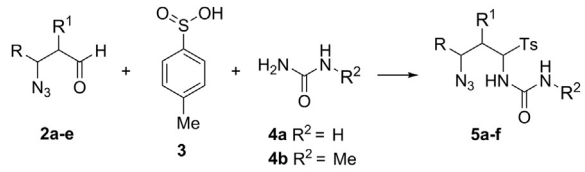
| Entry | **1** | **1**/$NaN_3$[b] | **2** | Molar ratio of **2**/**1**[a] after: | | | |
|---|---|---|---|---|---|---|---|
| | | | | 1 h | 2 h | 3 h | Work-up |
| 1 | **1b** | 1:1.5 | **2b** | 92:8 | 92:8 | 92:8 | 97:3 |
| 2 | **1b** | 1:2.5 | **2b** | 96:4 | 96:4 | 96:4 | 98:2 |
| 3 | **1c** | 1:1.5 | **2c** | — | 90:10 | 92:8 | 94:6 |
| 4 | **1d** | 1:2.5 | **2d** | 74:26 | 87:13 | — | 98:2 |
| 5 | **1e** | 1:2.5 | **2e** | 69:31 | 84:16 | — | 95:5 |

[a] According to $^1$H NMR spectroscopy for samples of reaction mixtures after 1, 2, 3 h (entries 1, 2, 4, 5: extracts in $CDCl_3$; entry 3: solutions in $D_2O$), and for crude products after work-up (in $CDCl_3$).
[b] Molar ratio.

Table 1 shows that the addition of $HN_3$ to crotonaldehyde (**1b**) proceeded rapidly (<1 h) at room temperature to give a 92:8 equilibrium mixture of **2b** and **1b**, respectively (entry 1). A greater excess of $NaN_3$ only slightly shifted this equilibrium to **2b** (entry 2). Compared with **1b**, the rate of the addition decreased insignificantly when pent-2-enal (**1c**) was used (entry 1 vs entry 3). In contrast to aldehydes **1a**–**c**, α-alkyl-substituted aldehydes **1d**,**e** reacted much more slowly even if 2.5 equiv of $NaN_3$ was used (entries 4 and 5).

Based on $^1$H NMR experiments, we developed a simple medium-scale procedure for preparation of azidoaldehydes **2b**–**e**. According to this procedure, an aqueous solution of $NaN_3$ (1.5–2.5 equiv) was added to a solution of aldehydes **1b**–**e** in AcOH followed by stirring of the resulting reaction mixture for 3–4 h at room temperature. Azidoaldehydes **2b**–**e** were obtained in 51–71% yield after extractive work-up, neutralization, drying, and distillation[18] of crude products. Compared with **2a**, compounds **2b**–**e** were stable upon distillation but gradually decomposed during storage at room temperature (slowly in $CDCl_3$ solutions, faster in liquid phase) (NMR spectroscopy data). Stability of azides **2b**–**e**, especially in $CDCl_3$ solutions, significantly increased upon storage at −18 °C.

We used freshly distilled 3-azidoaldehydes **2a**–**e** as starting materials for the synthesis of the required ureidoalkylation reagents. The synthesis involved three-component condensation of **2a**–**e**, *p*-toluenesulfinic acid (**3**), and urea (**4a**) or *N*-methylurea (**4b**) to give the corresponding *N*-[(3-azido-1-tosyl)alk-1-yl]ureas **5a**–**f** (Scheme 3).




**5 a** R = $R^1$ = $R^2$ = H; **b** R = $R^1$ = H, $R^2$ = Me; **c** R = Me, $R^1$ = $R^2$ = H; **d** R = Et, $R^1$ = $R^2$ = H; **e** R = $R^2$ = H, $R^1$ = Me; **f** R = $R^2$ = H, $R^1$ = Et.

**Scheme 3.** Synthesis of ureidoalkylation reagents, *N*-[(3-azido-1-tosyl)alk-1-yl]ureas **5a**–**f**.

Optimized reaction conditions for preparation of ureas **5a**–**f** and their yields are summarized in Table 2.

Three-component condensation of 3-azidopropanal (**2a**), sulfinic acid **3**, and urea (5 equiv) or *N*-methylurea (1.5 equiv) smoothly proceeded in water at room temperature for 24 h to give substituted ureas **5a**,**b** as white solids in 84 and 90% yields, respectively (entries 1 and 2).[20] In contrast, the reactions of other azidoaldehydes **2b**–**e** with acid **3** and urea in water at room temperature afforded only gummy materials containing the expected azidoalkyl ureas **5c**–**f** along with considerable amount of various

**Table 2**
Reaction of 3-azidoaldehydes **2a**–**e** with *p*-toluenesulfinic acid (**3**) and ureas **4a**,**b**

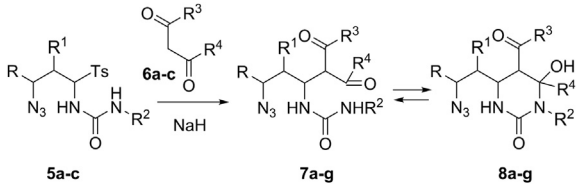
| Entry | 2 | 4 | Reaction conditions[a] | 5 | Yield[b] (%) | Isomer ratio[c] |
|---|---|---|---|---|---|---|
| 1 | **2a** | **4a** | $H_2O$, 24 h | **5a** | 84 | — |
| 2 | **2a** | **4b** | $H_2O$, 24 h | **5b** | 90 | — |
| 3 | **2b** | **4a** | 25% Aq HCOOH, 8 h | **5c** | 92 | 55:45 |
| 4 | **2c** | **4a** | 30% Aq EtOH, 16 h | **5d** | 92 | 58:42 |
| 5 | **2d** | **4a** | 30% Aq EtOH, 19 h | **5e** | 79 | 82:18 |
| 6 | **2e** | **4a** | 30% Aq EtOH, 18 h | **5f** | 83 | 63:37 |

[a] Room temperature; 1:1:5 molar ratio of **2**/**3**/**4** for the synthesis of **5a**,**c**–**f** and 1:1:1.5 molar ratio of **2**/**3**/**4** for the synthesis of **5b**.
[b] Isolated yields.
[c] According to $^1$H NMR spectra of the crude products.

byproducts (NMR spectroscopy data). Compound **5c** was successfully prepared in a yield of 92% by sequential addition of acid **3** and a fivefold excess of urea to a solution of 3-azidobutanal (**2b**) in 25% aqueous HCOOH (entry 3). However, only complex mixtures formed in the reactions of aldehydes **2c**–**e** with **3** and **4a** when aqueous HCOOH was used in various concentrations. Condensation of these aldehydes with **3** and **4a** cleanly proceeded in 30% aqueous EtOH to give the expected products **5d**–**f** in 79–92% yield (entries 4–6). Under optimal conditions (Table 2), sulfones **5a**–**f** precipitated from the reaction mixtures formed after the addition of all reagents as white solids. They were isolated by filtration with >95% purity according to $^1$H NMR spectra of the crude products and used in the ureidoalkylation step without additional purification. Compounds **5c**–**f** were obtained as mixtures of two diastereomers (Table 2).

## 2.2. Synthesis of 5-acyl-4-(β-azidoalkyl)-1,2,3,4-tetrahydropyrimidin-2-ones

According to the retrosynthetic plan (Scheme 1), the next step of the pyrido[4,3-*d*]pyrimidin-2-one scaffold synthesis involved two-step transformation of sulfones **5** into the corresponding 5-acyl-4-(β-azidoalkyl)-1,2,3,4-tetrahydropyrimidin-2-ones using our previously developed methodology for pyrimidine ring construction.[10] First, we studied ureidoalkylation of sodium enolates of acetylacetone, benzoylacetone, and dibenzoylmethane with sulfones **5a**–**c** in dry MeCN or THF (Scheme 4, Table 3). The enolates were generated by treatment of the corresponding CH-acids **6a**–**c** with NaH.




**Scheme 4.** Ureidoalkylation of Na-enolates of 1,3-diketones **6a**–**c** with sulfones **5a**–**c**.

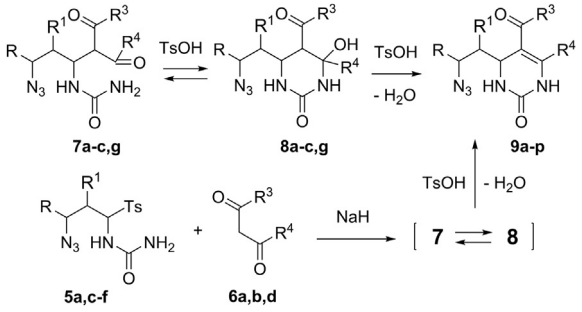
The reaction of sulfone **5a** with the Na-enolate of **6a** readily proceeded at room temperature in 7 h 45 min to give a product of nucleophilic substitution of the tosyl group, the corresponding ureido ketone **7a**, which spontaneously and completely cyclized into hydroxypyrimidinone **8a** under the reaction conditions. Pyrimidine **8a** was isolated in 75% yield as a single diastereomer (Table 3, entry 1). According to $^1$H NMR data, this diastereomer had (4*R**,5*R**,6*R**)-configuration with equatorial orientation of the substituents at C-5 and C-6 ($^3J_{5\text{-H},6\text{-H}}$=11.7, $^3J_{N(1)H,6\text{-H}}\approx$0 Hz)[21] and axial orientation of the hydroxyl group ($^4J_{5\text{-H,OH}}$=0.7 Hz) in DMSO-$d_6$.

In contrast to the reaction of **5a** with the Na-enolate of **6a**, all other reactions of **5a**–**c** with Na-enolates of **6a**–**c** (MeCN or THF, rt, 8–8.33 h) gave only the corresponding acyclic ureido ketones **7b**–**g** in 54–91% yield (Scheme 4; Table 3, entries 2–7).

The products **8a**, **7b**–**g** were readily isolated after removal of solvent followed by aqueous $NaHCO_3$ work-up and filtration with >95% purity ($^1$H NMR spectroscopy data) and were used in further syntheses without additional purification. Their yields were good, except compound **7d** (54%). The moderate yield of **7d** can be explained by partial loss of the product during aqueous work-up because of enhanced solubility of **7d** in water. Our attempt to improve yield of **7d** using extractive work-up of a mother liquor with $CHCl_3$ failed. Compounds **7b**,**e**,**g** were obtained as diastereomeric mixtures (Table 3).

We also attempted to react sulfone **5e** with the Na-enolate of **6b** in MeCN (rt, 8 h) and sulfone **5a** with the Na-enolate of **6d** (Scheme 4; $R^3$=Ph, $R^4$=COOEt) in THF (rt, 8 h). However, after removal of solvent and addition of saturated aqueous $NaHCO_3$ to the resulting residues, only gummy materials were obtained that did not solidify even upon prolonged manipulations. Therefore, it became evident that in these and similar cases the synthesis of 5-acyl-4-(β-azidoalkyl)-1,2,3,4-tetrahydropyrimidin-2-ones should be performed using a one-pot procedure directly from sulfones **5** without isolation of the ureidoalkylation products **7**, **8** from the reaction mixtures. Previously, we demonstrated that this one-pot procedure is often very effective for the pyrimidine synthesis.[10f,g,i]

Thus, we developed two different synthetic methods for preparation of tetrahydropyrimidines **9a**–**p** (Scheme 5). First, we




**Scheme 5.** Synthesis of 5-acyl-4-(β-azidoalkyl)-1,2,3,4-tetrahydropyrimidin-2-ones **9a**–**p**.

**Table 3**
Reaction of azidoalkyl ureas **5a**–**c** with 1,3-diketones **6a**–**c** in the presence of NaH at room temperature

| Entry | 5 | 6 | R | $R^1$ | $R^2$ | $R^3$ | $R^4$ | NaH/**6** molar ratio[a] | Solvent | Reaction time (h) | Product | Yield[b] (%) | Isomer ratio[c] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | **5a** | **6a** | H | H | H | Me | Me | 1.10:1.11 | MeCN | 7.75 | **8a** | 75 | [d] |
| 2 | **5a** | **6b** | H | H | H | Ph | Me | 1.00:1.02 | MeCN | 8.33 | **7b** | 79 | 52:48 |
| 3 | **5a** | **6c** | H | H | H | Ph | Ph | 1.05:1.01 | THF | 8 | **7c** | 90 | — |
| 4 | **5b** | **6a** | H | H | Me | Me | Me | 1.00:1.02 | MeCN | 8 | **7d** | 54 | — |
| 5 | **5b** | **6b** | H | H | Me | Ph | Me | 1.02:1.05 | MeCN | 8.25 | **7e** | 82 | 59:41 |
| 6 | **5b** | **6c** | H | H | Me | Ph | Ph | 1.05:1.00 | THF | 8.08 | **7f** | 91 | — |
| 7 | **5c** | **6b** | Me | H | H | Ph | Me | 1.01:1.02 | MeCN | 8 | **7g** | 75 | 27:28:19:26 |

[a] The amount of the corresponding sulfone **5** is 1.00 equiv.
[b] Isolated yields.
[c] According to $^1$H NMR spectra of the crude products.
[d] A single diastereomer with (4*R**,5*R**,6*R**)-configuration.

examined the transformation of hydroxypyrimidine **8a** and ureido ketones **7b**,**c**,**g** into the corresponding tetrahydropyrimidines **9a**,**f**,**g**,**k**. It was found that dehydration of **8a** cleanly proceeded in refluxing EtOH for 1 h in the presence of TsOH (0.19 equiv) to give pyrimidine **9a** in 77% yield (Table 4, entry 1). The yield of **9a** decreased to 63% when this reaction was carried out under similar conditions but in refluxing MeCN.

**Table 4**
Synthesis of 5-acyl-4-(β-azidoalkyl)-1,2,3,4-tetrahydropyrimidin-2-ones **9a**–**p**

| Entry | Starting material | R | $R^1$ | $R^3$ | $R^4$ | Reaction conditions | Product | Yield[a] (%) | Isomer ratio[b] |
|---|---|---|---|---|---|---|---|---|---|
| 1 | **8a** | H | H | Me | Me | TsOH (0.19 equiv), EtOH, reflux, 1 h | **9a** | 77 | — |
| 2 | **5a**+**6a** | H | H | Me | Me | (i) **6a** (1.03 equiv), NaH (1.01 equiv), THF, rt, 8 h (ii) TsOH (1.32 equiv), THF, reflux, 1.67 h | **9a** | 61 | — |
| 3 | **5c**+**6a** | Me | H | Me | Me | (i) **6a** (1.04 equiv), NaH (1.01 equiv), THF, rt, 8 h (ii) TsOH (1.32 equiv), THF, reflux, 1.92 h | **9b** | 47 | 86:14 |
| 4 | **5d**+**6a** | Et | H | Me | Me | (i) **6a** (1.06 equiv), NaH (1.02 equiv), THF, rt, 8 h (ii) TsOH (1.30 equiv), THF, reflux, 1.92 h | **9c** | 74 | 65:35 |
| 5 | **5e**+**6a** | H | Me | Me | Me | (i) **6a** (1.06 equiv), NaH (1.02 equiv), THF, rt, 8 h (ii) TsOH (1.30 equiv), THF, reflux, 1.92 h | **9d** | 63 | 56:44 |
| 6 | **5f**+**6a** | H | Et | Me | Me | (i) **6a** (1.03 equiv), NaH (1.01 equiv), THF, rt, 8 h (ii) TsOH (1.31 equiv), THF, reflux, 1.83 h | **9e** | 76 | 69:31 |
| 7 | **7b** | H | H | Ph | Me | TsOH (0.20 equiv), EtOH, reflux, 1 h | **9f** | 89 | — |
| 8 | **7g** | Me | H | Ph | Me | TsOH (0.21 equiv), EtOH, reflux, 45 min | **9g** | 88 | 55:45 |
| 9 | **5d**+**6b** | Et | H | Ph | Me | (i) **6b** (1.02 equiv), NaH (1.01 equiv), THF, rt, 8 h (ii) TsOH (1.31 equiv), THF, reflux, 1.5 h | **9h** | 82 | 55:45 |
| 10 | **5e**+**6b** | H | Me | Ph | Me | (i) **6b** (1.06 equiv), NaH (1.03 equiv), THF, rt, 8 h (ii) TsOH (1.30 equiv), THF, reflux, 1.58 h | **9i** | 79 | 50:50 |
| 11 | **5f**+**6b** | H | Et | Ph | Me | (i) **6b** (1.02 equiv), NaH (1.01 equiv), THF, rt, 8 h (ii) TsOH (1.30 equiv), THF, reflux, 1.83 h | **9j** | 73 | 67:33 |
| 12 | **7c** | H | H | Ph | Ph | TsOH (1.01 equiv), EtOH, reflux, 2.25 h | **9k** | 21 | — |
| 13 | **5a**+**6d** | H | H | Ph | COOEt | (i) **6d** (1.03 equiv), NaH (1.01 equiv), THF, rt, 8.17 h (ii) TsOH (1.32 equiv), THF, reflux, 3.17 min | **9l** | 60 | — |
| 14 | **5c**+**6d** | Me | H | Ph | COOEt | (i) **6d** (1.03 equiv), NaH (1.02 equiv), THF, rt, 8 h (ii) TsOH (1.30 equiv), THF, reflux, 2.5 h | **9m** | 62 | 63:37 |
| 15 | **5d**+**6d** | Et | H | Ph | COOEt | (i) **6d** (1.03 equiv), NaH (1.01 equiv), THF, rt, 8 h (ii) TsOH (1.40 equiv), THF, reflux, 2.33 h | **9n** | 73 | 62:38 |
| 16 | **5e**+**6d** | H | Me | Ph | COOEt | (i) **6d** (1.03 equiv), NaH (1.01 equiv), THF, rt, 8 h (ii) TsOH (1.43 equiv), THF, reflux, 2.33 h | **9o** | 19 | 60:40 |
| 17 | **5f**+**6d** | H | Et | Ph | COOEt | (i) **6d** (1.03 equiv), NaH (1.01 equiv), THF, rt, 8 h (ii) TsOH (1.40 equiv), THF, reflux, 2.33 h | **9p** | 14 | 50:50 |

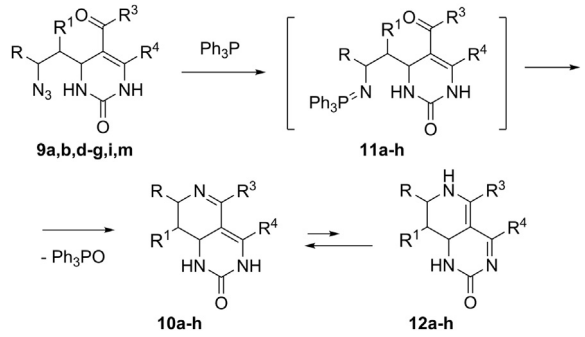
[a] Isolated yields.
[b] According to $^1$H NMR spectra of the crude products.

Ureido ketones **7b** and **7g** smoothly underwent cyclization–dehydration in refluxing EtOH in the presence of TsOH to give the corresponding pyrimidines **9f** and **9g** in high yields (entries 7 and 8). In contrast, the reduced electrophilicity of the benzoyl carbonyl groups in dibenzoylmethane derivative **7c** extremely hampered the cyclization–dehydration of this compound to afford pyrimidine **9k**. In this case greater amounts of TsOH (>0.5 equiv) and longer reaction times were required for completion of conversion of the starting material in refluxing EtOH or MeCN. These conditions led to formation of a significant amount of various byproducts that complicated isolation of **9k** and sharply decreased its yield. Compound **9k** was obtained in pure form only in 21% yield by refluxing **7c** in EtOH in the presence of 1.01 equiv of TsOH for 2 h 15 min followed by isolation of **9k** using silica gel column chromatography (entry 12). In this experiment dibenzoylmethane (**6c**) was isolated in a 30% yield as one of the byproducts.

Next, we developed a convenient one-pot synthesis of tetrahydropyrimidines **9a**–**e**,**h**–**j**,**l**–**p** based on the reaction of sulfones **5a**,**c**–**f** with Na-enolates of **6a**,**b**,**d** in THF (rt, 8–8.17 h) followed by the addition of 1.30–1.43 equiv of TsOH and heating at reflux for 1.5–3.17 h (Table 4, entries 2–6, 9–11, 13–17). The completion of the second step was monitored by TLC. Tetrahydropyrimidines **9** were isolated from the reaction mixtures after removal of the solvent, aqueous $NaHCO_3$ work-up of the resulting residues, and filtration of the obtained solids. Generally, the yields of pyrimidines **9** varied from moderate to high (47–82%) with the exception of compounds **9o**,**p**. The latter were isolated by silica gel column chromatography in only 19 and 14% yields, respectively (entries 16 and 17). Notably, the yield of pyrimidine **9a** obtained from **5a** and **6a** in the one-pot procedure was slightly higher (61%) than the overall yield in two steps (58%) (entry 2 vs entry 1).

## 2.3. Synthesis of pyrido[4,3-*d*]pyrimidin-2-ones

The final step of the synthesis of pyrido[4,3-*d*]pyrimidin-2-ones **10** was intramolecular Staudinger/aza-Wittig reaction of 5-acyl-4-(β-azidoalkyl)pyrimidines **9** promoted by $PPh_3$ (Scheme 6).




**Scheme 6.** Synthesis of pyrido[4,3-*d*]pyrimidin-2-ones **10a**–**h** from 5-acyl-4-(β-azidoalkyl)pyrimidines **9a**,**b**,**d**–**g**,**i**,**m** via intramolecular Staudinger/aza-Wittig reaction.

Initially, we studied the reaction of **9a** with $PPh_3$ (1.1 equiv) in various solvents (THF, MeCN, and 1,4-dioxane) at reflux for 1.5 h. The obtained reaction mixtures were evaporated in vacuo to dryness, and the composition of residues dissolved in DMSO-$d_6$ was

determined using $^1$H NMR spectroscopy. The starting material disappeared in all cases, and the expected pyridopyrimidine **10a** formed as the main heterocyclic product. However, the reaction in THF, besides 45% of **10a**, gave two other compounds in a ratio of 30:25 that seem to be intermediates of incomplete conversion of **9a** into **10a**. According to $^1$H NMR spectrum, one of them (30%) was iminophosphorane **11a**. These intermediates were absent in refluxing 1,4-dioxane, but significant amount of side products formed along with **10a**. Refluxing MeCN gave the better result furnishing pyridopyrimidine **10a** plus the above intermediates in a ratio of 83:13:4, respectively. An increase in the reaction time to 6 h was necessary to achieve complete conversion of **9a** into **10a** in MeCN at reflux ($^1$H NMR spectroscopy data).

The reaction of 5-benzoyl-substituted pyrimidine **9f** with $PPh_3$ (1.1 equiv) in refluxing THF for 6 h was studied. Although the starting material was consumed, no traces of the bicyclic product **10e** were detected in the $^1$H NMR spectrum of the crude reaction mixture.

