JOC The Journal of Organic Chemistry

Article

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Nucleophile-Mediated Ring Expansion of 5-Acyl-substituted 4-Mesyloxymethyl-1,2,3,4-tetrahydropyrimidin-2-ones in the Synthesis of 7-Membered Analogues of Biginelli Compounds and Related Heterocycles

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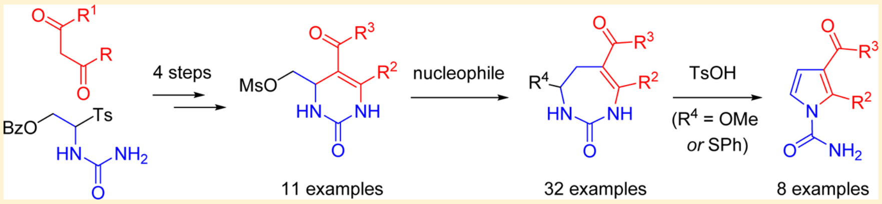
Supporting Information



ABSTRACT: A general six-step approach to alkyl 2-oxo-2,3,6,7-tetrahydro-1*H*-1,3-diazepine-5-carboxylates and 5-acyl-2,3,6,7-tetrahydro-1*H*-1,3-diazepin-2-ones based on the nucleophile-mediated ring expansion reaction of 5-functionalized 4-mesyloxymethyl-1,2,3,4-tetrahydropyrimidin-2-ones has been developed. Synthesis of the latter involved nucleophilic substitution of tosyl group in readily available *N*-[(2-benzoyloxy-1-tosyl)ethyl]urea with sodium enolates of β-oxoesters or 1,3-diketones, followed by dehydration or heterocyclization-dehydration of resulting products, removal of benzoyl protection, and conversion of hydroxymethyl group into mesyloxymethyl group. Conformations of the obtained tetrahydro-1*H*-1,3-diazepin-2-ones in solid state and solutions were established using X-ray diffraction and NMR spectroscopy. A plausible mechanism of tetrahydropyrimidine ring expansion based on DFT calculation at B3LYP/6-31+G(d,p) level and NMR monitoring experiments was discussed. The ring contraction reaction of methoxy- or phenylthio-diazepinones under acidic conditions resulted in the corresponding 3-functionalized 1-carbamoyl-1*H*-pyrroles.

INTRODUCTION

Monocyclic tetrahydro-1*H*-1,3-diazepin-2-ones, particularly alkyl 2-oxo-2,3,6,7-tetrahydro-1*H*-1,3-diazepine-5-carboxylates (e.g., **1**; Figure 1), are the representatives of rare heterocyclic scaffold.[1,2] In contrast to their six-membered analogues, so-called Biginelli compounds (e.g., **2**),[3] which are readily available and widely studied heterocycles with remarkable biological activities,[4,5] diazepines **1** remain practically unknown. Some of them were shown to be useful in the treatment of cardiovascular disorders.[6] However, extensive biological studies and synthetic applications of these heterocycles are hampered by their extremely low availability.

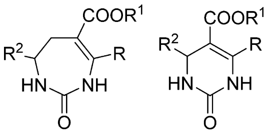

1 **2**

Figure 1. Structures of Biginelli compounds **2** and their seven-membered homoanalogues **1**.

The only described synthesis of diazepines **1** involves the reaction of ring expansion of alkyl 4-chloromethyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylates **3** under the action of nucleophilic reagents (Scheme 1).[6,7]

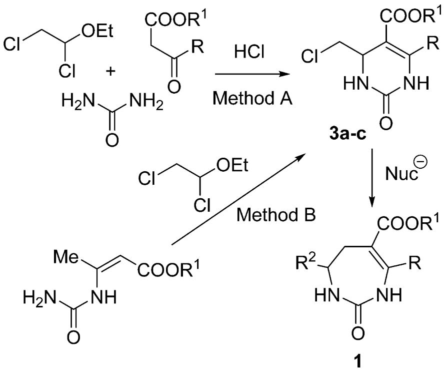
Principal limitations of this method are poor accessibility and low diversity of starting pyrimidines. Two 6-methyl-substituted pyrimidinones **3a**,**b** were synthesized by reacting 1,2-dichloroethyl ethyl ether with urea and alkyl acetoacetates (Method A)[7c] or with alkyl 3-ureidocrotonates (Method B)[7d] in 17−65% yields. 6-Phenyl-substituted pyrimidinone **3c** was prepared according to Method A in extremely low yield (2%). Obviously, the above methods are specific and cannot be applied for the preparation of target pyrimidines with other substituents at C4, C5, and C6 positions.

Previously, we have developed a general three-step approach to 5-functionalized 1,2,3,4-tetrahydropyrimidin-2-ones/thiones based on the reaction of readily available α-tosyl-substituted *N*-alkyl(thio)ureas with enolates of α-functionalized ketones followed by acid-catalyzed dehydration of the obtained

Received: May 31, 2017
Published: July 6, 2017

DOI: 10.1021/acs.joc.7b01348
J. Org. Chem. 2017, 82, 8085−8110

Scheme 1. Synthesis of 1,3-Diazepines 1 and Their Pyrimidine Precursors 3a−c



products.[8] However, the reaction between β-halogeno-α-tosyl-substituted *N*-alkylureas and sodium enolates of ethyl acetoacetate or ethyl benzoylacetate afforded the corresponding 5-ureido-4,5-dihydrofurans instead of expected tetrahydropyrimidinones (e.g., **3b**,**c**).[9] Therefore, we supposed that 5-functionalized 2,3,6,7-tetrahydro-1*H*-1,3-diazepin-2-ones **4** including diazepines **1** could be obtained via 4-hydroxymethyl-1,2,3,4-tetrahydropyrimidin-2-ones **5** starting from α-tosyl-substituted *N*-alkylurea bearing an acyloxy group at the β-position (Scheme 2).

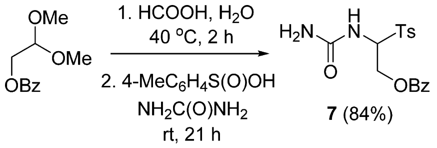
According to this strategy, various 5-tosyl- and 5-phenylthio-substituted diazepinones **4** (FG = Ts, PhS) were obtained.[10] We have found that not only 4-chloromethyl- but also 4-mesyloxy- and 4-tosyloxymethyl-pyrimidines underwent ring expansion under the action of nucleophiles. The leaving group (X) and substituents at the C5 and C6 positions (FG, R) of pyrimidine ring had a strong effect on the rate of this reaction, purity, and yield of the obtained diazepines. In continuation of our research on diazepine synthesis, herein we describe a general approach to various 5-acyl-substituted 4-mesyloxymethyl-1,2,3,4-tetrahydropyrimidin-2-ones and their nucleophile-mediated conversion into seven-membered analogues of Biginelli compounds, alkyl 2-oxo-2,3,6,7-tetrahydro-1*H*-1,3-diazepine-5-carboxylates **4** (FG = COOR′), and novel 5-acyl-2,3,6,7-tetrahydro-1*H*-1,3-diazepin-2-ones **4** (FG = COR′). The mechanism of the ring expansion reaction based on computational and experimental data was suggested. Structural characteristics of the obtained 1,3-diazepinones and their acid-catalyzed transformation into alkyl 1-carbamoyl-1*H*-pyrrole-3-carboxylates and 3-acyl-1-carbamoyl-1*H*-pyrroles are reported.

■ RESULTS AND DISCUSSION

Synthesis of Ethyl 4-Benzoyloxymethyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylates and 5-Acyl-4-benzoyloxymethyl-1,2,3,4-tetrahydropyrimidin-2-ones. In consistence with general approach to multifunctionalized tetrahydropyrimidines,[8] we used readily available *N*-[(2-benzoyloxy-1-tosyl)ethyl]urea (**7**) as a starting amidoalkylating reagent. Previously, this compound was obtained according to a four-step sequence starting from vinyl acetate. Bromination of vinyl acetate in methanol followed by substitution of bromine in the obtained acetal with sodium benzoate (DMF, reflux, 5 h) and hydrolysis of the resulting acetal **6** (80% aqueous HCOOH, rt, 4 h) afforded benzoyloxyethanal in 41% overall yield. All liquids were isolated and purified by distillation prior to use. The obtained aldehyde was reacted with *p*-toluenesulfinic acid and urea in water (rt, 24 h) to give **7** in 97% yield.[10a,c]

To simplify the preparation of sulfone **7** we used the solution obtained after hydrolysis of acetal **6** (without isolation of benzoyloxyethanal) for condensation with *p*-toluenesulfinic acid and urea. The reaction cleanly proceeded in 20% aqueous HCOOH at room temperature for 21 h (Scheme 3).

Scheme 3. Improved Synthesis of Sulfone 7



The product precipitated from the reaction mixture as a fine solid, the precipitate was filtered to give sulfone **7** in 84% yield with high purity (^{1}H NMR spectroscopic data) and was used in the next step without additional purification.

To demonstrate the flexibility of our approach to the diazepine precursors we used seven various CH-acids, four β-oxoesters **8a**−**d**, and three 1,3-diketones **8e**−**g** with different electrophilicity of ketone carbonyl groups. Sulfone **7** smoothly reacted with sodium enolates of **8a**−**g** (1.00−1.10 equiv) (rt, 8−8.5 h) generated by treatment of the corresponding CH-acids with NaH in appropriate solvent (MeCN or THF) to give (γ-oxoalkyl)ureas **9a**−**g** as a result of nucleophilic substitution of tosyl group. Ureas **9a**,**c**,**d**−**f** possessing keto group with relatively high electrophilicity spontaneously cyclized into the corresponding 4-hydroxypyrimidines **10a**,**c**,**d**−**f**. Compounds **10a**,**c**,**e**,**f** were dehydrated without isolation by adding of TsOH (1.30−1.43 equiv) to the obtained reaction mixtures followed by refluxing (2 h) to give tetrahydropyrimidines **11a**,**c**,**e**,**f** in 81−91% yields (Method A) (Table 1, entries 1, 3, 5, and 6).

Deprotonation of diethyl ester of 2-oxobutandioic acid (**8d**) under the action of NaH proceeded slowly in MeCN but rapidly completed in THF, therefore this solvent was used for reaction between sulfone **7** and the Na-enolate of **8d**. Dehydration of the *in situ* formed pyrimidine **10d** after the addition of TsOH (THF, reflux, 2 h) afforded a mixture of compound **11d** with significant amounts of side products. Therefore, we isolated pyrimidine **10d** before dehydration. This compound was obtained in 74% yield (Table 1, entry 4, step 1) as a single (4*R**,5*R**,6*R**)-diastereomer which, according to its ^{1}H NMR spectrum in DMSO-d_6, had equatorial orientation of

Scheme 2. Retrosynthesis of 5-Functionalized 2,3,6,7-Tetrahydro-1*H*-1,3-diazepin-2-ones 4

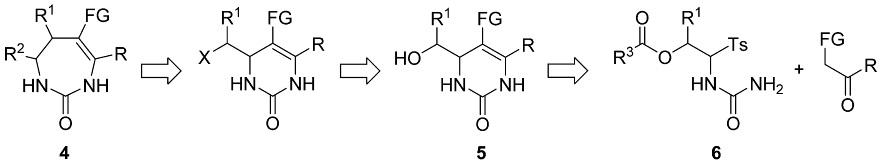
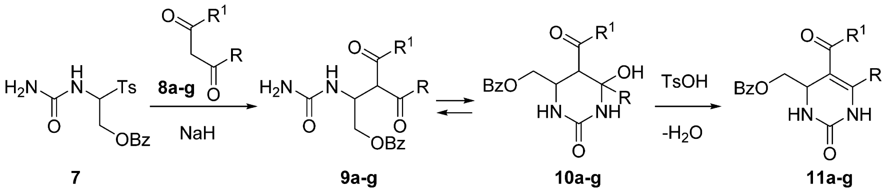


Table 1. Synthesis of 4-(Benzoyloxymethyl)tetrahydropyrimidines **11a−g** (Optimized Conditions)



entry	CH-acid	R	R^1	reaction conditions[a]	method[b]	product	yield (%)[c]
1	**8a**	Me	OEt	1. MeCN, NaH (1.10), **8a** (1.12), rt, 8 h 2. MeCN, TsOH (1.43), reflux, 2 h	A	**11a**	91
2[d]	**8b**	Ph	OEt	1. MeCN, NaH (1.00), **8b** (1.02), rt, 8 h 2. MeCN, TsOH (1.00), reflux, 5.5 h	B	**11b**	65
3	**8c**	Bu	OEt	1. MeCN, NaH (1.09), **8c** (1.10), rt, 8 h 2. MeCN, TsOH (1.42), reflux, 2 h	A	**11c**	81
4[e]	**8d**	COOEt	OEt	1. THF, NaH (1.09), **8d** (1.11), rt, 8.5 h 2. MeCN, TsOH (0.10), reflux, 1 h	B	**11d**	70
5	**8e**	Me	Me	1. MeCN, NaH (1.00), **8e** (1.02), rt, 8 h 2. MeCN, TsOH (1.30), reflux, 2 h	A	**11e**	86
6	**8f**	Me	Ph	1. MeCN, NaH (1.00), **8f** (1.05), rt, 8 h 2. MeCN, TsOH (1.30), reflux, 2 h	A	**11f**	86
7[f]	**8g**	Ph	Ph	1. THF, NaH (1.00), **8g** (1.05), rt, 8 h 2. EtOH, TsOH (0.50), reflux, 5 h	B	**11g**	73

[a] Number in parentheses is the amount of equivalents. [b] Method A and Method B: one pot and two-step synthesis, respectively (without or with isolation of the substitution product). [c] Isolated yields from sulfone **7**. [d] The first step afforded a 94:6 mixture of urea **9b** (two diastereomers in a ratio of 48:46) and pyrimidine **10b** [(4*R**,5*R**,6*R**)-diastereomer] which was isolated and used in the second step. [e] The first step gave (4*R**,5*R**,6*R**)-diastereomer of **10d** which was isolated and used in the second step. [f] The first step afforded **9g** which was isolated and used in the second step.

substituents at the C5 and C6 ($^3J_{\text{H-5,H-6}} = 11.5$, $^3J_{\text{H-6,N(1)H}} \approx 0$ Hz)[11] and axial orientation of the hydroxyl group ($^4J_{\text{H-5,OH}} = 1.3$ Hz). Hydroxypyrimidine **10d** was readily dehydrated in refluxing MeCN in the presence of TsOH (0.10 equiv) to give compound **11d** in 95% yield (entry 4, step 2). Thus, the overall yield of **11d** in two steps was 70% (Method B).

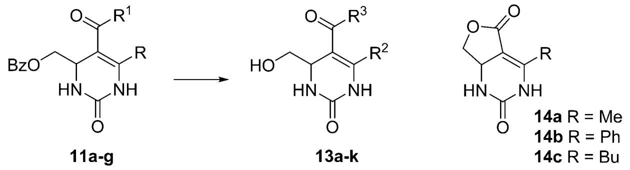
Method B was applied to the synthesis of pyrimidines **11b**,**g**. The reaction of sulfone **7** with the Na-enolate of ethyl benzoylacetate (**8b**) (1.00 equiv) smoothly proceeded in MeCN (rt, 8 h) to afford a 94:6 mixture of urea **9b** (two diastereomers in a ratio of 48:46) and pyrimidine **10b** (a single diastereomer) which was isolated in 90% yield (entry 2, step 1). Relatively low electrophilicity of the benzoyl carbonyl group resulted in slow cyclization of **9b** into **10b**. In the presence of 0.50 equiv of TsOH cyclization/dehydration of the obtained **9b**+**10b** mixture completed in refluxing MeCN for 9.5 h to give pyrimidine **11b**. The rate of this reaction was increased by the addition of a greater amount of the catalyst. Thus, with 1.00 equiv of TsOH the reaction completed in 5.5 h (MeCN, reflux) to give pyrimidine **11b** in 72% yield (entry 2, step 2). It should be noted that acid-catalyzed transformation of **9b**+**10b** mixtures according to Method A coincided with numerous side reactions.

Deprotonation of dibenzoylmethane (**8g**) with NaH in MeCN resulted in formation of a dense suspension of its enolate, which significantly complicated completion of this reaction. Therefore, dry THF was used as a solvent for generation of the Na-enolate of **8g** followed by its reaction with sulfone **7** to give urea **9g** in 89% yield. We have found that compound **9g** had a strong tendency to undergo isomerization to give *N*-[(1-benzoyloxy-4-oxo-4-phenyl)but-2-yl]-*N*′-benzoylurea (**12**).[12] Presumably, this reaction proceeds via cyclization of **9g** into **10g** followed by a base-promoted cleavage of the C4−C5 bond.[13] The amount of this side product increased up to 30 mol% with an increase in the basicity of the reaction media. Under the optimized reaction conditions (Table 1, entry 7, step 1), the formation of **12** was completely suppressed. TsOH-catalyzed cyclization/dehydration of urea **9g** in refluxing solvent proceeded with the formation of some amount of unidentified side products along with pyrimidine **11g**. The specific feature of ^{1}H NMR spectra of the isolated crude material was an increased integral intensity of the signals of aromatic protons. We estimated the amount of **11g** in a crude product as a ratio between expected integral intensity (15H) and the observed value of this intensity multiplied by 100. No starting material was detected by TLC in refluxing MeCN under the action of 0.5 equiv of TsOH after 1.5 h from the beginning of the reaction. According to ^{1}H NMR spectroscopic data, the isolated material contained about 50 mol% of compound **11g**. Purification of this material using column chromatography afforded pyrimidine **11g** in 49% yield. A similar result was obtained in toluene under these conditions. In refluxing EtOH in the presence of 0.5 equiv of TsOH the reaction completed after 5 h. The isolated material contained about 20 mol% of impurities (^{1}H NMR data) which were removed using Etheral work up. Pyrimidine **11g** was isolated in 82% yield without chromatography purification (entry 7, step 2).

Synthesis of Alkyl 4-Mesyloxymethyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylates and 5-Acyl-4-mesyloxymethyl-1,2,3,4-tetrahydropyrimidin-2-ones. Next, we removed the benzoyl protection in tetrahydropyrimidines **11a−g** to obtain 4-(hydroxymethyl)pyrimidines **13a−k** (Table 2).

Previously,[10] we successfully removed benzoyl protection using EtOH-H_2O solution of KOH at room temperature. Hydrolysis of compound **11a** readily proceeded under these conditions (TLC data), however, the isolation of product from

Table 2. Synthesis of 4-(Hydroxymethyl)pyrimidines **13a−k**



13	a	b	c	d	e	f	g	h	i	j	k
R^2	Me	Ph	Bu	COOMe	Me	Ph	Bu	COOEt	Me	Me	Ph
R^3	OMe	OMe	OMe	OMe	OEt	OEt	OEt	OEt	Me	Ph	Ph

entry	starting material	solvent	reaction conditions	product(s) (molar ratio)	yield of 13 (%)
1	**11a**	MeOH	NaOMe (0.28 equiv), rt, 6 h	**13a** + **13e** (66/34)	
2	**11a**	MeOH	NaOMe (0.26 equiv), reflux, 1.5 h	**13a** + **14a** (98/2)	89
3	**11b**	MeOH	NaOMe (0.89 equiv), rt, 27 h	**13b**	95
4	**11b**	MeOH	K_2CO_3 (1.50 equiv), rt, 24 h	**13b**	74
5	**11c**	MeOH	NaOMe (0.84 equiv), rt, 24 h	**13c**	85
6	**11d**	MeOH	NaOMe (1.80 equiv), reflux, 3 h	**13d**	83
7	**11a**	EtOH	NaOEt (0.34 equiv), rt, 6 h	**13e** + **14a** (95/5)	93
8	**11b**	EtOH-H_2O	KOH (1.47 equiv), rt, 50 min	**13f** + **14b** (67/33)	
9	**11b**	EtOH	KOH (1.27 equiv), 0 °C, 40 min	**13f** + **14b** (63/37)	
10	**11b**	EtOH	1. KOH (1.48 equiv), rt, 1.5 h 2. TsOH (1.96 equiv), reflux, 4 h	**13f** + **14b** (61/39)	
11	**11b**	EtOH	NaOEt (1.00 equiv), rt, 24 h	**13f** + **14b** (58/42)	
12	**11b**	EtOH	K_2CO_3 (1.50 equiv), rt, 7 days	**13f** + **14b** (95/5)	84
13	**11c**	EtOH	NaOEt (0.87 equiv), rt, 40 min	**13g** + **14c** (83/17)	
14	**11c**	EtOH-H_2O	KOH (1.30 equiv), rt, 55 min	**13g** + **14c** (98/2)	66
15	**11d**	EtOH	NaOEt (2.22 equiv), rt, 1 h	**13h**	79
16	**11e**	MeOH	MeONa (0.32 equiv), rt, 2.5 h	**13i**	88
17	**11f**	EtOH-H_2O	KOH (1.60 equiv), rt, 2 h	**13j**	90
18	**11g**	EtOH-H_2O	KOH (2.13 equiv), rt, 2.5 h	**13k**	91

the reaction mixture was complicated by its high solubility in water. Treatment of pyrimidine **11a** with NaOMe (0.28 equiv) in MeOH at room temperature for 6 h resulted in complete deprotection and partial re-esterification of 5-ethoxycarbonyl group to give a mixture of methyl and ethyl carboxylates **13a** and **13e** (Table 2, entry 1). Re-esterification (MeOH, NaOMe) completed at reflux after 1.5 h. The reaction mixture was neutralized with equivalent amount of conc. HCl, the solvent was removed under vacuum, the product was triturated with diethyl ether and filtered. According to ^1H NMR spectroscopic data, purity of the obtained pyrimidine **13a** was about 95%. The mass of this material was slightly higher than the theoretical one, indicating that the main impurity in the crude product was NaCl resulting from neutralization. Purification of this product using column chromatography on silica gel gave pure **13a** in 89% yield (entry 2). It should be noted that compound **13a** has low solubility in $CHCl_3$ which makes purification tedious. Both crude and purified pyrimidine **13a** contained 2 mol% of the corresponding lactone **14a** resulting from intramolecular esterification.[14] This side product was removed by crystallization to give an analytically pure sample. Reflux of 6-phenyl pyrimidine **11b** for 2.25 h in MeOH in the presence of NaOMe (0.28 equiv) led to formation of **13b** along with about 50 mol% of unidentified side products (^1H NMR data). Compound **13b** was obtained in 95% yield by treatment of **11b** with greater amount of NaOMe (0.89 equiv) at room temperature for 27 h (entry 3). Pyrimidine **13b** was also prepared from **11b** using K_2CO_3 in MeOH at room temperature, however in a lower yield (entry 3 vs entry 4). Formation of the corresponding lactone **14b** under these conditions was not observed. Treatment of pyrimidine **11c** with NaOMe in MeOH at room temperature resulted in clean formation of compound **13c** (entry 5). Re-esterification of 5,6-dicarboxylate **11d** was not completed under the action of NaOMe (1.03 equiv) in MeOH at room temperature for 24 h. Compound **13d** was obtained by refluxing **11d** in MeOH for 3 h in the presence of NaOMe (1.80 equiv) in 83% yield (entry 6).

To preserve the 5-ethoxycarbonyl group we carried out the removal of the benzoyl protection in **11a** under the action of NaOEt in EtOH (entry 7). Isolation and purification of crude **13e** was performed analogously to those described for **13a**. In this case, the amount of lactone **14a** was 5 mol%. We attempted to remove the benzoyl protection in **11b** using KOH in ethanol or aqueous ethanol. However, significant amount of lactone **14b** (33−37 mol%) along with **13f** formed under these conditions (entries 8 and 9). Treatment of a mixture of **13f** and **14b** with TsOH in refluxing EtOH did not result in lactone ring opening (entry 10). Almost the same mixture of products was obtained in the reaction between pyrimidine **11b** and NaOEt in EtOH at room temperature for 24 h (entry 11). The best result was achieved by treatment of **11b** with K_2CO_3 in EtOH. Though the reaction completed after 7 days, the amount of lactone **14b** in the isolated product was not higher than 5 mol% (^1H NMR data) (entry 12). Reaction of pyrimidine **11c** with NaOEt in EtOH resulted in the formation of 17 mol% of lactone **14c** along with the target product **13g** (entry 13). The use of KOH in aqueous ethanol was effective for clean preparation of pyrimidine **13g** from **11c** (entry 14). Pyrimidine **11d** reacted with NaOEt in EtOH at room temperature for 1 h to give **13h** in 79% yield without any traces of the corresponding lactone (entry 15).