Therefore, the results obtained show that the transformation of pyrimidines **9** into bicycles **10** is controlled predominantly by the intramolecular aza-Wittig reaction. Specifically, the rate of this step depends on electrophilicity of carbonyl group and steric factors in iminophosphoranes **11**. Based on these data, further we carried out all the pyrido[4,3-*d*]pyrimidines syntheses in refluxing MeCN for 5.5–8 h (Table 5).

**Table 5**
Synthesis of pyrido[4,3-*d*]pyrimidin-2-ones **10a**–**h** via intramolecular Staudinger/aza-Wittig reaction of 5-acyl-4-(β-azidoalkyl)pyrimidines **9a**,**b**,**d**–**g**,**i**,**m** promoted by $PPh_3$[a]

| Entry | Starting material[b] | Isomer ratio | R | $R^1$ | $R^3$ | $R^4$ | Time (h) | Product | Yield[c] (%) | Isomer ratio[d] |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | **9a** | — | H | H | Me | Me | 5.5 | **10a** | 94 | — |
| 2 | **9b** | 86:14 | Me | H | Me | Me | 7 | **10b** | 84 | 90:10 |
| 3 | **9d** | 56:44 | H | Me | Me | Me | 6 | **10c** | 87 | 57:43 |
| 4 | **9e** | 69:31 | Et | H | Me | Me | 6 | **10d** | 55 | 65:35 |
| 5 | **9f** | — | H | H | Ph | Me | 7 | **10e** | 95 | — |
| 6 | **9g** | 55:45 | Me | H | Ph | Me | 8 | **10f** | 96 | 54:46 |
| 7 | **9i** | 50:50 | H | Me | Ph | Me | 6 | **10g** | 90 | 49:51 |
| 8 | **9m** | 67:37 | Me | H | Ph | COOEt | 6 | **10h** | 26 | [e] |

[a] Reactions were carried out in refluxing MeCN in the presence of 1.13–1.18 equiv of $PPh_3$.
[b] Crude starting materials were used.
[c] Isolated yields.
[d] (7*R**,8a*S**)-**10**/(7*R**,8a*R**)-**10**. According to $^1$H NMR spectra of the crude products.
[e] A single diastereomer with (7*R**,8a*S**)-configuration was isolated by column chromatography.

Since compounds **10a**–**c** were slightly soluble in MeCN, they precipitated from the reaction mixtures and were isolated in pure form in 84–94% yield by filtration. Compounds **10d**–**h** were isolated in up to 96% yield using silica gel column chromatography of the residues obtained after evaporation of the reaction mixtures. Low yield of ethyl carboxylate **10h** (26%) is caused by formation of a huge amount of various byproducts ($^1$H NMR spectroscopy data).

According to NMR data, pyrido[4,3-*d*]pyrimidines **10b**–**d**,**f**,**g** formed as mixtures of two diastereomers in ratios that are close to isomer ratios in the starting pyrimidines **9b**,**d**,**e**,**g**,**i** (Table 5). Only compound **10h** was obtained as a single diastereomer indicating that the second isomer of **10h** did not form in the intramolecular aza-Wittig reaction of intermediate **11h**.

The structure of the obtained pyridopyrimidines was established by NMR spectroscopy. First, we determined in which tautomeric form these compounds exist, namely, in the form of 1,2,3,7,8,8a-hexahydropyrido[4,3-*d*]pyrimidin-2-ones **10** or 1,2,6,7,8,8a-hexahydropyrido[4,3-*d*]pyrimidin-2-ones **12** (Scheme 5).[22] The values of $^1$H NMR chemical shifts for the two NH protons (6.88–7.21 and 8.39–8.76 ppm) in DMSO-$d_6$ clearly indicated that both the protons are bonded to the ureido nitrogens. Therefore, we concluded that the obtained pyridopyrimidines in DMSO-$d_6$ solutions exist predominantly in the form of tautomer **10**. This conclusion is supported by a high geminal coupling constant between the 7-$H_A$ and 7-$H_B$ protons in **10a**,**c**,**e**,**g** (14.8–17.9 Hz), indicating that these protons are located at α-position to a double bond.[23] In addition, structures **10a**–**h** are confirmed by the absence of spin–spin coupling between one of the NH protons and the 7-H proton(s), which could be expected in the case of structures **12a**–**h**.

It should be noted that the signal of the $N_{(3)}H$ proton (8.39–8.76 ppm) in $^1$H NMR spectra of **10a**–**h** in DMSO-$d_6$ solutions appeared as an unusually broad singlet. In addition, $^{13}$C NMR spectra of these compounds (except **10h**) demonstrated a noticeable broadening of the signal of the C-4 carbon (135.7–138.5 ppm). These features of the NMR spectra could be explained by an exchanging process between tautomers **10** and **12**. To confirm this suggestion we performed ab initio calculations (B3LYP/6-311+G(d,p))[24] for pyridopyrimidines **10a**,**e** and **12a**,**e** in the gas phase and in DMSO solution using the polarizable continuum model (PCM). According to these calculations, in the gas phase, **10a**,**e** are considerably more stable tautomers than **12a**,**e** (6.94–10.23 kcal/mol). However, the computed difference in energies of tautomers **10a**,**e** and **12a**,**e** in DMSO solution becomes quite small (0.27–0.79 kcal/mol), suggesting that tautomeric equilibrium between **10a**,**e** and **12a**,**e** in favor of **10a**,**e** could take place in solutions.

The relative configurations of compounds **10b**–**d**,**f**–**h** were determined by $^1$H NMR spectroscopy. Large values of two vicinal coupling constants between 7-H, 8-H, and 8a-H protons in $^1$H NMR spectra of the major isomers of **10b**–**d**,**f**,**h** and the minor isomer of **10g** (7.3–11.9 Hz) allowed us to conclude that the tetrahydropyridine cycle of these compounds adopts a flattened chair conformation with a pseudo axial orientation of the 8a-H proton and a pseudo equatorial position of the alkyl group at C-7 (for **10b**,**d**,**f**,**h**) or C-8 (for **10c**,**g**). Therefore, the above mentioned diastereomers had (7*R**,8a*S**)-configuration. The relative configuration of the minor isomers of **10b**–**d**,**f** and the major isomer of **10g** was (7*R**,8a*R**).

## 3. Conclusion

A general four-step approach to 1,2,3,7,8,8a-hexahydropyrido[4,3-*d*]pyrimidin-2-ones via Staudinger/intramolecular aza-Wittig reaction of 5-acyl-4-(β-azidoalkyl)-1,2,3,4-tetrahydropyrimidin-2-ones promoted by $PPh_3$ was developed. Synthesis of the starting pyrimidinones included transformation of 3-azidoaldehydes into *N*-[(3-azido-1-tosyl)alkyl]ureas followed by reaction with enolates of dibenzoylmethane, benzoylacetone, acetylacetone, or ethyl 2,4-dioxo-4-phenylbutanoate and dehydration of the resulting products under acidic conditions. We believe that this approach to pyrido[4,3-*d*]pyrimidine scaffold is very promising since both components of the amidoalkylation reaction can be widely varied. Furthermore, the prepared hexahydropyrido[4,3-*d*]pyrimidin-2-ones can be aromatized or reduced by routine procedures expanding the synthetic utility of the method.

Medium-scale synthesis of 3-azidoaldehydes based on the reaction of α,β-unsaturated aldehydes with hydrazoic acid generated from sodium azide and aqueous acetic acid was also developed. High availability of 3-azidoaldehydes provides an opportunity for wider application of these compounds in organic synthesis.

## 4. Experimental section

### 4.1. General

All solvents were distilled before use. Petroleum ether had a distillation range of 40–70 °C. Dry solvents (MeCN, THF, 1,4-

dioxane) were obtained according to standard procedures. *p*-Toluenesulfinic acid (**3**) was synthesized by treatment of saturated aqueous solution of sodium *p*-toluenesulfinate[25] with hydrochloric acid at 0 °C, dried over $P_2O_5$, and stored at 0 °C. Sodium hydride (60% suspension in mineral oil) was thoroughly washed with dry pentane and dried under vacuum prior to use. 2-Ethylprop-2-enal (**1e**) with bp 91–93.5 °C/760 mmHg and 2-methylprop-2-enal (**1d**) with bp 67–68 °C/760 mmHg were used. Acrolein (**1a**) (90%, Aldrich) was used without distillation since it had no effect on the yield of 3-azidopropanal. Ethyl 2,4-dioxo-4-phenylbutanoate (**6d**) was prepared as described in the literature[26] and used without crystallization. All other reagents were purchased from commercial sources and used without additional purification. FTIR spectra were recorded using a Bruker Vector 22 spectrophotometer in Nujol for solid samples or in film for liquid samples. Band characteristics in the IR spectra are defined as very strong (vs), strong (s), medium (m), weak (w), shoulder (sh), and broad (br). $^1$H NMR and proton-decoupled $^{13}$C NMR spectra (solutions in DMSO-$d_6$ or $CDCl_3$) were acquired using a Bruker DPX 300 spectrometer at 300.13 MHz ($^1$H) and 75.48 MHz ($^{13}$C). $^1$H NMR chemical shifts are referenced to the residual proton signal in DMSO-$d_6$ (2.50 ppm) or $CDCl_3$ (7.25 ppm). In $^{13}$C NMR spectra, central signals of DMSO-$d_6$ (39.50 ppm) or $CDCl_3$ (77.00 ppm) were used as references. Multiplicities are reported as singlet (s), doublet (d), triplet (t), quartet (q), and some combinations of these, multiplet (m). Selective $^1$H–$^1$H decoupling and DEPT-135 experiments were used to aid in the assignment of $^1$H and $^{13}$C NMR signals. Elemental analyses (CHN) were performed by using a Thermo Finnigan Flash EA1112 apparatus. Thin-layer chromatography was carried out on Aldrich silica gel 60 $F_{254}$ aluminum backed plates in chloroform/methanol (9:1, v/v) and chloroform/methanol (5:1, v/v) as solvent systems. Spots were visualized with UV light or iodine vapors. Column chromatography was performed with Macherey–Nagel silica gel 60 (0.063–0.200 mm). All yields refer to isolated, spectroscopically and TLC pure compounds. The color of substances was white, if not otherwise mentioned. Evaporation of solvent from all the reaction mixtures formed after one-pot syntheses of pyrimidines **9** (from **5**) was carried out, at the beginning, upon cooling (temperature of water bath about 5–10 °C), and low vacuum (about 100 mmHg), otherwise the vigorous foaming complicated evaporation. Distillation of 3-azidoaldehydes **2a**–**c** was performed without protecting atmosphere since it had no effect on purity, yield or stability of products. All 3-azidoaldehydes started to decompose during the distillation if boiling temperature was higher than 70 °C. The geometry optimizations of compounds **10a**,**e** and **12a**,**e** were carried out at the B3LYP level of theory using Gaussian 09 suite[24] of quantum chemical programs. Pople's basis sets, 6-311+G(d,p), were employed for geometry optimization in both the gas phase and DMSO solution. The effect of continuum solvation was incorporated by using the polarizable continuum model (PCM).

## 4.2. Synthesis of 3-azidoaldehydes

*4.2.1. 3-Azidopropanal (**2a**).* A solution of $NaN_3$ (30.75 g, 0.473 mol) in $H_2O$ (115 mL) was added dropwise to a stirred, cooled (internal temperature −12 °C) solution of acrolein (**1a**) (17.68 g, 0.315 mol) in AcOH (45 mL). After the addition was completed, cooling was removed, the resulting emulsion was stirred for additional 30 min, and extracted with diethyl ether (2×100 mL, 3×50 mL). Combined extracts were washed with 7% aqueous solution of $Na_2CO_3$ (3×50 mL, 2×30 mL), $H_2O$ (2×50 mL), brine (3×50 mL, 2×30 mL), and dried overnight over $Na_2SO_4$ at +4 °C (transparent yellow liquid). Then the solvent was removed under reduced pressure, and the residue was subjected to *fast* vacuum distillation collecting the main fraction (a colorless liquid) in the receiving flask cooled in an ice bath. The collection began at bp 48 °C/20 mmHg and finished at 59 °C/15 mmHg (the pressure slightly decreased during distillation). The distilled **2a** (16.62 g, 53%) was very unstable and began to decompose (slow gas evolution) in the receiving flask at the time of distillation.[19] Therefore, 3-azidopropanal (**2a**) was used in the next step immediately after distillation. $^1$H NMR (300.13 MHz, DMSO-$d_6$) $\delta$: 9.68 (1H, t, $^3J$=1.2 Hz, CH=O), 3.58 (2H, t, $^3J$=6.2 Hz, $CH_2N_3$), 2.76 (2H, dt, $^3J$=6.2, $^3J$=1.2 Hz, $CH_2C$=O); $^{13}$C NMR (75.48 MHz, DMSO-$d_6$) $\delta$: 201.3 (C=O), 44.2 ($CH_2N_3$), 42.1 ($CH_2$C=O).

*4.2.2. 3-Azidobutanal (**2b**).* A solution of $NaN_3$ (16.05 g, 0.247 mol) in $H_2O$ (60 mL) was added dropwise to a stirred solution of but-2-enal (**1b**) (11.53 g, 0.164 mol) in AcOH (23 mL) cooled in an ice bath. After the addition was complete, cooling was removed, the resulting emulsion was warmed to room temperature (water bath), stirred for 4 h, and extracted with diethyl ether (100 mL, 4×50 mL). Combined extracts were washed with 7% aqueous solution of $Na_2CO_3$ (3×50 mL, 25 mL), $H_2O$ (3×50 mL), brine (3×25 mL), and dried overnight over $Na_2SO_4$ at +4 °C (transparent slightly yellow liquid). Then the solvent was removed under reduced pressure, and the residue was subjected to vacuum distillation to give **2b** (13.30 g, 72%) as a colorless liquid, which was immediately used in the next step. Bp 58–59.5 °C/18 mmHg. $n_D^{20}$ 1.4490. $^1$H NMR (300.13 MHz, $CDCl_3$) $\delta$: 9.72 (1H, dd, $^3J$=1.7, $^3J$=1.3 Hz, CH=O), 4.02 (1H, ddq, $^3J$=7.6, $^3J$=6.6, $^3J$=5.6 Hz, $CHN_3$), 2.62 (1H, ddd, $^2J$=17.4, $^3J$=7.6, $^3J$=1.7 Hz, $H_A$ in $CH_2C$=O), 2.52 (1H, ddd, $^2J$=17.4, $^3J$=5.6, $^3J$=1.3 Hz, $H_B$ in $CH_2C$=O), 1.30 (3H, d, $^3J$=6.6 Hz, $CH_3$); $^{13}$C NMR (75.48 MHz, $CDCl_3$) $\delta$: 199.3 (C=O), 52.1 ($CHN_3$), 49.4 ($CH_2$), 19.3 ($CH_3$); IR (neat) $\nu$, cm$^{-1}$: 2978 (m), 2936 (w), 2905 (w), 2877 (w) ($CH_2$, $CH_3$), 2836 (m), 2734 (m) (H–CO), 2118 (vs) ($N_3$), 1726 (s) (C=O), 1456 (m) ($CH_2$, $CH_3$), 1381 (m) ($CH_3$), 1265 (s) ($N_3$).

*4.2.3. 3-Azidopentanal (**2c**).* Compound **2c** was prepared from pent-2-enal (**1c**) (9.569 g, 113.75 mmol), $NaN_3$ (18.504 g, 284.55 mmol), $H_2O$ (60 mL), and AcOH (18 mL) as described for **2b**. The resulting emulsion was extracted with diethyl ether (2×25 mL, 2×20 mL). Combined extracts were washed with 7% aqueous solution of $Na_2CO_3$ (3×30 mL, 15 mL), $H_2O$ (2×30 mL), brine (3×15 mL), and dried for 1.5 h over $Na_2SO_4$ at room temperature (transparent slightly yellow liquid). Then the solvent was removed under reduced pressure, and the residue was subjected to vacuum distillation collecting the main fraction (a colorless liquid) in the receiving flask cooled in an ice bath. The distilled **2c** (10.292 g, 71%) was immediately used in the next step. Bp 32–35 °C/0.1 mmHg. $n_D^{20}$ 1.4506. $^1$H NMR (300.13 MHz, $CDCl_3$) $\delta$: 9.74 (1H, dd, $^3J$=1.6, $^3J$=1.3 Hz, CH=O), 3.79 (1H, dddd, $^3J$=7.6, $^3J$=6.5, $^3J$=6.5, $^3J$=5.4 Hz, $CHN_3$), 2.60 (1H, ddd, $^2J$=17.5, $^3J$=7.6, $^3J$=1.6 Hz, $H_A$ in $CH_2C$=O), 2.56 (1H, ddd, $^2J$=17.5, $^3J$=5.4, $^3J$=1.3 Hz, $H_B$ in $CH_2C$=O), 1.53–1.63 (2H, m, $CH_2$ in Et), 0.96 (3H, t, $^3J$=7.4 Hz, $CH_3$); $^{13}$C NMR (75.48 MHz, $CDCl_3$) $\delta$: 199.4 (C=O), 58.3 ($CHN_3$), 47.6 ($CH_2$CH=O), 27.4 ($CH_2$ in Et), 10.2 ($CH_3$); IR (neat) $\nu$, cm$^{-1}$: 2972 (m), 2936 (m), 2881 (m) ($CH_2$, $CH_3$), 2836 (m), 2733 (m) (H–CO), 2102 (vs) ($N_3$), 1726 (s) (C=O), 1463 (m) ($CH_2$, $CH_3$), 1385 (m) ($CH_3$), 1269 (s) ($N_3$).

*4.2.4. 3-Azido-2-methylpropanal (**2d**).* A solution of $NaN_3$ (11.582 g, 178.10 mmol) in $H_2O$ (35 mL) was added dropwise to a stirred solution of 2-methylprop-2-enal (**1d**) (4.993 g, 71.25 mmol) in AcOH (12 mL) cooled in an ice bath. After the addition was complete, cooling was removed, the resulting emulsion was warmed to room temperature (water bath), stirred for 3 h, and extracted with diethyl ether (4×20 mL). Combined extracts were washed with 7% aqueous solution of $Na_2CO_3$ (3×20 mL, 10 mL), $H_2O$ (2×30 mL), brine (3×15 mL), and dried for 1.5 h over $Na_2SO_4$ at room temperature (transparent slightly yellow liquid). The solvent was removed under reduced pressure, and the residue was subjected to vacuum distillation, collecting the main fraction (a colorless liquid) in the receiving flask cooled in an ice bath. The distilled **2d** (4.465 g, 55%) was

immediately used in the next step. Bp 66–67 °C/22 mmHg; 34–39 °C/1 mmHg. $n_D^{20}$ 1.4514. $^1$H NMR (300.13 MHz, $CDCl_3$) $\delta$: 9.67 (1H, d, $^3J$=0.9 Hz, CH=O), 3.59 (1H, dd, $^2J$=12.5, $^3J$=6.5 Hz, $H_A$ in $CH_2N_3$), 3.47 (1H, dd, $^2J$=12.5, $^3J$=5.7 Hz, $H_B$ in $CH_2N_3$), 2.62 (1H, dddq, $^3J$=7.3, $^3J$=6.5, $^3J$=5.7, $^3J$=0.9 Hz, CHC=O), 1.20 (3H, d, $^3J$=7.3 Hz, $CH_3$); $^{13}$C NMR (75.48 MHz, $CDCl_3$) $\delta$: 202.1 (C=O), 51.1 ($CH_2N_3$), 45.9 (CH), 11.3 ($CH_3$); IR (neat) $\nu$, cm$^{-1}$: 2978 (m), 2937 (m), 2878 (m) ($CH_2$, $CH_3$), 2825 (m), 2728 (m) (H–CO), 2104 (vs) ($N_3$), 1728 (s) (C=O), 1459 (m) ($CH_2$, $CH_3$), 1375 (w) ($CH_3$), 1281 (s) ($N_3$).

*4.2.5. 3-Azido-2-ethylpropanal (**2e**).* Compound **2e** was prepared from freshly distilled 2-ethylprop-2-enal (**1e**) (8.127 g, 96.61 mmol), $NaN_3$ (15.708 g, 241.55 mmol), $H_2O$ (50 mL), and AcOH (15 mL) as described for **2d**. The resulting emulsion was extracted with diethyl ether (2×25 mL, 2×20 mL). Combined extracts were washed with 7% aqueous solution of $Na_2CO_3$ (3×35 mL, 2×15 mL), $H_2O$ (2×35 mL), brine (3×15 mL), and dried for 1.5 h over $Na_2SO_4$ at room temperature (transparent slightly yellow liquid). The solvent was removed under reduced pressure, and the residue was subjected to vacuum distillation, collecting the main fraction (a colorless liquid) in the receiving flask cooled in an ice bath. The distilled **2e** (6.210 g, 51%) was immediately used in the next step. Bp 34–35 °C/0.1 mmHg. $n_D^{20}$ 1.4530. $^1$H NMR (300.13 MHz, $CDCl_3$) $\delta$: 9.66 (1H, d, $^3J$=1.5 Hz, CH=O), 3.58 (1H, dd, $^2J$=12.6, $^3J$=7.0 Hz, $H_A$ in $CH_2N_3$), 3.48 (1H, dd, $^2J$=12.6, $^3J$=5.2 Hz, $H_B$ in $CH_2N_3$), 2.45 (1H, ddddd, $^3J$=7.0, $^3J$=6.8, $^3J$=6.6, $^3J$=5.2, $^3J$=1.5 Hz, CHC=O), 1.76 (1H, ddq, $^2J$=14.1, $^3J$=7.5, $^3J$=6.8 Hz, $H_C$ in C$H_2$CH$_3$), 1.59 (1H, ddq, $^2J$=14.1, $^3J$=7.5, $^3J$=6.6 Hz, $H_D$ in C$H_2$CH$_3$), 0.96 (3H, t, $^3J$=7.5 Hz, $CH_3$); $^{13}$C NMR (75.48 MHz, $CDCl_3$) $\delta$: 202.3 (C=O), 52.5 (CH), 49.2 ($CH_2N_3$), 19.7 ($CH_2$ in Et), 11.0 ($CH_3$); IR (neat) $\nu$, cm$^{-1}$: 2970 (m), 2937 (m), 2878 (m) ($CH_2$, $CH_3$), 2824 (m), 2724 (m) (H–CO), 2104 (vs) ($N_3$), 1727 (s) (C=O), 1460 (m) ($CH_2$, $CH_3$), 1271 (s) ($N_3$).

### 4.3. Synthesis of *N*-[(3-azido-1-tosyl)alk-1-yl]ureas

*4.3.1. N-[(3-Azido-1-tosyl)prop-1-yl]urea (**5a**).* To a solution of freshly distilled 3-azidopropanal (**2a**) (12.32 g, 0.124 mol) in $H_2O$ (100 mL) at room temperature was added *p*-toluenesulfinic acid (19.43 g, 0.124 mol) under vigorous stirring followed by the addition of $H_2O$ (50 mL), and the resulting suspension was stirred for 30 min. Then urea (37.31 g, 0.621 mol) and $H_2O$ (100 mL) were added, and the reaction mixture was stirred at room temperature for 24 h. The obtained suspension was cooled to 0 °C, the precipitate was filtered, washed with ice-cold water, petroleum ether, and dried to give **5a** (30.89 g, 84%), which was used without further purification. Mp 108.5–110 °C (decomp., MeCN). $^1$H NMR (300.13 MHz, DMSO-$d_6$) $\delta$: 7.67–7.72 (2H, m, ArH), 7.39–7.45 (2H, m, ArH), 6.97 (1H, d, $^3J$=10.2 Hz, NH), 5.72 (2H, s, $NH_2$), 5.01 (1H, ddd, $^3J$=11.1, $^3J$=10.2, $^3J$=3.2 Hz, $CHSO_2$), 3.54 (1H, ddd, $^2J$=12.4, $^3J$=6.5, $^3J$=4.7 Hz, $H_A$ in $CH_2N_3$), 3.31 (1H, ddd, $^2J$=12.4, $^3J$=9.2, $^3J$=5.8 Hz, $H_B$ in $CH_2N_3$), 2.19 (1H, dddd, $^2J$=14.0, $^3J$=9.2, $^3J$=6.5, $^3J$=3.2 Hz, $H_C$ in C$H_2$CH$_2$N$_3$), 2.40 (3H, s, $CH_3$), 1.76 (1H, dddd, $^2J$=14.0, $^3J$=11.1, $^3J$=5.8, $^3J$=4.7 Hz, $H_D$ in C$H_2$CH$_2$N$_3$); $^{13}$C NMR (75.48 MHz, DMSO-$d_6$) $\delta$: 156.6 (C=O), 144.5 (C), 133.9 (C), 129.7 (2CH), 129.0 (2CH), 67.9 ($CHSO_2$), 46.9 ($CH_2N_3$), 26.6 (C$H_2$CH$_2$N$_3$), 21.2 ($CH_3$); IR (Nujol) $\nu$, cm$^{-1}$: 3463 (br s), 3351 (bs s), 3332 (br s), 3195 (br w) (NH), 3067 (w), 3056 (w), 3002 (w) ($CH_{arom}$), 2162 (m), 2123 (s), 2107 (s) ($N_3$), 1667 (vs) (amide-I), 1593 (m) ($CC_{arom}$), 1523 (s) (amide-II), 1283 (s), 1143 (s) ($SO_2$), 813 (m) ($CH_{arom}$). Anal. Calcd for $C_{11}H_{15}N_5O_3S$: C, 44.44; H, 5.09; N, 23.55. Found: C, 44.60; H, 5.41; N, 23.38.

*4.3.2. N-[(3-Azido-1-tosyl)prop-1-yl]-N′-methylurea (**5b**).* To a solution of freshly distilled 3-azidopropanal (**2a**) (16.617 g, 167.70 mmol) in $H_2O$ (100 mL) was added *p*-toluenesulfinic acid (26.199 g, 167.72 mmol) under vigorous stirring followed by the addition of $H_2O$ (50 mL). After 2 min, the resulting solid was triturated until the fine suspension formed, $H_2O$ (10 mL) was added, and the suspension was stirred at room temperature for 20 min. Then *N*-methylurea (18.699 g, 252.42 mmol) and $H_2O$ (50 mL) were added and the reaction mixture was stirred for 24 h. After 2, 4, and 6 h from the beginning of the reaction, the solid was triturated to obtain the fine suspension. After about 3 h from the beginning of the reaction the suspension became extremely dense, but after trituration it was fluid enough to be stirred normally. When the reaction was completed, the obtained mixture was cooled to 0 °C, the precipitate was filtered, washed with ice-cold water, petroleum ether, and dried to give **5b** (47.223 g, 90%), which was used without further purification. Mp 114.5–115 °C (decomp., MeCN); $^1$H NMR (300.13 MHz, DMSO-$d_6$) $\delta$: 7.66–7.71 (2H, m, ArH), 7.39–7.45 (2H, m, ArH), 6.88 (1H, d, $^3J$=10.2 Hz, N*H*CH), 5.84 (1H, q, $^3J$=4.7 Hz, N*H*Me), 5.04 (1H, ddd, $^3J$=10.2, $^3J$=11.1, $^3J$=3.3 Hz, $CHSO_2$), 3.51 (1H, ddd, $^2J$=12.4, $^3J$=6.7, $^3J$=4.8 Hz, $H_A$ in $CH_2N_3$), 3.31 (1H, ddd, $^2J$=12.4, $^3J$=9.0, $^3J$=6.0 Hz, $H_B$ in $CH_2N_3$), 2.41 (3H, s, $CH_3$ in Ts), 2.40 (3H, d, $^3J$=4.7 Hz, $NCH_3$), 2.17 (1H, dddd, $^2J$=13.9, $^3J$=9.0, $^3J$=6.7, $^3J$=3.3 Hz, $H_C$ in C$H_2$CH$_2$N$_3$), 1.78 (1H, dddd, $^2J$=13.9, $^3J$=11.1, $^3J$=6.0, $^3J$=4.8 Hz, $H_D$ in C$H_2$CH$_2$N$_3$); $^{13}$C NMR (75.48 MHz, DMSO-$d_6$) $\delta$: 156.6 (C=O), 144.4 (C), 133.8 (C), 129.5 (2CH), 128.9 (2CH), 68.4 ($CHSO_2$), 46.9 ($CH_2N_3$), 26.7 ($CH_2CH_2N_3$), 26.2 ($NCH_3$), 21.0 ($CH_3$ in Ts); IR (Nujol) $\nu$, cm$^{-1}$: 3373 (s), 3262 (s), 3179 (m) (NH), 3088 (w) ($CH_{arom}$), 2110 (s) ($N_3$), 1657 (s) (amide-I), 1595 (w) ($CC_{arom}$), 1560 (s) (amide-II), 1494 (w) ($CC_{arom}$), 1298 (s), 1124 (s) ($SO_2$), 820 (m) ($CH_{arom}$). Anal. Calcd for $C_{12}H_{17}N_5O_3S$: C, 46.29; H, 5.50; N, 22.49. Found: C, 46.59; H, 5.65; N, 22.10.

*4.3.3. N-[(3-Azido-1-tosyl)but-1-yl]urea (**5c**).* Freshly distilled 3-azidobutanal (**2b**) (6.588 g, 58.24 mmol) was dissolved in 80% formic acid (29 mL) and $H_2O$ (29 mL), and to the resulting colorless solution were subsequently added *p*-toluenesulfinic acid (9.099 g, 58.25 mmol) and $H_2O$ (20 mL). The mixture was stirred for 10 min, then urea (17.485 g, 291.13 mmol) and $H_2O$ (9 mL) were added. The resulting oily material partially dissolved, and new solid precipitated in 5 min. Then $H_2O$ (29 mL) was added, and the obtained suspension was stirred for 8 h, cooled to 0 °C, the precipitate was filtered, washed with ice-cold water until the smell of HCOOH disappeared, petroleum ether, and dried to give **5c** (16.758 g, 92%) as a 55:45 mixture of two diastereomers, which was used without further purification. After crystallization from MeCN the diastereomeric ratio changed to 60:40, respectively. Mp 119–120 °C (decomp., MeCN); $^1$H NMR of the major isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 7.67–7.73 (2H, m, ArH, overlap with signals of analogous protons of the minor isomer), 7.39–7.45 (2H, m, ArH, overlap with signals of analogous protons of the minor isomer), 7.04 (1H, d, $^3J$=10.2 Hz, NH), 5.71 (2H, br s, $NH_2$), 5.02 (1H, ddd, $^3J$=10.7, $^3J$=10.2, $^3J$=3.8 Hz, $CHSO_2$, partly overlap with signals of analogous proton of the minor isomer), 3.70 (1H, ddq, $^3J$=7.8, $^3J$=6.5, $^3J$=5.6 Hz, $CHN_3$), 2.40 (3H, s, $CH_3$ in Ts), 2.10 (1H, ddd, $^2J$=13.8, $^3J$=7.8, $^3J$=3.8 Hz, $H_A$ in C$H_2$CH), 1.83 (1H, ddd, $^2J$=13.8, $^3J$=10.7, $^3J$=5.6 Hz, $H_B$ in C$H_2$CH), 1.18 (3H, d, $^3J$=6.5 Hz, C$H_3$CH); $^1$H NMR of the minor isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 7.67–7.73 (2H, m, ArH, overlap with signals of analogous protons of the major isomer), 7.39–7.45 (2H, m, ArH, overlap with signals of analogous protons of the major isomer), 6.96 (1H, d, $^3J$=10.2 Hz, NH), 5.73 (2H, br s, $NH_2$), 5.02 (1H, ddd, $^3J$=11.7, $^3J$=10.2, $^3J$=2.6 Hz, $CHSO_2$, partly overlap with signals of analogous proton of the major isomer), 3.57 (1H, ddq, $^3J$=10.5, $^3J$=6.5, $^3J$=3.1 Hz, $CHN_3$), 2.40 (3H, s, $CH_3$ in Ts), 2.00 (1H, ddd, $^2J$=14.0, $^3J$=10.5, $^3J$=2.6 Hz, $H_A$ in C$H_2$CH), 1.70 (1H, ddd, $^2J$=14.0, $^3J$=11.7, $^3J$=3.1 Hz, $H_B$ in C$H_2$CH), 1.28 (3H, d, $^3J$=6.5 Hz, C$H_3$CH); $^{13}$C NMR of the major isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 156.4 (C=O), 144.51 (C), 133.8 (C), 129.66 (2CH), 129.1 (2CH), 67.6 ($CHSO_2$), 54.5 ($CHN_3$), 32.9 ($CH_2$), 21.2 ($CH_3$ in Ts), 18.4 (C$H_3$CH); $^{13}$C NMR of the minor isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 156.6 (C=O), 144.47 (C), 133.9 (C), 129.68 (2CH), 129.0 (2CH), 68.0 ($CHSO_2$), 54.1 ($CHN_3$), 33.2

($CH_2$), 21.2 ($CH_3$ in Ts), 19.5 ($CH_3CH$); IR (Nujol) $\nu$, $cm^{-1}$: 3452 (s), 3388 (s), 3358 (br w), 3324 (br m), 3273 (m), 3217 (m) (NH), 2114 (s), 2085 (s) ($N_3$), 1698 (s), 1668 (s) (amide-I), 1626 (w), 1598 (w) ($CC_{arom}$), 1520 (s) (amide-II), 1288 (s), 1144 (s) ($SO_2$), 816 (m) ($CH_{arom}$). Anal. Calcd for $C_{12}H_{17}N_5O_3S$: C, 46.29; H, 5.50; N, 22.49. Found: C, 46.36; H, 5.72; N, 22.54.

*4.3.4. N-[(3-Azido-1-tosyl)pent-1-yl]urea (**5d**).* Freshly distilled 3-azidopentanal (**2c**) (7.826 g, 61.56 mmol) was dissolved in EtOH (30 mL), and to the resulting colorless stirred solution were subsequently added *p*-toluenesulfinic acid (9.631 g, 61.65 mmol) and $H_2O$ (15 mL). *p*-Toluenesulfinic acid dissolved in 5 min. After that urea (18.486 g, 307.79 mmol) and $H_2O$ (15 mL) were added. After 5 min to the resulting solution was gradually added 60 mL of $H_2O$. After the addition of about 10–15 vol % of $H_2O$ the solid started to precipitate from the solution. As soon as the precipitation began, the addition of water was stopped, and the suspension was stirred for 10–15 min, then the remaining $H_2O$ was added. The obtained suspension was stirred at room temperature for 16 h, cooled to 0 °C, the precipitate was filtered, washed with ice-cold water, petroleum ether, and dried to give **5d** (18.488 g, 92%) as a 58:42 mixture of two diastereomers, which was used without further purification. After crystallization from MeCN the diastereomeric ratio changed to 55:45, respectively. Mp 117–117.5 °C (decomp., MeCN). $^1$H NMR of the major isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 7.68–7.73 (2H, m, ArH, overlap with signals of analogous protons of the minor isomer), 7.39–7.45 (2H, m, ArH, overlap with signals of analogous protons of the minor isomer), 6.96 (1H, d, $^3J$=10.2 Hz, NH), 5.69 (2H, br s, $NH_2$), 5.06 (1H, ddd, $^3J$=11.7, $^3J$=10.2, $^3J$=2.6 Hz, $CHSO_2$), 3.29–3.38 (1H, m, $CHN_3$), 2.40 (3H, s, $CH_3$ in Ts), 1.99 (1H, ddd, $^2J$=14.1, $^3J$=10.6, $^3J$=2.6 Hz, $H_A$ in C*H*$_2$CH), 1.75 (1H, ddd, $^2J$=14.1, $^3J$=11.7, $^3J$=2.9 Hz, $H_B$ in C*H*$_2$CH), 1.35–1.67 (2H, m, $CH_2$ in Et, overlap with signals of analogous protons of the minor isomer), 0.94 (3H, t, $^3J$=7.4 Hz, $CH_3$ in Et); $^1$H NMR of the minor isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 7.68–7.73 (2H, m, ArH, overlap with signals of analogous protons of the major isomer), 7.39–7.45 (2H, m, ArH, overlap with signals of analogous protons of the major isomer), 7.01 (1H, d, $^3J$=10.2 Hz, NH), 5.67 (2H, br s, $NH_2$), 5.04 (1H, ddd, $^3J$=10.2, $^3J$=10.2, $^3J$=4.0 Hz, $CHSO_2$), 3.50–3.58 (1H, m, $CHN_3$), 2.40 (3H, s, $CH_3$ in Ts), 2.19 (1H, ddd, $^2J$=14.1, $^3J$=7.0, $^3J$=4.0 Hz, $H_A$ in C*H*$_2$CH), 1.80 (1H, ddd, $^2J$=14.1, $^3J$=10.2, $^3J$=6.2 Hz, $H_B$ in C*H*$_2$CH), 1.35–1.67 (2H, m, $CH_2$ in Et, overlap with signals of analogous protons of the major isomer), 0.89 (3H, t, $^3J$=7.4 Hz, $CH_3$ in Et); $^{13}$C NMR of the major isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 156.5 (C=O), 144.36 (C), 133.9 (C), 129.6 (2CH), 128.88 (2CH), 68.0 ($CHSO_2$), 60.2 ($CHN_3$), 31.0 ($CH_2CHN_3$), 27.3 ($CH_2CH_3$), 21.1 ($CH_3$ in Ts), 10.1 ($CH_3CH_2$); $^{13}$C NMR of the minor isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 156.3 (C=O), 144.39 (C), 133.8 (C), 129.5 (2CH), 128.93 (2CH), 67.6 ($CHSO_2$), 60.7 ($CHN_3$), 31.1 ($CH_2CHN_3$), 25.9 ($CH_2CH_3$), 21.1 ($CH_3$ in Ts), 9.7 ($CH_3CH_2$); IR (Nujol) $\nu$, $cm^{-1}$: 3455 (s), 3384 (s), 3337 (br m), 3272 (m), 3218 (m) (NH), 3046 (w) ($CH_{arom}$), 2096 (s) ($N_3$), 1696 (s), 1665 (s) (amide-I), 1624 (w), 1598 (w) ($CC_{arom}$), 1517 (s) (amide-II), 1287 (s), 1142 (s) ($SO_2$), 817 (m) ($CH_{arom}$). Anal. Calcd for $C_{13}H_{19}N_5O_3S$: C, 47.99; H, 5.89; N, 21.52. Found: C, 48.12; H, 6.11; N, 21.55.

*4.3.5. N-[(3-Azido-2-methyl-1-tosyl)prop-1-yl]urea (**5e**).* Compound **5e** (23.870 g, 79%) as an 82:18 mixture of two diastereomers was prepared from freshly distilled aldehyde **2d** (10.953 g, 96.83 mmol), *p*-toluenesulfinic acid (15.153 g, 97.01 mmol), and urea (29.070 g, 484.02 mmol) in EtOH (48.5 mL) and $H_2O$ (145.5 mL) (19 h, rt) as described for **5d**. After crystallization from MeCN the diastereomeric ratio changed to 85:15, respectively. Mp 104.5 °C (decomp., MeCN). $^1$H NMR of the major isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 7.67–7.73 (2H, m, ArH), 7.38–7.44 (2H, m, ArH), 6.94 (1H, d, $^3J$=10.8 Hz, NHCO), 5.75 (2H, br s, $NH_2$), 5.10 (1H, dd, $^3J$=10.8, $^3J$=2.7 Hz, $CHSO_2$), 3.34 (1H, dd, $^2J$=12.2, $^3J$=5.8 Hz, $H_A$ in $CH_2N_3$), 3.15 (1H, dd, $^2J$=12.2, $^3J$=8.3 Hz, $H_B$ in $CH_2N_3$), 2.56 (1H, dddq, $^3J$=8.3, $^3J$=6.9, $^3J$=5.8, $^3J$=2.7 Hz, C*H*$CH_3$), 2.40 (3H, s, $CH_3$ in Ts), 1.04 (3H, d, $^3J$=6.9 Hz, C*H*$_3$CH); $^1$H NMR of the minor isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 7.67–7.73 (2H, m, ArH, overlap with signals of analogous protons of the major isomer), 7.38–7.44 (2H, m, ArH, overlap with signals of analogous protons of the major isomer), 6.96 (1H, d, $^3J$=10.8 Hz, NHCO), 5.69 (2H, br s, $NH_2$), 4.98 (1H, dd, $^3J$=10.8, $^3J$=5.3 Hz, $CHSO_2$), 3.73 (1H, dd, $^2J$=12.3, $^3J$=4.4 Hz, $H_A$ in $CH_2N_3$), 3.35 (1H, dd, $^2J$=12.3, $^3J$=7.7 Hz, $H_B$ in $CH_2N_3$), 2.46 (1H, dddq, $^3J$=7.7, $^3J$=6.9, $^3J$=5.3, $^3J$=4.4 Hz, C*H*$CH_3$), 2.40 (3H, s, $CH_3$ in Ts), 1.10 (3H, d, $^3J$=6.9 Hz, C*H*$_3$CH); $^{13}$C NMR of the major isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 156.6 (C=O), 144.3 (C), 135.0 (C), 129.6 (2CH), 128.5 (2CH), 69.8 ($CHSO_2$), 53.7 ($CH_2N_3$), 31.8 (*C*H$CH_3$), 21.0 ($CH_3$ in Ts), 12.2 (*C*H$_3$CH); $^{13}$C NMR of the minor isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 156.4 (C=O), 144.2 (C), 135.2 (C), 129.4 (2CH), 128.6 (2CH), 71.7 ($CHSO_2$), 53.1 ($CH_2N_3$), 33.3 (*C*H$CH_3$), 21.0 ($CH_3$ in Ts), 15.3 (*C*H$_3$CH); IR (Nujol) $\nu$, $cm^{-1}$: 3466 (s), 3375 (s), 3261 (br s), 3197 (m), 3054 (m) (NH), 2100 (s) ($N_3$), 1689 (m), 1660 (s) (amide-I), 1609 (m), 1592 (w) ($CC_{arom}$), 1542 (s) (amide-II), 1298 (s), 1149 (s) ($SO_2$), 821 (m) ($CH_{arom}$). Anal. Calcd for $C_{12}H_{17}N_5O_3S$: C, 46.29; H, 5.50; N, 22.49. Found: C, 46.55; H, 5.58; N, 22.51.

*4.3.6. N-[(3-Azido-2-ethyl-1-tosyl)prop-1-yl]urea (**5f**).* Compound **5f** (12.515 g, 83%) as a 63:37 mixture of two diastereomers was prepared from freshly distilled aldehyde **2e** (5.906 g, 46.45 mmol), *p*-toluenesulfinic acid (7.269 g, 46.53 mmol), and urea (13.948 g, 232.24 mmol) in EtOH (23 mL) and $H_2O$ (92 mL) (18 h, rt) as described for **5d**. After crystallization from MeCN the diastereomeric ratio changed to 65:35, respectively. Mp 102–102.5 °C (decomp., MeCN). $^1$H NMR of the major isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 7.66–7.74 (2H, m, ArH, overlap with signals of analogous protons of the minor isomer), 7.38–7.44 (2H, m, ArH, overlap with signals of analogous protons of the minor isomer), 6.90 (1H, d, $^3J$=10.8 Hz, NHCO), 5.76 (2H, br s, $NH_2$), 5.07 (1H, dd, $^3J$=10.8, $^3J$=3.8 Hz, $CHSO_2$), 3.81 (1H, dd, $^2J$=12.6, $^3J$=4.2 Hz, $H_A$ in $CH_2N_3$), 3.42 (1H, dd, $^2J$=12.6, $^3J$=7.3 Hz, $H_B$ in $CH_2N_3$), 2.39 (3H, s, $CH_3$ in Ts), 2.20–2.35 (1H, m, C*H*$CH_2CH_3$, overlap with signals of analogous proton of the minor isomer), 1.48–1.62 (1H, m, $H_C$ in C*H*$_2$CH$_3$), 1.31–1.46 (1H, m, $H_D$ in C*H*$_2$CH$_3$), 0.88 (3H, t, $^3J$=7.4 Hz, $CH_2CH_3$); $^1$H NMR of the minor isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 7.66–7.74 (2H, m, ArH, overlap with signals of analogous protons of the major isomer), 7.38–7.44 (2H, m, ArH, overlap with signals of analogous protons of the major isomer), 6.91 (1H, d, $^3J$=10.8 Hz, NHCO), 5.74 (2H, br s, $NH_2$), 5.11 (1H, dd, $^3J$=10.8, $^3J$=3.4 Hz, $CHSO_2$), 3.66 (1H, dd, $^2J$=12.6, $^3J$=4.4 Hz, $H_A$ in $CH_2N_3$), 3.17 (1H, dd, $^2J$=12.6, $^3J$=8.6 Hz, $H_B$ in $CH_2N_3$), 2.39 (3H, s, $CH_3$ in Ts), 2.20–2.35 (1H, m, C*H*$CH_2CH_3$, overlap with signals of analogous proton of the major isomer), 1.72–1.86 (1H, m, $H_C$ in C*H*$_2$CH$_3$), 1.09–1.28 (1H, m, $H_D$ in C*H*$_2$CH$_3$), 0.94 (3H, t, $^3J$=7.4 Hz, $CH_2CH_3$); $^{13}$C NMR of the major isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 156.5 (C=O), 144.30 (C), 135.0 (C), 129.56 (2CH), 128.6 (2CH), 69.86 ($CHSO_2$), 50.87 ($CH_2N_3$), 38.66 ($CHCH_2CH_3$), 22.1 ($CH_2$ in Et), 21.1 ($CH_3$ in Ts), 10.9 ($CH_3$ in Et); $^{13}$C NMR of the minor isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 156.6 (C=O), 144.26 (C), 135.1 (C), 129.57 (2CH), 128.5 (2CH), 69.94 (NCH), 50.85 ($CH_2N_3$), 38.67 (*C*H$CH_2CH_3$), 19.5 ($CH_2$ in Et), 21.1 ($CH_3$ in Ts), 11.3 ($CH_3$ in Et); IR (Nujol) $\nu$, $cm^{-1}$: 3500 (s), 3392 (s), 3249 (m), 3189 (br m), 3041 (m) (NH), 2105 (s) ($N_3$), 1686 (w), 1659 (s) (amide-I), 1598 (m) ($CC_{arom}$), 1552 (s) (amide-II), 1496 (w) ($CC_{arom}$), 1305 (s), 1142 (s) ($SO_2$), 818 (m) ($CH_{arom}$). Anal. Calcd for $C_{13}H_{19}N_5O_3S$: C, 47.99; H, 5.89; N, 21.52. Found: C, 48.20; H, 5.97; N, 21.62.