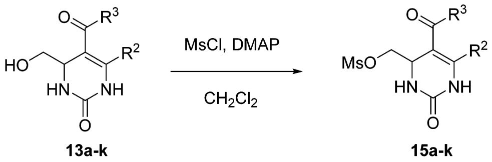
5-Acetyl-substituted pyrimidine **13i** was obtained from **11e** using methanolic solution of NaOMe (entry 16). For preparation of practically insoluble in water pyrimidines **13j** and **13k** from **11f** and **11g**, respectively, solution of KOH in aqueous EtOH was employed (entries 17 and 18). No side reactions proceeded with 5-acyl-substituted pyrimidines **11e−g** during the benzoyl protective group removal.

Previously,[10] for 5-tosyl- and 5-phenylthio-1,2,3,4-tetrahydropyrimidin-2-ones we compared the reactivity of 4-chloromethyl-, 4-tosyloxymethyl-, and 4-mesyloxymethyl-derivatives toward the reaction of ring expansion mediated by nucleophiles. The best results, including the rate and selectivity of the reaction, mildness of reaction conditions and yields of resulting diazepinones, were achieved with 4-mesyloxymethyl-derivatives. Therefore, we focused on the preparation of 4-(mesyloxymethyl)pyrimidines **15a−k** from the corresponding pyrimidines **13a−k**.

Carboxylates **15a–h** were prepared from crude pyrimidines **13b–d,f–h** and chromatographically purified pyrimidines **13a,e** under the action of MsCl (1.2 equiv) in the presence DMAP (1.4 equiv) in CH_2Cl_2 at room temperature for 1–1.5 h in good yields (Scheme 4). After completion of the reaction, the solvent was removed under vacuum, the residues were treated with water, and the resulting precipitates were filtered. Lactones **14a,c** (see Table 2) were completely washed out with water from crude **15a,e,g**. Lactone **14b** was removed from crude **15f** by crystallization. It is noteworthy that compounds **15a,e** are moderately soluble in water, therefore, their aqueous work up was performed carefully and rapidly. When crude pyrimidines **13a,e** obtained without chromatography purification were used to prepare **15a,e**, the yields of the isolated products were 63 and 78%, respectively. Compound **15h** was isolated from the reaction mixture using extraction. The amorphous material obtained after removal of solvent from the extract was used in the reaction of ring expansion. We were not able to obtain the crystalline solid of this compound.

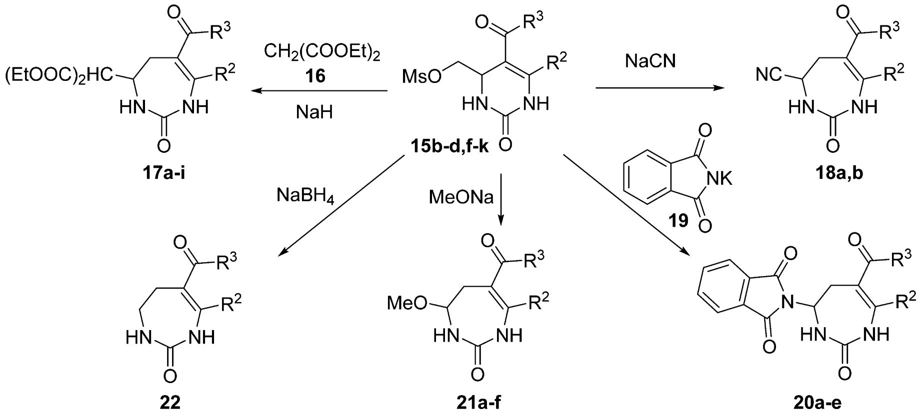
5-Acyl-substituted pyrimidines **13i–k** were reacted with MsCl (1.5 equiv) and DMAP (2.0 equiv) in CH_2Cl_2 at room temperature for 1.5 h to give mesyloxy-derivatives **15i–k**. With less excess of reagents or with NEt_3 instead of DMAP these reactions did not complete. Compounds **15i,j** were isolated as described for **15a–g** in good yields. It is noteworthy that

Scheme 4. Synthesis of 4-(Mesyloxymethyl)pyrimidines 15a–k



15	a	b	c	d	e	f	g	h	i	j	k
R^2	Me	Ph	Bu	COOMe	Me	Ph	Bu	COOEt	Me	Me	Ph
R^3	OMe	OMe	OMe	OMe	OEt	OEt	OEt	OEt	Me	Ph	Ph
Yield,%	81	93	80	64	88	66	82	67	70	92	96

Table 3. Diazepine Synthesis by Reaction of Pyrimidines 15b–d,f–k with *C*-, *H*-, *N*-, and *O*-nucleophiles



entry	15	R^2	R^3	solvent	reaction conditions	product	yield (%)[a]
1	**15b**	Ph	OMe	MeCN	**16** (1.14 equiv), NaH (1.10 equiv), rt, 1.67 h	**17a**	88
2	**15c**	Bu	OMe	MeCN	**16** (1.19 equiv), NaH (1.14 equiv), rt, 2 h	**17b**	91
3	**15d**	CO_2Me	OMe	MeCN	**16** (1.20 equiv), NaH (1.17 equiv), rt, 1 h	**17c**	86
4	**15f**	Ph	OEt	MeCN	**16** (1.16 equiv), NaH (1.11 equiv), rt, 1 h	**17d**	90
5	**15g**	Bu	OEt	MeCN	**16** (1.23 equiv), NaH (1.20 equiv), rt, 3.33 h	**17e**	94
6	**15h**	CO_2Et	OEt	MeCN	**16** (1.25 equiv), NaH (1.23 equiv), rt, 1 h	**17f**	70
7	**15i**	Me	Me	MeCN	**16** (1.26 equiv), NaH (1.19 equiv), rt, 1 h	**17g**	76
8	**15j**	Me	Ph	MeCN	**16** (1.19 equiv), NaH (1.11 equiv), rt, 1 h	**17h**	87
9	**15k**	Ph	Ph	MeCN	**16** (1.21 equiv), NaH (1.20 equiv), rt, 1.67 h	**17i**	79
10	**15b**	Ph	OMe	DMSO	NaCN (1.50 equiv), rt, 3 h	**18a**	87
11	**15k**	Ph	Ph	DMSO	NaCN (1.48 equiv), rt, 3 h	**18b**	83
12	**15b**	Ph	OMe	MeCN	**19** (1.30 equiv), reflux, 30 min	**20a**	95
13	**15c**	Bu	OMe	DMSO	**19** (1.30 equiv), rt, 2 h	**20b**	90
14	**15f**	Ph	OEt	MeCN	**19** (1.30 equiv), reflux, 1 h	**20c**	96
15	**15g**	Bu	OEt	DMSO	**19** (1.29 equiv), rt, 2 h	**20d**	84
16	**15j**	Me	Ph	DMSO	**19** (1.31 equiv), rt, 2 h	**20e**	92
17	**15b**	Ph	OMe	MeOH	NaOMe (2.49 equiv), rt, 1.67 h	**21a**	93
18	**15c**	Bu	OMe	MeOH	NaOMe (2.42 equiv), rt, 1.33 h	**21b**	90
19	**15d**	CO_2Me	OMe	MeOH	NaOMe (2.34 equiv), rt, 2 h	**21c**	75
20	**15i**	Me	Me	MeOH	NaOMe (2.61 equiv), rt, 2 h	**21d**	69
21	**15j**	Me	Ph	MeOH	NaOMe (2.56 equiv), rt, 2 h	**21e**	88
22	**15k**	Ph	Ph	MeOH	NaOMe (2.97 equiv), rt, 1.83 h	**21f**	95
23	**15b**	Ph	OMe	THF	$NaBH_4$ (1.50 equiv), reflux, 2 h	**22**	43

[a] Isolated yield.

DOI: 10.1021/acs.joc.7b01348
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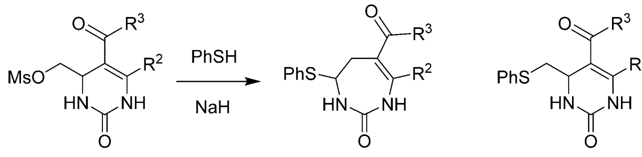
Table 4. Diazepine Synthesis by Reaction of Pyrimidines **15a−c,e−g,i−k** with PhSNa (Optimized Conditions)



15a-c,e-g,i-k **24a-i** **25a-i**

entry	15	R^2	R^3	solvent	reaction conditions[a]	product	yield (%)[b]
1	**15a**	Me	OMe	THF	PhSH (1.11 equiv), NaH (1.10 equiv), 2 h	**24a**	93
2	**15b**	Ph	OMe	THF	PhSH (1.25 equiv), NaH (1.16 equiv), 2.42 h	**24b**	94
3	**15c**	Bu	OMe	THF	PhSH (1.10 equiv), NaH (1.10 equiv), 2 h	**24c**	80
4	**15e**	Me	OEt	THF	PhSH (1.11 equiv), NaH (1.10 equiv), 2 h	**24d**	96
5	**15f**	Ph	OEt	THF	PhSH (1.21 equiv), NaH (1.15 equiv), 2 h	**24e**	95
6	**15g**	Bu	OEt	THF	PhSH (1.10 equiv), NaH (1.10 equiv), 2 h	**24f**	94
7	**15i**	Me	Me	MeCN	PhSH(1.10 equiv), NaH (1.10 equiv), 2 h	**24g**	80
8	**15j**	Me	Ph	MeCN	PhSH (1.10 equiv), NaH (1.10 equiv), 2 h	**24h**[c]	81
9	**15j**	Me	Ph	THF	PhSH (1.10 equiv), NaH (1.10 equiv), 2 h	**24h**[d]	88
10	**15k**	Ph	Ph	THF	PhSH (1.11 equiv), NaH (1.11 equiv), 2 h	**24i**	80

[a]At room temperature. [b]Isolated yield. [c]2 mol% of **25h** was detected in ^{1}H NMR spectrum. [d]3 mol% of **25h** was detected in ^{1}H NMR spectrum.

compound **15i** was moderately soluble in water. Analogous isolation of **15k** gave crude product containing about 20 mol% of DMAP (^{1}H NMR data). DMAP was removed by washing of the reaction mixture obtained after completion of mesylation with deluted HCl. Removal of solvent afforded pyrimidine **15k** in 96% yield.

Thus, we developed general five-step approach to a number of 5-acyl-substituted 4-mesyloxymethyl-1,2,3,4-tetrahydropyrimidin-2-ones which are the key precursors for diazepine synthesis. This approach is very flexible and gives access to the pyrimidines with a large variety of substituents at the C5 and C6 positions.

Synthesis of Functionalized 2,3,6,7-Tetrahydro-1*H*-1,3-diazepin-2-ones via Ring Expansion of 1,2,3,4-Tetrahydropyrimidin-2-ones. Pyrimidines **15a−k** were reacted with various *C*-, *N*-, *O*-, *H*-, and *S*-nucleophiles to give the target diazepines (Tables 3 and 4).

Diazepinones **17a−h** were readily obtained in good yields by reacting the corresponding pyrimidines **15b−d,f−j** with sodium diethyl malonate generated by the treatment of diethyl malonate (**16**) with NaH in MeCN at room temperature (Table 3, entries 1−8). Crude products isolated from the reaction between pyrimidine **15k** and sodium diethyl malonate (1.2 equiv) in MeCN or THF at room temperature contained some amount of unidentified side products. The crude material obtained from the reaction in MeCN was purified using silica gel column chromatography to give diazepine **17i** in 79% yield (entry 9).

We studied the reaction of pyrimidine **15b** with NaCN (1.5 equiv) in DMF and in DMSO at room temperature and found that in DMSO the yield of diazepine **18a** was higher than that in DMF. The reaction between pyrimidine **15k** and NaCN also smoothly proceeded in DMSO under these conditions. After completion of the reaction of **15b,k** with NaCN, the obtained mixtures were diluted with water and the resulting precipitates were filtered. The crude products were purified using column chromatography on silica gel to give cyanodiazepines **18a,b** in 87 and 83% yields, respectively (entries 10 and 11).

6-Phenyl-substituted carboxylates **15b,f** smoothly reacted with 1.30 equiv of potassium phthalimide (**19**) in refluxing MeCN to afford 7-phthalimidodiazepines **20a,c** in excellent yields (entries 12 and 14). Under these conditions from pyrimidines **15c,g** some amount of unidentified side products formed along with the target compounds **20b,d**. Reaction between **15j** and potassium phthalimide (1.28 equiv) in refluxing MeCN (1.25 h) afforded a 82:18 mixture of diazepine **20e** and another product. According to ^{1}H NMR spectroscopic data, the structure of this product was assigned as 4-methylene-5-phenyl-1,2,3,4,7,7a-hexahydrofuro[3,4-*d*]pyrimidin-2-one.[15] This compound resulted from intramolecular nucleophilic substitution of the OMs group by the carbonyl oxygen of the benzoyl group. We have found that diazepine **20e** can be cleanly prepared by reacting **15j** with potassium phthalimide (1.31 equiv) in DMSO at room temperature for 2 h. The reaction mixture was diluted with water after completion of the reaction and the obtained precipitate was filtered to give diazepine **20e** in 92% yield (entry 16). Analogously, 6-butyl-substituted carboxylates **15c,g** reacted with potassium phthalimide in DMSO to afford diazepines **20b,d** in good yields (entries 13 and 15).

Methoxy-diazepines **21a−f** were prepared by the reaction of pyrimidines **15b−d,i−k** with methanolic solution of NaOMe (2.34−2.97 equiv) at room temperature (1.33−2 h) in 69−95% yields (entries 17−22). It is noteworthy that methoxydiazepines **21** readily undergo the ring contraction reaction to give the corresponding 1-carbamoylpyrroles under acidic conditions (see below). Therefore, neutralization of the reaction mixtures after completion of the reaction was carried out with an equivalent amount of AcOH followed by addition of a small amount of $NaHCO_3$. After evaporation of the solvent in vacuum the products were isolated using aqueous work up. The moderate yields of compounds **21c,d** can be explained by their higher solubility in water compared with other diazepines **21a,b,e,f**. We found that the methoxy group in diazepines **21** has a tendency to undergo nucleophilic substitution reactions. For example, during crystallization of **21e** from EtOH we obtained a mixture of **21e** and the corresponding 7-ethoxy-derivative in a ratio of 90:10 (^{1}H NMR spectroscopic data).

Ring expansion of pyrimidine **15b** under the action of $NaBH_4$ (1.5 equiv) did not proceed in DMSO (3 h) or THF (1 h) at room temperature. Under these conditions in MeCN the starting material was consumed for 1 h, however, according to

^{1}H NMR spectroscopic data a complex mixture of products containing some amount of the target diazepine **22** was obtained. A similar mixture formed in the reaction of pyrimidine **15b** with NaBH$_4$ in refluxing THF (entry 23). Diazepine **22** was isolated from this mixture using column chromatography on silica gel in 43% yield.

Previously, we found that depending on the reaction conditions, ethyl 4-chloromethyl-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**23**) reacted with PhSNa or PhSK with or without PhSH to give (phenythio)diazepine **24d** or/and 4-(phenylthiomethyl)pyrimidine **25d** as a result of ring expansion or/and direct nucleophilic substitution of chlorine (Table 4).[16] The amount of pyrimidine **25d** increased with an increase in the amount of PhSH in the reaction mixture. The results obtained were explained by relatively low basicity of the thiophenolate-anion (pK_a = 10.3 in DMSO) together with its strong nucleophilicity. It is noteworthy that the basicity of nucleophile must be sufficient to provide deprotonation of N$_{(1)}$H in pyrimidine which is the first step of the ring expansion (see below). We studied the reaction of 4-(mesyloxymethyl)-pyrimidines **15a**–**c**,**f**,**g**,**i**–**k** with PhSNa under various conditions to prepare the corresponding diazepines **24a**–**i** in the maximum yield and purity. The results obtained under the optimal conditions are listed in Table 4.

In dry MeCN methyl carboxylate **15a** reacted at room temperature for 2 h with PhSNa generated by treatment of PhSH (1.11 equiv) with NaH (1.10 equiv) to give (phenylthio)diazepine **24a** along with considerable amount of unidentified side products. In THF under these conditions diazepines **24a** and **24d** were cleanly prepared from pyrimidines **15a** and **15e** in 93 and 96% yield, respectively (entries 1 and 4). For comparison, the reaction of ethyl 4-(chloromethyl)pyrimidine-5-carboxylate **23** with PhSNa (1.08 equiv) proceeded in MeCN (rt, 7 h) to give a 97:3 mixture of **24d** and **25d**, and in THF with 1.10 equiv of PhSNa (rt, 7 h) a mixture of **24d** and starting pyrimidine **23** in a ratio of 91:9 was isolated.[16] Reactions of other carboxylates **15b**,**c**,**f**,**g** with PhSNa smoothly proceeded in THF at room temperature to give the corresponding diazepinones **24b**,**c**,**e**,**f** in good yields (entries 2, 3, 5, and 6). It is noteworthy that a slight excess of PhSH in the reactions of **15b** and **15f** did not result in formation of pyrimidines **25b**,**e** (entries 2 and 5). In contrast, treatment of 4-butyl-substituted pyrimidine **15g** with PhSNa (1.14 equiv) in the presence of 0.02 equiv of PhSH in THF (rt, 2 h 45 min) afforded a mixture of **24f** and **25f** in a ratio of 93:7, respectively.

The crude product isolated from the reaction of 5-acetyl-substituted pyrimidine **15i** with PhSNa (1.10 equiv) and PhSH (0.02 equiv) in THF (rt, 1 h) was purified using column chromatography on silica gel followed by crystallization. After the first crystallization we obtained a 92:8 mixture of **24g** and **25g**, after the third crystallization this ratio was 97:3, however, small amounts of impurities were still detected in ^{1}H NMR spectrum. In MeCN this reaction cleanly proceeded to give diazepine **24g** in 80% yield without chromatography purification (entry 7). 5-Benzoyl-substituted pyrimidine **15j** was reacted with PhSNa (1.10 equiv) without any traces of PhSH (rt, 2 h) (entries 8 and 9). Both in MeCN and in THF the formation of diazepine **24h** was accompanied by some side reactions. The isolated crude materials were purified using column chromatography. Most of the impurities were removed, but small amounts of pyrimidine **25h** were observed in purified products (2 mol% for the MeCN reaction and 3 mol% for the THF reaction). This side product was completely removed by crystallization to give an analytically pure sample. Diazepine **24i** was obtained from pyrimidine **15k** under the action of PhSNa (1.11 equiv) in THF (entry 10). The crude product was purified using column chromatography on silica gel to give **24i** in 80% yield.

Structure of 5-Acyl-Substituted 2,3,6,7-Tetrahydro-1*H*-1,3-diazepin-2-ones. ^{1}H and ^{13}C NMR spectra of the obtained products **17a**–**i**, **18a**,**b**, **20a**–**e**, **21a**–**f**, **22**, and **24a**–**i** confirm their diazepinone structure. High value of geminal coupling between 6-H$_{(A)}$ and 6-H$_{(B)}$ (13.7–16.4 Hz), relatively high value of vicinal coupling between N$_{(1)}$H and 7-H (5.2–6.5 Hz), and long-range coupling between N$_{(1)}$H and 6-H$_{(A)}$ (0.7–1.1 Hz) in ^{1}H NMR spectra of **17**, **18**, **21**, and **24** in DMSO-d_6 are typical of diazepinone ring. Additionally, ^{1}H NMR spectra showed doublet of the methine proton in CH(COOEt)$_2$ (8.6–10.4 Hz) in the range of 4.89–4.07 ppm for compounds **17**, long-range coupling between 6-H$_{(B)}$ and 4-CH$_3$ (0.8–1.4 Hz) for 4-methyl-substituted compounds **17**, **21**, and **24**, and two multiplets of the 6-H and 7-H protons (each 2H) at 2.64–2.68 and 3.23–3.28 ppm for **22**. ^{13}C NMR spectra showed downfield shift of C7 carbon signal for **17** (49.0–53.4 ppm), **18** (45.5–45.9 ppm), **21** (80.6–85.3 ppm), and **24** (61.2–65.3 ppm) due to this atom has two electron-withdrawing substituents. The values of couplings between N$_{(1)}$H, 7-H, 6-H$_{(A)}$, and 6-H$_{(B)}$ ($^3J_{N(1)H,7\text{-}H}$ = 5.2–6.5 Hz, $^3J_{7\text{-}H,6\text{-}H(A)}$ = 5.4–6.7 Hz, and $^3J_{7\text{-}H,6\text{-}H(B)}$ = 1.4–3.8 Hz) indicate that compounds **17**, **18**, **21**, and **24** in DMSO-d_6 solution predominantly exist in a puckered conformation with a pseudo axial orientation of the substituent at the C7 position.

Analogously, the diazepine structure was unambiguously confirmed for 4-phthalimido-substituted compounds **20**. It should be noted that ^{1}H NMR spectroscopic characteristics of these compounds significantly differ from those of other diazepines. ^{1}H NMR spectra of **20** in DMSO-d_6 showed lower geminal coupling between 6-H$_{(A)}$ and 6-H$_{(B)}$ (13.5–14.0 Hz), low vicinal coupling constant between N$_{(1)}$H and 7-H (1.1–1.6 Hz), two very different vicinal couplings between 6-H$_{(A)}$ and 7-H (10.3–10.8 Hz) and 6-H$_{(B)}$ and 7-H (2.8–3.3 Hz). Therefore, in contrast to diazepines **17**, **18**, **21**, and **24**, orientation of the substituent at the C7 position of diazepines **20** is pseudo equatorial.

The structures of diazepines **18b**, **20b**, and **21a**,**b** were also confirmed by X-ray single-crystal analyses (Figures 2, 3, 4, and 5).[17]

The tetrahydrodiazepine ring of compounds **18b**, **20b**, and **21a** adopts a boat-like conformation. The mean-square plane in this conformation is formed by N1, C4, C5, and C7 atoms (maximum deviation from the plane is 0.03 Å). Atoms C6, C2, and N3 deviate from the plane by 0.73–0.76, 0.30–0.46, and 0.41–0.55 Å in the same direction, respectively. The heterocyclic ring of compound **21b** has a conformation of distorted envelope. The mean-square plane in this conformation is formed by N1, C2, N3, and C4 atoms (maximum deviation from the plane is 0.01 Å). Atoms C5, C6, and C7 deviate from the plane by 0.51, 1.18, and 0.21 Å, respectively. The cyano group in **18b** and 7-methoxy group in **21a** and **21b** have a pseudo axial orientation (the O–C7–C6–C5 or NC–C7–C6–C5 torsion angles are 46.1–55.1°), phthalimido group in diazepine **20b** has a pseudo equatorial orientation (the N–C7–C6–C5 torsion angle is 169.9°).

Mechanism of Tetrahydropyrimidinone Ring Expansion. The reactions of ring expansion are powerful synthetic tool in heterocyclic chemistry.[18] For instance, nucleophile-

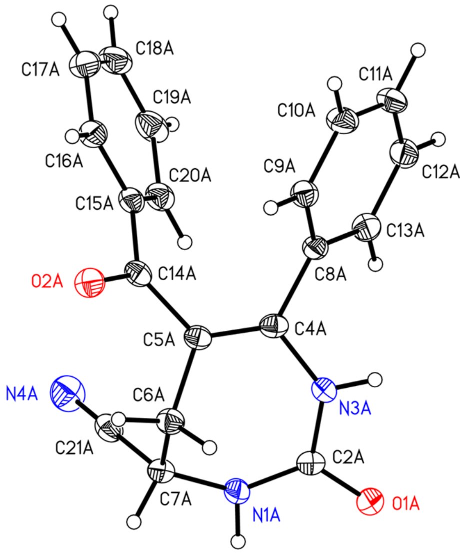


Figure 2. A view of molecular X-ray structure of **18b** with ellipsoids drawn at the 50% probability level.

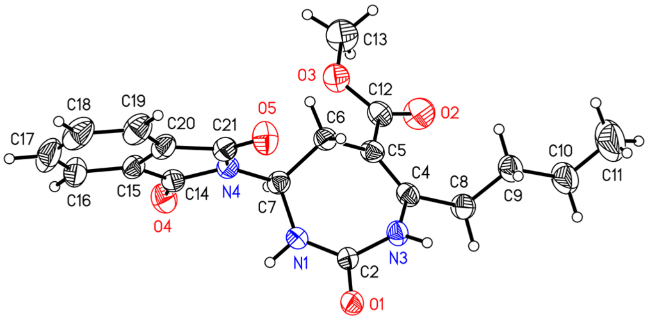


Figure 3. A view of molecular X-ray structure of **20b** with ellipsoids drawn at the 30% probability level.