### 4.4. Synthesis of 4-hydroxyhexahydropyrimidin-2-one 8a and *N*-(γ-oxoalkyl)ureas 7b–h

*4.4.1. 5-Acetyl-6-(2-azidoethyl)-4-hydroxy-4-methylhexahydropyrimidin2-one (**8a**).* To a stirred suspension of NaH (0.289 g,

12.04 mmol) in dry MeCN (8 mL) cooled in an ice-cold bath was added a solution of acetylacetone (**6a**) (1.218 g, 12.17 mmol) in MeCN (10 mL), and the resulting mixture was stirred for 25 min. The ice bath was removed, and to the obtained solution were added sulfone **5a** (3.252 g, 10.84 mmol) and MeCN (3 mL). The suspension was stirred at room temperature for 7 h 45 min, and solvent was removed under reduced pressure. The residue was triturated with petroleum ether (15 mL) and saturated aqueous solution of $NaHCO_3$ (9 mL), the obtained mixture was left overnight at room temperature and cooled to 0 °C. The precipitate was filtered, washed with ice-cold water, and petroleum ether. The obtained solid was dried in a vacuum desiccator (over $P_2O_5$) on the filter, cooled (−10 °C), washed with cold (−10 °C) diethyl ether (3×4 mL), and dried to give **8a** (1.974 g, 75%) as a single (4*R**,5*R**,6*R**)-diastereomer. Mp 160.5 °C (decomp., EtOH). $^1$H NMR (300.13 MHz, DMSO-$d_6$) $\delta$: 7.07 (1H, d, $^4J$=1.8 Hz, $N_{(3)}H$), 6.55 (1H, d, $^4J$=1.8 Hz, $N_{(1)}H$), 5.71 (1H, d, $^4J$=0.7 Hz, OH), 3.92 (1H, ddd, $^3J$=11.7, $^3J$=7.4, $^3J$=2.9 Hz, 6-H), 3.41–3.57 (2H, m, $CH_2N_3$), 2.45 (1H, dd, $^3J$=11.7, $^4J$=0.7 Hz, 5-H), 2.18 (3H, s, $CH_3$ in Ac), 1.40–1.66 (2H, m, C$H_2$C$H_2N_3$), 1.28 (3H, s, 4-$CH_3$); $^{13}$C NMR (75.48 MHz, DMSO-$d_6$) $\delta$: 207.6 (C=O in Ac), 154.5 (C-2), 78.0 (C-4), 61.0 (C-5), 46.4 ($CH_2N_3$), 45.9 (C-6), 32.0 (C$H_2$C$H_2N_3$), 30.4 ($CH_3$ in Ac), 27.5 (4-$CH_3$); IR (Nujol) $\nu$, cm$^{-1}$: 3298 (s), 3266 (s), 3100 (br s) (OH, NH), 2148 (m), 2108 (s), 2088 (s) ($N_3$), 1714 (s) (C=O in Ac), 1653 (vs) (amide-I), 1501 (s) (amide-II), 1135 (s) (C–O). Anal. Calcd for $C_9H_{15}N_5O_3$: C, 44.81; H, 6.27; N, 29.03. Found: C, 45.01; H, 6.26; N, 29.16.

*4.4.2. N-[(1-Azido-4-benzoyl-5-oxo)hex-3-yl]urea (**7b**).* To a mixture of benzoylacetone (**6b**) (1.083 g, 6.68 mmol) and NaH (0.158 g, 6.58 mmol) was added dry MeCN (12 mL), the mixture was stirred at room temperature for 26 min, and to the resulting suspension were added sulfone **5a** (1.945 g, 6.54 mmol) and MeCN (6 mL). The suspension was stirred at room temperature for 8 h, and the solvent was removed under reduced pressure. To a solid residue were added saturated aqueous solution of $NaHCO_3$ (2 mL) and petroleum ether (10 mL), the obtained mixture was triturated until complete crystallization, and the resulting suspension was left overnight at room temperature and cooled to 0 °C. The precipitate was filtered, washed with ice-cold water, and petroleum ether. The obtained solid was dried in a vacuum desiccator (over $P_2O_5$) on the filter, cooled (−10 °C), washed with cold (−10 °C) diethyl ether (3×5 mL), and dried to give **7b** (2.222 g, 79%) as a mixture of two diastereomers (52:48). After two crystallizations from EtOH the diastereomeric ratio changed to 48:52, respectively. Mp 124.5–125.0 °C (decomp., EtOH). $^1$H NMR of the 48:52 diastereomeric mixture (after two crystallizations) (300.13 MHz, DMSO-$d_6$) $\delta$: 7.94–8.01 (2H, m, ArH in both isomers), 7.63–7.72 (1H, m, ArH in both isomers), 7.50–7.60 (2H, m, ArH in both isomers), 6.19 (0.52H, d, $^3J$=9.7 Hz, NH in the major isomer), 6.05 (0.48H, d, $^3J$=9.6 Hz, NH in the minor isomer), 5.65 (1.04H, br s, $NH_2$ in the major isomer), 5.59 (0.96H, br s, $NH_2$ in the minor isomer), 5.20 (0.52H, d, $^3J$=4.9 Hz, C*H*C=O in the major isomer), 5.04 (0.48H, d, $^3J$=7.7 Hz, C*H*C=O in the minor isomer), 4.43–4.56 (1H, m, CHN in both isomers), 3.22–3.43 (2H, m, $CH_2N_3$ in both isomers), 2.26 (1.56H, s, $CH_3$ in the major isomer), 2.13 (1.44H, s, $CH_3$ in the minor isomer), 1.56–1.82 (2H, m, C$H_2$C$H_2N_3$ in both isomers); $^{13}$C NMR of the 48:52 diastereomeric mixture (75.48 MHz, DMSO-$d_6$) $\delta$: 204.5, 203.7 (C=O in Ac), 197.2, 195.4 (C=O in Bz), 158.2, 158.0 ($CONH_2$), 136.7, 136.2 (C), 133.9, 133.6 (CH), 129.0, 128.8 (2CH), 128.5, 128.2 (2CH), 65.5, 63.3 (*C*HC=O), 48.1, 47.8 ($CH_2N_3$), 47.0, 46.6 (CHN), 32.7, 32.5 (C$H_2$C$H_2N_3$), 29.5, 28.7 ($CH_3$); IR (Nujol) $\nu$, cm$^{-1}$: 3420 (s), 3404 (s), 3366 (s), 3212 (br s) (NH), 3087 (w) ($CH_{arom}$), 2151 (m), 2104 (vs) ($N_3$), 1717 (s), 1708 (s) (C=O), 1662 (s), 1651 (vs) (amide-I), 1617 (m), 1610 (m), 1595 (m), 1578 (m) ($CC_{arom}$), 1542 (s), 1522 (s) (amide-II), 771 (s), 697 (s) ($CH_{arom}$). Anal. Calcd for $C_{14}H_{17}N_5O_3$: C, 55.44; H, 5.65; N, 23.09. Found: C, 55.56; H, 5.71; N, 23.02.

*4.4.3. N-[(5-Azido-2-benzoyl-1-oxo-1-phenyl)pent-3-yl]urea (**7c**).* To a mixture of dibenzoylmethane (**6c**) (1.214 g, 5.41 mmol) and NaH (0.122 g, 5.07 mmol) was added dry THF (11 mL), the mixture was stirred in an ice-cold bath for 12 min, and to the resulting solution were added sulfone **5a** (1.492 g, 5.02 mmol) and THF (7 mL). The reaction mixture was stirred at room temperature for 8 h, and the solvent was removed under reduced pressure. To a solid residue were added saturated aqueous solution of $NaHCO_3$ (6 mL) and petroleum ether (10 mL), the obtained mixture was triturated until complete crystallization, and the resulting suspension was left overnight at room temperature and cooled to 0 °C. The precipitate was filtered, washed with ice-cold water and petroleum ether. The obtained solid was dried in a vacuum desiccator (over $P_2O_5$) on the filter, cooled (−10 °C), washed with cold (−10 °C) diethyl ether (3×5 mL), and dried to give **7c** (1.654 g, 90%). Mp 154.5 °C (decomp., EtOH). $^1$H NMR (300.13 MHz, DMSO-$d_6$) $\delta$: 7.93–8.05 (4H, m, ArH), 7.47–7.71 (6H, m, ArH), 6.20 (1H, d, $^3J$=9.4 Hz, NH), 6.08 (1H, d, $^3J$=4.8 Hz, CHC=O), 5.56 (2H, br s, $NH_2$), 4.46 (1H, dddd, $^3J$=10.1, $^3J$=9.4, $^3J$=4.8, $^3J$=3.9 Hz, CHN), 3.41 (1H, ddd, $^2J$=12.4, $^3J$=7.1, $^3J$=5.2 Hz, $H_A$ in $CH_2N_3$), 3.30 (1H, ddd, $^2J$=12.4, $^3J$=8.2, $^3J$=6.7 Hz, $H_B$ in $CH_2N_3$), 1.77–2.00 (2H, m, C$H_2$C$H_2N_3$); $^{13}$C NMR (75.48 MHz, DMSO-$d_6$) $\delta$: 196.3 (C=O in Bz), 195.6 (C=O in Bz), 158.0 ($CONH_2$), 136.2 (C), 135.7 (C), 133.73 (CH), 133.67 (CH), 129.0 (2CH), 128.9 (2CH), 128.5 (2CH), 128.2 (2CH), 58.4 (*C*HC=O), 48.1 ($CH_2N_3$), 47.3 (CHN), 32.3 (C$H_2$C$H_2N_3$); IR (Nujol) $\nu$, cm$^{-1}$: 3414 (s), 3360 (s), 3197 (br s) (NH), 3060 (w) ($CH_{arom}$), 2097 (s) ($N_3$), 1691 (s) (C=O), 1658 (s) (amide-I), 1625 (w), 1595 (w), 1578 (w) ($CC_{arom}$), 1542 (s) (amide-II), 763 (m), 688 (m) ($CH_{arom}$). Anal. Calcd for $C_{19}H_{19}N_5O_3$: C, 62.46; H, 5.24; N, 19.17. Found: C, 62.41; H, 5.30; N, 19.00.

*4.4.4. N-[(4-Acetyl-1-azido-5-oxo)hex-3-yl]-N′-methylurea (**7d**).* Compound **7d** (1.167 g, 54%) was prepared from acetylacetone (**6a**) (0.866 g, 8.65 mmol), NaH (0.203 g, 8.45 mmol), and sulfone **5b** (2.630 g, 8.45 mmol) in dry MeCN (20 mL) (8 h, rt) as described for **8a**. Mp 118–118.5 °C (decomp., EtOH). $^1$H NMR (300.13 MHz, DMSO-$d_6$) $\delta$: 5.93 (1H, d, $^3J$=9.6 Hz, NH), 5.93 (1H, q, $^3J$=4.7 Hz, N*H*$CH_3$), 4.36 (1H, dddd, $^3J$=9.6, $^3J$=8.0, $^3J$=6.8, $^3J$=5.7 Hz, CHN), 4.14 (1H, d, $^3J$=6.8 Hz, CHC=O), 3.20–3.37 (2H, m, $CH_2N_3$), 2.51 (3H, d, $^3J$=4.7 Hz, $NCH_3$), 2.19 (3H, s, $CH_3$ in Ac), 2.09 (3H, s, $CH_3$ in Ac), 1.53–1.68 (2H, m, C$H_2$C$H_2N_3$); $^{13}$C NMR (75.48 MHz, DMSO-$d_6$) $\delta$: 204.6 (C=O in Ac), 204.1 (C=O in Ac), 158.0 (CONH), 69.8 (*C*HC=O), 47.9 ($CH_2N_3$), 46.4 (CHN), 32.6 (C$H_2$C$H_2N_3$), 30.15 ($CH_3$ in Ac), 30.08 ($CH_3$ in Ac), 26.2 ($NCH_3$); IR (Nujol) $\nu$, cm$^{-1}$: 3352 (s) (NH), 2105 (s) ($N_3$), 1722 (s), 1701 (m) (C=O), 1638 (s) (amide-I), 1566 (s), 1531 (m) (amide-II). Anal. Calcd for $C_{10}H_{17}N_5O_3$: C, 47.05; H, 6.71; N, 27.43. Found: C, 46.98; H, 6.80; N, 27.12.

*4.4.5. N-[(1-Azido-4-benzoyl-5-oxo)hex-3-yl]-N′-methylurea (**7e**).* Compound **7e** (1.616 g, 82%) as a mixture of two diastereomers (59:41) was prepared from benzoylacetone (**6b**) (1.054 g, 6.50 mmol), NaH (0.152 g, 6.33 mmol), and sulfone **5b** (1.934 g, 6.21 mmol) in dry MeCN (18 mL) (8 h 15 min, rt) as described for **7b**. After crystallization from MeCN the diastereomeric ratio did not change. Mp 123.5–124 °C (decomp., MeCN). $^1$H NMR of the 59:41 diastereomeric mixture (300.13 MHz, DMSO-$d_6$) $\delta$: 7.94–8.01 (2H, m, ArH in both isomers), 7.62–7.72 (1H, m, ArH in both isomers), 7.50–7.60 (2H, m, ArH in both isomers), 6.08 (0.59H, d, $^3J$=9.6 Hz, NH in the major isomer), 6.02 (0.59H, q, $^3J$=4.7 Hz, N*H*$CH_3$ in the major isomer), 5.97 (0.41H, d, $^3J$=9.5 Hz, NH in the minor isomer), 5.89 (0.41H, q, $^3J$=4.6 Hz, N*H*$CH_3$ in the minor isomer), 5.19 (0.59H, d, $^3J$=5.0 Hz, CHC=O in the major isomer), 5.04 (0.41H, d, $^3J$=8.0 Hz, CHC=O in the minor isomer), 4.45–4.57 (1H,

m, CHN in both isomers), 3.21–3.41 (2H, m, $CH_2N_3$ in both isomers), 2.51 (1.23H, d, $^3J$=4.6 Hz, $NCH_3$ in the minor isomer), 2.50 (1.77H, d, $^3J$=4.7 Hz, $NCH_3$ in the major isomer), 2.25 (1.77H, s, $CH_3C$=O in the major isomer), 2.12 (1.23H, s, $CH_3C$=O in the minor isomer), 1.55–1.84 (2H, m, $CH_2CH_2N_3$ in both isomers); $^{13}$C NMR of the major isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 204.3 (C=O in Ac), 197.1 (C=O in Bz), 158.1 (CONH), 136.7 (C), 133.6 (CH), 128.8 (2CH), 128.2 (2CH), 63.4 (*C*HC=O), 48.0 ($CH_2N_3$), 46.9 (CHN), 32.4 ($CH_2CH_2N_3$), 29.5 ($CH_3$ in Ac), 26.1 ($NCH_3$); $^{13}$C NMR of the minor isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 203.5 (C=O in Ac), 195.4 (C=O in Bz), 158.0 (CONH), 136.3 (C), 133.8 (CH), 128.9 (2CH), 128.5 (2CH), 65.6 (*C*HC=O), 47.7 ($CH_2N_3$), 47.3 (CHN), 32.5 ($CH_2CH_2N_3$), 28.6 ($CH_3$ in Ac), 26.2 ($NCH_3$); IR (Nujol) $\nu$, cm$^{-1}$: 3379 (s), 3303 (br s) (NH), 3064 (w) ($CH_{arom}$), 2098 (s) ($N_3$), 1712 (s) (C=O in Ac), 1666 (s) (C=O in Bz), 1626 (s) (amide-I), 1598 (w) ($CC_{arom}$), 1565 (s) (amide-II), 1508 (w) ($CC_{arom}$), 771 (m) ($CH_{arom}$). Anal. Calcd for $C_{15}H_{19}N_5O_3$: C, 56.77; H, 6.03; N, 22.07. Found: C, 56.88; H, 5.94; N, 22.23.

*4.4.6. N-[(5-Azido-2-benzoyl-1-oxo-5-phenyl)pent-3-yl]-N′-methylurea (**7f**).* Compound **7f** (3.375 g, 91%) was prepared from dibenzoylmethane (**6c**) (2.346 g, 10.25 mmol), NaH (0.234 g, 9.76 mmol), and sulfone **5b** (3.033 g, 9.74 mmol) in dry THF (18 mL) (8 h 5 min, rt) as described for **7c**. Mp 139 °C (decomp., EtOH). $^1$H NMR (300.13 MHz, DMSO-$d_6$) $\delta$: 7.95–8.03 (4H, m, ArH), 7.61–7.70 (2H, m, ArH), 7.48–7.58 (4H, m, ArH), 6.11 (1H, d, $^3J$=9.0 Hz, NH), 6.09 (1H, d, $^3J$=5.1 Hz, CHC=O), 5.94 (1H, q, $^3J$=4.7 Hz, N*H*$CH_3$), 4.49 (1H, dddd, $^3J$=10.4, $^3J$=9.0, $^3J$=5.1, $^3J$=3.8 Hz, CHN), 3.40 (1H, ddd, $^2J$=12.4, $^3J$=7.3, $^3J$=5.2 Hz, $H_A$ in $CH_2N_3$), 3.29 (1H, ddd, $^2J$=12.4, $^3J$=8.3, $^3J$=6.6 Hz, $H_B$ in $CH_2N_3$), 2.44 (3H, d, $^3J$=4.7 Hz, $NCH_3$), 1.95 (1H, dddd, $^2J$=13.8, $^3J$=10.4, $^3J$=6.6, $^3J$=5.2 Hz, $H_C$ in $CH_2CH_2N_3$), 1.81 (1H, dddd, $^2J$=13.8, $^3J$=8.3, $^3J$=7.3, $^3J$=3.8 Hz, $H_D$ in $CH_2CH_2N_3$); $^{13}$C NMR (75.48 MHz, DMSO-$d_6$) $\delta$: 196.3 (C=O in Bz), 195.5 (C=O in Bz), 158.0 ($CONH_2$), 136.1 (C), 135.8 (C), 133.73 (CH), 133.70 (CH), 129.0 (2CH), 128.9 (2CH), 128.4 (2CH), 128.3 (2CH), 58.5 (*C*HC=O), 48.1 ($CH_2N_3$), 47.7 (CHN), 32.1 ($CH_2CH_2N_3$), 26.1 ($NCH_3$); IR (Nujol) $\nu$, cm$^{-1}$: 3421 (m), 3366 (m), 3308 (br m) (NH), 3057 (w) ($CH_{arom}$), 2097 (s) ($N_3$), 1692 (s) (C=O), 1664 (s), 1638 (m) (amide-I), 1592 (w) ($CC_{arom}$), 1550 (s) (amide-II), 762 (m), 688 (s) ($CH_{arom}$). Anal. Calcd for $C_{20}H_{21}N_5O_3$: C, 63.31; H, 5.58; N, 18.46. Found: C, 63.44; H, 5.57; N, 18.46.

*4.4.7. N-[(6-Azido-3-benzoyl-2-oxo)hept-4-yl]urea (**7g**).* Compound **7g** (1.399 g, 75%) as a mixture of four diastereomers (27:28:19:26) was prepared from benzoylacetone (**6b**) (0.983 g, 6.06 mmol), NaH (0.143 g, 5.96 mmol), and sulfone **5c** (1.839 g, 5.91 mmol) in dry MeCN (19 mL) (8 h, rt) as described for **7b**. Recrystallization from AcOEt or MeCN gave compound **7g** with isomer ratios of 21:50:10:19 or 42:27:22:9, respectively. Mp 131.5–132 °C (decomp., MeCN). $^1$H NMR the 42:27:22:9 diastereomeric mixture (300.13 MHz, DMSO-$d_6$) $\delta$: 7.93–8.01 (2H, m, ArH), 7.62–7.72 (1H, m, ArH), 7.50–7.60 (2H, m, ArH), 6.22 (0.42H, $^3J$=9.8 Hz, NH), 6.19 (0.27H, $^3J$=9.5 Hz, NH), 6.09 (0.22H, $^3J$=9.8 Hz, NH), 6.03 (0.09H, $^3J$=9.4 Hz, NH), 5.63 (1.38H, br s, $NH_2$), 5.59 (0.44H, br s, $NH_2$), 5.56 (0.18H, br s, $NH_2$), 5.20 (0.27H, d, $^3J$=4.7 Hz, CHC=O), 5.19 (0.42H, d, $^3J$=4.9 Hz, CHC=O), 5.03 (0.22H, d, $^3J$=7.8 Hz, CHC=O), 5.01 (0.09H, d, $^3J$=7.6 Hz, CHC=O), 4.47–4.60 (1H, m, CHN), 3.45–3.60 (1H, m, $CHN_3$), 2.27 (2.07H, s, $CH_3$ in Ac), 2.13 (0.27H, s, $CH_3$ in Ac), 2.12 (0.66H, s, $CH_3$ in Ac), 1.35–1.84 (2H, m, $CH_2$), 1.23 (0.66H, d, $^3J$=6.4 Hz, $CH_3$), 1.21 (2.07H, d, $^3J\approx$6.5 Hz, $CH_3$), 1.18 (0.27H, d, $^3J\approx$6.5 Hz, $CH_3$); $^{13}$C NMR of the 42:27:22:9 diastereomeric mixture (signals of only three isomers are presented; signals of the 42% isomer are in italics) (75.48 MHz, DMSO-$d_6$) $\delta$: *204.6*, 204.4, 203.7 (C=O in Ac), 197.31, *197.27*, 195.4 (C=O in Bz), 158.2, *158.0*, 157.9 ($CONH_2$), *136.74*, 136.68, 136.2 (C), 133.9, *133.63*, 133.59 (CH), 128.9, *128.84*, 128.81 (2CH), 128.6, *128.25*, 128.22 (2CH), 65.7, 63.5, *63.3* (CHC=O), 55.2, *55.0*, 54.6 ($CHN_3$), 46.6, 46.5, *46.1* (CHN), *39.7*, 39.4 ($CH_2$), 29.59, *29.55*, 28.7 ($CH_3$ in Ac), 19.8, 18.5, *18.4* ($CH_3$); IR (Nujol) $\nu$, cm$^{-1}$: 3411 (s), 3374 (m), 3203 (br s) (NH), 3086 (w), 3060 (w) ($CH_{arom}$), 2111 (s) ($N_3$), 1712 (s) (C=O in Ac), 1667 (sh), 1654 (s) (C=O in Bz and amide-I), 1622 (w), 1596 (w), 1579 (w) ($CC_{arom}$), 1534 (sh), 1523 (s) (amide-II), 766 (m), 690 (m) ($CH_{arom}$). Anal. Calcd for $C_{15}H_{19}N_5O_3$: C, 56.77; H, 6.03; N, 22.07. Found: C, 56.94; H, 6.22; N, 21.77.

### 4.5. Synthesis of 5-acyl-4-(azidoalkyl)-1,2,3,4-tetrahydropyrimidin-2-ones

*4.5.1. 5-Acetyl-4-(2-azidoethyl)-6-methyl-1,2,3,4-tetrahydropyrimidin-2-one (**9a**). Method A*: a solution of compound **8a** (1.737 g, 7.20 mmol) and *p*-TsOH·$H_2O$ (0.263 g, 1.38 mmol) in EtOH (20 mL) was heated at reflux for 1 h under stirring, and then the solvent was removed in vacuum. The oily residue was triturated with saturated aqueous solution of $NaHCO_3$ (3 mL) and petroleum ether (10 mL), and the obtained suspension was cooled to 0 °C. The precipitate was filtered, washed with ice-cold water, petroleum ether, cold (−10 °C) diethyl ether (2×5 mL), and dried to give **9a** (1.231 g, 77%) as a white solid. Mp 150.0–150.5 °C (decomp., MeCN). $^1$H NMR (300.13 MHz, DMSO-$d_6$) $\delta$: 9.05 (1H, br d, $^4J$=1.9 Hz, $N_{(1)}H$), 7.55 (1H, br dd, $^3J$=3.9, $^4J$=1.9 Hz, $N_{(3)}H$), 4.20 (1H, ddd, $^3J$=7.8, $^3J$=4.1, $^3J$=3.9 Hz, 4-H), 3.30–3.44 (2H, m, $CH_2N_3$), 2.21 (3H, s, $CH_3$ in Ac), 2.19 (3H, s, 6-$CH_3$), 1.49–1.67 (2H, m, $CH_2CH_2N_3$). $^{13}$C NMR (75.48 MHz, DMSO-$d_6$) $\delta$: 193.9 (C=O in Ac), 152.6 (C-2), 148.1 (C-6), 110.0 (C-5), 47.9 (C-4), 46.6 ($CH_2N_3$), 35.1 ($CH_2CH_2N_3$), 30.3 ($CH_3$ in Ac), 18.9 (6-$CH_3$). IR (Nujol) $\nu$, cm$^{-1}$: 3364 (w), 3230 (s), 3113 (s) (NH), 2172 (m), 2122 (m), 2095 (s) ($N_3$), 1713 (vs) (amide-I), 1669 (s) (C=O), 1598 (s) (C=C). Anal. Calcd for $C_9H_{13}N_5O_2$, %: C, 48.42; H, 5.87; N, 31.37. Found: C, 48.40; H, 5.86; N, 31.47.

*Method B*: to a stirred suspension of NaH (0.337 g, 14.04 mmol) in dry THF (10 mL) cooled in an ice-cold bath was added a solution of acetylacetone (**6a**) (1.437 g, 14.35 mmol) in THF (10 mL), and the resulting mixture was stirred for 25 min. The ice bath was removed, and to the obtained solution were added sulfone **5a** (4.129 g, 13.88 mmol) and THF (5 mL). The suspension was stirred at room temperature for 8 h, *p*-TsOH·$H_2O$ (3.481 g, 18.30 mmol) was added, and the reaction mixture was heated at reflux under stirring for 1 h 40 min. Vigorous foaming occurred for about 30 min from the beginning of reflux and then faded away (use of a straight condenser and periodic shaking of the flask during foaming are recommended). The solvent was removed under reduced pressure. The residue was triturated with petroleum ether (3×15 mL), petroleum ether was decanted, saturated aqueous solution of $NaHCO_3$ (10 mL), solid $NaHCO_3$ (1.500 g, 17.85 mmol), and petroleum ether (15 mL) were added, the obtained mixture was triturated until crystallization was complete, left overnight at room temperature, and cooled to 0 °C. The precipitate was filtered, washed with ice-cold water and petroleum ether. The obtained solid was dried in a vacuum desiccator (over $P_2O_5$) on the filter, cooled (−10 °C), washed with cold (−10 °C) diethyl ether (3×4 mL), and dried to give **9a** (1.879 g, 61%) as a white solid.

*4.5.2. 5-Acetyl-4-(2-azidoprop-1-yl)-6-methyl-1,2,3,4-tetrahydropyrimidin-2-one (**9b**).* Pyrimidine **9b** (1.267 g, 47%) as a mixture of two diastereomers (86:14) was prepared from acetylacetone (**6a**) (1.193 g, 11.91 mmol), NaH (0.279 g, 11.61 mmol), and sulfone **5c** (3.569 g, 11.46 mmol) in dry THF (25 mL) (rt, 8 h), followed by treatment with *p*-TsOH·$H_2O$ (2.875 g, 15.12 mmol) (THF, reflux, 1 h 55 min) as described for **9a** in method B. After crystallization from MeCN the diastereomeric ratio changed to 97:3, respectively. Mp 191–192 °C (decomp., MeCN). $^1$H NMR of the major isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 9.04 (1H, d, $^4J$=2.1 Hz, $N_{(1)}H$), 7.67 (1H, dd, $^3J$=4.1, $^4J$=2.1 Hz, $N_{(3)}H$), 4.23 (1H, ddd, $^3J$=9.8, $^3J$=4.1, $^3J$=2.7 Hz, 4-H), 3.73 (1H, ddq, $^3J$=10.8, $^3J$=6.5, $^3J$=2.9 Hz, $CHN_3$),

2.18 (6H, s, 6-$CH_3$ and $CH_3$ in Ac), 1.51 (1H, ddd, $^2J$=14.1, $^3J$=9.8, $^3J$=2.9 Hz, $CH_A$ in $CH_2$), 1.31 (1H, ddd, $^2J$=14.1, $^3J$=10.8, $^3J$=2.7 Hz, $CH_B$ in $CH_2$), 1.23 (3H, d, $^3J$=6.5 Hz, C*H*$_3$CHN$_3$); $^1$H NMR of the minor isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 9.08 (1H, br s, $N_{(1)}H$), 7.48 (1H, br s, $N_{(3)}H$), 3.50–3.62 (1H, m, $CHN_3$), 1.62–1.71 (1H, m, $CH_A$ in $CH_2$), signals of other protons partly or completely overlap with signals of analogous protons of the major isomer; $^{13}$C NMR of the major isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 193.7 (C=O in Ac), 152.6 (C-2), 148.0 (C-6), 110.3 (C-5), 53.3 ($CHN_3$), 47.6 (C-4), 42.4 ($CH_2$), 30.1 ($CH_3$ in Ac), 19.6 ($CH_3$), 18.9 (6-$CH_3$); IR (Nujol) $\nu$, cm$^{-1}$: 3230 (br s), 3188 (sh), 3111 (br s) (NH), 2110 (s), 2078 (m) ($N_3$), 1713 (vs) (amide-I), 1675 (s) (C=O), 1606 (s) (C=C). Anal. Calcd for $C_{10}H_{15}N_5O_2$: C, 50.62; H, 6.37; N, 29.52. Found: C, 50.74; H, 6.31; N, 29.42.

*4.5.3. 5-Acetyl-4-(2-azidobut-1-yl)-6-methyl-1,2,3,4-tetrahydropyrimidin-2-one (**9c**).* Pyrimidine **9c** (1.496 g, 74%) as a mixture of two diastereomers (65:35) was prepared from acetylacetone (**6a**) (0.853 g, 8.52 mmol), NaH (0.197 g, 8.22 mmol), and sulfone **5d** (2.628 g, 8.08 mmol) in dry THF (20 mL) (rt, 8 h), followed by treatment with *p*-TsOH·$H_2O$ (2.038 g, 10.71 mmol) (THF, reflux, 1 h 55 min) as described for **9a** in method B. After crystallization from EtOH the diastereomeric ratio changed to 80:20, respectively. Mp 172–173 °C (decomp., EtOH). $^1$H NMR of the 80:20 diastereomeric mixture (300.13 MHz, DMSO-$d_6$) $\delta$: 9.05 (0.2H, d, $^4J$=2.0 Hz, $N_{(1)}H$ in the minor isomer), 9.02 (0.8H, d, $^4J$=2.0 Hz, $N_{(1)}H$ in the major isomer), 7.66 (0.8H, dd, $^3J$=4.0, $^4J$=2.0 Hz, $N_{(3)}H$ in the major isomer), 7.45 (0.2H, dd, $^3J$=3.9, $^4J$=2.0 Hz, $N_{(3)}H$ in the minor isomer), 4.25 (0.8H, ddd, $^3J$=9.8, $^3J$=4.0, $^3J$=2.7 Hz, 4-H in the major isomer), 4.18–4.24 (0.2H, m, 4-H in the minor isomer, signals partly overlap with the 4-H proton signals of the major isomer), 3.48–3.57 (0.8H, m, $CHN_3$ in the major isomer), 3.34–3.42 (0.2H, m, $CHN_3$ in the minor isomer), 2.23 and 2.21 (0.6H and 0.6H, two s, 6-$CH_3$ and $COCH_3$ in the minor isomer), 2.190 and 2.186 (2.4H and 2.4H, two s, 6-$CH_3$ and $COCH_3$ in the major isomer), 1.36–1.72 (3.2H, m, $CH_A$ of the $CH_2CHN_3$ fragment and C*H*$_2$CH$_3$ in the major isomer, C*H*$_2$CHC*H*$_2$ in the minor isomer), 1.30 (0.8H, ddd, $^2J$=14.1, $^3J$=10.8, $^3J$=2.7 Hz, $CH_B$ of the $CH_2CHN_3$ fragment in the major isomer), 0.92 (0.6H, t, $^3J$=7.3 Hz, $CH_3$ in the minor isomer), 0.91 (2.4H, t, $^3J$=7.3 Hz, $CH_3$ in the major isomer); $^{13}$C NMR of the major isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 193.7 (C=O in Ac), 152.5 (C-2), 147.9 (C-6), 110.3 (C-5), 59.2 ($CHN_3$), 47.7 (C-4), 40.1 ($CH_2$), 30.0 ($CH_3$ in Ac), 27.4 ($CH_2$ in Et), 18.8 (6-$CH_3$), 10.1 ($CH_3$ in Et); $^{13}$C NMR of the minor isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 193.8 (C=O in Ac), 152.6 (C-2), 148.0 (C-6), 110.6 (C-5), 59.9 ($CHN_3$), 47.8 (C-4), 39.9 ($CH_2$), 30.4 ($CH_3$ in Ac), 26.4 ($CH_2$ in Et), 19.0 (6-$CH_3$), 9.8 ($CH_3$ in Et); IR (Nujol) $\nu$, cm$^{-1}$: 3353 (m), 3236 (br s), 3117 (br s) (NH), 2103 (vs) ($N_3$), 1711 (vs) (amide-I), 1675 (s) (C=O), 1607 (s) (C=C). Anal. Calcd for $C_{11}H_{17}N_5O_2$: C, 52.58; H, 6.82; N, 27.87. Found: C, 52.79; H, 6.82; N, 27.81.

*4.5.4. 5-Acetyl-4-(1-azidoprop-2-yl)-6-methyl-1,2,3,4-tetrahydropyrimidin-2-one (**9d**).* Pyrimidine **9d** (1.110 g, 63%) as a mixture of two diastereomers (56:44) was prepared from acetylacetone (**6a**) (0.789 g, 7.88 mmol), NaH (0.181 g, 7.52 mmol), and sulfone **5e** (2.307 g, 7.41 mmol) in THF (20 mL) (rt, 8 h), followed by treatment with *p*-TsOH·$H_2O$ (1.866 g, 9.81 mmol) (THF, reflux, 1 h 55 min) as described for **9a** in method B. After crystallization from MeCN the diastereomeric ratio changed to 60:40, respectively. Mp 162–165 °C (decomp., MeCN). $^1$H NMR of the major isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 8.95 (1H, br d, $^4J$=1.9 Hz, $N_{(1)}H$), 7.40 (1H, br dd, $^3J$=3.8, $^4J$=1.9 Hz, $N_{(3)}H$), 4.31 (1H, dd, $^3J$=3.8, $^3J$=2.7 Hz, 4-H), 3.35 (1H, dd, $^2J$=12.3, $^3J$=8.6 Hz, $CH_A$ in $CH_2N_3$), 3.23 (1H, dd, $^2J$=12.3, $^3J$=6.6 Hz, $CH_B$ in $CH_2N_3$), 2.21 and 2.19 (3H and 3H, two s, 6-$CH_3$ and $CH_3$ in Ac), 1.58–1.79 (1H, m, C*H*CH$_3$, signals overlap with signals of the analogous proton of the minor isomer), 0.75 (3H, d, $^3J$=6.9 Hz, CHC*H*$_3$); $^1$H NMR of the minor isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 9.02 (1H, br d, $^4J$=2.0 Hz, $N_{(1)}H$), 7.53 (1H, br dd, $^3J$=3.8, $^4J$=2.0 Hz, $N_{(3)}H$), 4.17 (1H, dd, $^3J$=5.0, $^3J$=3.8 Hz, 4-H), 3.38 (1H, dd, $^2J$=12.2, $^3J$=4.9 Hz, $CH_A$ in $CH_2N_3$), 3.10 (1H, dd, $^2J$=12.2, $^3J$=7.9 Hz, $CH_B$ in $CH_2N_3$), 2.24 and 2.21 (3H and 3H, two s, 6-$CH_3$ and $CH_3$ in Ac), 1.58–1.79 (1H, m, C*H*CH$_3$, signals overlap with signals of the analogous proton of the major isomer), 0.86 (3H, d, $^3J$=7.0 Hz, CHC*H*$_3$); $^{13}$C NMR of the major isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 194.3 (C=O in Ac), 152.9 (C-2), 148.3 (C-6), 108.3 (C-5), 52.8 ($CH_2N_3$), 51.6 (C-4), 39.74 (*C*HCH$_3$), 30.2 ($CH_3$ in Ac), 18.9 (6-$CH_3$), 11.0 (*C*H$_3$CH); $^{13}$C NMR of the minor isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 194.4 (C=O in Ac), 152.7 (C-2), 148.1 (C-6), 108.9 (C-5), 52.9 (C-4), 52.6 ($CH_2N_3$), 39.66 (*C*HCH$_3$), 30.5 ($CH_3$ in Ac), 19.0 (6-$CH_3$), 14.1 (*C*H$_3$CH); IR (Nujol) $\nu$, cm$^{-1}$: 3276 (br vs), 3123 (br s) (NH), 2095 (vs) ($N_3$), 1704 (vs) (amide-I), 1603 (vs) (C=O, C=C). Anal. Calcd for $C_{10}H_{15}N_5O_2$: C, 50.62; H, 6.37; N, 29.52. Found: C, 50.78; H, 6.38; N, 29.57.

*4.5.5. 5-Acetyl-4-(1-azidobut-2-yl)-6-methyl-1,2,3,4-tetrahydropyrimidin-2-one (**9e**).* Pyrimidine **9e** (2.240 g, 76%) as a mixture of two diastereomers (69:31) was prepared from acetylacetone (**6a**) (1.203 g, 12.01 mmol), NaH (0.282 g, 11.77 mmol), and sulfone **5f** (3.793 g, 11.66 mmol) in THF (25 mL) (rt, 8 h), followed by treatment with *p*-TsOH·$H_2O$ (2.914 g, 15.32 mmol) (THF, reflux, 1 h 50 min) as described for **9a** in method B. After crystallization from EtOH the diastereomeric ratio changed to 73:27, respectively. Mp 144–145 °C (decomp., EtOH). $^1$H NMR of the major isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 8.97 (1H, br d, $^4J$=2.0 Hz, $N_{(1)}H$), 7.45 (1H, br dd, $^3J$=4.1, $^4J$=2.0 Hz, $N_{(3)}H$), 4.32 (1H, dd, $^3J$=4.1, $^3J$=3.6 Hz, 4-H), 3.41 (1H, dd, $^2J$=12.5, $^3J$=4.5 Hz, $CH_A$ in $CH_2N_3$), 3.20 (1H, dd, $^2J$=12.5, $^3J$=6.3 Hz, $CH_B$ in $CH_2N_3$), 2.23 and 2.21 (3H and 3H, two s, 6-$CH_3$ and $CH_3$ in Ac), 1.28–1.47 (3H, m, C*H*C*H*$_2$CH$_3$, overlap with signals of the $CH_2$ protons of the minor isomer), 0.89 (3H, t, $^3J$=7.2 Hz, $CH_3$ in Et); $^1$H NMR of the minor isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 8.92 (1H, br d, $^4J$=2.0 Hz, $N_{(1)}H$), 7.40 (1H, br dd, $^3J$=3.8, $^4J$=2.0 Hz, $N_{(3)}H$), 4.38 (1H, dd, $^3J$=3.8, $^3J$=2.8 Hz, 4-H), 3.41 (1H, dd, $^2J$=12.5, $^3J$=5.1 Hz, $CH_A$ in $CH_2N_3$), 3.36 (1H, dd, $^2J$=12.5, $^3J$=8.6 Hz, $CH_B$ in $CH_2N_3$), 2.21 and 2.18 (3H and 3H, two s, 6-$CH_3$ and $CH_3$ in Ac), 1.28–1.47 (2H, m, $CH_2$ in Et, overlap with signals of the $CHCH_2$ protons of the major isomer), 1.00–1.11 (1H, m, C*H*Et), 0.84 (3H, t, $^3J$=7.3 Hz, $CH_3$ in Et); $^{13}$C NMR of the major isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 194.2 (C=O in Ac), 152.6 (C-2), 148.3 (C-6), 108.9 (C-5), 50.9 (C-4), 50.5 ($CH_2N_3$), 45.8 (*C*H–Et), 30.5 ($CH_3$ in Ac), 20.5 ($CH_2$ in Et), 19.0 (6-$CH_3$), 11.4 ($CH_3$ in Et); $^{13}$C NMR of the minor isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 194.4 (C=O in Ac), 152.7 (C-2), 148.1 (C-6), 108.5 (C-5), 51.3 (C-4), 50.1 ($CH_2N_3$), 46.3 (*C*H–Et), 30.1 ($CH_3$ in Ac), 18.3 ($CH_2$ in Et), 18.9 (6-$CH_3$), 11.6 ($CH_3$ in Et); IR (Nujol) $\nu$, cm$^{-1}$: 3350 (m), 3230 (br s), 3111 (br s) (NH), 2098 (vs) ($N_3$), 1708 (vs) (amide-I), 1675 (s) (C=O), 1606 (s) (C=C). Anal. Calcd for $C_{11}H_{17}N_5O_2$: C, 52.58; H, 6.82; N, 27.87. Found: C, 52.62; H, 6.84; N, 27.88.

*4.5.6. 4-(2-Azidoethyl)-5-benzoyl-6-methyl-1,2,3,4-tetrahydropyrimidin-2-one (**9f**).* Pyrimidine **9e** (0.700 g, 89%) as a slightly yellow solid was prepared from urea **7b** (0.835 g, 2.75 mmol) and *p*-TsOH·$H_2O$ (0.109 g, 0.57 mmol) in EtOH (13 mL) (reflux, 1 h) as described for **9a** in method A. Mp 186.0–186.5 °C (decomp., EtOH). $^1$H NMR (300.13 MHz, DMSO-$d_6$) $\delta$: 9.10 (1H, br d, $^4J$=1.9 Hz, $N_{(1)}H$), 7.43–7.59 (6H, m, Ph and $N_{(3)}H$), 4.25 (1H, dt, $^3J$=6.0, $^3J$=3.7 Hz, 4-H), 3.31–3.44 (2H, m, $CH_2N_3$), 1.68 (2H, ddd, $^3J$=7.2, $^3J$=6.6, $^3J$=6.0 Hz, C*H*$_2$CH$_2$N$_3$), 1.61 (3H, s, 6-$CH_3$); $^{13}$C NMR (75.48 MHz, DMSO-$d_6$) $\delta$: 194.2 (C=O in Bz), 152.5 (C-2), 146.7 (C-6), 141.1 (C), 131.3 (CH), 128.6 (2CH), 127.8 (2CH), 108.0 (C-5), 49.1 (C-4), 46.5 ($CH_2N_3$), 35.3 ($CH_2$), 18.6 (6-$CH_3$); IR (Nujol) $\nu$, cm$^{-1}$: 3291 (br vs), 3175 (br m) (NH), 3056 (w) ($CH_{arom}$), 2100 (sh), 2086 (s) ($N_3$), 1710 (s) (amide-I), 1678 (vs), 1653 (m) (C=O), 1601 (s), 1591 (s), 1572 (s)

(C=C, $CC_{arom}$), 743 (s), 712 (m) ($CH_{arom}$). Anal. Calcd for $C_{14}H_{15}N_5O_2 \cdot 0.07C_2H_5OH$: C, 58.86; H, 5.39; N, 24.27. Found: C, 58.89; H, 5.57; N, 23.95.