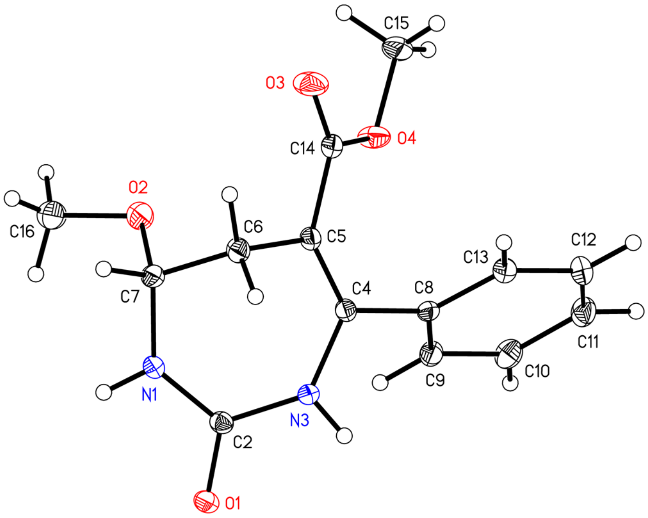


Figure 4. A view of molecular X-ray structure of **21a** with ellipsoids drawn at the 50% probability level.

mediated one-carbon atom ring expansion reactions of nitrogen-containing heterocycles of general structure **A** (Scheme 5) provides a simple access to azepines from 1,4-dihydropyridines,[19] dibenzoazepines from 9,10-dihydroacridines,[20] diazepines from tetrahydropyrimidines.[6,7,10]

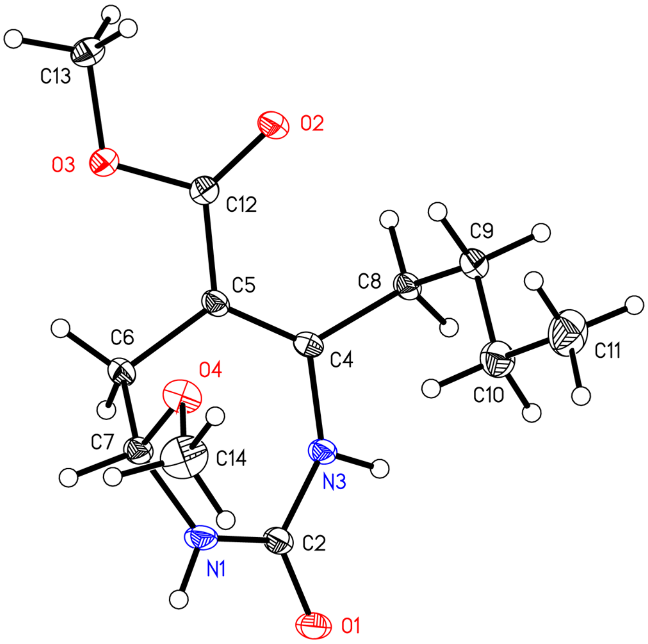
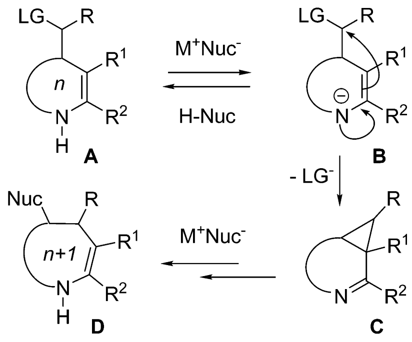


Figure 5. A view of molecular X-ray structure of **21b** with ellipsoids drawn at the 50% probability level.

Scheme 5. Proposed One-Carbon Atom Ring Expansion Pathway

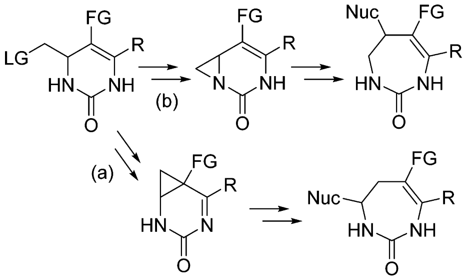


The reported data indicate that the basicity of nucleophile plays an important role for initiation of all these reactions, since they start from the abstraction of proton from NH group to give anion **B**. Subsequent intramolecular substitution of good-leaving group results in bicyclic intermediates **C** whose transformations via cyclopropane ring opening lead to ring expansion products **D**.

However, a general proposed mechanism of the ring expansion outlined in Scheme 5 was based mainly on speculative insights. No experimental evidence of the formation of cyclopropane intermediates **C** was reported. It should be noted that the reaction of ring expansion of $N_{(1)}$-unsubstituted tetrahydropyrimidines to tetrahydro-1,3-diazepines could proceed not only via cyclopropane intermediates (Scheme 6, route a) but also via aziridine ones (route b). Ring expansion reactions involving aziridine intermediates are well documented.[21]

Obviously, formation of 7- or 6-substituted diazepines could be expected following pathway a or b, respectively. Our experimental and reported data showed that the only isolated products were 7-substituted diazepines, which proves that the reaction proceeds via pathway a. Thus, we attempted to

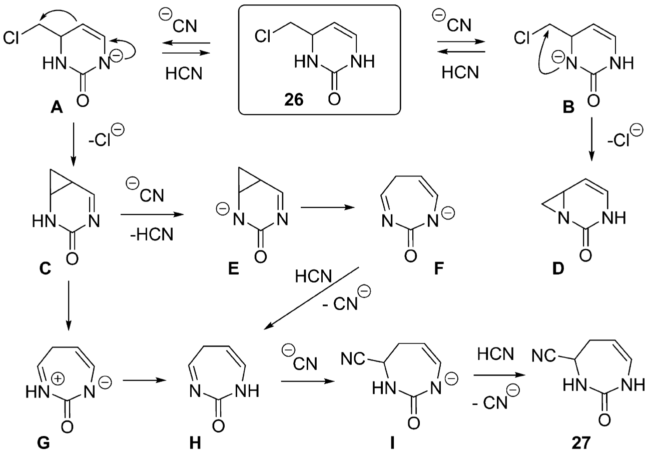
Scheme 6. Two Possible Pathways of One-Carbon Atom Ring Expansion of Pyrimidines



rationalize the mechanism of the pyrimidine ring expansion including the reason for exclusive formation of cyclopropane intermediates.

Using 4-chloromethyl-1,2,3,4-tetrahydropyrimidin-2-one (**26**) as a model compound and DFT methodology, we performed the B3LYP/6-31+G(d,p) calculations for both routes (a and b) of its reaction with cyanide-ion in the gas phase and in MeCN solution (Scheme 7). Three principal steps for both the proposed pathways were calculated: (a) deprotonation of $N_{(1)}H$ and $N_{(3)}H$ in **26** under the action of nucleophile resulting in the corresponding anions **A** and **B**; (b) formation of cyclopropane or aziridine bicyclic intermediates **C** and **D** from anions **A** and **B**, respectively; (c) cyclopropane ring opening in intermediate **C** to give ring expansion products followed by their transformation into the final diazepinone **27**.

Scheme 7. Two Plausible Pathways of the Ring Expansion of Pyrimidine 26 into Diazepine 27 under the Action of Cyanide-Anion



Calculations showed that deprotonation of the $N_{(1)}H$ group to give anion **A** was much more preferable than formation of anion **B**. Higher stability of anion **A** compared with **B** (ΔG = 5.29 kcal/mol in the gas phase and 4.09 kcal/mol in MeCN) can be explained by effective delocalization of negative charge in this anion. Thus, the equilibrium concentration of anion **B** leading to aziridine intermediate **D** (route b) is extremely low, therefore the ring expansion proceeds via cyclopropane intermediate **C** (route a).

Intramolecular nucleophilic substitution of chlorine in the most stable conformations of pyrimidine anions **A** and **B** with antiperiplanar relationship between chlorine and the C5 or $N_{(3)}$ atoms, respectively, lead to intermediates **C** and **D**. For both reactions relatively low activation barriers (ΔG = 8.04 and 9.10 kcal/mol in the gas phase, 8.74 and 9.52 kcal/mol in MeCN, respectively) and a decrease in the Gibbs free energies were found (Figure 6).

Under basic conditions, bicycle **C** can transform into intermediate dihydrodiazepinone **H** following two possible pathways (Scheme 7): (1) NH deprotonation followed by ring expansion (**C** → **E** → **F** → **H**) or (2) electrocyclic opening of cyclopropane ring (**C**→ **G** → **H**). The energy barrier ΔG for transformation of **C** into **G** was found to be 10.31 kcal/mol in the gas phase and 8.12 kcal/mol in MeCN. In contrast, anion **E** resulted from NH deprotonation of **C** is extremely unstable. This anion undergoes ring expansion to give diazepine anion **F** without energy barrier (ΔG = 0 kcal/mol) in the gas phase or with a very low barrier (ΔG = 0.06 kcal/mol) in MeCN. Further detailed calculations using CN-anion as a base showed that the prereaction complex of cyclopropane intermediate **C** with this anion undergoes both the zero-bridge cleavage and NH deprotonation with an activation barrier of ΔG = 4.45 kcal/mol (the gas phase, 298 K, 1 atm) to give the postreaction complex of anion **F** with HCN. Ring expansion of the prereaction complex of intermediate **C** and CN-anion in MeCN solution proceeds via zero-bridge cleavage with an energy barrier of G = 6.17 kcal/mol to provide the complex **G**·CN^-. The initial ring expansion products further form dihydrodiazepinone **H** followed by the addition of HCN to the C=N double bond to give the target diazepine **27**. It should be noted that transformation of bicycle **C** into diazepine **H** promoted by bases is a thermodynamically favorable process with ΔG = −9.86 kcal/mol and ΔG = −8.16 kcal/mol in the gas phase and MeCN, respectively (298 K, 1 atm).

We believe that the nucleophile-promoted ring expansion of 5-functionalized pyrimidines **15a–k** into diazepines **17**, **18**, **20–22**, and **24** proceeds, in general, analogously to that described above for **26** (Scheme 8). However, we suppose that the presence of an electron-withdrawing group at the C5 in the starting compounds may assist the reaction.

According to the above-discussed mechanism, transformation of pyrimidinones **15a–k** into diazepinones **17**, **18**, **20–22**, and **24** includes two consecutive reaction sets. The first set is the pyrimidine ring expansion controlled only by basicity of the nucleophile to result in dihydrodiazepinones **A**, and the second is nucleophilic addition to the latter determined by nucleophilicity of the nucleophile to give the final products. The first set of reactions can proceed without nucleophile under the action of an appropriate non-nucleophilic base (e.g., DBU). To confirm this hypothesis, a solution of **23** (conc. 0.042 mol/L) in DMSO-d_6 was treated with DBU (1.47 equiv) in an NMR tube and the progress of the reactions was monitored by ^1H NMR spectroscopy at 25 °C (Table 5).

The reaction of **23** proceeded very fast and after 11 min only 24% of the starting material was observed (entry 3). Dihydrodiazepinone **30** and tricyclic bis-diazepinone **32**[22] in a ratio of 66:34 (after 3 days) were formed as stable final products of this transformation (entry 5). In addition to **30** and **32**, ^1H NMR spectra of the reaction mixture showed the signals of three compounds: bicyclic cyclopropane intermediate **28**, dihydrodiazepinone **29**, and anion **31** (the conjugated base of **30**) (entries 1–4). The formation of compounds **28** and **29** confirms the plausible pathway of the ring expansion reaction discussed above. In the absence of nucleophiles the initially formed ring expansion product dihydrodiazepinone **29** affords **30** and its conjugated base **31** as a result of acylimine-enamide tautomerization promoted by DBU. Dimerization of compound

DOI: 10.1021/acs.joc.7b01348
J. Org. Chem. 2017, 82, 8085–8110

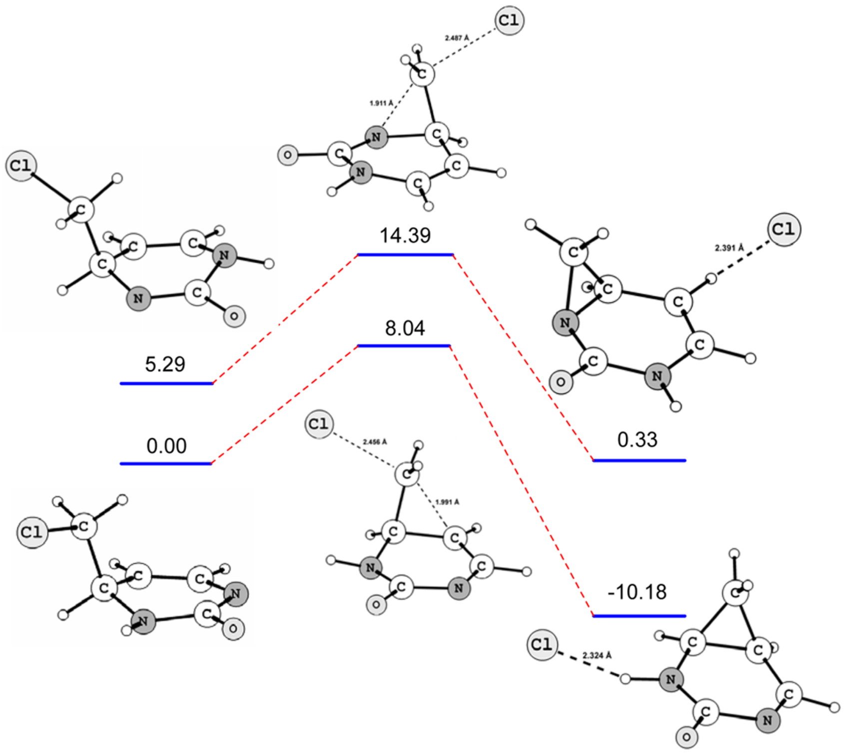
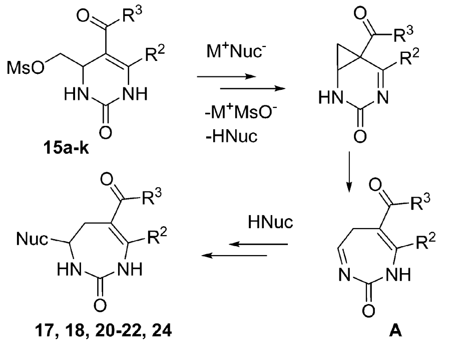


Figure 6. Gibbs free energy profiles (B3LYP/6-31+G(d,p)) for cyclopropane and aziridine intermediates formation via intramolecular nucleophilic substitution of chlorine in N(1)- and N(3)-anions of 4-chloromethyl-1,2,3,4-tetrahydropyrimidin-2-one (**26**) in gas phase. Free energies in kcal/mol at 298 K and 1 atm.

Scheme 8. Plausible Pathway of Ring Expansion of Pyrimidines 15a−k under Action of Nucleophiles

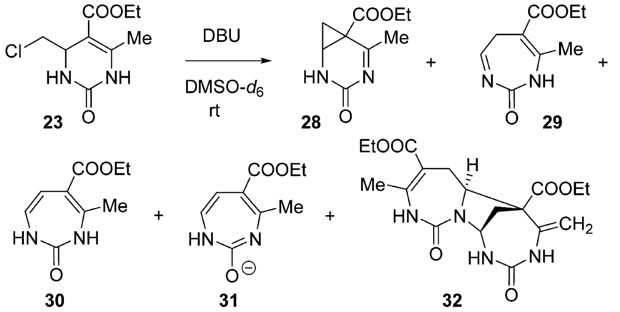


29 possessing imine and enamide moieties proceeds in the presence of DBU and gives tricycle **32**.

Generally, similar results were obtained in an NMR tube reaction of **23** using a greater concentration of substrate (0.113 mol/L) and greater excess of DBU (2.16 equiv). However, under these conditions the concentration of dihydrodiazepinone **29** was too low to detect its signals. The starting material was practically consumed after 3 h and a 3:13:28:21:35 mixture of compounds **23**, **28**, **30**, **31**, and **32** was observed. After 2 days all the intermediates disappeared, and a mixture of **30** and **32** in a ratio of 61:39 was obtained.

^1H NMR monitoring of the DBU promoted transformation of 4-mesyloxymethyl-substituted pyrimidine **15a** (conc. 0.069 mol/L) in DMSO-d_6 gave results similar to those described above, except that the starting material was completely consumed after 1 h, since OMs group is a better leaving group than chlorine.

Table 5. Distribution of the Products upon the Treatment of Pyrimidine 23 with DBU in DMSO-d_6



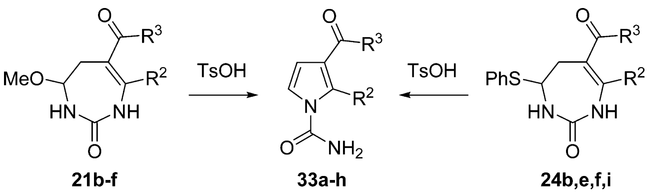
entry	reaction time	23	28	29	30	31	32
1	2 min	73	4	4	4	5	10
2	5 min	28	9	3	23	12	25
3	11 min	24	11	2	24	14	25
4	166 min	4	6	0	50	9	31
5	3 days	0	0	0	66	0	34

(product distribution, % for columns 23–32)

Preparative syntheses of the mixtures of dihydrodiazepinone **30** and tricyclic bis-diazepinone **32** were performed by treatment of pyrimidine **23** (conc. 0.20 mol/L) with DBU (1.41−1.50 equiv) in dry DMF or DMSO at room temperature for 20 h followed by removal of the solvent under vacuum (oil pump, at less than 60 °C), trituration of the residue with ice-cold water and filtration. As a result, mixtures of **30**[23] and **32** in a ratio of 34:66 (in DMF) and 50:50 (in DMSO) were obtained (yield 61−73%).

Synthesis of 1-Carbamoylpyrroles via Ring Contraction. Previously, Bullock et al. reported an example of HCl-promoted transformation of methyl 7-methoxy-tetrahydrodiazepine-5-carboxylate into methyl 1-carbamoyl-1*H*-pyrrole-3-carboxylate.[7d] Recently, we demonstrated that 5-phenylthio- and 5-tosyl-substituted 7-methoxy- or 7-phenylthiodiazepines undergo the reaction of ring contraction in the presence of TsOH to give the corresponding 1-carbamoylpyrroles.[10c,d] Since 3-functionalized 1-carbamoylpyrroles are poorly explored pyrrole derivatives,[24] the synthesis of new representatives of these compounds is of significant importance. Therefore, we studied the reaction of the obtained diazepines **21** and **24** with TsOH (0.10 equiv) in refluxing solvent. In EtOH or MeCN the reaction of 7-methoxydiazepine **21e** with TsOH completed in 30 min to give 3-benzoyl-substituted pyrrole **33g** in 92 and 96% yield, respectively (Table 6, entries 7 and 8).

Table 6. Synthesis of 1-Carbamoylpyrroles 33a−h via the Reaction of Ring Contraction of Diazepinones 21 and 24[a]



entry	starting material	R^2	R^3	solvent	product	yield (%)[b]
1	**24b**	Ph	OMe	MeCN	**33a**	88
2	**24e**	Ph	OEt	MeCN	**33b**	94
3	**24f**	Bu	OEt	MeCN	**33c**	93
4	**21b**	Bu	OMe	MeCN	**33d**	94
5	**21c**	CO_2Me	OMe	MeCN	**33e**	87
6	**21d**	Me	Me	MeCN	**33f**	79
7	**21e**	Me	Ph	EtOH	**33g**	92
8	**21e**	Me	Ph	MeCN	**33g**	96
9	**21f**	Ph	Ph	MeCN	**33h**	94
10	**24i**	Ph	Ph	MeCN	**33h**	96

[a] Reaction conditions: TsOH (0.10 equiv), refluxing solvent, 30 min. [b] Isolated yield.

Since the solvent had only a slight effect on the yield and purity of pyrrole **33g**, for all further reactions MeCN was used. Under these conditions, 3-acetyl-substituted pyrrole **33f** was obtained from **21d** in 79% yield (entry 6). Both 7-methoxydiazepine **21f** and 7-phenylthiodiazepine **24i** smoothly reacted with TsOH to give compound **33h** in 94 and 96% yields, respectively (entries 9 and 10). Analogously, pyrrole-3-carboxylates **33a−c** and **33d,e** were prepared in good yields from 7-phenylthiodiazepines **24b,e,f** and 7-methoxydiazepines **21b,c**, respectively (entries 1−5).

We developed a convenient one-pot procedure for preparation of pyrrole **33f** from pyrimidine **15i** without isolation of intermediate methoxydiazepine **21d** via the ring expansion/ring contraction sequence. According to this procedure, to the reaction mixture formed after the reaction of **15i** with NaOMe in MeOH was added TsOH followed by reflux for 30 min to give pyrrole **33f** in 55% yield. It should be noted that the overall yield of pyrrole **33f** from pyrimidine **15i** using two steps was also 55%.

The structures of carbamoyl pyrroles **33a,f** were confirmed by X-ray single-crystal analyses (Figures 7 and 8).[17]

Conformations of **33a** and **33f** are generally similar. Due to conjugation between pyrrole ring, carbamoyl group, and acetyl group, compound **33f** adopts an approximately planar conformation with orientation of both carbonyl oxygens toward the 2-Me group. The angles between the planes of the pyrrole ring and above groups are 9.6° and 5.0°, respectively. The bulky phenyl group in compound **33a** causes an increase in the angle between the planes of the pyrrole ring and carbamoyl moiety to 23.63°, while the pyrrole ring and methoxycarbonyl substituent lie almost in the same plane (angle 4.0°). The phenyl and pyrrole rings in **33a** form an angle of 69.0°.

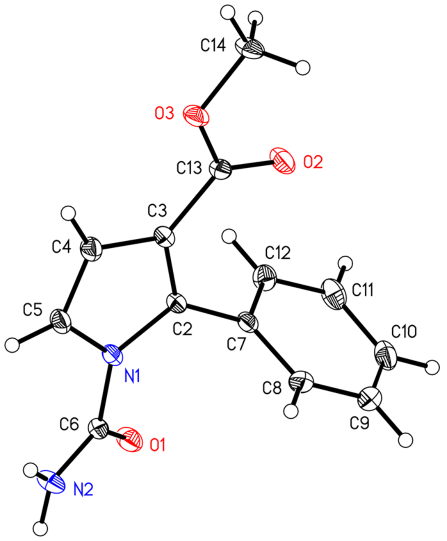


Figure 7. A view of molecular X-ray structure of **33a** with ellipsoids drawn at the 50% probability level.

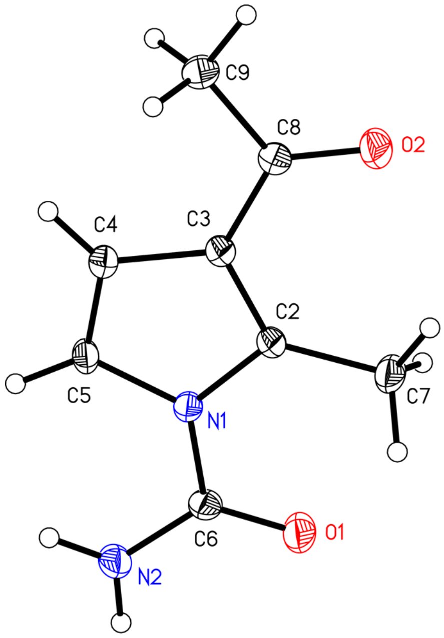


Figure 8. A view of molecular X-ray structure of **33f** with ellipsoids drawn at the 50% probability level.

■ CONCLUSION

A general five-step multigram protocol for preparation of alkyl 4-mesyloxymethyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylates and 5-acyl-4-mesyloxymethyl-1,2,3,4-tetrahydropyrimidin-2-ones has been developed. The synthesis involved nucleophilic substitution of the tosyl group in readily available

N-[(2-benzoyloxy-1-tosyl)ethyl]urea with Na-enolates of *β*-oxoesters or 1,3-diketones, followed by acid-catalyzed dehydration or heterocyclization-dehydration of the resulting products, removal of benzoyl protection, and conversion of hydroxymethyl group into mesyloxymethyl group. The pyrimidinones obtained can serve as versatile precursors in the synthesis of 5-functionalyzed 2,3,6,7-tetrahydro-1*H*-1,3-diazepin-2-ones via nucleophile-mediated ring expansion reaction using NaCN, sodium diethyl malonate, NaOMe, potassium phthalimide, PhSNa, and $NaBH_4$ as a nucleophile. A plausible mechanism of pyrimidine ring expansion based on experimental data, DFT calculations at B3LYP/6-31+G(d,p) level, and NMR monitoring experiments was proposed. This mechanism involved the following subsequent steps: $N_{(1)}H$ deprotonation under the action of nucleophile, intramolecular nucleophilic substitution of mesyloxy group to give cyclopropane bicyclic intermediates, nucleophile-mediated cyclopropane ring opening leading to 2,5-dihydro-1*H*-1,3-diazepin-2-ones, and addition of nucleophile to the C=N bond to afford final diazepinones. Conformations of the obtained tetrahydro-1*H*-1,3-diazepin-2-ones in solid state and solutions were established using X-ray diffraction and NMR spectroscopy. We believe that general and flexible synthesis of multifunctionalized 1,3-diazepines described in this article will give a strong impulse for further development of their chemistry. We demonstrated that 7-methoxy- or 7-phenylthio-diazepinones in the presence of TsOH undergo the ring contraction reaction to give access to the corresponding 3-functionalized 1-carbamoyl-1*H*-pyrroles.