*4.5.7. 4-(2-Azidoprop-1-yl)-5-benzoyl-6-methyl-1,2,3,4-tetrahydropyrimidin-2-one (**9g**).* Pyrimidine **9g** (1.410 g, 88%) as a mixture of two diastereomers (55:45) was prepared from urea **7g** (1.683 g, 5.30 mmol) and *p*-TsOH·$H_2O$ (0.207 g, 1.09 mmol) in EtOH (15 mL) (reflux, 45 min) as described for **9a** in method A. After crystallization from MeCN the diastereomeric ratio did not change. Mp 168.5–171 °C (decomp., MeCN). $^1$H NMR of the major isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 9.08 (1H, br d, $^4J$=1.8 Hz, $N_{(1)}H$), 7.70 (1H, br dd, $^3J$=3.8, $^4J$=1.8 Hz, $N_{(3)}H$), 7.43–7.59 (5H, m, Ph, overlap with the Ph and $N_{(3)}H$ proton signals of the minor isomer), 4.25 (1H, ddd, $^3J$=9.7, $^3J$=3.8, $^3J$=3.1 Hz, 4-H), 3.71 (1H, ddq, $^3J$=10.4, $^3J$=6.5, $^3J$=3.2 Hz, $CHN_3$), 1.60 (3H, s, 6-$CH_3$), 1.51–1.72 (1H, m, $CH_A$ in $CH_2$, overlap with the $CH_2$ proton signals of the minor isomer), 1.43 (1H, ddd, $^2J$=14.1, $^3J$=10.4, $^3J$=3.2 Hz, $CH_B$ in $CH_2$), 1.21 (3H, d, $^3J$=6.5 Hz, C*H*$_3$CHN$_3$); $^1$H NMR of the minor isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 9.14 (1H, br d, $^4J \approx 1.6$ Hz, $N_{(1)}H$), 7.43–7.59 (6H, m, Ph and $N_{(3)}H$, overlap with the Ph proton signals of the major isomer), 4.20 (1H, ddd, $^3J$=7.5, $^3J$=5.1, $^3J$=3.8 Hz, 4-H), 3.56 (1H, ddq, $^3J$=6.8, $^3J$=6.8, $^3J$=6.5 Hz, $CHN_3$), 1.66 (3H, s, 6-$CH_3$), 1.51–1.72 (2H, m, $CH_2$, overlap with the $CH_A$ proton signals of the major isomer), 1.16 (3H, d, $^3J$=6.5 Hz, C*H*$_3$CHN$_3$); $^{13}$C NMR of the major isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 194.1 (C=O in Bz), 152.56 (C-2), 146.6 (C-6), 141.1 (C), 131.28 (CH), 128.54 (2CH), 127.7 (2CH), 109.5 (C-5), 53.2 ($CHN_3$), 48.8 (C-4), 42.6 ($CH_2$), 19.5 (*C*H$_3$CHN$_3$), 18.6 (6-$CH_3$); $^{13}$C NMR of the minor isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 194.2 (C=O in Bz), 152.63 (C-2), 146.8 (C-6), 140.9 (C), 131.33 (CH), 128.52 (2CH), 127.7 (2CH), 109.3 (C-5), 53.8 ($CHN_3$), 49.0 (C-4), 42.6 ($CH_2$), 19.0 (*C*H$_3$CHN$_3$), 18.4 (6-$CH_3$); IR (Nujol) $\nu$, cm$^{-1}$: 3255 (sh), 3235 (br s), 3114 (br s) (NH), 3026 (w) ($CH_{arom}$), 2113 (s), 2091 (m), ($N_3$), 1704 (vs) (amide-I), 1649 (m), 1625 (s) (C=O, C=C), 1594 (m), 1573 (w) ($CC_{arom}$), 739 (m), 702 (m) ($CH_{arom}$). Anal. Calcd for $C_{15}H_{17}N_5O_2$: C, 60.19; H, 5.72; N, 23.40. Found: C, 60.24; H, 5.66; N, 23.35.

*4.5.8. 4-(2-Azidobut-1-yl)-5-benzoyl-6-methyl-1,2,3,4-tetrahydropyrimidin-2-one (**9h**).* Pyrimidine **9h** (2.290 g, 82%) as a mixture of two diastereomers (55:45) was prepared from benzoylacetone (**6b**) (1.476 g, 9.10 mmol), NaH (0.215 g, 8.94 mmol), and sulfone **5d** (2.893 g, 8.89 mmol) in dry THF (22 mL) (rt, 8 h), followed by treatment with *p*-TsOH·$H_2O$ (2.214 g, 11.64 mmol) (THF, reflux, 1 h 30 min) as described for **9a** in method B. After crystallization from MeCN the diastereomeric ratio did not change. Mp 164–165.5 °C (decomp., MeCN). $^1$H NMR of the major isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 9.10 (1H, br d, $^4J$=1.9 Hz, $N_{(1)}H$), 7.73 (1H, dd, $^3J$=3.8, $^4J$=1.9 Hz, $N_{(3)}H$), 7.42–7.59 (5H, m, Ph, overlap with the Ph and $N_{(3)}H$ proton signals of the minor isomer), 4.27 (1H, ddd, $^3J$=9.6, $^3J$=3.8, $^3J$=2.8 Hz, 4-H), 3.46–3.55 (1H, m, $CHN_3$), 1.61 (3H, s, 6-$CH_3$), 1.33–1.67 (4H, m, C*H*$_2$CHC*H*$_2$, overlap with signals of analogous protons of the minor isomer), 0.90 (3H, t, $^3J$=7.4 Hz, $CH_3$ in Et); $^1$H NMR of the minor isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 9.15 (1H, br d, $^4J$=1.9 Hz, $N_{(1)}H$), 7.42–7.59 (6H, m, Ph and $N_{(3)}H$, overlap with the Ph proton signals of the major isomer), 4.22 (1H, ddd, $^3J$=6.4, $^3J$=6.4, $^3J$=3.8 Hz, 4-H), 3.35–3.43 (1H, m, $CHN_3$), 1.65 (3H, s, 6-$CH_3$), 1.33–1.67 (4H, m, C*H*$_2$CHC*H*$_2$, overlap with signals of analogous protons of the major isomer), 0.87 (3H, t, $^3J$=7.4 Hz, $CH_3$ in Et); $^{13}$C NMR of the major isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 194.1 (C=O in Bz), 152.6 (C-2), 146.7 (C-6), 141.2 (C), 131.3 (CH), 128.6 (2CH), 127.75 (2CH), 109.5 (C-5), 59.1 ($CHN_3$), 48.9 (C-4), 40.3 ($CH_2$), 27.4 ($CH_2$ in Et), 18.6 (6-$CH_3$), 10.2 ($CH_3$ in Et); $^{13}$C NMR of the minor isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 194.2 (C=O in Bz), 152.7 (C-2), 146.9 (C-6), 141.0 (C), 131.4 (CH), 128.6 (2CH), 127.77 (2CH), 109.3 (C-5), 59.8 ($CHN_3$), 49.1 (C-4), 40.2 ($CH_2$), 26.5 ($CH_2$ in Et), 18.5 (6-$CH_3$), 9.8 ($CH_3$ in Et); IR (Nujol) $\nu$, cm$^{-1}$: 3236 (br s), 3100 (br s) (NH), 3030 (w) ($CH_{arom}$), 2100 (s) ($N_3$), 1701 (vs) (amide-I), 1650 (s), 1629 (s) (C=O, C=C), 1599 (m), 1577 (w) ($CC_{arom}$), 738 (m), 703 (m) ($CH_{arom}$). Anal. Calcd for $C_{16}H_{19}N_5O_2$: C, 61.33; H, 6.11; N, 22.35. Found: C, 61.04; H, 6.03; N, 22.34.

*4.5.9. 4-(1-Azidoprop-1-yl)-5-benzoyl-6-methyl-1,2,3,4-tetrahydropyrimidin-2-one (**9i**).* Pyrimidine **9i** (0.991 g, 79%) as a mixture of two diastereomers (50:50) was prepared from benzoylacetone (**6b**) (0.727 g, 4.48 mmol), NaH (0.104 g, 4.33 mmol), and sulfone **5e** (1.312 g, 4.21 mmol) in THF (18 mL) (rt, 8 h), followed by treatment with *p*-TsOH·$H_2O$ (1.076 g, 5.66 mmol) (THF, reflux, 1 h 35 min) as described for **9a** in method B. After crystallization from MeCN the diastereomeric ratio changed to 51:49. Mp 177.5–178.5 °C (decomp., MeCN). $^1$H NMR of the first isomer (49%) (300.13 MHz, DMSO-$d_6$) $\delta$: 8.94 (1H, br d, $^4J$=1.9 Hz, $N_{(1)}H$), 7.44–7.61 (5H, m, Ph, overlap with the Ph and $N_{(3)}H$ proton signals of the second isomer), 7.40 (1H, br dd, $^3J$=3.6, $^4J$=1.9 Hz, $N_{(3)}H$), 4.39 (1H, dd, $^3J$=3.6, $^3J$=3.0 Hz, 4-H), 3.32 (1H, dd, $^2J$=12.4, $^3J$=8.1 Hz, $CH_A$ in $CH_2N_3$), 3.22 (1H, dd, $^2J$=12.4, $^3J$=6.6 Hz, $CH_B$ in $CH_2N_3$), 1.65 (3H, s, 6-$CH_3$), 1.62–1.85 (1H, m, C*H*$CH_3$, overlap with signals of the analogous proton of the second isomer and signals of the 6-Me groups of both isomers), 0.84 (3H, d, $^3J$=6.9 Hz, CHC*H*$_3$); $^1$H NMR of the second isomer (51%) (300.13 MHz, DMSO-$d_6$) $\delta$: 9.02 (1H, br d, $^4J$=1.9 Hz, $N_{(1)}H$), 7.44–7.61 (6H, m, Ph and $N_{(3)}H$, overlap with the Ph proton signals of the first isomer), 4.23 (1H, dd, $^3J$=4.9, $^3J$=3.9 Hz, 4-H), 3.37 (1H, dd, $^2J$=12.3, $^3J$=5.1 Hz, $CH_A$ in $CH_2N_3$), 3.13 (1H, dd, $^2J$=12.3, $^3J$=7.5 Hz, $CH_B$ in $CH_2N_3$), 1.69 (3H, s, 6-$CH_3$), 1.62–1.85 (1H, m, C*H*$CH_3$, overlap with signals of the analogous proton of the first isomer and signals of the 6-Me groups of both isomers), 0.86 (3H, d, $^3J$=6.9 Hz, CHC*H*$_3$); $^{13}$C NMR of the 49:51 diastereomeric mixture (75.48 MHz, DMSO-$d_6$) $\delta$: 194.6, 194.6 (C=O in Bz), 152.9, 152.8 (C-2), 146.3, 146.1 (C-6), 140.9, 140.6 (C), 131.50, 131.45 (CH), 128.6, 128.6 (2CH), 127.9, 127.8 (2CH), 107.59, 107.55 (C-5), 54.0, 52.9 (C-4), 52.59, 52.56 ($CH_2N_3$), 40.3, 39.8 (*C*HCH$_3$), 18.24, 18.17 (6-$CH_3$), 13.7, 11.3 (*C*H$_3$CH); IR (Nujol) $\nu$, cm$^{-1}$: 3228 (br s), 3104 (br s) (NH), 2102 (s) ($N_3$), 1702 (vs) (amide-I), 1648 (m), 1628 (s) (C=C, C=O), 1595 (w), 1578 (w) ($CC_{arom}$), 739 (m), 704 (m) ($CH_{arom}$). Anal. Calcd for $C_{15}H_{17}N_5O_2$: C, 60.19; H, 5.72; N, 23.40. Found: C, 60.12; H, 5.83; N, 23.29.

*4.5.10. 4-(1-Azidobut-2-yl)-5-benzoyl-6-methyl-1,2,3,4-tetrahydropyrimidin-2-one (**9j**).* Pyrimidine **9j** (1.927 g, 73%) as a mixture of two diastereomers (67:33) was prepared from benzoylacetone (**6b**) (1.394 g, 8.59 mmol), NaH (0.203 g, 8.45 mmol), and sulfone **5f** (2.733 g, 8.40 mmol) in THF (25 mL) (rt, 8 h), followed by treatment with *p*-TsOH·$H_2O$ (2.092 g, 10.99 mmol) (THF, reflux, 1 h 50 min) as described for **9a** in method B. After crystallization from MeCN the diastereomeric ratio changed to 76:24, respectively. Mp 163.5–165.5 °C (decomp., MeCN). $^1$H NMR of the major isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 9.03 (1H, br d, $^4J$=1.8 Hz, $N_{(1)}H$), 7.42–7.60 (6H, m, Ph and $N_{(3)}H$, overlap with signals of analogous protons of the minor isomer), 4.37 (1H, t, $^3J_1$+$^3J_2$=7.3 Hz, 4-H), 3.48 (1H, dd, $^2J$=12.5, $^3J$=4.7 Hz, $CH_A$ in $CH_2N_3$), 3.25 (1H, dd, $^2J$=12.5, $^3J$=6.4 Hz, $CH_B$ in $CH_2N_3$), 1.70 (3H, s, 6-$CH_3$), 1.02–1.52 (3H, m, C*H*C*H*$_2$CH$_3$, overlap with signals of analogous protons of the minor isomer), 0.75 (3H, t, $^3J$=7.3 Hz, $CH_3$ in Et); $^1$H NMR of the minor isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 8.96 (1H, br d, $^4J$=1.8 Hz, $N_{(1)}H$), 7.42–7.60 (6H, m, Ph and $N_{(3)}H$, overlap with signals of analogous protons of the major isomer), 4.44 (1H, t, $^3J_1$+$^3J_2$=6.7 Hz, 4-H), 3.32–3.43 (2H, m, $CH_2N_3$), 1.66 (3H, s, 6-$CH_3$), 1.02–1.52 (3H, m, C*H*C*H*$_2$CH$_3$, overlap with signals of analogous protons of the major isomer), 0.84 (3H, t, $^3J$=7.3 Hz, $CH_3$ in Et); $^{13}$C NMR of the major isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 194.6 (C=O in Bz), 152.7 (C-2), 146.5 (C-6), 140.8 (C), 131.5 (CH), 128.58 (2CH), 127.9 (2CH), 107.8 (C-5), 52.2 (C-4), 50.5 ($CH_2N_3$), 46.4 (*C*H–Et), 20.3 ($CH_2$ in Et), 18.3 (6-$CH_3$), 11.2 ($CH_3$ in Et); $^{13}$C NMR of the minor isomer (75.48 MHz,

DMSO-$d_6$) $\delta$: 194.7 (C=O in Bz), 152.9 (C-2), 145.8 (C-6), 140.7 (C), 131.6 (CH), 128.64 (2CH), 127.9 (2CH), 107.7 (C-5), 52.5 (C-4), 50.0 ($CH_2N_3$), 46.6 (*C*H–Et), 18.8 ($CH_2$ in Et), 18.2 (6-$CH_3$), 11.7 ($CH_3$ in Et); IR (Nujol) $\nu$, $cm^{-1}$: 3229 (br s), 3103 (br s) (NH), 3028 (w) ($CH_{arom}$), 2097 (s) ($N_3$), 1701 (vs) (amide-I), 1649 (m), 1631 (s) (C=O, C=C), 1598 (w), 1578 (w) ($CC_{arom}$), 740 (m), 703 (m) ($CH_{arom}$). Anal. Calcd for $C_{16}H_{19}N_5O_2$: C, 61.33; H, 6.11; N, 22.35. Found: C, 61.35; H, 6.20; N, 22.19.

*4.5.11. 4-(2-Azidoethyl)-5-benzoyl-6-phenyl-1,2,3,4-tetrahydropyrimidin-2-one (**9k**).* A solution of compound **7c** (0.981 g, 2.68 mmol) and *p*-TsOH·$H_2O$ (0.516 g, 2.71 mmol) in EtOH (20 mL) was heated at reflux for 2 h 15 min under stirring, and then the solvent was removed in vacuum. The residue was dissolved in $CHCl_3$ (10 mL) and subsequently washed with saturated aqueous solution of $NaHCO_3$ (5 mL, 3×3 mL), $H_2O$ (2×5 mL), brine (2×5 mL), and dried over $Na_2SO_4$. After removal of solvent, the residue was purified using column chromatography on silica gel 60 (6.9 g) eluting with $CHCl_3$/MeOH (from 1:0 to 100:1) to give **9k** (0.191 g, 21%). Mp 171.5–173 °C (decomp., AcOEt/hexane, 1:1). $^1$H NMR (300.13 MHz, DMSO-$d_6$) $\delta$: 9.35 (1H, d, $^4J$=1.8 Hz, $N_{(1)}H$), 7.68 (1H, dd, $^3J$=3.8, $^4J$=1.8 Hz, $N_{(3)}H$), 7.26–7.32 (2H, m, ArH), 6.98–7.18 (8H, m, ArH), 4.28 (1H, ddd, $^3J$=7.3, $^3J$=4.7, $^3J$=3.8 Hz, 4-H), 3.46–3.61 (2H, m, $CH_2N_3$), 1.85–2.02 (2H, m, C$H_2$$CH_2N_3$); $^{13}$C NMR (75.48 MHz, DMSO-$d_6$) $\delta$: 194.7 (C=O in Bz), 152.8 (C-2), 148.9 (C-6), 139.5 (C), 133.4 (C), 130.6 (CH), 129.7 (2CH), 129.6 (CH), 128.5 (2CH), 127.6 (2CH), 127.4 (2CH), 108.7 (C-5), 49.9 (C-4), 46.7 ($CH_2N_3$), 35.1 (C$H_2$$CH_2N_3$); IR (Nujol) $\nu$, $cm^{-1}$: 3208 (br s), 3116 (br s) (NH), 3031 (w) ($CH_{arom}$), 2091 (s) ($N_3$), 1704 (vs) (amide-I), 1618 (sh), 1597 (s), 1569 (s) (C=O, C=C), 1492 (w) ($CC_{arom}$), 730 (s), 700 (m) ($CH_{arom}$). Anal. Calcd for $C_{19}H_{17}N_5O_2$: C, 65.70; H, 4.93; N, 20.16. Found: C, 65.38; H, 4.93; N, 19.82.

*4.5.12. Ethyl 6-(2-azidoethyl)-5-benzoyl-2-oxo-1,2,3,6-tetrahydropyrimidine-4-carboxylate (**9l**).* Pyrimidine **9l** (1.093 g, 60%) was prepared from **6d** (1.202 g, 5.46 mmol), NaH (0.129 g, 5.37 mmol), and sulfone **5a** (1.577 g, 5.30 mmol) in THF (20 mL) (rt, 8 h 10 min), followed by treatment with *p*-TsOH·$H_2O$ (1.334 g, 5.90 mmol) (THF, reflux, 3 h 10 min) as described for **9a** in method B. The analytically pure sample (0.273 g) was obtained by purification of 0.355 g of crude **9l** using column chromatography on silica gel 60 (4.1 g) eluting with MeOH/$CHCl_3$ (from 0:1 to 1:95) followed by crystallization from EtOH (18 mL). Mp 174.5–175 °C (decomp., EtOH). $^1$H NMR (300.13 MHz, DMSO-$d_6$) $\delta$: 8.99 (1H, br s, $N_{(3)}H$), 7.70–7.75 (2H, m, ArH), 7.62 (1H, br d, $^3J$=3.4 Hz, $N_{(1)}H$), 7.58–7.64 (1H, m, ArH), 7.47–7.53 (2H, m, ArH), 4.25 (1H, ddd, $^3J$=7.2, $^3J$=4.8, $^3J$=3.4 Hz, 6-H), 3.58–3.72 (2H, m, $OCH_2$), 3.39–3.52 (2H, m, $CH_2N_3$), 1.69–1.85 (2H, m, C$H_2$$CH_2N_3$), 0.87 (3H, t, $^3J$=7.1 Hz, $CH_3$); $^{13}$C NMR (75.48 MHz, DMSO-$d_6$) $\delta$: 193.2 (C=O in Bz), 161.2 (C=O in COOEt), 152.2 (C-2), 137.8 (C-4), 134.0 (C), 132.8 (CH), 128.6 (2CH), 128.1 (2CH), 114.5 (C-5), 61.7 ($OCH_2$), 49.9 (C-6), 46.2 ($CH_2N_3$), 34.5 (C$H_2$$CH_2N_3$), 13.0 ($CH_3$); IR (Nujol) $\nu$, $cm^{-1}$: 3216 (br s), 3112 (br s) (NH), 2138 (m), 2097 (s) ($N_3$), 1731 (s) (C=O in COOEt), 1708 (vs) (amide-I), 1643 (s) (C=O in Bz, C=C), 1596 (w), 1578 (w) ($CC_{arom}$), 1292 (s), 1217 (s), 1079 (s) (C–O), 714 (s) ($CH_{arom}$). Anal. Calcd for $C_{16}H_{17}N_5O_4$: C, 55.97; H, 4.99; N, 20.40. Found: C, 55.87; H, 4.95; N, 20.06.

*4.5.13. Ethyl 6-(2-azidoprop-1-yl)-5-benzoyl-2-oxo-1,2,3,6-tetrahydropyrimidine-4-carboxylate (**9m**).* Pyrimidine **9m** (1.093 g, 60%) as a mixture of two diastereomers (63:37) was prepared from **6d** (1.676 g, 7.61 mmol), NaH (0.180 g, 7.50 mmol), and sulfone **5c** (2.300 g, 7.39 mmol) in THF (20 mL) (rt, 8 h), followed by treatment with *p*-TsOH·$H_2O$ (1.859 g, 9.77 mmol) (THF, reflux, 2 h 30 min) as described for **9a** in method B. After crystallization from MeCN the diastereomeric ratio changed to 78:22, respectively. Mp 180–181 °C (decomp., MeCN). $^1$H NMR of the major isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 8.98 (1H, d, $^4J$=1.9 Hz, $N_{(3)}H$), 7.77 (1H, dd, $^3J$=3.5, $^4J$=1.9 Hz, $N_{(1)}H$), 7.46–7.74 (5H, m, Ph), 4.23 (1H, ddd, $^3J$=9.9, $^3J$=3.5, $^3J$=2.8 Hz, 6-H), 3.82 (1H, ddq, $^3J$=10.9, $^3J$=6.5, $^3J$=2.8 Hz, $CHN_3$), 3.64 (2H, q, $^3J$=7.1 Hz, $OCH_2$), 1.73 (1H, ddd, $^2J$=14.1, $^3J$=9.9, $^3J$=2.8 Hz, $CH_A$ in $CH_2$), 1.48 (1H, ddd, $^2J$=14.1, $^3J$=10.9, $^3J$=2.8 Hz, $CH_B$ in $CH_2$), 1.24 (3H, d, $^3J$=6.5 Hz, C$H_3$$CHN_3$), 0.86 (3H, t, $^3J$=7.1 Hz, $CH_3$ in COOEt); $^1$H NMR of the minor isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 9.08 (1H, d, $^4J$=1.9 Hz, $N_{(3)}H$), 7.46–7.74 (6H, m, Ph and $N_{(1)}H$, overlap with the Ph proton signals of the major isomer), 4.21–4.27 (1H, m, 6-H, overlap with signals of analogous proton of the major isomer), 3.64 (2H, q, $^3J$=7.1 Hz, $OCH_2$), 3.59–3.69 (1H, m, $CHN_3$, overlap with signals of the $OCH_2$ protons of both isomers), 1.64–1.83 (2H, m, C$H_2$$CHN_3$, partly overlap with signals of the $CH_A$ proton of the major isomer), 1.19 (3H, d, $^3J$=6.5 Hz, C$H_3$$CHN_3$), 0.88 (3H, t, $^3J$=7.1 Hz, $CH_3$ in COOEt); $^{13}$C NMR of the major isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 193.15 (C=O in Bz), 161.2 (C=O in COOEt), 152.2 (C-2), 137.9 (C-4), 134.0 (C), 132.8 (CH), 128.62 (2CH), 128.1 (2CH), 114.8 (C-5), 61.70 ($OCH_2$), 52.9 ($CHN_3$), 49.6 (C-6), 41.7 (C$H_2$$CHN_3$), 19.4 (C$H_3$$CHN_3$), 13.0 ($CH_3$ in COOEt); $^{13}$C NMR of the minor isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 193.12 (C=O in Bz), 161.3 (C=O in COOEt), 152.3 (C-2), 138.0 (C-4), 134.7 (C), 132.7 (CH), 128.59 (2CH), 128.1 (2CH), 114.4 (C-5), 61.72 ($OCH_2$), 53.6 ($CHN_3$), 49.7 (C-6), 41.7 (C$H_2$$CHN_3$), 18.9 (C$H_3$$CHN_3$), 13.0 ($CH_3$ in COOEt); IR (Nujol) $\nu$, $cm^{-1}$: 3222 (br s), 3115 (br s) (NH), 2119 (s), 2099 (s) ($N_3$), 1736 (s) (C=O in COOEt), 1706 (vs) (amide-I), 1679 (m), 1649 (s) (C=O in Bz, C=C), 1595 (w), 1577 (w) ($CC_{arom}$), 1254 (s), 1217 (s), 1085 (m) (C–O), 715 (s) ($CH_{arom}$). Anal. Calcd for $C_{17}H_{19}N_5O_4$: C, 57.14; H, 5.36; N, 19.60. Found: C, 57.19; H, 5.36; N, 19.61.