■ EXPERIMENTAL SECTION

General Procedures. All solvents were distilled before use. EtOH (95%) was used unless otherwise indicated. Petroleum ether had a distillation range of 40−60 °C. Dry solvents (MeCN, THF, CH_2Cl_2, MeOH, EtOH, DMF, DMSO, $CHCl_3$) were obtained according to the standard procedures and used in the reactions. Sodium hydride (60% suspension in mineral oil) was washed with anhydrous hexane and dried in vacuum prior to use. Ethyl acetoacetate and ethyl benzoylacetate were dried over $MgSO_4$ and then distilled in vacuum. Mesyl chloride was distilled in vacuum prior to use. Diethyl ester of 2-oxobutandioic acid (bp 78−86 °C/0.1 mm) was prepared by reaction of ethyl acetate with diethyl oxalate in the presence of sodium as described in ref 25. Ethyl ester of 3-oxoheptanoic acid (bp 105−115 °C/20 mm) was prepared analogously to a published procedure including acylation of ethyl acetoacetate with butyryl chloride followed by retro-Claisen reaction.[26] *p*-Toluenesulfinic acid was synthesized by treatment of a saturated aqueous solution of sodium *p*-toluenesulfinate[27] with hydrochloric acid at 0 °C, dried over P_2O_5, and stored at −18 °C. All other reagents and solvents were purchased from commercial sources and used without additional purification. IR spectra (in Nujol) were recorded on a FT-IR spectrophotometer. Peak intensities in the IR spectra are defined as strong (s), medium (m), or weak (w), shoulder (sh). NMR spectra (solutions in DMSO-d_6) were recorded on a spectrometer at 300.13 MHz (^1H) and 75.48 MHz (^{13}C) and calibrated using residual undeuterated solvent (DMSO-d_6: $\delta H = 2.50$ ppm, $\delta C = 39.50$ ppm) as an internal reference. Multiplicities are reported as singlet (s), doublet (d), triplet (t), quartet (q), and some combinations of these, multiplet (m). $^1H-^1H$ spin−spin decoupling, DEPT 135, exchange of NH and OH-protons with D_2O were used to attribute some signals. Chemical shifts are reported in units of parts per million and all coupling constants are reported in hertz (Hz). Thin layer chromatography (TLC) was performed on silica gel plates Kieselgel 60 F254 (Merck) in $CHCl_3$/MeOH (20:1, v/v) and $CHCl_3$/MeOH (9:1, v/v) as solvent systems. Spots were visualized with UV light. Column chromatography was performed with Macherey−Nagel silica gel 60 (0.063−0.200 mm). All yields refer to isolated, spectroscopically and TLC pure material. The color of the solids is white if not otherwise mentioned. Single crystals of compounds **18b**, **20b**, **21a**, **21b**, **33a**, and **33f** suitable for X-ray crystallographic analysis were obtained by slow evaporation of saturated solutions in EtOH (for **18b**, **20b**, **33a**,**f**) and MeOH (for **21a**,**b**) at room temperature. For details on the X-ray diffraction experiments, see the Supporting Information. With compounds **11a**,**c**,**e**,**f** at the beginning of reflux (dehydration step) the reaction mixture may become very dense and vigorous foam formation may proceed. In this case the flask should be manually shaken. For all these compounds the reaction mixture became fluid after 20−30 min from the beginning of the reflux, but weak foam formation proceeded during all the reaction time. In all cases when the coarse suspension of product was obtained after triturating with saturated aqueous $NaHCO_3$ (and petroleum ether), stirring of the mixture was used for better grinding of the precipitate.

The geometry optimizations of all key stationary points were carried out at the B3LYP level of theory using Gaussian 09 suite of quantum chemical programs.[28] Pople's basis sets, 6-31+G(d,p), was employed for geometry optimization in the gas phase and in solution. The effect of continuum solvation was incorporated using the polarizable continuum model. Since MeCN was the typical solvent in the reactions studied, we chose the dielectric constant of MeCN ($\varepsilon = 36.6$) in the condensed-phase calculations. Enthalpies and Gibbs free energies were obtained by adding unscaled zero-point vibration energy corrections (ZPVE) and thermal contributions to the energies. All transition states were optimized and characterized as a first order saddle point by harmonic vibration frequency analysis. The only one imaginary frequency of the first-order saddle point was subjected to visual inspection to examine whether it represented the desired reaction coordinate. The intrinsic reaction coordinate (IRC) analysis was performed to authenticate that the transition state pertains to the desired reaction coordinate. The IRC calculations were performed at the B3LYP/6-31+G(d,p) level of theory.

*N-[(2-Benzoyloxy-1-tosyl)ethyl]urea (**7**).* To a freshly distilled 2-benzoyloxyethanal dimethyl acetal (12.340 g, 58.67 mmol) was added 80% formic acid (29 mL), the resulting solution was stirred in a water bath at 40 °C for 2 h, then *p*-toluenesulfinic acid (9.170 g, 5870 mmol) and H_2O (29 mL) were added. The mixture was stirred at room temperature for 25 min, and to the resulting clear solution were added urea (17.620 g, 193.37 mmol) and H_2O (58 mL). Urea dissolved in 5 min followed by precipitation of a fine solid. The suspension was stirred for 21 h and cooled to 0 °C. The precipitate was filtered, washed with ice-cold water (8 × 20 mL) so that the smell of formic acid disappeared and petroleum ether, and dried to give **7** (17.811 g, 84%), which was used without additional purification. Mp 127−131 °C (decomp., MeCN) (mp lit.[10a] 127−131 °C). ^1H NMR (300.13 MHz, DMSO-d_6) δ 7.86−7.91 (m, 2H, ArH), 7.71−7.76 (m, 2H, ArH), 7.64−7.71 (m, 1H, ArH), 7.49−7.55 (m, 2H, ArH), 7.38−7.44 (m, 2H, ArH), 7.13 (d, $^3J = 10.4$ Hz, 1H, NH), 5.91 (s, 2H, NH_2), 5.47 (ddd, $^3J = 10.4$, $^3J = 4.9$, $^3J = 4.7$ Hz, 1H, CHN), 4.69 (dd, $^2J = 12.1$, $^3J = 4.9$ Hz, 1H, H_A in OCH_2), 4.61 (dd, $^2J = 12.1$, $^3J = 4.7$ Hz, 1H, H_B in OCH_2), 2.37 (s, 3H, CH_3).

*N-[(1-Benzoyloxy-4-oxo-4-phenyl-3-ethoxycarbonyl)but-2-yl]urea (**9b**).* To a cooled in an ice bath, stirred suspension of NaH (0.251 g, 10.48 mmol) in dry MeCN (10 mL) was added a solution of ethyl benzoylacetate (**8b**) (2.115 g, 10.72 mmol) in MeCN (8 mL), and the solution was stirred for 15 min, then urea **7** (3.797 g, 10.48 mmol) and MeCN (7 mL) were added. The resulting suspension was stirred at room temperature for 8 h, and the solvent was removed under vacuum. The residue was triturated with petroleum ether (2 × 15 mL), and then with saturated aqueous $NaHCO_3$ (6 mL) and petroleum ether (15 mL) until crystallization was complete. The obtained suspension was left at room temperature overnight, and cooled (0 °C). The precipitate was filtered, washed with ice-cold H_2O and petroleum ether. The obtained solid was dried in vacuum desiccator (over P_2O_5) on the filter, cooled (−10 °C), washed with cold (−10 °C) diethyl ether (3 × 10 mL), and dried to give a 94:6 mixture (3.759 g, 90%) of urea **9b** (two diastereomers in a ratio of 48:46) and pyrimidine **10b** [a single (4*R**,5*R**,6*R**)-diastereomer] as a light yellow solid. The analytically pure sample of **9b** (diastereomeric ratio 51:49, white solid) was obtained by crystallization from AcOEt/hexane (2:1, v/v). Mp 95−98 °C (AcOEt−hexane, 2:1); IR (Nujol) ν_{max} 3460 (s), 3338 (br s), 3294 (br s), 3224 (br m) (OH, NH), 3031 (w) (CH_{arom}), 1725 (vs), 1717 (sh) (C═O in COOEt and OBz), 1683 (vs) (C═O in Bz), 1660 (vs) (amide-I), 1600 (m), 1582 (w), 1568 (m) (CC_{arom}), 1543 (br m) (amide-II), 1492 (w) (CC_{arom}), 1272 (br vs), 1178 (s), 1114 (s) (C−O), 763 (m), 713 (s), 688 (m) (CH_{arom}) cm^{-1}; ^{1}H NMR of the 51:49 diastereomeric mixture (300.13 MHz, DMSO-d_6) δ 7.88−8.03 (m, 4H, ArH in both isomers), 7.61−7.71 (m, 2H, ArH in both isomers), 7.46−7.59 (m, 4H, ArH in both isomers), 6.35 (d, ^{3}J = 9.5 Hz, 0.49H, NH in minor isomer), 6.28 (d, ^{3}J = 9.1 Hz, 0.51H, NH in major isomer), 5.69 (s, 1.02H, NH_2 in major isomer), 5.68 (s, 0.98H, NH_2 in minor isomer), 5.07 (d, ^{3}J = 6.6 Hz, 0.49H, C*H*Bz in minor isomer), 5.01 (d, ^{3}J = 7.3 Hz, 0.51H, C*H*Bz in major isomer), 4.72−4.84 (m, 1H, CHN in both isomers), 4.39 (dd, ^{2}J = 11.1, ^{3}J = 6.0 Hz, 0.51H, H_A in BzOC*H*$_2$ of major isomer), 4.37 (dd, ^{2}J = 11.1, ^{3}J = 5.5 Hz, 0.51H, H_B in BzOC*H*$_2$ of major isomer), 4.33 (d, ^{3}J = 5.6 Hz, 0.98H, BzOC*H*$_2$ in minor isomer), 4.00−4.16 (m, 2H, OC*H*$_2$CH$_3$ in both isomers), 1.10 (t, ^{3}J = 7.1 Hz, 1.53H, CH_3 in major isomer), 1.06 (t, ^{3}J = 7.1 Hz, 1.47H, CH_3 in minor isomer); ^{13}C NMR of the 51:49 diastereomeric mixture (75.48 MHz, DMSO-d_6) δ 194.3, 193.6 (C═O in Bz), 168.0, 167.9 (C═O in COOEt), 165.46, 165.44 (C═O in OBz), 158.0, 157.9 ($CONH_2$), 136.1, 135.6 (C), 134.0, 133.9 (CH), 133.42, 133.41 (CH), 129.40, 129.39 (C), 129.29, 129.28 (2CH), 129.0, 128.9 (2CH), 128.7, 128.6 (2CH), 128.4 (2CH), 65.6, 65.2 ($BzOCH_2$), 61.2, 61.1 (CH_2 in OEt), 55.0, 54.1 (CHBz), 48.3, 48.0 (CHN), 13.8, 13.7 (CH_3). Anal. Calcd for $C_{21}H_{22}N_2O_6$: C 63.31, H 5.57, N 7.03. Found: C 63.17, H 5.49, N 7.04.

^{1}H NMR of hydroxypyrimidine **10b** (300.13 MHz, DMSO-d_6) δ 7.17 (br d, ^{4}J = 1.8 Hz, 1H, $N_{(3)}H$), 6.94 (br d, ^{4}J = 1.8 Hz, 1H, $N_{(1)}H$), 6.34 (d, ^{4}J = 0.9 Hz, 1H, OH), 3.51−3.67 (m, 2H, CH_2 in OEt), 2.86 (dd, ^{3}J = 10.2, ^{4}J = 0.9 Hz, 1H, H-5), 0.61 (t, ^{3}J = 7.1 Hz, 3H, CH_3), signals of other protons overlap with proton signals of the corresponding acyclic isomers; ^{13}C NMR of hydroxypyrimidine **10b** (for nonaromatic carbon atoms) (75.48 MHz, DMSO-d_6) δ 168.5 (C═O in COOEt), 165.4 (C═O in OBz), 154.9 (C-2), 81.9 (C-4), 65.2 ($BzOCH_2$), 59.6 (CH_2 in OEt), 52.9 (C-5), 48.5 (C-6), 13.4 (CH_3).

*N-[(3-Benzoyl-1-benzoyloxy-4-oxo-4-phenyl)but-2-yl]urea (**9g**).* To a mixture of dibenzoylmethane (**8g**) (2.445 g, 10.90 mmol) and NaH (0.249 g, 10.37 mmol) was added dry THF (16 mL), the resulting mixture was stirred in an ice bath for 25 min, then urea **7** (3.758 g, 10.37 mmol) and THF (10 mL) were added. The obtained suspension was stirred at room temperature for 8 h, and solvent was removed under vacuum. The residue was triturated with petroleum ether (10 mL) and saturated aqueous $NaHCO_3$ (8 mL), the obtained suspension was left at room temperature overnight, and cooled (0 °C). The precipitate was filtered, washed with ice-cold H_2O 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 × 15 mL), and dried to give **9g** (3.975 g, 89%). Mp 156.5−157.5 °C (EtOH); IR (Nujol) ν_{max} 3447 (s), 3368 (s), 3297 (m), 3221 (br m), 3185 (br m), 3113 (w) (NH), 3065 (m) (CH_{arom}), 1732 (s) (C═O in OBz), 1680 (vs) (C═O in Bz), 1654 (s) (amide-I), 1610 (m), 1595 (m), 1580 (m) (CC_{arom}), 1529 (s) (amide-II), 1494 (w) (CC_{arom}), 1264 (vs), 1105 (s) (C−O), 759 (m), 715 (m), 704 (s), 684 (s) (CH_{arom}) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 7.96−8.06 (m, 4H, ArH), 7.83−7.89 (m, 2H, ArH), 7.60−7.70 (m, 3H, ArH), 7.43−7.57 (m, 6H, ArH), 6.35 (d, ^{3}J = 9.5 Hz, 1H, NH), 6.21 (d, ^{3}J = 5.4 Hz, 1H, C*H*Bz), 5.68 (br s, 2H, NH_2), 4.90 (dddd, ^{3}J = 9.5, ^{3}J = 6.6, ^{3}J = 5.5, ^{3}J = 5.4 Hz, 1H, CHN), 4.46 (dd, ^{2}J = 11.0, ^{3}J = 5.5 Hz, 1H, H_A in BzOC*H*$_2$), 4.44 (dd, ^{2}J = 11.0, ^{3}J = 6.6 Hz, 1H, H_B in BzOC*H*$_2$); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 195.7 (C═O in Bz), 195.1 (C═O in Bz), 165.4 (C═O in OBz), 158.0 ($CONH_2$), 136.0 (C), 135.4 (C), 133.9 (CH), 133.8 (CH), 133.3 (CH), 129.4 (C), 129.2 (2CH), 129.02 (2CH), 128.96 (2CH), 128.55 (2CH), 128.50 (2CH), 128.3 (2CH), 65.7 (OCH_2), 56.4 (CHBz), 48.9 (CHN). Anal. Calcd for $C_{25}H_{22}N_2O_5$: C, 69.76; H, 5.15; N, 6.51. Found: C, 69.38; H, 5.21; N, 6.59.

*Diethyl 6-(Benzoyloxymethyl)-4-hydroxy-2-oxohexahydropyrimidine-4,5-dicarboxylate (**10d**).* To a cooled in an ice bath, stirred suspension of NaH (0.253 g, 10.53 mmol) in dry THF (10 mL) was added a solution of diethyl ester of 2-oxobutandioic acid (**8d**) (2.001 g, 10.63 mmol) in THF (6 mL) over 5 min, the mixture was stirred for 15 min, then urea **7** (3.482 g, 9.61 mmol) and THF (5 mL) were added. The obtained suspension was stirred at room temperature for 8.5 h, and the solvent was removed under vacuum. The oily residue was triturated with petroleum ether (2 × 15 mL), then with saturated aqueous $NaHCO_3$ (6 mL) and petroleum ether (10 mL). The obtained suspension was left at room temperature overnight, and cooled (0 °C). The precipitate was filtered, rapidly washed with ice-cold H_2O (4 × 8 mL), petroleum ether, and dried to give **10d** (2.795 g, 74%) as a single (4*R**,5*R**,6*R**)-diastereomer. Mp 154−155 °C (decomp, MeCN); IR (Nujol) ν_{max} 3492 (s), 3436 (s), 3342 (br w), 3217 (br s), 3093 (br s) (OH, NH), 1759 (s), 1748 (s), 1741 (s), 1725 (vs) (C═O), 1689 (vs) (amide-I), 1600 (w), 1583 (w) (CC_{arom}), 1497 (m) (amide-II), 1297 (s), 1276 (vs), 1179 (s), 1117 (s), 1098 (s), 1026 (s) (C−O), 717 (s) (CH_{arom}) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 7.94−7.99 (m, 2H, ArH), 7.65−7.71 (m, 1H, ArH), 7.64 (br d, ^{4}J = 1.9 Hz, 1H, $N_{(3)}H$), 7.51−7.58 (m, 2H, ArH), 6.92 (br d, ^{4}J = 1.9 Hz, 1H, $N_{(1)}H$), 6.62 (d, ^{4}J = 1.3 Hz, 1H, OH), 4.42 (dd, ^{2}J = 11.5, ^{3}J = 3.3 Hz, 1H, H_A in BzOC*H*$_2$), 4.39 (dd, ^{2}J = 11.5, ^{3}J = 3.8 Hz, 1H, H_B in BzOC*H*$_2$), 4.07 (ddd, ^{3}J = 11.5, ^{3}J = 3.8, ^{3}J = 3.3 Hz, 1H, H-6), 3.91−4.23 (m, 4H, CH_2 in 4-COOEt and 5-COOEt), 3.13 (dd, ^{3}J = 11.5, ^{4}J = 1.3 Hz, 1H, H-5), 1.24 (t, ^{3}J = 7.1 Hz, 3H, CH_3 in 4-COOEt), 1.08 (t, ^{3}J = 7.1 Hz, 3H, CH_3 in 5-COOEt); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 169.3 (C═O in 5-COOEt), 167.7 (C═O in 4-COOEt), 165.5 (C═O in OBz), 153.7 (C-2), 133.6 (CH), 129.5 (C), 129.2 (2CH), 128.8 (2CH), 80.9 (C-4), 65.0 ($BzOCH_2$), 61.6 (CH_2 in 4-COOEt), 60.7 (CH_2 in 5-COOEt), 47.3 (C-6), 46.3 (C-5), 13.9 (CH_3 in OEt), 13.6 (CH_3 in OEt). Anal. Calcd for $C_{18}H_{22}N_2O_8$: C, 54.82; H, 5.62; N, 7.10. Found: C, 54.74; H, 5.65; N, 7.05.

*Ethyl 4-(Benzoyloxymethyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**11a**).* To a cooled in an ice bath, stirred suspension of NaH (0.214 g, 8.91 mmol) in dry MeCN (7 mL) was added a solution of ethyl acetoacetate (**8a**) (1.178 g, 9.05 mmol) in MeCN (10 mL) over 5 min, the resulting suspension was stirred for 20 min, then urea **7** (2.932 g, 8.09 mmol) and MeCN (8 mL) were added. The reaction mixture was stirred at room temperature for 8 h, then TsOH·H_2O (2.206 g, 11.60 mmol) was added, and the obtained suspension was refluxed under stirring for 2 h. The solvent was removed under vacuum. To the residue were added $NaHCO_3$ (0.933 g) and saturated aqueous $NaHCO_3$ (15 mL), and the mixture was triturated until crystallization was completed. The obtained suspension was left at room temperature overnight, and cooled (0 °C). The precipitate was filtered, washed with ice-cold H_2O 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 × 8 mL), and dried to give **11a** (2.349 g, 91%). Mp 214.5−215 °C (decomp, EtOH); IR (Nujol) ν_{max} 3263 (br s), 3124 (br m) (NH), 3061 (w) (CH_{arom}), 1731 (s) (C═O in OBz), 1711 (s) (C═O in COOEt), 1683 (vs) (amide-I), 1661 (s) (C═C), 1604 (w), 1492 (w) (CC_{arom}), 1275 (s), 1243 (vs), 1117 (s), 1103 (s), 1072 (s) (C−O), 719 (s) (CH_{arom}) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 9.24 (br d, ^{4}J = 2.0 Hz, 1H, $N_{(1)}H$), 7.94−7.99 (m, 2H, ArH), 7.63−7.70 (m, 1H, ArH), 7.49−7.56 (m, 3H, ArH and $N_{(3)}H$), 4.44 (ddd, ^{3}J = 5.0, ^{3}J = 3.5, ^{3}J = 3.5 Hz, 1H, H-4), 4.26 (dd, ^{2}J = 10.9, ^{3}J = 5.0 Hz, 1H, H_A in BzOC*H*$_2$), 4.11 (dd, ^{2}J = 10.9, ^{3}J = 3.5 Hz, 1H, H_B in BzOC*H*$_2$), 4.05 (q, ^{3}J = 7.1 Hz, 2H, CH_2 in OEt), 2.18 (s, 3H, 6-CH_3), 1.17 (t, ^{3}J = 7.1 Hz, 3H, CH_3 in OEt); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 165.6 (C═O in OBz), 165.1 (C═O in COOEt), 152.6 (C-2), 150.7 (C-6), 133.4 (CH), 129.5 (C), 129.3 (2CH), 128.6 (2CH), 94.8 (C-5), 67.0 ($BzOCH_2$), 59.3 (CH_2 in OEt), 49.9 (C-4), 17.8 (6-CH_3), 14.1 (CH_3 in OEt). Anal. Calcd for $C_{16}H_{18}N_2O_5$: C, 60.37; H, 5.70; N, 8.80. Found: C, 60.45; H 5.79; N, 8.77.

*Ethyl 4-(Benzoyloxymethyl)-2-oxo-6-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**11b**).* A solution of urea **9b** (6.413 g, 16.10 mmol) and TsOH·H_2O (3.078 g, 16.18 mmol) in MeCN (40 mL) was refluxed under stirring for 5.5 h, and the solvent was removed under vacuum. The residue was triturated with petroleum ether (2 × 20 mL), then with saturated aqueous NaHCO$_3$ (10 mL) and petroleum ether (10 mL) until crystallization was complete. The resulting suspension was cooled (0 °C), the precipitate was filtered, washed with ice-cold H$_2$O and petroleum ether. The obtained solid was dried in a vacuum desiccator (over P$_2$O$_5$) on the filter, cooled (−10 °C), washed with cold (−10 °C) diethyl ether (4 × 10 mL), and dried to give **11b** (4.392 g, 72%) as a light yellow solid. The analytically pure sample (white solid) was obtained by crystallization from MeCN. Mp 157−158 °C (MeCN); IR (Nujol) ν_{max} 3249 (br s), 3122 (br m), 3105 (br m) (NH), 3067 (w), 3034 (w) (CH$_{arom}$), 1722 (s) (C=O in OBz), 1700 (vs) (C=O in COOEt), 1688 (vs) (amide-I), 1652 (m) (C=C), 1603 (w), 1492 (w) (CC$_{arom}$), 1275 (s), 1261 (s), 1122 (s), 1107 (s), 1067 (m) (C−O), 766 (s), 715 (s), 701 (m) (CH$_{arom}$) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 9.30 (br d, ^4J = 1.9 Hz, 1H, N$_{(1)}$H), 8.00−8.05 (m, 2H, ArH), 7.62−7.69 (m, 1H, ArH), 7.56 (br dd, ^3J = 2.9, ^4J = 1.9 Hz, 1H, N$_{(3)}$H), 7.48−7.55 (m, 2H, ArH), 7.15−7.42 (m, 5H, ArH), 4.49−4.56 (m, 2H, H-4 and H$_A$ in BzOC*H*$_2$), 4.19−4.26 (m, 1H, H$_B$ in BzOC*H*$_2$), 3.69−3.84 (m, 2H, CH$_2$ in OEt), 0.77 (t, ^3J = 7.1 Hz, 3H, CH$_3$ in OEt); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 165.8 (C=O in OBz), 164.9 (C=O in COOEt), 152.5 (C-2), 150.9 (C-6), 135.0 (C), 133.4 (CH), 129.5 (C), 129.4 (2CH), 128.8 (CH), 128.7 (2CH), 128.1 (2CH), 127.6 (2CH), 95.9 (C-5), 67.3 (BzOCH$_2$), 59.1 (CH$_2$ in OEt), 50.7 (C-4), 13.4 (CH$_3$). Anal. Calcd for C$_{21}$H$_{20}$N$_2$O$_5$: C, 66.31; H, 5.30; N, 7.36. Found: C, 66.37; H, 5.51; N, 7.34.

*Ethyl 4-(Benzoyloxymethyl)-6-butyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**11c**).* Compound **11c** (2.347 g, 81%) was obtained from NaH (0.211 g, 8.81 mmol), ethyl ester of 3-oxoheptanoic acid (**8c**) (1.524 g, 8.85 mmol) and urea **7** (2.919 g, 8.06 mmol) in dry MeCN (18 mL) (rt, 8 h), then TsOH·H$_2$O (2.177 g, 11.45 mmol) (reflux, 2 h) as described for **11a**. Mp 143−144 °C (EtOH); IR (Nujol) ν_{max} 3249 (br s), 3203 (sh), 3124 (br m) (NH), 3063 (w) (CH$_{arom}$), 1730 (s) (C=O in OBz), 1711 (vs) (C=O in COOEt), 1683 (s) (amide-I), 1655 (m), 1643 (m) (C=C), 1603 (w) (CC$_{arom}$), 1269 (s), 1246 (s), 1105 (s), 1080 (m) (C−O), 715 (s) (CH$_{arom}$) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 9.22 (br d, ^4J = 2.0 Hz, 1H, N$_{(1)}$H), 7.93−7.98 (m, 2H, ArH), 7.63−7.69 (m, 1H, ArH), 7.48−7.55 (m, 2H, ArH), 7.49 (br dd, ^3J = 3.3, ^4J = 2.0 Hz, 1H, N$_{(3)}$H, signals partly overlap with signals of aromatic protons), 4.44 (ddd, ^3J = 4.5, ^3J = 3.3, ^3J = 3.2 Hz, 1H, H-4), 4.33 (dd, ^2J = 10.9, ^3J = 4.5 Hz, 1H, H$_A$ in BzOC*H*$_2$), 4.08 (dd, ^2J = 10.9, ^3J = 3.2 Hz, 1H, H$_B$ in BzOC*H*$_2$), 4.06 (q, ^3J = 7.1 Hz, 2H, CH$_2$ in OEt), 2.43−2.70 (m, 2H, C*H*$_2$CH$_2$CH$_2$CH$_3$), 1.16−1.41 (m, 4H, CH$_2$C*H*$_2$C*H*$_2$CH$_3$), 1.18 (t, ^3J = 7.1 Hz, 3H, CH$_3$ in OEt), 0.76 (t, ^3J = 7.2 Hz, 3H, CH$_3$ in Bu); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 165.6 (C=O in OBz), 164.8 (C=O in COOEt), 154.9 (C-6), 152.9 (C-2), 133.4 (CH), 129.5 (C), 129.4 (2CH), 128.6 (2CH), 94.3 (C-5), 67.1 (BzOCH$_2$), 59.3 (CH$_2$ in OEt), 50.1 (C-4), 30.40 (*C*H$_2$CH$_2$CH$_2$CH$_3$), 30.37 (CH$_2$*C*H$_2$CH$_2$CH$_3$), 22.0 (CH$_2$CH$_2$*C*H$_2$CH$_3$), 14.1 (CH$_3$ in OEt), 13.7 (CH$_3$ in Bu). Anal. Calcd for C$_{19}$H$_{24}$N$_2$O$_5$: C, 63.32; H, 6.71; N, 7.77. Found: C, 63.39; H, 6.80; N, 7.75.

*Diethyl 6-(Benzoyloxymethyl)-2-oxo-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylate (**11d**).* A solution of pyrimidine **10d** (4.450 g, 11.28 mmol) and TsOH·H$_2$O (0.217 g, 1.13 mmol) in MeCN (40 mL) was refluxed under stirring for 1 h, and the solvent was removed under vacuum. The residue was triturated with saturated aqueous NaHCO$_3$ (15 mL), and the obtained mixture was stirred at room temperature for 1 h. The resulting fine suspension was cooled (0 °C). The precipitate was filtered, washed with ice-cold H$_2$O and petroleum ether. The obtained solid was dried in a vacuum desiccator (over P$_2$O$_5$) on the filter, cooled (−10 °C), washed with cold (−10 °C) diethyl ether (2 × 10 mL), and dried to give **11d** (4.021 g, 95%). Mp 102−104 °C (EtOH); IR (Nujol) ν_{max} 3390 (m), 3358 (m), 3224 (br m), 3203 (br s), 3111 (br s) (NH), 3063 (w), 3035 (w) (CH$_{arom}$), 1759 (s) (C=O in 4-COOEt), 1730 (s) (C=O in OBz), 1702 (br vs) (C=O in 5-COOEt and amide-I), 1660 (s) (C=C), 1603 (w), 1493 (w) (CC$_{arom}$), 1281 (s), 1238 (s), 1215 (s), 1121 (s), 1105 (s), 1074 (m) (C−O), 713 (s) (CH$_{arom}$) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 9.93 (br d, ^4J = 1.9 Hz, 1H, N$_{(3)}$H), 7.95−8.00 (m, 2H, ArH), 7.64−7.70 (m, 1H, ArH, signals partly overlap with signals of N$_{(1)}$H), 7.65 (br dd, ^3J = 3.2, ^4J = 1.9 Hz, 1H, N$_{(1)}$H, signals partly overlap with signals of aromatic protons), 7.48−7.55 (m, 2H, ArH), 4.48 (ddd, ^3J = 3.8, ^3J = 3.2, ^3J = 3.0 Hz, 1H, H-6), 4.30 (dd, ^2J = 11.1, ^3J = 3.8 Hz, 1H, H$_A$ in BzOC*H*$_2$), 4.23 (dd, ^2J = 11.1, ^3J = 3.0 Hz, 1H, H$_B$ in BzOC*H*$_2$), 4.10−4.26 (m, 2H, CH$_2$ in 5-COOEt), 4.06 (q, ^3J = 7.1 Hz, 2H, CH$_2$ in 4-COOEt), 1.22 (t, ^3J = 7.1 Hz, 3H, CH$_3$ in OEt), 1.15 (t, ^3J = 7.1 Hz, 3H, CH$_3$ in OEt); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 165.6 (C=O in OBz), 163.4 (C=O in COOEt), 162.4 (C=O in COOEt), 151.9 (C-2), 143.2 (C-4), 133.5 (CH), 129.4 (C), 129.4 (2CH), 128.7 (2CH), 95.4 (C-5), 66.9 (BzOCH$_2$), 61.8 (CH$_2$ in OEt), 60.3 (CH$_2$ in OEt), 49.7 (C-6), 13.9 (CH$_3$ in OEt), 13.6 (CH$_3$ in OEt). Anal. Calcd for C$_{18}$H$_{20}$N$_2$O$_7$: C, 57.44; H, 5.36; N, 7.44. Found: C, 57.56; H, 5.38; N, 7.40.

*5-Acetyl-4-(benzoyloxymethyl)-6-methyl-1,2,3,4-tetrahydropyrimidin-2-one (**11e**).* Compound **11e** (2.607 g, 86%) as a light yellow solid was obtained from NaH (0.251 g, 10.47 mmol), acetylacetone (**8e**) (1.067 g, 10.66 mmol), and urea **7** (3.792 g, 10.47 mmol) in dry MeCN (26 mL) (rt, 8 h), then TsOH·H$_2$O (2.588 g, 13.61 mmol) (reflux, 2 h) as described for **11a**. The analytically pure sample (white solid) was obtained by crystallization from EtOH. Mp 208.5−209.5 °C (decomp, EtOH); IR (Nujol) ν_{max} 3269 (br s), 3125 (br s) (NH), 1734 (m), 1726 (s) (C=O in OBz), 1711 (vs), 1705 (sh) (amide-I), 1678 (s), 1644 (m), 1628 (s), 1604 (s) (C=O in Ac and C=C), 1562 (w), 1492 (w) (CC$_{arom}$), 1281 (s), 1240 (s), 1116 (s) (C−O), 714 (m) (CH$_{arom}$) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 9.21 (br d, ^4J = 2.1 Hz, 1H, N$_{(1)}$H), 7.96−8.01 (m, 2H, ArH), 7.63−7.70 (m, 1H, ArH), 7.59 (br dd, ^3J = 3.6, ^4J = 2.1 Hz, 1H, N$_{(3)}$H), 7.49−7.56 (m, 2H, ArH), 4.53 (ddd, ^3J = 5.7, ^3J = 3.6, ^3J = 3.4 Hz, 1H, H-4), 4.16 (dd, ^2J = 11.0, ^3J = 5.7 Hz, 1H, H$_A$ in OCH$_2$), 4.08 (dd, ^2J = 11.0, ^3J = 3.4 Hz, 1H, H$_B$ in OCH$_2$), 2.26 (s, 3H, CH$_3$ in Ac), 2.21 (s, 3H, 6-CH$_3$); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 194.0 (C=O in Ac), 165.8 (C=O in OBz), 152.7 (C-2), 150.0 (C-6), 133.4 (CH), 129.6 (C), 129.4 (2CH), 128.7 (2CH), 106.1 (C-5), 67.0 (OCH$_2$), 49.9 (C-4), 30.5 (CH$_3$ in Ac), 19.1 (6-CH$_3$). Anal. Calcd for C$_{15}$H$_{16}$N$_2$O$_4$: C, 62.49; H, 5.59; N, 9.72. Found: C, 62.29; H, 5.52; N, 9.54.

*5-Benzoyl-4-(benzoyloxymethyl)-6-methyl-1,2,3,4-tetrahydropyrimidin-2-one (**11f**).* To a mixture of benzoylacetone (**8f**) (1.953 g, 12.04 mmol) and NaH (0.276 g, 11.48 mmol) was added dry MeCN (14 mL), the resulting suspension was stirred at room temperature for 25 min, then urea **7** (4.162 g, 11.48 mmol) and MeCN (5 mL) were added. The reaction mixture was stirred at room temperature for 8 h, then TsOH·H$_2$O (2.839 g, 14.93 mmol) was added, and the obtained suspension was refluxed under stirring for 2 h. The solvent was removed under vacuum. To the residue were added NaHCO$_3$ (1.196 g), saturated aqueous NaHCO$_3$ (8 mL), and petroleum ether (6 mL), and the mixture was triturated until crystallization was completed. The obtained suspension was left at room temperature overnight, and cooled (0 °C). The precipitate was filtered, washed with ice-cold H$_2$O and petroleum ether. The obtained solid was dried in a vacuum desiccator (over P$_2$O$_5$) on the filter, cooled (−10 °C), washed with cold (−10 °C) diethyl ether (3 × 10 mL), and dried to give **11f** (2.036 g, 86%) as a light yellow solid. The analytically pure sample (white solid) was obtained by crystallization from EtOH. Mp 213-214 °C (decomp, EtOH); IR (Nujol) ν_{max} 3234 (br s), 3106 (br s) (NH), 1726 (s) (C=O in OBz), 1698 (s) (amide-I), 1657 (m) (C=C), 1639 (s) (C=O in 5-Bz), 1599 (w), 1579 (w) (CC$_{arom}$), 1281 (s), 1247 (s), 1121 (m) (C−O), 758 (m), 705 (s) (CH$_{arom}$) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 9.26 (br d, ^4J = 1.9 Hz, 1H, N$_{(1)}$H), 7.91−7.96 (m, 2H, ArH), 7.61−7.68 (m, 2H, N$_{(3)}$H and ArH), 7.40−7.57 (m, 7H, ArH), 4.55 (ddd, ^3J = 5.4, ^3J = 4.2, ^3J = 3.4 Hz, 1H, H-4), 4.28 (dd, ^2J = 10.8, ^3J = 5.4 Hz, 1H, H$_A$ in OCH$_2$), 4.17 (dd, ^2J = 10.8, ^3J = 4.2 Hz, 1H, H$_B$ in OCH$_2$), 1.61 (s, 3H, CH$_3$); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 194.0 (C=O in 5-Bz), 165.6 (C=O in OBz), 152.5 (C-2), 148.2 (C-6), 141.0 (C), 133.3 (CH), 131.3 (CH), 129.4 (C), 129.3 (2CH), 128.6 (2CH), 128.5 (2CH), 127.8 (2CH), 105.4 (C-5), 67.0 (OCH$_2$), 51.0 (C-4), 18.7 (CH_3). Anal. Calcd for $C_{20}H_{18}N_2O_4$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.54; H, 5.19; N, 7.94.

*5-Benzoyl-4-(benzoyloxymethyl)-6-phenyl-1,2,3,4-tetrahydrohydropyrimidin-2-one (**11g**).* A solution of urea **9g** (7.434 g, 17.27 mmol) and TsOH·H_2O (1.650 g, 8.67 mmol) in EtOH (50 mL) was refluxed under stirring for 5 h, and the solvent was removed under vacuum. To the residue were added $NaHCO_3$ (0.705 g, 8.38 mmol) and saturated aqueous $NaHCO_3$ (15 mL), and the obtained mixture was stirred at room temperature for 1 h. The resulting fine suspension was cooled (0 °C). The precipitate was filtered, washed with ice-cold H_2O and petroleum ether. The obtained solid was dried in a vacuum desiccator (over P_2O_5), triturated with diethyl ether (10 mL) until the suspension was obtained, and cooled (−10 °C). The precipitate was filtered, washed with cold (−10 °C) diethyl ether (4 × 10 mL), and dried. To the obtained solid was added saturated aqueous $NaHCO_3$ (10 mL) and the suspension was left at room temperature for 2 h, and cooled. The precipitate was filtered, washed with ice-cold H_2O and petroleum ether, and dried to give **11g** (5.831 g, 82%). The analytically pure sample (light yellow solid) was obtained by crystallization from MeCN. Mp 188−189 °C (MeCN); IR (Nujol) ν_{max} 3221 (br s), 3102 (br s), 3089 (br s), 3064 (sh) (NH), 1717 (s) (C=O in OBz), 1700 (vs) (amide-I), 1616 (br s) (C=O in 5-Bz and C=C), 1600 (w), 1577 (m), 1495 (w) (CC_{arom}), 1271 (vs), 1253 (s), 1116 (s) (C−O), 712 (s), 698 (m) (CH_{arom}) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6) δ 9.51 (br d, ^4J = 1.8 Hz, 1H, $N_{(1)}H$), 7.96−8.01 (m, 2H, ArH), 7.75 (br dd, ^3J = 2.9, ^4J = 1.8 Hz, 1H, $N_{(3)}H$), 7.60−7.66 (m, 1H, ArH), 7.44−7.51 (m, 2H, ArH), 6.95−7.30 (m, 10H, ArH), 4.55−4.63 (m, 2H, H-4 and H_A in OCH_2), 4.33−4.40 (m, 1H, H_B in OCH_2); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 194.7 (C=O in 5-Bz), 165.8 (C=O in OBz), 152.8 (C-2), 150.5 (C-6), 139.5 (C), 133.35 (C), 133.33 (CH), 130.5 (CH), 129.7 (CH), 129.5 (2CH), 129.44 (C), 129.37 (2CH), 128.6 (2CH), 128.5 (2CH), 127.6 (2CH), 127.3 (2CH), 104.9 (C-5), 67.5 (OCH_2), 51.9 (C-4). Anal. Calcd for $C_{25}H_{20}N_2O_4$: C, 72.80; H, 4.89; N, 6.79. Found: C, 72.46; H, 4.87; N, 6.83.

*Methyl 4-Hydroxymethyl-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**13a**).* To a solution of Na (0.031 g, 1.34 mmol) in dry MeOH (20.4 mL) was added pyrimidine **11a** (1.638 g, 5.14 mmol), the resulting mixture was refluxed under stirring for 1.5 h, and cooled to room temperature. To the obtained solution was added conc. HCl (0.112 mL, 1.34 mmol), and the solvent was removed under vacuum. The residue was triturated with diethyl ether, and the obtained suspension was cooled. The precipitate was filtered, washed with diethyl ether, and dried. The crude product (1.045 g) was purified by column chromatography on silica gel 60 (10.05 g) eluting with $CHCl_3$/MeOH (from 25:1 to 10:1) to give **13a** (0.918 g, 89%). Mp 191.5−193.5 °C (decomp, EtOH); IR (Nujol) ν_{max} 3341 (br s), 3263 (br s), 3155 (br s) (NH, OH), 1720 (sh), 1709 (vs), 1679 (m) (C=O and amide-I), 1647 (s) (C=C), 1238 (s), 1224 (s), 1083 (s), 1031 (s) (C−O) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6) δ 8.91 (br d, ^4J = 2.0 Hz, 1H, $N_{(1)}H$), 7.07 (br dd, ^3J = 3.4, ^4J = 2.0 Hz, 1H, $N_{(3)}H$), 4.75 (t, ^3J = 5.7 Hz, 1H, OH), 4.03 (dtq, ^3J = 4.8, ^3J = 3.4, ^5J = 0.6 Hz, 1H, H-4), 3.59 (s, 3H, OCH_3), 3.25 (dd, ^3J = 5.7, ^3J = 4.8 Hz, 2H, OCH_2), 2.16 (d, ^5J = 0.6 Hz, 3H, 6-CH_3). ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 165.9 (C=O in COOMe), 152.6 (C-2), 149.9 (C-6), 95.7 (C-5), 64.2 (CH_2OH), 53.0 (C-4), 50.6 (OCH_3), 17.8 (6-CH_3). Anal. Calcd for $C_8H_{12}N_2O_4$: C, 48.00; H, 6.04; N, 13.99. Found: C, 48.12; H, 6.18; N, 13.65.

*Methyl 4-Hydroxymethyl-2-oxo-6-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**13b**).* To a solution of Na (0.171 g, 7.45 mmol) in dry MeOH (50 mL) was added pyrimidine **11b** (3.175 g, 8.35 mmol) and the resulting mixture was stirred at room temperature for 27 h. The obtained suspension was cooled in an ice bath, neutralized with conc. HCl (0.630 mL, 7.55 mmol), concentrated under vacuum until the dense suspension formed, and cooled (−10 °C). The precipitate was filtered on a cooled (−10 °C) filter, washed with cold MeOH (4 × 6 mL), cold diethyl ether (4 × 10 mL), and dried to give **13b** (2.069 g, 95%). Mp 222−223.5 °C (decomp, EtOH); IR (Nujol) ν_{max} 3302 (br s), 3269 (br s), 3147 (br w) (OH, NH), 3068 (w), 3035 (w), 3020 (w) (CH_{arom}), 1688 (br vs) (C=O), 1669 (br s) (amide-I and C=C), 1599 (m) (CC_{arom}), 1265 (s), 1238 (m), 1190 (s), 1098 (s) (C−O), 765 (m), 701 (m) (CH_{arom}) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6) δ 9.01 (br d, ^4J = 1.9 Hz, 1H, $N_{(1)}H$), 7.23−7.42 (m, 5H, ArH), 7.22 (br dd, ^3J = 3.4, ^4J = 1.9 Hz, 1H, $N_{(3)}H$), 4.92 (t, ^3J = 5.8 Hz, 1H, OH), 4.12 (ddd, ^3J = 5.8, ^3J = 3.8, ^3J = 3.4 Hz, 1H, H-4), 3.44 (ddd, ^2J = 10.9, ^3J = 5.8, ^3J = 5.8 Hz, 1H, H_A in OCH_2), 3.41 (ddd, ^2J = 10.9, ^3J = 5.8, ^3J = 3.8 Hz, 1H, H_B in OCH_2), 3.32 (s, 3H, OCH_3); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 165.5 (C=O in COOMe), 152.6 (C-2), 150.4 (C-6), 135.1 (C), 128.8 (CH), 128.3 (2CH), 127.6 (2CH), 96.8 (C-5), 64.2 (CH_2OH), 53.5 (C-4), 50.5 (OCH_3). Anal. Calcd for $C_{13}H_{14}N_2O_4$: C, 59.54; H, 5.38; N, 10.68. Found: C, 59.57; H, 5.34; N, 10.53.

*Methyl 6-Butyl-4-(hydroxymethyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**13c**).* Compound **13c** (1.715 g, 85%) was obtained from pyrimidine **11c** (3.005 g, 8.34 mmol) and Na (0.161 g, 7.00 mmol) in dry MeOH (50 mL) (rt, 24 h 15 min) as described for **13b**. Mp 168.5−169.5 °C (EtOH); IR (Nujol) ν_{max} 3292 (br s), 3226 (br s), 3112 (br s) (NH, OH), 1688 (br vs), 1682 (sh) (C=O and amide-I), 1654 (s) (C=C), 1282 (s), 1258 (s), 1190 (s), 1094 (s) (C−O) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6) δ 8.95 (br d, ^4J = 2.0 Hz, 1H, $N_{(1)}H$), 7.14 (br dd, ^3J = 3.4, ^4J = 2.0 Hz, 1H, $N_{(3)}H$), 4.82 (t, ^3J = 5.6 Hz, 1H, OH), 4.01 (ddd, ^3J = 5.8, ^3J = 4.2, ^3J = 3.4 Hz, 1H, H-4), 3.59 (s, 3H, OCH_3), 3.24 (ddd, ^2J = 10.9, ^3J = 5.6, ^3J = 4.2 Hz, 1H, H_A in OCH_2), 3.22 (ddd, ^2J = 10.9, ^3J = 5.8, ^3J = 5.6 Hz, 1H, H_B in OCH_2), 2.63−2.72 (m, 1H, H_A in $\mathit{CH_2}CH_2CH_2CH_3$), 2.40−2.49 (m, 1H, H_B in $\mathit{CH_2}CH_2CH_2CH_3$), 1.22−1.49 (m, 4H, $CH_2\mathit{CH_2CH_2}CH_3$), 0.86 (t, ^3J = 7.2 Hz, 3H, CH_3 in Bu); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 165.6 (C=O in COOMe), 154.5 (C-6), 153.0 (C-2), 95.3 (C-5), 64.1 (CH_2OH), 52.9 (C-4), 50.8 (OCH_3), 30.36 ($CH_2CH_2CH_2CH_3$), 30.32 ($CH_2CH_2CH_2CH_3$), 22.0 ($CH_2CH_2CH_2CH_3$), 13.8 (CH_3 in Bu). Anal. Calcd for $C_{11}H_{18}N_2O_4$: C, 54.53; H, 7.49; N, 11.56. Found: C, 54.52; H, 7.55; N, 11.52.

*Dimethyl 6-Hydroxymethyl-2-oxo-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylate (**13d**).* To a solution of Na (0.335 g, 14.55 mmol) in dry MeOH (50 mL) was added pyrimidine **11d** (3.049 g, 8.10 mmol) and the resulting mixture was refluxed under stirring for 3 h. The obtained suspension was cooled in an ice bath, neutralized with conc. HCl (1.250 mL, 14.98 mmol), and the solvent was removed under vacuum. The residue was triturated with diethyl ether (5 mL) until crystallization was complete, the precipitate was filtered, and washed with diethyl ether (5 × 5 mL). The obtained solid was collected in a 10 mL round-bottom flask, triturated with saturated aqueous $NaHCO_3$ (1 mL) and H_2O (1 mL). The suspension was cooled (0 °C), the precipitate was filtered on a cold (−10 °C) filter, rapidly washed with ice-cold H_2O (3 × 2 mL), petroleum ether, and dried to give **13d** (1.648 g, 83%) as a pale yellow solid. The analytically pure sample (white solid) was obtained by crystallization from H_2O. Mp 201.5−203.5 °C (decomp, H_2O); IR (Nujol) ν_{max} 3424 (s), 3266 (br s), 3232 (sh), 3103 (br s) (NH, OH), 1743 (s), 1711 (s) (C=O), 1695 (s) (amide-I), 1642 (s) (C=C), 1514 (m) (amide-II), 1266 (s), 1234 (s), 1112 (s), 1091 (m) (C−O) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6) δ 9.56 (br d, ^4J = 2.0 Hz, 1H, $N_{(3)}H$), 7.28 (br dd, ^3J = 3.2, ^4J = 2.0 Hz, 1H, $N_{(1)}H$), 4.96 (t, ^3J = 5.6 Hz, 1H, OH), 4.05 (dt, ^3J = 4.3, ^3J = 3.2 Hz, 1H, H-6), 3.74 (s, 3H, OCH_3), 3.60 (s, 3H, OCH_3), 3.33 (dd, ^3J = 5.6, ^3J = 4.3 Hz, 2H, OCH_2); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 164.3 (C=O in COOMe), 163.3 (C=O in COOMe), 152.0 (C-2), 142.5 (C-4), 96.9 (C-5), 63.8 (CH_2OH), 52.7 (OMe), 52.6 (C-6), 51.5 (OMe). Anal. Calcd for $C_9H_{12}N_2O_6$: C, 44.27; H 4.95; N, 11.47. Found: C, 44.20; H, 4.88; N, 11.49.