*4.5.14. Ethyl 6-(2-azidobut-1-yl)-5-benzoyl-2-oxo-1,2,3,6-tetrahydropyrimidine-4-carboxylate (**9n**).* Pyrimidine **9n** (1.483 g, 73%) as a mixture of two diastereomers (62:38) was prepared from **6d** (1.245 g, 5.66 mmol), NaH (0.133 g, 5.55 mmol), and sulfone **5d** (1.791 g, 5.50 mmol) in THF (19 mL) (rt, 8 h), followed by treatment with *p*-TsOH·$H_2O$ (1.478 g, 7.77 mmol) (THF, reflux, 2 h 20 min) as described for **9a** in method B. The analytically pure sample (0.223 g; mixture of two diastereomers, 65:35) was obtained by purification of 0.405 g of crude **9n** using column chromatography on silica gel 60 (4.2 g) eluting with MeOH/$CHCl_3$ (from 0:1 to 1:100) followed by crystallization from EtOH (3 mL). Mp 123–124 °C (decomp., EtOH). $^1$H NMR of the 65:35 diastereomeric mixture (300.13 MHz, DMSO-$d_6$) $\delta$: 9.14 (0.35H, br s, $N_{(3)}H$ in the minor isomer), 9.05 (0.65H, br s, $N_{(3)}H$ in the major isomer), 7.82 (0.65H, d, $^3J$=3.6 Hz, $N_{(1)}H$ in the major isomer), 7.46–7.74 (5.35H, m, Ph in both isomers and $N_{(1)}H$ in the minor isomer), 4.24 (0.65H, ddd, $^3J$=9.9, $^3J$=3.6, $^3J$=2.6 Hz, 6-H in the major isomer), 4.22–4.28 (0.35H, m, 6-H in the minor isomer, overlap with signals of analogous proton of the major isomer), 3.55–3.69 (2.65H, m, $OCH_2$ in both isomers and $CHN_3$ in the major isomer), 3.42–3.50 (0.35H, m, $CHN_3$ in the minor isomer), 1.36–1.80 (4H, m, C$H_2$CHC$H_2$ in both isomers), 0.91 (1.95H, t, $^3J$=7.3 Hz, C$H_3$$CH_2$CH in the major isomer), 0.87 (1.05H, t, $^3J$=7.1 Hz, C$H_3$$CH_2$O in the minor isomer), 0.87 (1.05H, t, $^3J$=7.3 Hz, C$H_3$$CH_2$CH in the minor isomer), 0.86 (1.95H, t, $^3J$=7.1 Hz, C$H_3$$CH_2$O in the major isomer); $^{13}$C NMR of the major isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 193.2 (C=O in Bz), 161.3 (C=O in COOEt), 152.3 (C-2), 138.0 (C-4), 134.2 (C), 132.81 (CH), 128.66 (2CH), 128.1 (2CH), 114.8 (C-5), 61.76 ($OCH_2$), 58.7 ($CHN_3$), 49.6 (C-6), 39.5 (CHC$H_2$CH), 27.4 ($CH_3$C$H_2$CH), 13.0 ($CH_3$ in COOEt), 10.1 ($CH_3CH_2CH$); $^{13}$C NMR of the major isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 193.2 (C=O in Bz), 161.4 (C=O in COOEt), 152.4 (C-2), 138.1 (C-4), 135.0 (C), 132.75 (CH), 128.63 (2CH), 128.1 (2CH), 114.3 (C-5), 61.77 ($OCH_2$), 59.6 ($CHN_3$), 49.8 (C-6), 39.5 (CHC$H_2$CH), 26.5 ($CH_3$C$H_2$CH), 13.0 ($CH_3$ in COOEt), 9.8 ($CH_3CH_2CH$); IR (Nujol) $\nu$, $cm^{-1}$: 3230 (br s), 3125 (m), 3094 (m) (NH), 2098 (s) ($N_3$), 1721 (s) (C=O in COOEt), 1702 (vs) (amide-I),

1658 (s) (C=O in Bz, C=C), 1595 (w), 1578 (w) ($CC_{arom}$), 1293 (m), 1213 (s), 1073 (m) (C–O), 718 (s) ($CH_{arom}$). Anal. Calcd for $C_{18}H_{21}N_5O_4$: C, 58.21; H, 5.70; N, 18.86. Found: C, 58.22; H, 5.72; N, 18.77.

*4.5.15. Ethyl 6-(1-azidoprop-2-yl)-5-benzoyl-2-oxo-1,2,3,6-tetrahydropyrimidine-4-carboxylate (**9o**).* Pyrimidine **9o** (two diastereomers, 60:40) along with unidentified byproducts was prepared from **6d** (1.276 g, 5.79 mmol), NaH (0.136 g, 5.68 mmol), and sulfone **5e** (1.744 g, 5.60 mmol) in THF (18 mL) (rt, 8 h), followed by treatment with *p*-TsOH·$H_2O$ (1.520 g, 7.99 mmol) (THF, reflux, 2 h 20 min) as described for **9a** in method B. Pure **9o** (0.387 g, 19%) was isolated from the crude product (1.174 g) using column chromatography on silica gel 60 (18 g) eluting with $CHCl_3$/petroleum ether (from 2:1 to 1:0), then $CHCl_3$/MeOH (100:1). After crystallization from EtOH the diastereomeric ratio was 64:36, respectively. Mp 155.5–156.5 °C (decomp., EtOH). $^1$H NMR of the major isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 8.89 (1H, br s, $N_{(3)}H$), 7.47–7.76 (6H, m, Ph and $N_{(1)}H$, overlap with signals of analogous protons of the minor isomer), 4.37 (1H, dd, $^3J$=3.2, $^3J$=2.4 Hz, 6-H), 3.54–3.78 (2H, m, $OCH_2$, overlap with signals of analogous protons of the minor isomer), 3.38 (1H, dd, $^2J$=12.4, $^3J$=8.7 Hz, $CH_A$ in $CH_2N_3$), 3.30 (1H, dd, $^2J$=12.4, $^3J$=6.4 Hz, $CH_B$ in $CH_2N_3$), 1.75 (1H, dddq, $^3J$=8.7, $^3J$=6.9, $^3J$=6.4, $^3J$=2.4 Hz, C*H*$CH_3$), 0.91 (3H, d, $^3J$=6.9 Hz, CH$CH_3$), 0.88 (3H, t, $^3J$=7.1 Hz, $CH_3$ in COOEt); $^1$H NMR of the minor isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 9.04 (1H, br s, $N_{(3)}H$), 7.47–7.76 (6H, m, Ph and $N_{(1)}H$, overlap with signals of analogous protons of the major isomer), 4.28 (1H, dd, $^3J$=4.3, $^3J$=3.4 Hz, 6-H), 3.54–3.78 (2H, m, $OCH_2$, overlap with signals of analogous protons of the major isomer), 3.42 (1H, dd, $^2J$=12.3, $^3J$=5.4 Hz, $CH_A$ in $CH_2N_3$), 3.20 (1H, dd, $^2J$=12.3, $^3J$=7.5 Hz, $CH_B$ in $CH_2N_3$), 1.87 (1H, dddq, $^3J$=7.5, $^3J$=6.9, $^3J$=5.4, $^3J$=4.3 Hz, C*H*$CH_3$), 0.92 (3H, d, $^3J$=6.9 Hz, CH$CH_3$), 0.90 (3H, t, $^3J$=7.1 Hz, $CH_3$ in COOEt); $^{13}$C NMR of the major isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 193.32 (C=O in Bz), 161.2 (C=O in COOEt), 152.7 (C-2), 137.7 (C-4), 134.3 (C), 132.9 (CH), 128.7 (2CH), 128.1 (2CH), 113.6 (C-5), 61.7 ($OCH_2$), 53.5 (C-6), 52.1 ($CH_2N_3$), 39.0 ($CH_3$*C*H), 13.0 ($CH_3$ in COOEt), 10.9 (*C*$H_3$CH); $^{13}$C NMR of the minor isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 193.27 (C=O in Bz), 161.3 (C=O in COOEt), 152.5 (C-2), 137.7 (C-4), 135.5 (C), 132.8 (CH), 128.6 (2CH), 128.2 (2CH), 112.7 (C-5), 61.7 ($OCH_2$), 54.7 (C-6), 52.3 ($CH_2N_3$), 39.8 ($CH_3$*C*H), 13.0 ($CH_3$ in COOEt), 13.6 (*C*$H_3$CH); IR (Nujol) $\nu$, cm$^{-1}$: 3230 (br s), 3126 (m), 3089 (m) (NH), 2105 (s) ($N_3$), 1727 (s) (C=O in COOEt), 1697 (vs) (amide-I), 1663 (s) (C=O in Bz, C=C), 1596 (w), 1579 (w), 1488 (w) ($CC_{arom}$), 1291 (s), 1219 (s), 1073 (m) (C–O), 719 (s) ($CH_{arom}$). Anal. Calcd for $C_{17}H_{19}N_5O_4$: C, 57.14; H, 5.36; N, 19.60. Found: C, 57.18; H, 5.38; N, 19.58.

*4.5.16. Ethyl 6-(1-azidobut-2-yl)-5-benzoyl-2-oxo-1,2,3,6-tetrahydropyrimidine-4-carboxylate (**9p**).* Pyrimidine **9p** (two diastereomers, 50:50) along with unidentified byproducts was prepared from **6d** (1.367 g, 6.21 mmol), NaH (0.146 g, 6.10 mmol), and sulfone **5f** (1.959 g, 6.02 mmol) in THF (20 mL) (rt, 8 h), followed by treatment with *p*-TsOH·$H_2O$ (1.627 g, 8.55 mmol) (THF, reflux, 2 h 20 min) as described for **9a** in method B. Pure **9p** (0.309 g, 14%) was isolated from the crude product (1.432 g) using column chromatography on silica gel 60 (18 g) eluting with $CHCl_3$/petroleum ether (from 20:1 to 1:0), then $CHCl_3$/MeOH (from 200:1 to 80:1). After crystallization from EtOH the diastereomeric ratio was 65:35. Mp 147–148 °C (decomp., EtOH). $^1$H NMR of the first isomer (65% in analytically pure form) (300.13 MHz, DMSO-$d_6$) $\delta$: 8.93 (1H, br s, $N_{(3)}H$), 7.46–7.75 (6H, m, Ph and $N_{(1)}H$, overlap with signals of analogous protons of the second isomer), 4.43 (1H, dd, $^3J$=3.2, $^3J$=2.5 Hz, 6-H), 3.55–3.79 (2H, m, $OCH_2$, overlap with signals of analogous protons of the second isomer), 3.49 (1H, dd, $^2J$=12.6, $^3J$=4.9 Hz, $CH_A$ in $CH_2N_3$), 3.41 (1H, dd, $^2J$=12.6, $^3J$=9.4 Hz, $CH_B$ in $CH_2N_3$), 1.07–1.64 (3H, m, C*HCH*$_2$$CH_3$, overlap with signals of analogous protons of the second isomer), 0.87 (3H, t, $^3J$=7.1 Hz, $CHCH_2CH_3$), 0.87 (3H, t, $^3J$=7.1 Hz, $CH_3$ in COOEt); $^1$H NMR of the second isomer (35% in analytically pure form) (300.13 MHz, DMSO-$d_6$) $\delta$: 9.07 (1H, br s, $N_{(3)}H$), 7.46–7.75 (6H, m, Ph and $N_{(1)}H$, overlap with signals of analogous protons of the first isomer), 4.40 (1H, dd, $^3J$=3.5, $^3J$=3.4 Hz, 6-H), 3.55–3.79 (2H, m, $OCH_2$, overlap with signals of analogous protons of the first isomer), 3.51 (1H, dd, $^2J$=12.6, $^3J$=5.4 Hz, $CH_A$ in $CH_2N_3$), 3.32 (1H, dd, $^2J$=12.6, $^3J$=6.3 Hz, $CH_B$ in $CH_2N_3$), 1.07–1.64 (3H, m, C*HCH*$_2$$CH_3$, overlap with signals of analogous protons of the first isomer), 0.89 (3H, t, $^3J$=7.1 Hz, $CH_3$ in COOEt), 0.80 (3H, t, $^3J$=7.3 Hz, $CHCH_2CH_3$); $^{13}$C NMR of the first isomer (65% in analytically pure form) (75.48 MHz, DMSO-$d_6$) $\delta$: 193.4 (C=O in Bz), 161.2 (C=O in COOEt), 152.6 (C-2), 137.6 (C-4), 134.3 (C), 133.1 (CH), 128.8 (2CH), 128.1 (2CH), 113.9 (C-5), 61.80 ($OCH_2$), 53.4 (C-6), 49.5 ($CH_2N_3$), 45.8 ($CH_3CH_2CH$), 18.8 ($CH_3CH_2CH$), 13.04 ($CH_3$ in COOEt), 11.6 (*C*$H_3$CH$_2$CH); $^{13}$C NMR of the second isomer (35% in analytically pure form) (75.48 MHz, DMSO-$d_6$) $\delta$: 193.3 (C=O in Bz), 161.4 (C=O in COOEt), 152.5 (C-2), 137.9 (C-4), 135.6 (C), 132.8 (CH), 128.7 (2CH), 128.2 (2CH), 113.0 (C-5), 61.79 ($OCH_2$), 53.0 (C-6), 50.4 ($CH_2N_3$), 45.9 ($CH_3CH_2CH$), 20.3 ($CH_3CH_2CH$), 13.06 ($CH_3$ in COOEt), 11.3 (*C*$H_3$CH$_2$CH); IR (Nujol) $\nu$, cm$^{-1}$: 3213 (br s), 3092 (br s) (NH), 2102 (s) ($N_3$), 1730 (s) (C=O in COOEt), 1702 (vs) (amide-I), 1669 (s) (C=O in Bz, C=C), 1596 (w), 1579 (w) ($CC_{arom}$), 1291 (s), 1220 (s), 1078 (m) (C–O), 717 (s) ($CH_{arom}$). Anal. Calcd for $C_{18}H_{21}N_5O_4$: C, 58.21; H, 5.70; N, 18.86. Found: C, 58.50; H, 5.73; N, 18.51.

### 4.6. Synthesis of pyrido[4,3-*d*]pyrimidin-2-ones

*4.6.1. 4,5-Dimethyl-1,2,3,7,8,8a-hexahydropyrido[4,3-d]pyrimidin-2-one (**10a**).* To pyrimidine **9a** (1.271 g, 5.69 mmol) and $PPh_3$ (1.694 g, 6.46 mmol) was added dry MeCN (16 mL), and the obtained mixture was heated at reflux under stirring for 5 h 30 min. A clear solution formed at the beginning of reflux, and after 10 min the product precipitated to give a suspension. After the reaction was complete, the mixture was evaporated in vacuo to half of its volume, the resulting suspension was cooled to −10 °C, and the precipitate was filtered on a cold (−10 °C) filter, successively washed with MeCN (4×4 mL, −10 °C), diethyl ether (2×5 mL), petroleum ether, and dried to give **10a** (0.963 g, 94%) as a white solid. Mp 229.5 °C (decomp.; EtOH). $^1$H NMR (300.13 MHz, DMSO-$d_6$) $\delta$: 8.42 (1H, br s, $N_{(3)}H$), 7.01 (1H, s, $N_{(1)}H$), 3.99 (1H, ddq, $^3J$=10.8, $^3J$=4.8, $^5J$=1.4 Hz, 8a-H), 3.52 (1H, dddq, $^2J$=16.4, $^3J$=4.7, $^3J$=2.9, $^5J$=1.1 Hz, 7-$H_A$), 3.29 (1H, dddq, $^2J$=16.4, $^3J$=11.4, $^3J$=4.2, $^5J$=2.0 Hz, 7-$H_B$), 2.13 (3H, dd, $^5J$=2.0, $^5J$=1.1 Hz, 5-$CH_3$), 2.05 (3H, d, $^5J$=1.4 Hz, 4-$CH_3$), 1.84 (1H, dddd, $^2J$=12.4, $^3J$=4.8, $^3J$=4.2, $^3J$=2.9 Hz, 8-$H_A$), 1.41 (1H, dddd, $^2J$=12.4, $^3J$=11.4, $^3J$=10.8, $^3J$=4.7 Hz, 8-$H_B$); $^{13}$C NMR (75.48 MHz, DMSO-$d_6$) $\delta$: 160.3 (C-5), 154.3 (C-2), 137.4 (br) (C-4), 104.2 (C-4a), 48.9 (C-8a), 46.6 (C-7), 29.3 (C-8), 28.1 (5-$CH_3$), 18.6 (4-$CH_3$); IR (Nujol) $\nu$, cm$^{-1}$: 3213 (s), 3105 (s), 3082 (s) (NH), 1692 (vs) (amide-I), 1639 (s) (C=C), 1593 (s) (C=N). Anal. Calcd for $C_9H_{13}N_3O$: C, 60.32; H, 7.31; N, 23.45. Found: C, 60.12; H, 7.30; N, 23.58.

*4.6.2. 4,5,7-Trimethyl-1,2,3,7,8,8a-hexahydropyrido[4,3-d]pyrimidin-2-one (**10b**).* Compound **10b** (0.393 g, 84%) as a mixture of (7*R**,8a*S**)- and (7*R**,8a*R**)-diastereomers (90:10) was prepared from pyrimidine **9b** (0.576 g, 2.43 mmol; a 86:14 isomeric mixture) and $PPh_3$ (0.729 g, 2.78 mmol) in MeCN (9 mL) (reflux, 7 h) as described for **10a**. After crystallization from MeCN the diastereomeric ratio did not change. Mp 183.5–185 °C (decomp., MeCN). $^1$H NMR of the major isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 8.47 (1H, br s, $N_{(3)}H$), 7.02 (1H, s, $N_{(1)}H$), 4.04 (1H, ddq, $^3J$=11.9, $^3J$=4.6, $^5J$=1.4 Hz, 8a-H), 3.22–3.35 (1H, m, 7-H, overlaps with HOD), 2.12 (3H, d, $^5J$=2.1 Hz, 5-$CH_3$), 2.06 (3H, d, $^5J$=1.4 Hz, 4-$CH_3$), 1.96 (1H, ddd, $^2J$=12.1, $^3J$=4.6, $^3J$=3.6 Hz, 8-$H_A$), 1.16 (3H, d, $^3J$=6.8 Hz, 7-$CH_3$),

1.04 (1H, ddd, $^2J$=12.1, $^3J$=11.9, $^3J$=11.4 Hz, 8-$H_B$); $^1$H NMR of the minor isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 6.90 (1H, s, $N_{(1)}H$), 3.94 (1H, ddq, $^3J$=6.7, $^3J$=6.2, $^5J$=1.4 Hz, 8a-H), 2.13 (3H, d, $^5J\approx$2 Hz, 5-$CH_3$, partly overlaps with the 5-$CH_3$ of the major isomer), 2.02 (3H, d, $^5J$=1.4 Hz, 4-$CH_3$), 1.58 (1H, ddd, $^2J$=13.1, $^3J$=6.7, $^3J$=4.5 Hz, 8-$H_A$), 1.43 (1H, ddd, $^2J$=13.1, $^3J$=6.2, $^3J$=6.2 Hz, 8-$H_B$), 1.12 (3H, d, $^3J$=6.9 Hz, 7-$CH_3$). Signals of the 7-H and $N_{(3)}H$ protons overlap with signals of analogous protons of the major isomer; $^{13}$C NMR of the major isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 158.8 (C-5), 154.6 (C-2), 138.5 (C-4), 103.9 (C-4a), 51.2 (C-8a), 49.2 (C-7), 36.6 (C-8), 28.0 (5-$CH_3$), 23.6 (7-$CH_3$), 18.8 (4-$CH_3$); $^{13}$C NMR of the minor isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 160.6 (C-5), 154.7 (C-2), 137.1 (C-4), 104.0 (C-4a), 50.2 (C-8a), 45.3 (C-7), 35.3 (C-8), 27.4 (5-$CH_3$), 22.1 (7-$CH_3$), 18.0 (4-$CH_3$); IR (Nujol) $\nu$, cm$^{-1}$: 3229 (br s), 3107 (br s) (NH), 1713 (vs) (amide-I), 1648 (m), 1631 (s) (C=C), 1581 (s) (C=N). Anal. Calcd for $C_{10}H_{15}N_3O$: C, 62.15; H, 7.82; N, 21.74. Found: C, 62.14; H, 7.68; N, 21.71.