*Ethyl 4-Hydroxymethyl-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**13e**).* To a solution of Na (0.028 g, 1.20 mmol) in dry EtOH (10.4 mL) was added pyrimidine **11a** (1.112 g, 3.49 mmol), the resulting mixture was stirred at room temperature for 6 h, neutralized with conc. HCl (0.100 mL, 1.20 mmol), and the solvent was removed under vacuum. The residue was triturated with diethyl ether, and the obtained suspension was cooled. The precipitate was filtered, washed with diethyl ether, and dried. The crude product (0.789 g) was purified by column chromatography on silica gel 60 (10.05 g) eluting with $CHCl_3$/MeOH (from 100:4 to 100:8) to give **13e** (0.696 g, 93%). Mp 198.5−200 °C (decomp, EtOH); IR (Nujol)

ν_{max} 3475 (br s), 3241 (br s), 3122 (br s) (NH, OH), 1708 (s) (C═O), 1688 (s) (amide-I), 1646 (s) (C═C), 1231 (s), 1104 (s), 1059 (s) (C–O) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 8.91 (br d, ^4J = 2.0 Hz, 1H, N$_{(1)}$H), 7.09 (br dd, ^3J = 3.4, ^4J = 2.0 Hz, 1H, N$_{(3)}$H), 4.77 (t, ^3J = 5.7 Hz, 1H, OH), 3.98–4.13 (m, 3H, CH$_2$ in OEt and H-4), 3.25 (dd, ^3J = 5.7, ^3J = 4.8 Hz, 2H, C*H*$_2$OH), 2.16 (d, ^5J = 0.6 Hz, 3H, 6-CH$_3$), 1.18 (t, ^3J = 7.1 Hz, 3H, CH$_3$ in OEt); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 165.5 (C═O in COOEt), 152.8 (C-2), 149.7 (C-6), 95.9 (C-5), 64.2 (CH$_2$OH), 59.0 (CH$_2$ in OEt), 53.0 (C-4), 17.9 (6-CH$_3$), 14.3 (CH$_3$ in OEt). Anal. Calcd for $C_9H_{14}N_2O_4$: C, 50.46, H, 6.59; N, 13.08. Found: C, 50.42; H, 6.79; N, 13.07.

*Ethyl 4-Hydroxymethyl-2-oxo-6-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**13f**).* A suspension of pyrimidine **11b** (3.187 g, 8.38 mmol) and finely powdered K_2CO_3 (1.736 g, 12.56 mmol) in EtOH (50 mL) was stirred at room temperature for 7 days, cooled in an ice bath, neutralized with 15% aqueous HCl to pH 6, and the solvent was removed under vacuum. The residue was triturated with petroleum ether (10 mL) and saturated aqueous $NaHCO_3$ (10 mL) until crystallization was completed. The obtained suspension was cooled (0 °C). The precipitate was filtered, washed with ice-cold H_2O 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 (2 × 5 mL), and dried to give **13f** (1.945 g, 84%) as a light yellow solid. The analytically pure sample (white solid) was obtained by crystallization from EtOH. Mp 180.5–181 °C (decomp, EtOH); IR (Nujol) ν_{max} 3289 (br vs), 3144 (br m) (NH, OH), 3058 (w) (CH$_{arom}$), 1686 (vs) (C═O), 1657 (vs) (amide-I and C═C), 1599 (m), 1489 (w) (CC$_{arom}$), 1267 (s), 1237 (m), 1189 (m), 1097 (s) (C–O), 768 (m), 702 (m) (CH$_{arom}$) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 8.99 (br d, ^4J = 2.0 Hz, 1H, N$_{(1)}$H), 7.22–7.43 (m, 5H, ArH), 7.19 (br dd, ^3J = 3.4, ^4J = 2.0 Hz, 1H, N$_{(3)}$H), 4.91 (t, ^3J = 5.8 Hz, 1H, OH), 4.11 (ddd, ^3J = 5.8, ^3J = 3.8, ^3J = 3.4 Hz, 1H, H-4), 3.76 (q, ^3J = 7.1 Hz, 2H, CH$_2$ in OEt), 3.44 (ddd, ^2J = 10.9, ^3J = 5.8, ^3J = 5.8 Hz, 1H, H$_A$ in C*H*$_2$OH), 3.41 (ddd, ^2J = 10.9, ^3J = 5.8, ^3J = 3.8 Hz, 1H, H$_B$ in C*H*$_2$OH), 0.77 (t, ^3J = 7.1 Hz, 3H, CH$_3$ in OEt); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 165.3 (C═O in COOEt), 152.6 (C-2), 150.2 (C-6), 135.4 (C), 128.7 (CH), 128.3 (2CH), 127.6 (2CH), 97.1 (C-5), 64.2 (CH$_2$OH), 58.9 (CH$_2$ in OEt), 53.6 (C-4), 13.5 (CH$_3$ in OEt). Anal. Calcd for $C_{14}H_{16}N_2O_4$: C, 60.86; H, 5.84; N, 10.14. Found: C, 60.70; H, 5.97; N, 10.09.

*Ethyl 6-Butyl-4-(hydroxymethyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**13g**).* To a solution of KOH (0.683 g, 12.7 mmol) in H_2O (8 mL) were added pyrimidine **11c** (3.137 g, 8.70 mmol) and EtOH (25 mL). The reaction mixture was stirred at room temperature for 1 h, cooled in an ice bath, neutralized with 15% aqueous HCl to pH 6, and the solvent was removed under vacuum. The residue was triturated with petroleum ether (15 mL), then with saturated aqueous $NaHCO_3$ (5 mL) and petroleum ether (15 mL) until crystallization was completed. The obtained suspension was cooled (0 °C). The precipitate was filtered, washed with ice-cold H_2O, petroleum ether, cold diethyl ether (3 × 5 mL), and dried to give **13g** (1.477 g, 66%). Mp 141–142 °C (MeCN); IR (Nujol) ν_{max} 3303 (br s), 3230 (br s), 3116 (br s) (NH, OH), 1685 (br vs) (C═O and amide-I), 1653 (s) (C═C), 1276 (s), 1250 (s), 1091 (s) (C–O) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 8.88 (br d, ^4J = 2.0 Hz, 1H, N$_{(1)}$H), 7.07 (br dd, ^3J = 3.4, ^4J = 2.0 Hz, 1H, N$_{(3)}$H), 4.77 (t, ^3J = 5.6 Hz, 1H, OH), 3.99–4.14 (m, 2H, CH$_2$ in OEt, signals partly overlap with signals of the H-4 proton), 4.02 (ddd, ^3J = 5.6, ^3J = 4.1, ^3J = 3.4 Hz, 1H, H-4, signals partly overlap with signals of the CH$_2$ protons in OEt), 3.25 (ddd, ^2J = 10.8, ^3J = 5.6, ^3J = 4.1 Hz, 1H, H$_A$ in OCH$_2$), 3.23 (ddd, ^2J = 10.8, ^3J = 5.6, ^3J = 5.6 Hz, 1H, H$_B$ in OCH$_2$), 2.63–2.72 (m, 1H, H$_A$ in C*H*$_2$CH$_2$CH$_2$CH$_3$), 2.40–2.49 (m, 1H, H$_B$ in C*H*$_2$CH$_2$CH$_2$CH$_3$), 1.23–1.50 (m, 4H, CH$_2$C*H*$_2$C*H*$_2$CH$_3$), 1.18 (t, ^3J = 7.1 Hz, 3H, CH$_3$ in OEt), 0.87 (t, ^3J = 7.2 Hz, 3H, CH$_3$ in Bu); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 165.2 (C═O in COOEt), 154.0 (C-6), 152.9 (C-2), 95.6 (C-5), 64.0 (CH$_2$OH), 59.0 (CH$_2$ in OEt), 52.9 (C-4), 30.39 (*C*H$_2$CH$_2$CH$_2$CH$_3$), 30.36 (CH$_2$*C*H$_2$CH$_2$CH$_3$), 22.0 (CH$_2$CH$_2$*C*H$_2$CH$_3$), 14.2 (CH$_3$ in OEt), 13.7 (CH$_3$ in Bu). Anal. Calcd for $C_{12}H_{20}N_2O_4$: C, 56.24; H, 7.87; N, 10.93. Found: C, 56.26; H, 7.87; N, 10.90.

*Diethyl 6-Hydroxymethyl-2-oxo-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylate (**13h**).* To a solution of Na (0.388 g, 16.72 mmol) in dry EtOH (46 mL) was added pyrimidine **11d** (2.770 g, 7.36 mmol) and the resulting mixture was stirred at room temperature for 1 h. The obtained solution was cooled in an ice bath, neutralized with conc. HCl (1.40 mL, 16.78 mmol), and the solvent was removed under vacuum. The residue was triturated with petroleum ether (2 × 15 mL) until crystallization was complete. The precipitate was filtered, and washed with petroleum ether. The obtained solid was cooled (−10 °C) on the filter, rapidly washed with cold saturated aqueous $NaHCO_3$ (3 mL), ice-cold H_2O (2 × 3 mL), petroleum ether, and dried to give **13h** (1.585 g, 79%). Mp 114–116.5 °C (EtOAc); IR (Nujol) ν_{max} 3422 (sh), 3387 (br s), 3291 (br s), 3102 (br m) (NH, OH), 1738 (s) (C═O), 1697 (sh), 1689 (vs) (C═O and amide-I), 1639 (s) (C═C), 1256 (s), 1228 (s), 1106 (s) (C–O) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 9.53 (br s, 1H, N$_{(3)}$H), 7.25 (br d, ^3J = 3.2 Hz, 1H, N$_{(1)}$H), 4.95 (t, ^3J = 5.5 Hz, 1H, OH), 4.19 (q, ^3J = 7.1 Hz, 2H, CH$_2$ in 4-COOEt), 3.98–4.13 (m, 2H, CH$_2$ in 5-COOEt, signals partly overlap with signals of the H-6 proton), 4.05 (dt, ^3J = 4.3, ^3J = 3.2 Hz, H-6, signals partly overlap with signals of the CH$_2$ protons in 5-COOEt), 3.33 (dd, ^3J = 5.5, ^3J = 4.3 Hz, 2H, C*H*$_2$OH), 1.26 (t, ^3J = 7.1 Hz, 3H, CH$_3$ in OEt), 1.15 (t, ^3J = 7.1 Hz, 3H, CH$_3$ in OEt); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 163.8 (C═O in COOEt), 162.7 (C═O in COOEt), 152.1 (C-2), 142.3 (C-4), 96.9 (C-5), 63.8 (CH$_2$OH), 61.6 (CH$_2$ in OEt), 60.0 (CH$_2$ in OEt), 52.6 (C-6), 13.9 (CH$_3$ in OEt), 13.6 (CH$_3$ in OEt). Anal. Calcd for $C_{11}H_{16}N_2O_6$: C, 48.53; H, 5.92; N, 10.29. Found: C, 48.71; H, 5.83; N, 10.12.

*5-Acetyl-4-hydroxymethyl-6-methyl-1,2,3,4-tetrahydropyrimidin-2-one (**13i**).* Compd **13i** (1.355 g, 88%) was obtained from pyrimidine **11e** (2.399 g, 8.32 mmol) and Na (0.062 g, 2.68 mmol) in dry MeOH (34 mL) (rt, 2.5 h) as described for **13b**. Mp 210–210.5 °C (decomp, EtOH); IR (Nujol) ν_{max} 3321 (br s), 3230 (br s), 3117 (br s) (OH, NH), 1705 (s) (amide-I), 1668 (s) (C═O), 1598 (s) (C═C), 1064 (s) (C–O) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 8.89 (br d, ^4J = 2.0 Hz, 1H, N$_{(1)}$H), 7.18 (br dd, ^3J = 3.6, ^4J = 2.0 Hz, 1H, N$_{(3)}$H), 4.77 (t, ^3J = 5.6 Hz, 1H, OH), 4.11 (dt, ^3J = 5.5, ^3J = 3.6 Hz, 1H, H-4), 3.22 (dd, ^3J = 5.6, ^3J = 5.5 Hz, 2H, OCH$_2$), 2.19 (s, 3H, CH$_3$ in Ac), 2.16 (s, 3H, 6-CH$_3$); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 194.3 (C═O in Ac), 152.7 (C-2), 148.5 (C-6), 107.2 (C-5), 64.2 (CH$_2$OH), 53.0 (C-4), 30.1 (CH$_3$ in Ac), 18.8 (6-CH$_3$). Anal. Calcd for $C_8H_{12}N_2O_3$: C, 52.17; H, 6.57; N, 15.21. Found: C, 52.13; H, 6.51; N, 15.03.

*5-Benzoyl-4-(hydroxymethyl)-6-methyl-1,2,3,4-tetrahydrohydropyrimidin-2-one (**13j**).* Compd **13j** (3.856 g, 90%) was obtained from pyrimidine **11f** (6.103 g, 17.42 mmol) and KOH (1.568 g, 27.95 mmol) in H_2O (15 mL) and EtOH (41 mL) (rt, 2 h) as described for **13g**. Mp 211.5–212.5 °C (decomp, EtOH); IR (Nujol) ν_{max} 3320 (br s), 3253 (br s), 3220 (sh), 3138 (br s) (NH, OH), 3026 (w) (CH$_{arom}$), 1696 (br s) (amide-I), 1658 (s) (C═O). 1627 (s) (C═C), 1598 (m), 1578 (w) (CC$_{arom}$), 1074 (s), 1036 (s) (C–O), 734 (m), 699 (m) (CH$_{arom}$) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 8.93 (br d, ^4J = 1.9 Hz, 1H, N$_{(1)}$H), 7.42–7.58 (m, 5H, ArH), 7.23 (br dd, ^3J = 3.4, ^4J = 1.9 Hz, 1H, N$_{(3)}$H), 4.82 (t, ^3J = 5.5 Hz, 1H, OH), 4.15 (dt, ^3J = 5.3, ^3J = 3.4 Hz, 1H, H-4), 3.29 (dd, ^3J = 5.5, ^3J = 5.3 Hz, 2H, OCH$_2$), 1.61 (s, 3H, CH$_3$). ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 194.6 (C═O), 152.7 (C-2), 146.5 (C-6), 141.3 (C), 131.2 (CH), 128.5 (2CH), 127.9 (2CH), 106.9 (C-5), 64.4 (CH$_2$OH), 54.2 (C-4), 18.4 (CH$_3$). Anal. Calcd for $C_{13}H_{14}N_2O_3$: C, 63.40; H, 5.73; N, 11.38. Found: C, 63.32; H, 5.64; N, 11.34.

*5-Benzoyl-4-(hydroxymethyl)-6-phenyl-1,2,3,4-tetrahydrohydropyrimidin-2-one (**13k**).* Compd **13k** (3.954 g, 91%) was obtained from pyrimidine **11g** (5.813 g, 14.09 mmol) and KOH (1.688 g, 30.09 mmol) in H_2O (10 mL) and EtOH (36 mL) (rt, 2.5 h) as described for **13g**. Mp 225–225.5 °C (decomp, EtOH); IR (Nujol) ν_{max} 3568 (s), 3298 (s), 3199 (br m), 3080 (br s) (NH, OH), 3028 (w) (CH$_{arom}$), 1691 (vs) (amide-I), 1619 (s) (C═O and C═C), 1599 (w), 1577 (m), 1492 (w) (CC$_{arom}$), 1027 (s) (C–O), 739 (m), 722 (m), 696 (m) (CH$_{arom}$) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 9.13 (br d, ^4J = 2.0 Hz, 1H, N$_{(1)}$H), 7.33 (br dd, ^3J = 3.3, ^4J = 2.0 Hz, 1H, N$_{(3)}$H, signals partly overlap with signals of aromatic protons), 7.28–7.34 (m, 2H, ArH, signals partly overlap with signal of the N$_{(3)}$H proton), 6.99−7.18 (m, 8H, ArH), 4.94 (t, ^3J = 5.6 Hz, 1H, OH), 4.21 (ddd, ^3J = 6.0, ^3J = 4.1, ^3J = 3.3 Hz, 1H, H-4), 3.55 (ddd, ^2J = 10.7, ^3J = 5.6, ^3J = 4.1 Hz, 1H, H_A in OCH_2), 3.52 (ddd, ^2J = 10.7, ^3J = 6.0, ^3J = 5.6 Hz, 1H, H_B in OCH_2); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 195.2 (C=O in Bz), 153.0 (C-2), 148.8 (C-6), 139.7 (C), 133.7 (C), 130.6 (CH), 129.5 (2CH), 129.4 (CH), 128.6 (2CH), 127.6 (2CH), 127.3 (2CH), 106.8 (C-5), 64.2 (CH_2OH), 55.1 (C-4). Anal. Calcd for $C_{18}H_{16}N_2O_3$: C, 70.12; H, 5.23; N, 9.09. Found: C, 69.80; H, 5.17; N, 8.96.

*Methyl 4-(Mesyloxymethyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**15a**).* To a cooled in an ice bath, stirred suspension of pyrimidine **13a** (0.896 g, 4.48 mmol) and DMAP (0.783 g, 6.41 mmol) in CH_2Cl_2 (10 mL) was added a solution of MsCl (0.626 g, 5.47 mmol) in CH_2Cl_2 (10 mL) over 2 min. The obtained suspension was stirred at room temperature for 1 h, and the solvent was removed under vacuum. The residue was dried in vacuum until the stable foam was formed. The foam was dissolved in ice-cold H_2O (2 mL), after 2 min the solid precipitated from the solution. The resulting suspension was cooled (0 °C). The precipitate was filtered on cooled (−10 °C) filter, rapidly washed with ice-cold H_2O (4 × 2 mL), petroleum ether, cold diethyl ether (3 × 2 mL), and dried to give **15a** (1.006 g, 81%). Mp 128.5−129 °C (decomp, EtOH); IR (Nujol) ν_{max} 3248 (br s), 3121 (br m), 3112 (br m) (NH), 1719 (s) (C=O and amide-I), 1661 (s) (C=C), 1335 (s) (SO_2), 1229 (s) (C−O), 1180 (s) (SO_2), 1102 (m) (C−O) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 9.20 (br d, ^4J = 2.1 Hz, 1H, $N_{(1)}H$), 7.49 (br dd, ^3J = 3.6, ^4J = 2.1 Hz, 1H, $N_{(3)}H$), 4.35 (dddq, ^3J = 5.2, ^3J = 3.7, ^3J = 3.6, ^5J = 0.6 Hz, 1H, H-4), 4.05 (dd, ^2J = 10.2, ^3J = 5.2 Hz, 1H, H_A in OCH_2), 4.03 (dd, ^2J = 10.2, ^3J = 3.7 Hz, 1H, H_B in OCH_2), 3.63 (s, 3H, OCH_3), 3.13 (s, 3H, CH_3SO_3), 2.20 (d, ^5J = 0.6 Hz, 3H, 6-CH_3); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 165.4 (C=O in COOMe), 152.1 (C-2), 151.5 (C-6), 93.5 (C-5), 71.9 (OCH_2), 51.0 (OCH_3), 50.1 (C-4), 36.7 (CH_3SO_3), 18.0 (6-CH_3). Anal. Calcd for $C_9H_{14}N_2O_6S$: C, 38.85; H, 5.07; N, 10.07. Found: C, 39.04; H, 5.25; N, 10.07.

*Methyl 4-(Mesyloxymethyl)-2-oxo-6-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**15b**).* Compd **15b** (4.097 g, 93%) was obtained from pyrimidine **13b** (3.411 g, 13.01 mmol), DMAP (2.223 g, 18.19 mmol) and MsCl (1.790 g, 15.62 mmol) in CH_2Cl_2 (50 mL) (rt, 1.5 h) as described for **15a**. Mp 152.5−153 °C (decomp, EtOAc/MeCN, 16:7 v/v); IR (Nujol) ν_{max} 3342 (m), 3230 (br m), 3121 (sh), 3104 (br m) (NH), 3025 (w) (CH_{arom}), 1713 (s) (C=O), 1687 (s) (amide-I), 1656 (w) (C=C), 1320 (s) (SO_2), 1259 (m) (C−O), 1163 (s) (SO_2), 1098 (s) (C−O), 769 (s), 704 (m) (CH_{arom}) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 9.33 (br d, ^4J = 2.0 Hz, 1H, $N_{(1)}H$), 7.60 (br dd, ^3J = 3.5, ^4J = 2.0 Hz, 1H, $N_{(3)}H$), 7.25−7.45 (m, 5H, ArH), 4.44 (ddd, ^3J = 5.4, ^3J = 3.5, ^3J = 3.0 Hz, 1H, H-4), 4.26 (dd, ^2J = 10.3, ^3J = 5.4 Hz, 1H, H_A in OCH_2), 4.17 (dd, ^2J = 10.3, ^3J = 3.0 Hz, 1H, H_B in OCH_2), 3.34 (s, 3H, OCH_3), 3.19 (s, 3H, CH_3SO_3); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 165.0 (C=O in COOMe), 152.0 (C-2), 151.8 (C-6), 134.6 (C), 129.1 (CH), 128.3 (2CH), 127.6 (2CH), 94.4 (C-5), 72.0 (OCH_2), 50.7 (OCH_3), 50.6 (C-4), 36.9 (CH_3SO_3). Anal. Calcd for $C_{14}H_{16}N_2O_6S$: C, 49.41; H, 4.74; N, 8.23. Found: C, 49.29; H, 4.76; N, 8.28.

*Methyl 6-Butyl-4-(mesyloxymethyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**15c**).* Compd **15c** (3.038 g, 80%) was obtained from pyrimidine **13c** (2.871 g, 11.85 mmol), DMAP (2.029 g, 16.61 mmol) and MsCl (1.635 g, 14.27 mmol) in CH_2Cl_2 (50 mL) (rt, 1.5 h) as described for **15a**. Mp 123−124 °C (decomp, EtOH); IR (Nujol) ν 3376 (sh), 3367 (s), 3217 (br m), 3103 (br s), 3021 (w), 3007 (w) (NH), 1708 (s) (C=O), 1697 (s) (amide-I), 1631 (s) (C=C), 1353 (s) (SO_2), 1227 (s) (C−O), 1174 (s) (SO_2), 1106 (s) (C−O) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 9.24 (br d, ^4J = 2.0 Hz, 1H, $N_{(1)}H$), 7.54 (br dd, ^3J = 3.5, ^4J = 2.0 Hz, 1H, $N_{(3)}H$), 4.34 (ddd, ^3J = 5.0, ^3J = 3.9, ^3J = 3.5 Hz, 1H, H-4), 4.03 (dd, ^2J = 10.2, ^3J = 5.0 Hz, 1H, H_A in OCH_2), 4.01 (dd, ^2J = 10.2, ^3J = 3.9 Hz, 1H, H_B in OCH_2), 3.62 (s, 3H, OCH_3), 3.14 (s, 3H, CH_3SO_3), 2.50−2.68 (m, 2H, $\mathit{CH_2}CH_2CH_2CH_3$), 1.22−1.53 (m, 4H, $CH_2\mathit{CH_2CH_2}CH_3$), 0.87 (t, ^3J = 7.2 Hz, 3H, CH_3 in Bu); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 165.1 (C=O in COOMe), 156.0 (C-6), 152.4 (C-2), 93.0 (C-5), 71.9 (OCH_2), 51.1 (OCH_3), 50.1 (C-4), 36.7 (CH_3SO_3), 30.4 ($CH_2\mathit{CH_2}CH_2CH_3$), 30.3 ($\mathit{CH_2}CH_2CH_2CH_3$), 22.0 ($CH_2CH_2\mathit{CH_2}CH_3$), 13.8 ($CH_3$ in Bu). Anal. Calcd for $C_{12}H_{20}N_2O_6S$: C, 44.99; H, 6.29; N, 8.74. Found: C, 45.11; H, 6.44; N, 8.66.

*Dimethyl 6-(Mesyloxymethyl)-2-oxo-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylate (**15d**).* To a cooled in an ice bath, stirred suspension of pyrimidine **13d** (1.637 g, 6.70 mmol) and DMAP (1.663 g, 13.61 mmol) in CH_2Cl_2 (8 mL) was added a solution of MsCl (1.161 g, 10.13 mmol) in CH_2Cl_2 (6 mL) over 2 min. The obtained suspension was stirred for 5 min, then at room temperature for 1 h 25 min, and the solvent was removed under vacuum. The residue was dissolved in ice-cold water (3 mL), and left upon cooling (0 °C) for 1 h. The obtained precipitate was filtered on a cold (−10 °C) filter, rapidly washed with ice-cold H_2O (3 × 2 mL), petroleum ether, cold diethyl ether (2 × 5 mL), and dried to give **15d** (1.391 g, 64%) as a pale brown solid. The analytically pure sample (0.139 g, white solid) was obtained from crude **15d** (0.303 g) by column chromatography on silica gel 60 (10 g) eluting with MeOH/$CHCl_3$ (1:100) followed by crystallization from MeCN (2.2 mL). Mp 143−145 °C (decomp, MeCN); IR (Nujol) ν_{max} 3321 (s), 3220 (m), 3083 (br m), 3033 (w), 3011 (w) (NH), 1749 (s) (C=O in 4-COOMe), 1718 (s) (C=O in 5-COOMe), 1702 (s) (amide-I), 1650 (s) (C=C), 1348 (s) (SO_2), 1245 (s), 1220 (s) (C−O), 1172 (s) (SO_2), 1116 (s), 1092 (s) (C−O) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 9.89 (br d, ^4J = 2.0 Hz, 1H, $N_{(3)}H$), 7.64 (br dd, ^3J = 3.1, ^4J = 2.0 Hz, 1H, $N_{(1)}H$), 4.42 (ddd, ^3J = 4.5, ^3J = 3.1, ^3J = 3.0 Hz, 1H, H-6), 4.16 (dd, ^2J = 10.5, ^3J = 4.5 Hz, 1H, H_A in OCH_2), 4.11 (dd, ^2J = 10.5, ^3J = 3.0 Hz, 1H, H_B in OCH_2), 3.76 (s, 3H, OCH_3), 3.63 (s, 3H, OCH_3), 3.15 (s, 3H, CH_3SO_3); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 163.7 (C=O in COOMe), 162.8 (C=O in COOMe), 151.4 (C-2), 143.5 (C-4), 94.5 (C-5), 71.7 (OCH_2), 52.9 (OCH_3), 51.8 (OCH_3), 49.8 (C-6), 36.7 (CH_3SO_3). Anal. Calcd for $C_{10}H_{14}N_2O_8S$: C, 37.27; H, 4.38; N, 8.69. Found: C, 37.35; H, 4.60; N, 8.76.

*Ethyl 4-(Mesyloxymethyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**15e**).* Compd **15e** (0.808 g, 88%) was obtained from pyrimidine **13e** (0.676 g, 3.16 mmol), DMAP (0.547 g, 4.48 mmol), and MsCl (0.442 g, 3.86 mmol) in CH_2Cl_2 (20 mL) (rt, 1 h) as described for **15a**. Mp 132.5−133 °C (decomp, EtOH); IR (Nujol) ν_{max} 3246 (br s), 3114 (br s), 3027 (w), 3015 (w) (NH), 1712 (vs) (C=O and amide-I), 1661 (s) (C=C), 1338 (s) (SO_2), 1227 (s) (C−O), 1181 (s) (SO_2), 1104 (s) (C−O) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 9.18 (br d, ^4J = 2.0 Hz, 1H, $N_{(1)}H$), 7.50 (br dd, ^3J = 3.6, ^4J = 2.0 Hz, 1H, $N_{(3)}H$), 4.36 (dddq, ^3J = 5.0, ^3J = 4.0, ^3J = 3.6, ^5J = 0.5 Hz, 1H, H-4), 4.01−4.16 (m, 2H, CH_2 in OEt), 4.05 (dd, ^2J = 10.2, ^3J = 5.0 Hz, 1H, H_A in CH_2OMs), 4.03 (dd, ^2J = 10.2, ^3J = 4.0 Hz, 1H, H_B in CH_2OMs), 3.13 (s, 3H, CH_3SO_3), 2.20 (d, ^5J = 0.5 Hz, 3H, 6-CH_3), 1.20 (t, ^3J = 7.1 Hz, 3H, CH_3 in OEt); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 164.8 (C=O in COOEt), 152.0 (C-2), 151.2 (C-6), 93.6 (C-5), 71.8 (CH_2OMs), 59.3 (CH_2 in OEt), 50.1 (C-4), 36.7 (CH_3SO_3), 17.8 (6-CH_3), 14.1 (CH_3 in OEt). Anal. Calcd for $C_{10}H_{16}N_2O_6S$: C, 41.09; H, 5.52; N, 9.58. Found: C, 41.41; H, 5.79; N, 9.64.

*Ethyl 4-(Mesyloxymethyl)-2-oxo-6-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**15f**).* Compd **15f** (0.748 g, 66%) was obtained from pyrimidine **13f** (0.891 g, 3.22 mmol), DMAP (0.555 g, 4.54 mmol), and MsCl (0.465 g, 4.06 mmol) in CH_2Cl_2 (17 mL) (rt, 1 h 20 min) as described for **15a** followed by crystallization from EtOAc (24 mL). Mp 146−146.5 °C (decomp, EtOAc); IR (Nujol) ν_{max} 3421 (s), 3214 (br m), 3204 (br m), 3108 (br m) (NH), 3024 (w), 3008 (w) (CH_{arom}), 1700 (vs) (C=O), 1686 (vs) (amide-I), 1655 (m) (C=C), 1599 (w) (CC_{arom}), 1352 (s) (SO_2), 1243 (s) (C−O), 1180 (s) (SO_2), 1098 (s) (C−O), 762 (m), 697 (m) (CH_{arom}) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 9.35 (br d, ^4J = 2.0 Hz, 1H, $N_{(1)}H$), 7.62 (br dd, ^3J = 3.5, ^4J = 2.0 Hz, 1H, $N_{(3)}H$), 7.25−7.45 (m, 5H, ArH), 4.43 (ddd, ^3J = 5.4, ^3J = 3.5, ^3J = 2.9 Hz, 1H, H-4), 4.26 (dd, ^2J = 10.3, ^3J = 5.4 Hz, 1H, H_A in CH_2OMs), 4.16 (dd, ^2J = 10.3, ^3J = 2.9 Hz, 1H, H_B in CH_2OMs), 3.70−3.85 (m, 2H, CH_2 in OEt), 3.20 (s, 3H, CH_3SO_3), 0.78 (t, ^3J = 7.1 Hz, 3H, CH_3 in OEt); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 164.9 (C=O in COOEt), 152.1 (C-2), 151.6 (C-6), 134.9 (C), 129.0 (CH), 128.4 (2CH), 127.7 (2CH), 94.6 (C-5), 72.1 (CH_2OMs), 59.2 (CH_2 in OEt), 50.7 (C-4), 36.9 (CH_3SO_3), 13.5

(CH_3 in OEt). Anal. Calcd for $C_{15}H_{18}N_2O_6S$: C, 50.84; H, 5.12; N, 7.91. Found: C, 50.95; H, 5.37; N, 8.03.

Ethyl 6-Butyl-4-(mesyloxymethyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (15g). Compd **15g** (2.906 g, 82%) was obtained from pyrimidine **13g** (2.723 g, 10.62 mmol), DMAP (1.807 g, 14.79 mmol), and MsCl (1.459 g, 12.74 mmol) in CH_2Cl_2 (50 mL) (rt, 1 h 10 min) as described for **15a**. Mp 94.5−96 °C (EtOAc/petroleum ether, 5:11); IR (Nujol) ν_{max} 3383 (w), 3331 (s), 3228 (br m), 3167 (w), 3121 (sh), 3103 (br m), 3037 (m) (NH), 1719 (vs) (C=O), 1705 (vs) (amide-I), 1645 (s) (C=C), 1318 (s) (SO_2), 1227 (s) (C−O), 1170 (s) (SO_2), 1083 (s) (C−O) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6) δ 9.18 (br d, ^4J = 2.0 Hz, 1H, $N_{(1)}H$), 7.50 (br dd, ^3J = 3.6, ^4J = 2.0 Hz, 1H, $N_{(3)}H$), 4.35 (dt, ^3J = 4.5, ^3J = 3.6 Hz, 1H, H-4), 4.01−4.16 (m, 2H, CH_2 in OEt), 4.03 (d, ^3J = 4.5 Hz, 2H, CH_2OMs), 3.13 (s, 3H, CH_3SO_3), 2.50−2.69 (m, 2H, $CH_2CH_2CH_2CH_3$), 1.25−1.52 (m, 4H, $CH_2CH_2CH_2CH_3$), 1.20 (t, ^3J = 7.1 Hz, 3H, CH_3 in OEt), 0.87 (t, ^3J = 7.2 Hz, 3H, CH_3 in Bu); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 164.6 (C=O in COOEt), 155.5 (C-6), 152.3 (C-2), 93.2 (C-5), 71.7 (CH_2OMs), 59.4 (CH_2 in OEt), 50.1 (C-4), 36.7 (CH_3SO_3), 30.4 ($CH_2CH_2CH_2CH_3$), 30.3 ($CH_2CH_2CH_2CH_3$), 22.0 ($CH_2CH_2CH_2CH_3$), 14.1 (CH_3 in OEt), 13.7 (CH_3 in Bu). Anal. Calcd for $C_{13}H_{22}N_2O_6S$: C, 46.70; H, 6.63; N, 8.38. Found: C, 46.90; H, 6.56; N, 8.40.

Diethyl 6-(Mesyloxymethyl)-2-oxo-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylate (15h). To a cooled in an ice bath, stirred suspension of pyrimidine **13h** (0.686 g, 2.52 mmol) and DMAP (0.434 g, 3.55 mmol) in CH_2Cl_2 (8 mL) was added a solution of MsCl (0.356 g, 3.11 mmol) in CH_2Cl_2 (7 mL) over 2 min. The reaction mixture was stirred for 5 min, then at room temperature for 55 min, and the solvent was removed under vacuum. The residue was dissolved in $CHCl_3$ (40 mL), washed with H_2O (4 × 3 mL), brine (2 × 3 mL), and the solvent was removed under vacuum. The residue was purified using column chromatography on silica gel 60 (20 g) eluting with $CHCl_3$/MeOH (from 100:0 to 100:1) to give **15h** (0.587 g, 67%) as a white amorphous solid. Mp 38−40 °C; IR (Nujol) ν_{max} 3315 (sh), 3240 (br s), 3104 (br s) (NH), 1746 (s) (C=O in 4-COOEt), 1721 (s) (C=O in 5-COOEt), 1710 (s), 1692 (s) (amide-I), 1653 (s) (C=C), 1342 (s) (SO_2), 1214 (s) (C−O), 1171 (s) (SO_2), 1104 (s) (C−O) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6) δ 9.88 (br d, ^4J = 2.0 Hz, 1H, $N_{(3)}H$), 7.64 (br dd, ^3J = 3.2, ^4J = 2.0 Hz, 1H, $N_{(1)}H$), 4.42 (ddd, ^3J = 4.6, ^3J = 3.2, ^3J = 3.1 Hz, 1H, H-6), 4.21 (q, ^3J = 7.1 Hz, 2H, CH_2 in 4-COOEt), 4.16 (dd, ^2J = 10.5, ^3J = 4.6 Hz, 1H, H_A in CH_2OMs, signals partly overlap with signals of the CH_2 group in 5-COOEt), 4.11 (dd, ^2J = 10.5, ^3J = 3.1 Hz, 1H, H_B in CH_2OMs, signals partly overlap with signals of the CH_2 group in 5-COOEt), 4.01−4.16 (m, 2H, CH_2 in 5-COOEt, signals partly overlap with signals of CH_2 group in CH_2OMs), 3.15 (s, 3H, CH_3SO_3), 1.26 (t, ^3J = 7.1 Hz, 3H, CH_3 in OEt), 1.17 (t, ^3J = 7.1 Hz, 3H, CH_3 in OEt); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 163.2 (C=O in COOEt), 162.3 (C=O in COOEt), 151.5 (C-2), 143.4 (C-4), 94.4 (C-5), 71.6 (CH_2OMs), 61.9 (CH_2 in OEt), 60.4 (CH_2 in OEt), 49.9 (C-6), 36.7 (CH_3SO_3), 13.9 (CH_3 in OEt), 13.6 (CH_3 in OEt). Anal. Calcd for $C_{12}H_{18}N_2O_8S\cdot0.1H_2O$: C, 40.93; H, 5.21; N, 7.95. Found: C, 40.72; H, 5.12; N, 7.76.[29]

5-Acetyl-4-(mesyloxymethyl)-6-methyl-1,2,3,4-tetrahydropyrimidine-2-one (15i). Compd **15i** (1.348 g, 70%) as a light yellow solid was obtained from pyrimidine **13i** (1.353 g, 7.35 mmol), DMAP (1.778 g, 14.56 mmol), and MsCl (1.272 g, 11.11 mmol) in CH_2Cl_2 (25 mL) (rt, 1 h) as described for **15a**. The analytically pure sample (white solid) was obtained by crystallization from EtOAc. Mp 103.5−105 °C (decomp, EtOAc); IR (Nujol) ν_{max} 3345 (s), 3215 (m), 3096 (br s), 3023 (w), 3005 (w) (NH), 1703 (vs) (amide-I), 1625 (vs) (C=O and C=C), 1353 (m), 1168 (s) (SO_2) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6) δ 9.22 (br d, ^4J = 2.0 Hz, 1H, $N_{(1)}H$), 7.61 (br dd, ^3J = 3.7, ^4J = 2.0 Hz, 1H, $N_{(3)}H$), 4.42 (dt, ^3J = 4.8, ^3J = 3.7 Hz, 1H, H-4), 3.96 (d, ^3J = 4.8 Hz, 2H, OCH_2), 3.14 (s, 3H, CH_3SO_3), 2.25 (s, 3H, CH_3 in Ac), 2.23 (s, 3H, 6-CH_3); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 193.8 (C=O in Ac), 152.2 (C-2), 150.5 (C-6), 105.3 (C-5), 71.6 (OCH_2), 50.0 (C-4), 36.7 (CH_3SO_3), 30.5 (CH_3 in Ac), 19.2 (6-CH_3). Anal. Calcd for $C_9H_{14}N_2O_5S$: C, 41.21; H, 5.38; N, 10.68. Found: C, 41.23; H, 5.46; N, 10.48.

5-Benzoyl-4-(mesyloxymethyl)-6-methyl-1,2,3,4-tetrahydropyrimidin-2-one (15j). Compd **15j** (3.092 g, 92%) as a light yellow solid was obtained from pyrimidine **13j** (2.547 g, 10.34 mmol), DMAP (2.521 g, 20.64 mmol), and MsCl (1.788 g, 15.61 mmol) in CH_2Cl_2 (50 mL) (rt, 1 h) as described for **15a**. Mp 131−132 °C (acetone); IR (Nujol) ν_{max} 3317 (s), 3212 (br s), 3124 (br s) (NH), 1726 (s) (amide-I), 1613 (s) (C=O and C=C), 1577 (w), 1488 (w) (CC_{arom}), 1322 (s), 1167 (s) (SO_2), 750 (m), 701 (m) (CH_{arom}) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6) δ 9.24 (br d, ^4J = 2.1 Hz, 1H, $N_{(1)}H$), 7.61 (br dd, ^3J = 3.5, ^4J = 2.1 Hz, 1H, $N_{(3)}H$), 7.43−7.58 (m, 5H, ArH), 4.46 (dt, ^3J = 4.8, ^3J = 3.5 Hz, 1H, H-4), 4.10 (d, ^3J = 4.8 Hz, 2H, OCH_2), 3.14 (s, 3H, CH_3SO_3), 1.60 (s, 3H, 6-CH_3); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 193.9 (C=O in Bz), 152.0 (C-2), 149.2 (C-6), 141.1 (C), 131.3 (CH), 128.5 (2CH), 127.7 (2CH), 104.3 (C-5), 71.6 (OCH_2), 51.0 (C-4), 36.7 (CH_3SO_3), 18.8 (6-CH_3). Anal. Calcd for $C_{14}H_{16}N_2O_5S$: C, 51.84; H, 4.97; N, 8.64. Found: C, 51.73; H, 4.95; N, 8.92.

5-Benzoyl-4-(mesyloxymethyl)-6-phenyl-1,2,3,4-tetrahydropyrimidin-2-one (15k). To a cooled in an ice bath, stirred suspension of pyrimidine **13k** (2.046 g, 6.64 mmol) and DMAP (1.613 g, 13.20 mmol) in CH_2Cl_2 (25 mL) was added a solution of MsCl (1.153 g, 10.07 mmol) in CH_2Cl_2 (25 mL) over 2 min. The obtained suspension was stirred for 5 min, the ice bath was removed and stirring was continued at room temperature for 1 h 25 min. The resulting solution was washed with H_2O (4 × 25 mL), 1% aqueous solution of HCl (3 × 10 mL), H_2O (2 × 25 mL), brine (2 × 25 mL), and the solvent was removed under vacuum. The residue was triturated with H_2O (10 mL) and petroleum ether (10 mL) until crystallization was completed. The obtained suspension was cooled (0 °C), the precipitate was filtered, washed with ice-cold H_2O and petroleum ether, and dried to give **15k** (2.455 g, 96%) as a light yellow solid. Mp 140.5−141.5 °C (decomp, EtOH); IR (Nujol) ν_{max} 3232 (br s), 3178 (sh), 3123 (br s) (NH), 1711 (vs) (amide-I), 1601 (s), 1592 (s) (C=O and C=C), 1570 (m), 1495 (w) (CC_{arom}), 1354 (s), 1174 (s) (SO_2), 732 (m), 698 (m) (CH_{arom}) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6) δ 9.51 (br d, ^4J = 2.0 Hz, 1H, $N_{(1)}H$), 7.75 (br dd, ^3J = 3.5, ^4J = 2.0 Hz, 1H, $N_{(3)}H$), 6.98−7.31 (m, 10H, ArH), 4.50 (ddd, ^3J = 5.6, ^3J = 3.5, ^3J = 3.4 Hz, 1H, H-4), 4.37 (dd, ^2J = 10.1, ^3J = 5.6 Hz, 1H, H_A in OCH_2), 4.33 (dd, ^2J = 10.1, ^3J = 3.4 Hz, 1H, H_B in OCH_2), 3.20 (s, 3H, CH_3SO_3); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 194.5 (C=O in Bz), 152.3 (C-2), 151.4 (C-6), 139.4 (C), 133.2 (C), 130.6 (CH), 129.9 (CH), 129.8 (2CH), 128.5 (2CH), 127.6 (2CH), 127.3 (2CH), 103.6 (C-5), 72.1 (OCH_2), 51.8 (C-4), 36.8 (CH_3SO_3). Anal. Calcd for $C_{19}H_{18}N_2O_5S$: C, 59.06; H, 4.70; N, 7.25. Found: C, 59.12; H, 4.72; N, 7.33.

Methyl 7-[Di(ethoxycarbonyl)methyl]-2-oxo-4-phenyl-2,3,6,7-tetrahydro-1H-1,3-diazepine-5-carboxylate (17a). To a cooled in an ice bath, stirred suspension of NaH (0.021 g, 0.87 mmol) in dry MeCN (1 mL) was added a solution of diethyl malonate (**16**) (0.143 g, 0.89 mmol) in MeCN (2 mL) over 2 min. The resulting mixture was stirred for 6 min, then pyrimidine **15b** (0.267 g, 0.79 mmol) and MeCN (2 mL) were added. The obtained suspension was stirred at room temperature for 1 h 40 min, and the solvent was removed under vacuum. The oily residue was triturated with petroleum ether (3 mL), saturated aqueous $NaHCO_3$ (1 mL) and H_2O (1 mL) until crystallization was completed. The obtained suspension was cooled (0 °C), the precipitate was filtered, washed with ice-cold H_2O, petroleum ether, and dried to give **17a** (0.280 g, 88%). Mp 128.5−129.5 °C (EtOH); IR (Nujol) ν_{max} 3229 (br s), 3085 (br s) (NH), 1730 (vs) (C=O), 1704 (m), 1685 (s) (amide-I), 1644 (s) (C=C), 1494 (w) (CC_{arom}), 1302 (s), 1255 (s), 1150 (s), 1035 (s) (C−O), 768 (s), 699 (s) (CH_{arom}) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6) δ 8.38 (br d, ^4J = 2.0 Hz, 1H, $N_{(3)}H$), 7.33−7.42 (m, 3H, ArH), 7.19−7.26 (m, 2H, ArH), 7.19 (br dd, ^3J = 5.2, ^4J = 2.0 Hz, 1H, $N_{(1)}H$, signals partly overlap with signals of aromatic protons), 4.02−4.23 (m, 4H, two OCH_2), 4.01 (dddd, ^3J = 9.2, ^3J = 6.5, ^3J = 5.2, ^3J = 2.5 Hz, 1H, H-7), 3.58 [d, ^3J = 9.2 Hz, 1H, $CH(COOEt)_2$], 3.23 (s, 3H, OCH_3), 2.92 (dd, ^2J = 15.0, ^3J = 6.5 Hz, 1H, H_A-6), 2.74 (dd, ^2J = 15.0, ^3J = 2.5 Hz, 1H, H_B-6), 1.20 (t, ^3J = 7.1 Hz, 3H, CH_3 in OEt), 1.16 (t, ^3J = 7.1 Hz, 3H, CH_3 in OEt); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 168.6 (C═O in COOMe), 166.7 (C═O in COOEt), 166.5 (C═O in COOEt), 154.7 (C-2), 147.2 (C-4), 137.3 (C), 129.0 (CH), 128.5 (2CH), 127.8 (2CH), 107.6 (C-5), 61.4 (OCH$_2$), 61.3 (OCH$_2$), 56.3 [CH(COOEt)$_2$], 52.8 (C-7), 50.9 (OCH$_3$), 31.3 (C-6), 13.8 (CH$_3$ in OEt), 13.7 (CH$_3$ in OEt). Anal. Calcd for $C_{20}H_{24}N_2O_7$: C, 59.40; H, 5.98; N, 6.93. Found: C, 59.47; H, 5.94; N, 6.82.

*Methyl 4-Butyl-7-[di(ethoxycarbonyl)methyl]-2-oxo-2,3,6,7-tetrahydro-1H-1,3-diazepine-5-carboxylate (**17b**).* Compd **17b** (0.727 g, 91%) was obtained from pyrimidine **15c** (0.667 g, 2.08 mmol), NaH (0.057 g, 2.38 mmol), and diethyl malonate (**16**) (0.398 g, 2.49 mmol) in dry MeCN (10 mL) (rt, 2 h) as described for **17a**. Mp 127.5−128.5 °C (EtOH); IR (Nujol) ν_{max} 3228 (br s), 3100 (br s) (NH), 1736 (vs) (C═O), 1714 (s), 1694 (s) (amide-I), 1634 (s) (C═C), 1277 (s), 1240 (s), 1159 (s), 1092 (m), 1033 (m) (C−O) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 8.39 (br d, ^4J = 1.9 Hz, 1H, N$_{(3)}$H), 7.21 (br dd, ^3J = 6.0, ^4J = 1.9 Hz, 1H, N$_{(1)}$H), 4.01−4.20 (m, 4H, two OCH$_2$), 3.90 (dddd, ^3J = 9.9, ^3J = 6.2, ^3J = 6.0, ^3J = 2.1 Hz, 1H, H-7), 3.56 (s, 3H, OCH$_3$), 3.38 [d, ^3J = 9.9 Hz, 1H, *C*H(COOEt)$_2$], 2.93 (dd, ^2J = 15.3, ^3J = 6.2 Hz, 1H, H$_A$-6), 2.70−2.79 (m, 1H, H$_A$ in *C*H$_2$CH$_2$CH$_2$CH$_3$), 2.49 (dd, ^2J = 15.3, ^3J = 2.1 Hz, 1H, H$_B$-6), 2.34−2.43 (m, 1H, H$_B$ in *C*H$_2$CH$_2$CH$_2$CH$_3$), 1.25−1.55 (m, 4H, CH$_2$*C*H$_2$*C*H$_2$CH$_3$), 1.17 (t, ^3J = 7.1 Hz, 3H, CH$_3$ in OEt), 1.16 (t, ^3J = 7.1 Hz, 3H, CH$_3$ in OEt), 0.89 (t, J = 7.2 Hz, 3H, CH$_3$ in Bu); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 167.5 (C═O in COOMe), 166.7 (C═O in COOEt), 166.3 (C═O in COOEt), 155.0 (C-2), 152.0 (C-4), 104.1 (C-5), 61.2 (OCH$_2$), 61.1 (OCH$_2$), 56.0 [(CH(COOEt)$_2$], 51.7 (C-7), 51.0 (OCH$_3$), 32.4 (C-6), 30.9 (*C*H$_2$CH$_2$CH$_2$CH$_3$), 30.6 (CH$_2$*C*H$_2$CH$_2$CH$_3$), 21.8 (CH$_2$CH$_2$*C*H$_2$CH$_3$), 13.72 (CH$_3$ in Bu), 13.71 (CH$_3$ in OEt), 13.68 (CH$_3$ in OEt). Anal. Calcd for $C_{18}H_{28}N_2O_7$: C, 56.24; H, 7.34; N, 7.29. Found: C, 56.28; H, 7.42; N, 7.24.