*4.6.3. 4,5,8-Trimethyl-1,2,3,7,8,8a-hexahydropyrido[4,3-d]pyrimidin-2-one (**10c**).* Compound **10c** (0.538 g, 87%) as a mixture of (8*R**,8a*S**)- and (8*R**,8a*R**)-diastereomers (57:43) was prepared from pyrimidine **9d** (0.760 g, 3.20 mmol; a 56:44 isomeric mixture) and $PPh_3$ (0.952 g, 3.63 mmol) in MeCN (8 mL) (reflux, 6 h) as described for **10a**. After crystallization from MeCN the diastereomeric ratio changed to 55:45, respectively. Mp 201.5–202 °C (decomp., MeCN). $^1$H NMR of the major isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 8.48 (1H, br s, $N_{(3)}H$), 7.00 (1H, s, $N_{(1)}H$), 3.58 (1H, dq, $^3J$=10.5, $^5J$=1.3 Hz, 8a-H), 3.51 (1H, ddq, $^2J$=16.5, $^3J$=4.5, $^5J$=0.9 Hz, 7-$H_A$), 2.90 (1H, ddq, $^2J$=16.5, $^3J$=10.9, $^5J$=2.2 Hz, 7-$H_B$), 2.12 (3H, dd, $^5J$=2.2, $^5J$=0.9 Hz, 5-$CH_3$), 2.05 (3H, d, $^5J$=1.3 Hz, 4-$CH_3$), 1.49 (1H, dddq, $^3J$=10.9, $^3J$=10.5, $^3J$=6.4, $^3J$=4.5 Hz, 8-H), 0.94 (3H, d, $^3J$=6.4 Hz, 8-$CH_3$); $^1$H NMR of the minor isomer (300.13 MHz, DMSO-$d_6$) $\delta$: ≈8.40 (1H, br s, $N_{(3)}H$, partly overlaps with the $N_{(3)}H$ signal of the major isomer), 6.91 (1H, s, $N_{(1)}H$), 4.17 (1H, dq, $^3J$=4.3, $^5J$=1.3 Hz, 8a-H), 3.49 (1H, ddq, $^2J$=17.2, $^3J$=4.2, $^5J$=2.1 Hz, 7-$H_A$), 3.42 (1H, ddq, $^2J$=17.2, $^3J$=1.9, $^5J$=1.2 Hz, 7-$H_B$), 2.13 (3H, dd, $^5J$=2.1, $^5J$=1.2 Hz, 5-$CH_3$), 2.05 (3H, d, $^5J$=1.3 Hz, 4-$CH_3$), 1.87 (1H, dddq, $^3J$=6.9, $^3J$=4.3, $^3J$=4.2, $^3J$=1.9 Hz, 8-H), 0.78 (3H, d, $^3J$=6.9 Hz, 8-$CH_3$); $^{13}$C NMR of the major isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 160.7 (C-5), 154.8 (C-2), 138.0 (C-4), 104.3 (C-4a), 55.4 (C-8a), 54.8 (C-7), 33.5 (C-8), 28.0 (5-$CH_3$), 18.7 (4-$CH_3$), 15.5 (8-$CH_3$); $^{13}$C NMR of the minor isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 159.5 (C-5), 153.6 (C-2), 138.2 (C-4), 100.7 (C-4a), 53.9 (C-7), 52.8 (C-8a), 30.0 (C-8), 28.3 (5-$CH_3$), 18.8 (4-$CH_3$), 11.9 (8-$CH_3$); IR (Nujol) $\nu$, cm$^{-1}$: 3214 (br s), 3097 (br s) (NH), 1699 (vs) (amide-I), 1654 (s), 1631 (s) (C=C), 1595 (s) (C=N). Anal. Calcd for $C_{10}H_{15}N_3O$: C, 62.15; H, 7.82; N, 21.74. Found: C, 62.12; H, 7.93; N, 21.64.

*4.6.4. 7-Ethyl-4,5-dimethyl-1,2,3,7,8,8a-hexahydropyrido[4,3-d]pyrimidin-2-one (**10d**).* A solution of pyrimidine **9e** (0.803 g, 3.20 mmol; a 69:31 isomeric mixture) and $PPh_3$ (0.947 g, 3.61 mmol) in dry MeCN (9 mL) was heated at reflux under stirring for 6 h, and the solvent was removed under vacuum to give a residue containing (7*R**,8a*S**)- and (7*R**,8a*R**)-diastereomeric mixture of **10d** (65:35). This residue was purified by column chromatography on silica gel 60 (21 g) eluting with $CHCl_3$/MeOH (from 1:0 to 10:1). The main fraction was concentrated in vacuo, the solid residue was triturated with hexane (2 mL), the precipitate was filtered and dried to give **10d** (0.365 g, 55%) as a light yellow solid. An analytical sample (two diastereomers, 62:38) was obtained by recrystallization from $CH_3CN$. Mp 156.5–157.5 °C (decomp., MeCN). $^1$H NMR of the major isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 8.45 (1H, br s, $N_{(3)}H$), 7.01 (1H, s, $N_{(1)}H$), 4.03 (1H, ddq, $^3J$=11.9, $^3J$=4.7, $^5J$=1.3 Hz, 8a-H), 3.01–3.13 (1H, m, 7-H), 2.13 (3H, d, $^5J\approx$2.1 Hz, 5-$CH_3$, partly overlaps with the 5-$CH_3$ of the minor isomer), 2.06 (3H, d, $^5J$=1.3 Hz, 4-$CH_3$), 1.95 (1H, ddd, $^2J$=12.0, $^3J$=4.7, $^3J$=3.5 Hz, 8-$H_A$), 1.27–1.61 (2H, m, $CH_2$ in Et, overlap with the 8-H and $CH_2$ proton signals of the minor isomer), 1.03 (1H, ddd, $^2J$=12.0, $^3J$=11.9, $^3J$=11.6 Hz, 8-$H_B$), 0.92 (3H, t, $^3J$=7.4 Hz, $CH_3$ in Et); $^1$H NMR of the minor isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 8.45 (1H, br s, $N_{(3)}H$), 6.88 (1H, s, $N_{(1)}H$), 3.90 (1H, ddq, $^3J$=6.3, $^3J$=5.5, $^5J$=1.3 Hz, 8a-H), 2.86–2.95 (1H, m, 7-H), 2.14 (3H, d, $^5J\approx$1.7 Hz, 5-$CH_3$, partly overlaps with the 5-$CH_3$ of the major isomer), 2.01 (3H, d, $^5J$=1.3 Hz, 4-$CH_3$), 1.60 (1H, ddd, $^2J$=13.3, $^3J$=5.5, $^3J$=4.1 Hz, 8-$H_A$), 1.27–1.61 (2H, m, $CH_2$ in Et, overlap with the $CH_2$ proton signals of the major isomer), 1.38 (1H, ddd, $^2J$=13.3, $^3J$=7.3, $^3J$=6.3 Hz, 8-$H_B$), 0.93 (3H, t, $^3J$=7.4 Hz, $CH_3$ in Et); $^{13}$C NMR of the major isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 158.7 (C-5), 154.6 (C-2), 137.8 (C-4), 104.4 (C-4a), 56.9 (C-8a), 49.4 (C-7), 34.2 (C-8), 30.0 ($CH_2$ in Et), 28.2 (5-$CH_3$), 18.7 (4-$CH_3$), 10.4 ($CH_3$ in Et); $^{13}$C NMR of the minor isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 161.1 (C-5), 154.9 (C-2), 136.5 (C-4), 104.4 (C-4a), 56.4 (C-8a), 45.5 (C-7), 33.2 (C-8), 28.7 ($CH_2$ in Et), 27.2 (5-$CH_3$), 17.7 (4-$CH_3$), 11.0 ($CH_3$ in Et); IR (Nujol) $\nu$, cm$^{-1}$: 3224 (br s), 3108 (br s) (NH), 1699 (vs) (amide-I), 1653 (s), 1636 (s) (C=C), 1582 (s) (C=N). Anal. Calcd for $C_{11}H_{17}N_3O$: C, 63.74; H, 8.27; N, 20.27. Found: C, 63.68; H, 8.27; N, 20.38.

*4.6.5. 4-Methyl-5-phenyl-1,2,3,7,8,8a-hexahydropyrido[4,3-d]pyrimidin-2-one (**10e**).* A solution of pyrimidine **9f** (0.507 g, 1.78 mmol) and $PPh_3$ (0.529 g, 2.02 mmol) in dry MeCN (40 mL) was heated at reflux for 7 h under stirring, and then the solvent was removed under vacuum. The residue was purified by column chromatography on silica gel 60 (17 g) eluting with $CHCl_3$/MeOH (from 1:0 to 20:1) to give compound **10e** (0.403 g, 95%) as a slightly yellow solid. Mp 197.0–197.5 °C (decomp., MeCN). $^1$H NMR (300.13 MHz, DMSO-$d_6$) $\delta$: 8.53 (1H, br s, $N_{(3)}H$), 7.05 (1H, s, $N_{(1)}H$), 7.34–7.48 (5H, m, ArH), 4.14 (1H, ddq, $^3J$=5.8, $^3J$=5.8, $^5J$=1.4 Hz, 8a-H), 3.77 (1H, ddd, $^2J$=14.8, $^3J$=6.4, $^3J$=4.4 Hz, 7-$H_A$), 3.33 (1H, ddd, $^2J$=14.8, $^3J$=7.5, $^3J$=4.4 Hz, 7-$H_B$), 1.75 (1H, dddd, $^2J$=13.3, $^3J$=6.4, $^3J$=5.8, $^3J$=4.4 Hz, 8-$H_A$), 1.67 (1H, dddd, $^2J$=13.3, $^3J$=7.5, $^3J$=5.8, $^3J$=4.4 Hz, 8-$H_B$), 1.30 (3H, d, $^5J$=1.4 Hz, 4-$CH_3$); $^{13}$C NMR (75.48 MHz, DMSO-$d_6$) $\delta$: 165.7 (C-5), 154.0 (C-2), 141.4 (C), 136.3 (C-4), 128.9 (CH), 128.2 (2CH), 127.5 (2CH), 103.1 (C-4a), 47.6 (C-8a), 47.3 (C-7), 31.6 (C-8), 17.8 ($CH_3$); IR (Nujol) $\nu$, cm$^{-1}$: 3188 (s), 3127 (s), 3086 (s), 3060 (sh) (NH), 1717 (vs) (amide-I), 1645 (s) (C=C), 1584 (m) ($CC_{arom}$), 1557 (s) (C=N), 1490 (m) ($CC_{arom}$), 702 (s) ($CH_{arom}$). Anal. Calcd for $C_{14}H_{15}N_3O$: C, 69.69; H, 6.27; N, 17.42. Found: C, 69.49; H, 6.33; N, 17.41.

*4.6.6. 4,7-Dimethyl-5-phenyl-1,2,3,7,8,8a-hexahydropyrido[4,3-d]pyrimidin-2-one (**10f**).* A solution of pyrimidine **9g** (0.509 g, 1.70 mmol; a 55:45 isomeric mixture) and $PPh_3$ (0.522 g, 1.99 mmol) in dry MeCN (21 mL) was heated at reflux for 8 h under stirring, and then the solvent was removed under vacuum to give a residue containing (8*R**,8a*S**)- and (8*R**,8a*R**)-diastereomeric mixture of **10f** (54:46). The residue was purified by column chromatography on silica gel 60 (15 g) eluting with $CHCl_3$/MeOH (from 1:0 to 20:1) to give a 51:49 diastereomeric mixture of compound **10f** (0.394 g, 96%) as a slightly yellow solid. After crystallization from MeCN the diastereomeric ratio changed to 76:24, respectively. This compound was highly hygroscopic. $^1$H NMR analysis (increased quantity of residual water in DMSO-$d_6$ solution) and elemental analysis data showed that immediately after purification it contained 25 mol % of water. Further manipulations (additional column chromatographic purification, repeated crystallizations from MeCN, and prolonged drying under high vacuum over $P_2O_5$) gave only gradual increase of water content ($^1$H NMR and elemental analysis data). Mp 119.5–122.5 (decomp., MeCN). $^1$H NMR of the major isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 8.47 (1H, br s, $N_{(3)}H$), 7.26–7.41 (5H, m, Ph), 7.17 (1H, s, $N_{(1)}H$), 4.18 (1H, ddq, $^3J$=11.6, $^3J$=4.3, $^5J$=1.3 Hz, 8a-H), 3.63 (1H, ddq, $^3J$=10.3, $^3J$=6.9, $^3J$=4.3 Hz, 7-H), 2.07 (1H, ddd, $^2J$=12.2, $^3J$=4.3, $^3J$=4.3 Hz, 8-$H_A$), 1.27 (1H, ddd,

$^2J$=12.2, $^3J$=11.6, $^3J$=10.3 Hz, 8-$H_B$), 1.26 (3H, d, $^3J$=6.9 Hz, 7-$CH_3$), 1.20 (3H, d, $^5J$=1.3 Hz, 4-$CH_3$); $^1$H NMR of the minor isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 8.59 (1H, br s, $N_{(3)}H$), 7.49–7.56 (2H, m, $H_{arom}$), 7.34–7.45 (3H, m, $H_{arom}$), 6.97 (1H, s, $N_{(1)}H$), 4.14 (1H, ddq, $^3J$=7.0, $^3J$=2.1, $^5J$=1.4 Hz, 8a-H), 3.12 (1H, ddq, $^3J$=10.3, $^3J$=6.5, $^3J$=3.2 Hz, 7-H), 1.80 (1H, ddd, $^2J$=13.6, $^3J$=3.2, $^3J$=2.1 Hz, 8-$H_A$), 1.35 (3H, d, $^5J$=1.4 Hz, 4-$CH_3$), 1.34 (3H, d, $^3J$=6.5 Hz, 7-$CH_3$), 1.26 (1H, ddd, $^2J$=13.6, $^3J$=10.3, $^3J$=7.0 Hz, 8-$H_B$); $^{13}$C NMR of the major isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 162.5 (C-5), 153.8 (C-2), 142.6 (C), 137.7 (C-4), 128.1 (CH), 128.0 (2CH), 127.6 (2CH), 103.1 (C-4a), 53.1 (C-8a), 49.6 (C-7), 38.6 (C-8), 23.2 (7-$CH_3$), 18.3 (4-$CH_3$); $^{13}$C NMR of the minor isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 165.3 (C-5), 154.6 (C-2), 140.5 (C), 135.8 (C-4), 129.2 (CH), 128.2 (2CH), 127.5 (2CH), 103.2 (C-4a), 51.7 (C-8a), 46.5 (C-7), 38.5 (C-8), 22.6 (7-$CH_3$), 17.4 (4-$CH_3$); IR (Nujol) $\nu$, cm$^{-1}$: 3501 (s) ($H_2O$), 3175 (br s), 3101 (sh), 3086 (br s), 3067 (sh), 3030 (w) (NH), 1715 (vs) (amide-I), 1658 (m), 1622 (s) (C=C), 1586 (w) ($CC_{arom}$), 1555 (s) (C=N), 1488 (w) ($CC_{arom}$), 772 (s), 699 (s) ($CH_{arom}$). Anal. Calcd for $C_{15}H_{17}N_3O\cdot 0.25H_2O$: C, 69.34; H, 6.79; N, 16.17. Found: C, 69.37; H, 6.83; N, 16.13.

*4.6.7. 4,8-Dimethyl-5-phenyl-1,2,3,7,8,8a-hexahydropyrido[4,3-d] pyrimidin-2-one (**10g**).* A solution of pyrimidine **9i** (0.512 g, 1.71 mmol; a 50:50 isomeric mixture) and $PPh_3$ (0.527 g, 2.01 mmol) in dry MeCN (26 mL) was heated at reflux for 6 h under stirring, and then the solvent was removed under vacuum to give a residue containing (8*R**,8a*S**)- and (8*R**,8a*R**)-diastereomeric mixture of **10g** (49:51). The residue was purified by column chromatography on silica gel 60 (10 g) eluting with $CHCl_3$/MeOH (from 1:0 to 12.5:1) to give a 51:49 diastereomeric mixture of compound **10g** (0.395 g, 90%) as a slightly yellow solid. After two crystallizations from MeCN the diastereomeric ratio changed to 82:18, respectively. According to $^1$H NMR analysis (increased quantity of residual water in DMSO-$d_6$ solution) and elemental analysis data, this compound formed a strong solvate with water (10 mol %). Further manipulations (repeated crystallizations from MeCN and prolonged drying under high vacuum over $P_2O_5$) did not change water content ($^1$H NMR and elemental analysis data). Mp 209.5–211.5 °C (decomp., MeCN). $^1$H NMR of the major isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 8.39 (1H, br s, $N_{(3)}H$), 7.34–7.44 (5H, m, Ph, overlap with signals of analogous protons of the minor isomer), 6.98 (1H, br d, $^3J$=1.3 Hz, $N_{(1)}H$), 4.29 (1H, ddq, $^3J$=4.3, $^3J$=1.3, $^5J$=1.3 Hz, 8a-H), 3.82 (1H, dd, $^2J$=17.9, $^3J$=4.9 Hz, 7-$H_A$), 3.58 (1H, dd, $^2J$=17.9, $^3J$=1.8 Hz, 7-$H_B$), 2.13 (3H, dd, $^5J$=2.1, $^5J$=1.2 Hz, 5-$CH_3$), 1.96 (1H, dddq, $^3J$=6.9, $^3J$=4.9, $^3J$=4.3, $^3J$=1.8 Hz, 8-H), 1.24 (3H, d, $^5J$=1.3 Hz, 4-$CH_3$), 0.92 (3H, d, $^3J$=6.9 Hz, 8-$CH_3$); $^1$H NMR of the minor isomer (300.13 MHz, DMSO-$d_6$) $\delta$: 8.54 (1H, br s, $N_{(3)}H$), 7.34–7.44 (5H, m, Ph, overlap with signals of analogous protons of the major isomer), 7.21 (1H, br d, $^3J$=1.5 Hz, $N_{(1)}H$), 3.70 (1H, dd, $^2J$=16.8, $^3J$=5.1 Hz, 7-$H_A$), 3.67 (1H, ddq, $^3J$=8.7, $^3J$=1.5, $^5J$=1.3 Hz, 8a-H), 3.37 (1H, dd, $^2J$=16.8, $^3J$=8.8 Hz, 7-$H_B$), 1.86 (1H, dddq, $^3J$=8.8, $^3J$=8.7, $^3J$=6.6, $^3J$=5.1 Hz, 8-Ha), 1.25 (3H, d, $^5J$=1.3 Hz, 4-$CH_3$), 0.91 (3H, d, $^3J$=6.6 Hz, 8-$CH_3$); $^{13}$C NMR of the major isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 164.7 (C-5), 153.4 (C-2), 141.8 (C), 136.3 (C-4), 128.7 (CH), 128.2 (2CH), 127.5 (2CH), 102.9 (C-4a), 56.1 (C-7), 55.2 (C-8a), 37.1 (C-8), 18.1 (4-$CH_3$), 15.7 (8-$CH_3$); $^{13}$C NMR of the minor isomer (75.48 MHz, DMSO-$d_6$) $\delta$: 163.5 (C-5), 152.9 (C-2), 142.3 (C), 135.7 (C-4), 128.4 (CH), 128.1 (2CH), 99.3 (C-4a), 55.5 (C-7), 53.0 (C-8a), 33.1 (C-8), 12.4 (8-$CH_3$). Signals of other carbons were not detectable; IR (Nujol) $\nu$, cm$^{-1}$: 3229 (br s), 3112 (br s) (NH), 1697 (vs) (amide-I), 1667 (m), 1627 (m) (C=C), 1589 (w) ($CC_{arom}$), 1561 (m) (C=N), 779 (s), 705 (s) ($CH_{arom}$). Anal. Calcd for $C_{15}H_{17}N_3O\cdot 0.1H_2O$: C, 70.07; H, 6.74; N, 16.34. Found: C, 70.04; H, 6.73; N, 16.60.

*4.6.8. Ethyl 7-methyl-2-oxo-5-phenyl-1,2,3,7,8,8a-hexahydropyrido [4,3-d]pyrimidin-4-carboxylate (**10h**).* A solution of pyrimidine **9m** (0.554 g, 1.55 mmol; a 63:37 isomeric mixture) and $PPh_3$ (0.462 g, 1.76 mmol) in dry MeCN (25 mL) was heated at reflux under stirring for 6 h, and the solvent was removed under vacuum. The residue was purified by column chromatography on silica gel 60 (10 g) eluting with $CHCl_3$/MeOH (from 1:0 to 100:1) to give (7*R**,8a*S**)-**10h** (0.127 g, 26%) as a slightly yellow solid. Mp 190.5–191.5 °C (decomp., MeCN). $^1$H NMR (300.13 MHz, DMSO-$d_6$) $\delta$: 8.76 (1H, d, $^4J$=1.7 Hz, $N_{(3)}H$), 7.47–7.55 (2H, m, ArH), 7.31–7.41 (3H, m, ArH), 7.18 (1H, d, $^4J$=1.7 Hz, $N_{(1)}H$), 4.27 (1H, dd, $^3J$=7.3, $^3J$=2.1 Hz, 8a-H), 3.62 (1H, dq, $^2J$=10.7, $^3J$=7.1 Hz, $H_A$ in $OCH_2$), 3.23 (1H, dq, $^2J$=10.7, $^3J$=7.1 Hz, $H_B$ in $OCH_2$), 3.22 (1H, ddq, $^3J$=10.3, $^3J$=6.7, $^3J$=3.6 Hz, 7-H, partly overlap with the $OCH_B$ proton signals), 1.87 (1H, ddd, $^2J$=13.7, $^3J$=3.6, $^3J$=2.1 Hz, 8-$H_A$), 1.39 (3H, d, $^3J$=6.7 Hz, 7-$CH_3$), 1.35 (1H, ddd, $^2J$=13.7, $^3J$=10.3, $^3J$=7.3 Hz, 8-$H_B$), 0.79 (3H, t, $^3J$=7.1 Hz, $CH_3$ in OEt); $^{13}$C NMR (75.48 MHz, DMSO-$d_6$) $\delta$: 163.6 (C-5), 161.8 (C=O in COOEt), 153.7 (C-2), 139.2 (C), 130.3 (C-4), 129.3 (CH), 128.0 (2CH), 126.8 (2CH), 108.6 (C-4a), 61.1 ($OCH_2$), 52.0 (C-8a), 46.6 (C-7), 37.4 (C-8), 22.5 (7-$CH_3$), 13.1 ($CH_3$ in OEt); IR (Nujol) $\nu$, cm$^{-1}$: 3312 (s), 3278 (s), 3153 (br w), 3127 (br w), 3109 (br w) (NH), 3052 (w) ($CH_{arom}$), 1727 (s) (C=O in COOEt), 1708 (s) (amide-I), 1680 (s), 1650 (s) (C=C), 1588 (w) ($CC_{arom}$), 1567 (m) (C=N), 1198 (s) (C–O), 771 (s), 701 (s) ($CH_{arom}$). Anal. Calcd for $C_{17}H_{19}N_3O_3$: C, 65.16; H, 6.11; N, 13.41. Found: C, 65.13; H, 6.14; N, 13.38.

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## Supplementary data

Copies of IR, $^1$H and $^{13}$C NMR spectra of all the synthesized compounds, and computational data. Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2014.06.128. These data include MOL files and InChiKeys of the most important compounds described in this article.

## References and notes

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16. It is probably due to potential explosion hazards of 3-azidoaldehydes.
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18. Caution! Although we never experienced any accidents with azides **2** on scales described within this article, we recommend great caution. These compounds may be explosive and must be manipulated behind splash shields.
19. After 2 h of storage at −18 °C under argon, the distilled **2a** turned into dark brown liquid (strong gas evolution). $^{1}$H and $^{13}$C NMR spectra of **2a** in $CDCl_3$ (30 min after destillation) showed the presence of three main components in a ratio of 86:4:10, namely azidoaldehyde **2a**, acroleine **1a**, and a non-carbonyl compound, which was identified as 1,3-diazidopropan-1-ol (**13**).[27] Therefore, spontaneous decomposition of azidoaldehyde **2a** in $CDCl_3$ solution includes slow $HN_3$ elimination followed by addition of $HN_3$ to the carbonyl group of azidoaldehyde **2a** to give compound **12**. Addition of hydrazoic acid to aldehydes to provide α-azido alcohols has been recently reported.[28]
20. Excesses of ureas **4a,b** were used to prevent formation of *N*,*N*′-disubstituted side products (see Ref. 10i).
21. Previously[29] we proposed a convenient criterion for the determination of the substituent orientation at C-4 and C-6 in hexahydropyrimidine-2-thiones(ones), which was based on the values of vicinal coupling constants $J_{N(1)H,6\text{-}H}$ and $J_{N(3)H,4\text{-}H}$.
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