*Dimethyl 7-[Di(ethoxycarbonyl)methyl]-2-oxo-2,3,6,7-tetrahydro-1H-1,3-diazepine-4,5-dicarboxylate (**17c**).* Compd **17c** (0.716 g, 86%) as a slightly creamy solid was obtained from pyrimidine **15d** (0.695 g, 2.16 mmol), NaH (0.061 g, 2.53 mmol), and diethyl malonate (**16**) (0.415 g, 2.59 mmol) in dry MeCN (8 mL) (rt, 1 h) as described for **17a**. The analytically pure sample (white solid) was obtained by crystallization from EtOH. Mp 223−224.5 °C (EtOH); IR (Nujol) ν_{max} 3268 (br m), 3244 (br m), 3107 (br m) (NH), 1758 (s), 1753 (sh), 1730 (vs) (C═O), 1717 (s), 1702 (s) (amide-I), 1639 (s) (C═C), 1535 (m) (amide-II), 1295 (s), 1268 (s), 1237 (vs), 1157 (s) (C−O) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 9.26 (br d, ^4J = 1.9 Hz, 1H, N$_{(3)}$H), 7.77 (br dd, ^3J = 6.5, ^4J = 1.9 Hz, 1H, N$_{(1)}$H), 4.03−4.21 (m, 4H, two OCH$_2$), 3.91 (dddd, ^3J = 10.4, ^3J = 6.5, ^3J = 5.9, ^3J = 2.5 Hz, 1H, H-7), 3.71 (s, 3H, OCH$_3$), 3.57 (s, 3H, OCH$_3$), 3.47 [d, ^3J = 10.4 Hz, 1H, *C*H(COOEt)$_2$], 2.84 (dd, ^2J = 16.4, ^3J = 5.9 Hz, 1H, H$_A$-6), 2.56 (dd, ^2J = 16.4, ^3J = 2.5 Hz, 1H, H$_B$-6), 1.18 (t, ^3J = 7.1 Hz, 3H, CH$_3$ in OEt), 1.15 (t, ^3J = 7.1 Hz, 3H, CH$_3$ in OEt); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 166.52 (C═O in COOMe), 166.51 (C═O in COOEt), 166.3 (C═O in COOEt), 164.6 (C═O in COOMe), 154.8 (C-2), 140.3 (C-4), 103.2 (C-5), 61.51 (OCH$_2$), 61.50 (OCH$_2$), 54.9 [CH(COOEt)$_2$], 52.6 (OCH$_3$), 51.9 (OCH$_3$), 49.0 (C-7), 30.7 (C-6), 13.8 (CH$_3$ in OEt), 13.7 (CH$_3$ in OEt). Anal. Calcd for $C_{16}H_{22}N_2O_9$: C, 49.74; H, 5.74; N, 7.25. Found: C, 49.80; H, 5.73; N, 7.07.

*Ethyl 7-[Di(ethoxycarbonyl)methyl]-2-oxo-4-phenyl-2,3,6,7-tetrahydro-1H-1,3-diazepine-5-carboxylate (**17d**).* Compd **17d** (0.424 g, 90%) was obtained from pyrimidine **15f** (0.401 g, 1.13 mmol), NaH (0.030 g, 1.25 mmol), and diethyl malonate (**16**) (0.210 g, 1.31 mmol) in dry MeCN (5.5 mL) (rt, 1 h) as described for **17a**. Mp 125−126 °C (EtOH); IR (Nujol) ν_{max} 3268 (m), 3231 (br m), 3093 (m), 3056 (m) (NH), 1737 (vs) (C═O), 1715 (m), 1677 (vs) (amide-I), 1628 (s) (C═C), 1600 (w), 1494 (w) (CC$_{arom}$), 1293 (s), 1242 (s), 1150 (s) (C−O), 764 (m), 700 (m) (CH$_{arom}$) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 8.42 (br d, ^4J = 2.0 Hz, 1H, N$_{(3)}$H), 7.33−7.43 (m, 3H, ArH), 7.26 (br dd, ^3J = 5.3, ^4J = 2.0 Hz, 1H, N$_{(1)}$H), 7.19−7.24 (m, 2H, ArH), 4.01−4.22 [m, 4H, two OCH$_2$ in CH(COOEt)$_2$], 4.00 (dddd, ^3J = 9.3, ^3J = 6.5, ^3J = 5.3, ^3J = 2.5 Hz, 1H, H-7), 3.67 (q, ^3J = 7.1 Hz, 2H, OCH$_2$ in 5-COOEt), 3.58 [d, ^3J = 9.3 Hz, 1H, *C*H(COOEt)$_2$], 2.92 (dd, ^2J = 15.0, ^3J = 6.5 Hz, 1H, H$_A$-6), 2.72 (dd, ^2J = 15.0, ^3J = 2.5 Hz, 1H, H$_B$-6), 1.19 [t, ^3J = 7.1 Hz, 3H, CH$_3$ in CH(COOEt)$_2$], 1.15 [t, ^3J = 7.1 Hz, 3H, CH$_3$ in CH(COOEt)$_2$], 0.67 (t, ^3J = 7.1 Hz, 3H, CH$_3$ in 5-COOEt); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 168.4 (C═O in 5-COOEt), 166.8 [C═O in CH(COOEt)$_2$], 166.6 [C═O in CH(COOEt)$_2$], 154.8 (C-2), 147.1 (C-4), 137.6 (C), 128.9 (CH), 128.6 (2CH), 127.9 (2CH), 107.8 (C-5), 61.5 [OCH$_2$ in CH(COOEt)$_2$], 61.4 [OCH$_2$ in CH(COOEt)$_2$], 59.5 (OCH$_2$ in 5-COOEt), 56.2 [CH(COOEt)$_2$], 52.7 (C-7), 31.4 (C-6), 13.9 [CH$_3$ in CH(COOEt)$_2$], 13.8 [CH$_3$ in CH(COOEt)$_2$], 13.3 (CH$_3$ in 5-COOEt). Anal. Calcd for $C_{21}H_{26}N_2O_7$: C, 60.28; H, 6.26; N, 6.70. Found: C, 60.25; H, 6.14; N, 6.62.

*Ethyl 4-Butyl-7-[di(ethoxycarbonyl)methyl]-2-oxo-2,3,6,7-tetrahydro-1H-1,3-diazepine-5-carboxylate (**17e**).* Compd **17e** (0.958 g, 94%) was obtained from pyrimidine **15g** (0.852 g, 2.55 mmol), NaH (0.074 g, 3.07 mmol), and diethyl malonate (**16**) (0.503 g, 3.13 mmol) in dry MeCN (10.5 mL) (rt, 2 h 20 min) as described for **17a**. Mp 122.5−123.5 °C (EtOH); IR (Nujol) ν_{max} 3229 (br s), 3100 (br s) (NH), 1737 (vs) (C═O), 1709 (s), 1695 (s) (amide-I), 1634 (s) (C═C), 1275 (s), 1237 (vs), 1159 (s) (C−O) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 8.41 (br d, ^4J = 1.9 Hz, 1H, N$_{(3)}$H), 7.27 (br dd, ^3J = 6.0, ^4J = 1.9 Hz, 1H, N$_{(1)}$H), 3.94−4.20 (m, 6H, three OCH$_2$), 3.89 (dddd, ^3J = 9.9, ^3J = 6.2, ^3J = 6.0, ^3J = 2.1 Hz, 1H, H-7), 3.37 [d, ^3J = 9.9 Hz, 1H, *C*H(COOEt)$_2$], 2.94 (dd, ^2J = 15.3, ^3J = 6.2 Hz, 1H, H$_A$-6), 2.69−2.78 (m, 1H, H$_A$ in *C*H$_2$CH$_2$CH$_2$CH$_3$), 2.47 (dd, ^2J = 15.3, ^3J = 2.1 Hz, 1H, H$_B$-6), 2.32−2.41 (m, 1H, H$_B$ in *C*H$_2$CH$_2$CH$_2$CH$_3$), 1.23−1.57 (m, 4H, CH$_2$*C*H$_2$*C*H$_2$CH$_3$), 1.17 [t, ^3J = 7.1 Hz, 3H, CH$_3$ in CH(COOEt)$_2$], 1.16 [t, ^3J = 7.1 Hz, 3H, CH$_3$ in CH(COOEt)$_2$], 1.15 (t, ^3J = 7.1 Hz, 3H, CH$_3$ in 5-COOEt), 0.88 (t, ^3J = 7.2 Hz, 3H, CH$_3$ in Bu); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 167.3 (C═O in 5-COOEt), 166.8 [C═O in CH(COOEt)$_2$], 166.4 [(C═O in CH(COOEt)$_2$], 155.1 (C-2), 151.6 (C-4), 104.4 (C-5), 61.3 [OCH$_2$ in CH(COOEt)$_2$], 61.2 [OCH$_2$ in CH(COOEt)$_2$], 59.6 (OCH$_2$ in 5-COOEt), 56.1 [CH(COOEt)$_2$], 51.6 (C-7), 32.6 (C-6), 31.0 (*C*H$_2$CH$_2$CH$_2$CH$_3$), 30.7 (CH$_2$*C*H$_2$CH$_2$CH$_3$), 22.0 (CH$_2$CH$_2$*C*H$_2$CH$_3$), 14.1 (CH$_3$ in 5-COOEt), 13.9 (CH$_3$ in Bu), 13.79 [CH$_3$ in CH(COOEt)$_2$], 13.76 [CH$_3$ in CH(COOEt)$_2$]. Anal. Calcd for $C_{19}H_{30}N_2O_7$: C, 57.27; H, 7.59; N, 7.03. Found: C, 57.40; H, 7.40; N, 6.85.

*Diethyl 7-[Di(ethoxycarbonyl)methyl]-2-oxo-2,3,6,7-tetrahydro-1H-1,3-diazepine-4,5-dicarboxylate (**17f**).* To a cooled in an ice bath, stirred suspension of NaH (0.096 g, 3.99 mmol) in dry MeCN (5 mL) was added a solution of diethyl malonate (**16**) (0.650 g, 4.06 mmol) in MeCN (7 mL) over 2 min. The suspension was stirred for 20 min, then solution of pyrimidine **15h** (1.140 g, 3.25 mmol) in MeCN (10 mL) was added. The resulting mixture was stirred at room temperature for 1 h, and the solvent was removed under vacuum. The oily residue was triturated with petroleum ether (4 × 8 mL), then with petroleum ether (8 mL) and H$_2$O (3 mL) until crystallization was completed. The obtained suspension was cooled, the precipitate was filtered, washed with ice-cold H$_2$O, petroleum ether, and dried to give **17f** (0.940 g, 70%) as a light brown solid. The analytically pure sample (white solid) was obtained by crystallization from EtOAc−petroleum ether (1:2 v/v). Mp 118.5−120 °C (petroleum ether−EtOAc); IR (Nujol) ν_{max} 3298 (br s), 3114 (br m) (NH), 1740 (vs), 1732 (sh) (C═O), 1699 (vs) (amide-I), 1626 (s) (C═C), 1542 (m) (amide-II), 1281 (s), 1236 (vs), 1158 (s) (C−O) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 9.19 (br s, 1H, N$_{(3)}$H), 7.72 (br d, ^3J = 6.3 Hz, 1H, N$_{(1)}$H), 3.98−4.21 (m, 8H, four OCH$_2$), 3.91 (dddd, ^3J = 10.3, ^3J = 6.3, ^3J = 6.1, ^3J = 2.5 Hz, 1H, H-7), 3.47 [d, ^3J = 10.3 Hz, 1H, *C*H(COOEt)$_2$], 2.84 (dd, ^2J = 16.3, ^3J = 6.1 Hz, 1H, H$_A$-6), 2.55 (dd, ^2J = 16.3, ^3J = 2.5 Hz, 1H, H$_B$-6), 1.25 (t, ^3J = 7.2 Hz, 3H, CH$_3$ in 4-COOEt), 1.18 [t, ^3J = 7.1 Hz, 3H, CH$_3$ in CH(COOEt)$_2$], 1.15 [t, ^3J = 7.1 Hz, 3H, CH$_3$ in CH(COOEt)$_2$], 1.14 (t, ^3J = 7.1 Hz, 3H, CH$_3$ in 5-COOEt); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 166.5 [C═O in CH(COOEt)$_2$], 166.3 [C═O in CH(COOEt)$_2$], 166.1 (C═O in 5-COOEt), 164.1 (C═O in 4-COOEt), 154.9 (C-2), 140.0 (C-4), 103.8 (C-5), 61.6 (OCH$_2$ in 4-COOEt), 61.50 [OCH$_2$ in CH(COOEt)$_2$], 61.45 [OCH$_2$ in CH(COOEt)$_2$], 60.4 (OCH$_2$ in 5-COOEt), 55.0 [CH(COOEt)$_2$], 49.2 (C-7), 30.83 (C-6), 13.85 (CH$_3$ in 4-COOEt), 13.76 [CH$_3$ in CH(COOEt)$_2$], 13.7 [CH$_3$ in CH(COOEt)$_2$], 13.6

(CH_3 in 5-COOEt). Anal. Calcd for $C_{18}H_{26}N_2O_9$: C, 52.17; H, 6.32; N, 6.76. Found: C, 52.05; H, 6.31; N, 6.69.

5-Acetyl-7-[di(ethoxycarbonyl)methyl]-4-methyl-2,3,6,7-tetrahydro-1H-1,3-diazepin-2-one (17g). Compd **17g** (0.389 g, 76%) was obtained from pyrimidine **15i** (0.413 g, 1.58 mmol), NaH (0.045 g, 0.88 mmol), and diethyl malonate (**16**) (0.318 g, 1.98 mmol) in dry MeCN (8 mL) (rt, 1 h) as described for **17a**. Mp 110−111 °C (petroleum ether−AcOEt, 1:1 v/v); IR (Nujol) ν_{max} 3369 (br s), 3231 (m), 3126 (br m), 3107 (m), 3096 (m) (NH), 1741 (m), 1722 (s) (C═O in COOEt), 1684 (s) (amide-I), 1667 (s) (C═O in Ac), 1603 (s) (C═C), 1274 (s), 1241 (s), 1157 (s), 1030 (s) (C−O) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6) δ 8.41 (br d, $^4J = 2.0$ Hz, 1H, $N_{(3)}H$), 7.21 (br dd, $^3J = 5.4$, $^4J = 2.0$ Hz, 1H, $N_{(1)}H$), 4.01−4.20 (m, 4H, two OCH_2), 3.89 (dddd, $^3J = 9.2$, $^3J = 6.7$, $^3J = 5.4$, $^3J = 2.1$ Hz, 1H, H-7), 3.45 [d, $^3J = 9.2$ Hz, 1H, $CH(COOEt)_2$], 2.88 (dd, $^2J = 15.2$, $^3J = 6.7$ Hz, 1H, H_A-6), 2.56 (ddq, $^2J = 15.2$, $^3J = 2.1$, $^5J = 0.8$ Hz, 1H, H_B-6), 2.14 (s, 3H, CH_3 in Ac), 2.10 (d, $^5J = 0.8$ Hz, 3H, 4-CH_3), 1.18 (t, $^3J = 7.1$ Hz, 3H, CH_3 in OEt), 1.15 (t, $^3J = 7.1$ Hz, 3H, CH_3 in OEt); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 198.2 (C═O in Ac), 166.9 (C═O in COOEt), 166.6 (C═O in COOEt), 154.7 (C-2), 145.6 (C-4), 115.1 (C-5), 61.35 (OCH_2), 61.30 (OCH_2), 55.8 [$CH(COOEt)_2$], 51.7 (C-7), 30.9 (C-6), 30.0 (CH_3 in Ac), 20.8 (4-CH_3), 13.8 (CH_3 in OEt), 13.7 (CH_3 in OEt). Anal. Calcd for $C_{15}H_{22}N_2O_6$: C, 55.21; H, 6.80; N, 8.58. Found: C, 55.23; H, 6.86; N, 8.80.

5-Benzoyl-7-[di(ethoxycarbonyl)methyl]-4-methyl-2,3,6,7-tetrahydro-1H-1,3-diazepin-2-one (17h). Compd **17h** (0.237 g, 87%) was obtained from pyrimidine **15j** (0.227 g, 0.70 mmol), NaH (0.019 g, 0.78 mmol), and diethyl malonate (**16**) (0.134 g, 0.84 mmol) in dry MeCN (5 mL) (rt, 1 h) as described for **17a**. Mp 137.5−139 °C (MeCN); IR (Nujol) ν_{max} 3288 (s), 3223 (br m), 3138 (m), 3099 (m) (NH), 1738 (m), 1720 (vs) (C═O in COOEt), 1690 (s) (amide-I), 1656 (s) (C═O in Bz), 1615 (s) (C═C), 1597 (w), 1580 (w), 1496 (w) (CC_{arom}), 1267 (s), 1166 (s), 1028 (s) (C−O), 722 (m), 693 (m) (CH_{arom}) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6) δ 8.44 (br d, $^4J = 2.0$ Hz, 1H, $N_{(3)}H$), 7.63−7.68 (m, 2H, ArH), 7.54−7.60 (m, 1H, ArH), 7.44−7.51 (m, 2H, ArH), 7.25 (br dd, $^3J = 5.9$, $^4J = 2.0$ Hz, 1H, $N_{(1)}H$), 4.05−4.21 (m, 2H, OCH_2), 3.91 (dddd, $^3J = 9.9$, $^3J = 5.9$, $^3J = 5.5$, $^3J = 3.1$ Hz, 1H, H-7), 3.87−4.04 (m, 2H, OCH_2), 3.62 [d, $^3J = 9.9$ Hz, 1H, $CH(COOEt)_2$], 2.71 (dd, $^2J = 15.4$, $^3J = 5.5$ Hz, 1H, H_A-6), 2.67 (ddq, $^2J = 15.4$, $^3J = 3.1$, $^5J = 1.4$ Hz, 1H, H_B-6), 1.72 (br s, 3H, 4-CH_3), 1.17 (t, $^3J = 7.1$ Hz, 3H, CH_3 in OEt), 1.00 (t, $^3J = 7.1$ Hz, 3H, CH_3 in OEt); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 196.9 (C═O in Bz), 166.9 (C═O in COOEt), 166.4 (C═O in COOEt), 155.0 (C-2), 142.5 (C-4), 139.1 (C), 132.1 (CH), 128.53 (2CH), 128.52 (2CH), 113.3 (C-5), 61.3 (OCH_2), 61.1 (OCH_2), 55.8 [$CH(COOEt)_2$], 51.3 (C-7), 32.8 (C-6), 20.8 (4-CH_3), 13.7 (CH_3 in OEt), 13.5 (CH_3 in OEt). Anal. Calcd for $C_{20}H_{24}N_2O_6$: C, 61.85; H, 6.23; N, 7.21. Found: C, 61.79; H, 6.28; N, 7.20.

5-Benzoyl-7-[di(ethoxycarbonyl)methyl]-4-phenyl-2,3,6,7-tetrahydro-1H-1,3-diazepin-2-one (17i). Compd **17i** (0.612 g, 79%) was obtained from pyrimidine **15k** (0.663 g, 1.72 mmol), NaH (0.049 g, 2.05 mmol), and diethyl malonate (**16**) (0.333 g, 2.08 mmol) in dry MeCN (10 mL) (rt, 2 h) as described for **17a**, followed by purification of the crude product using column chromatography on silica gel 60 (23g) eluting with petroleum ether/$CHCl_3$ (from 1:2 to 1:4). Mp 127−129 °C (EtOAc−hexane, 2:1 v/v); IR (Nujol) ν_{max} 3269 (m), 3222 (br m), 3084 (m), 3060 (m) (NH), 1755 (s), 1732 (s) (C═O in COOEt), 1680 (vs) (amide-I), 1610 (br vs) (C═O in COPh and C═C), 1577 (m), 1492 (w) (CC_{arom}), 1294 (vs), 1179 (s), 1034 (m) (C−O), 766 (m), 722 (m), 698 (m) (CH_{arom}) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6) δ 8.50 (br d, $^4J = 1.9$ Hz, 1H, $N_{(3)}H$), 7.45−7.50 (m, 2H, ArH), 7.26−7.33 (m, 1H, ArH), 7.15−7.22 (m, 2H, ArH), 7.05−7.15 (m, 6H, ArH and $N_{(1)}H$), 4.07−4.23 (m, 2H, OCH_2), 4.07 (dddd, $^3J = 8.6$, $^3J = 5.8$, $^3J = 4.3$, $^3J = 3.8$ Hz, 1H, H-7), 3.91−4.08 (m, 2H, OCH_2), 3.80 [d, $^3J = 8.6$ Hz, 1H, $CH(COOEt)_2$], 2.95 (dd, $^2J = 14.7$, $^3J = 5.8$ Hz, 1H, H_A-6), 2.92 (dd, $^2J = 14.7$, $^3J = 3.8$ Hz, 1H, H_B-6), 1.18 (t, $^3J = 7.1$ Hz, 3H, CH_3 in OEt), 1.10 (t, $^3J = 7.1$ Hz, 3H, CH_3 in OEt); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 197.0 (C═O in Bz), 166.9 (C═O in COOEt), 166.6 (C═O in COOEt), 155.2 (C-2), 145.9 (C-4), 138.3 (C), 136.2 (C), 131.5 (CH), 129.8 (2CH), 129.4 (CH), 128.8 (2CH), 127.8 (2 × 2CH), 117.1 (C-5), 61.4 (OCH_2), 61.2 (OCH_2), 56.3 [$CH(COOEt)_2$], 53.4 (C-7), 32.5 (C-6), 13.8 (CH_3 in OEt), 13.5 (CH_3 in OEt). Anal. Calcd for $C_{25}H_{26}N_2O_6$: C, 66.66; H, 5.82; N, 6.22. Found: C, 66.32; H, 5.85; N, 6.14.

Methyl 7-Cyano-2-oxo-4-phenyl-2,3,6,7-tetrahydro-1H-1,3-diazepine-5-carboxylate (18a). A suspension of pyrimidine **15b** (0.786 g, 2.31 mmol) and finely powdered NaCN (0.169 g, 3.46 mmol) in dry DMSO (2 mL) was stirred at room temperature for 3 h, then ice-cold H_2O (12 mL) was added. The obtained oily residue was triturated until crystallization was complete. The suspension was cooled, the precipitate was filtered, washed with ice-cold H_2O, petroleum ether, and dried. The obtained solid (0.604 g) was purified using column chromatography on silica gel (12.55 g) eluting with $CHCl_3$/MeOH (from 100:1 to 100:2) to give **18a** (0.545 g, 87%). Mp 233−234 °C (decomp, EtOH); IR (Nujol) ν_{max} 3278 (s), 3141 (w), 3106 (br m) (NH), 3060 (w), 3023 (w) (CH_{arom}), 2244 (vw) (CN), 1688 (vs), 1677 (vs) (C═O and amide-I), 1625 (s) (C═C), 1598 (w), 1492 (w) (CC_{arom}), 1299 (s), 1189 (s) (C−O), 763 (s), 698 (s) (CH_{arom}) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6) δ 8.69 (br d, $^4J = 2.1$ Hz, 1H, $N_{(3)}H$), 7.85 (br doublet of unresolved dd, $^3J = 6.0$, $^4J = 2.1$, $^4J \approx 1.1$ Hz, 1H, $N_{(1)}H$), 7.34−7.44 (m, 3H, ArH), 7.20−7.27 (m, 2H, ArH), 4.77 (ddd, $^3J = 6.0$, $^3J = 5.3$, $^3J = 2.9$ Hz, 1H, H-7), 3.28 (s, 3H, OCH_3), 3.24 (ddd, $^2J = 15.3$, $^3J = 5.3$, $^4J = 1.1$ Hz, 1H, H_A-6), 2.82 (dd, $^2J = 15.3$, $^3J = 2.9$ Hz, 1H, H_B-6); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 168.2 (C═O in COOMe), 154.0 (C-2), 148.4 (C-4), 137.0 (C), 129.2 (CH), 128.7 (2CH), 127.9 (2CH), 118.9 (CN), 108.1 (C-5), 51.1 (OCH_3), 45.5 (C-7), 31.5 (C-6). Anal. Calcd for $C_{14}H_{13}N_3O_3$: C, 61.99; H, 4.83; N, 15.49. Found: C, 62.09; H, 4.92; N, 15.23.

5-Benzoyl-7-cyano-4-phenyl-2,3,6,7-tetrahydro-1H-1,3-diazepin-2-one (18b). Compd **18b** (0.701 g, 83%) was obtained from pyrimidine **15k** (1.033 g, 2.67 mmol) and NaCN (0.194 g, 3.96 mmol) in dry DMSO (3 mL) (rt, 3 h) as described for **18a**. The crude product (0.815 g) was purified using column chromatography on silica gel (24.61 g) eluting with $CHCl_3$/MeOH (from 100:0 to 100:1). Mp 190.5−191.5 °C (decomp, EtOH); IR (Nujol) ν_{max} 3476 (br s), 3261 (br s), 3219 (w), 3198 (w), 3102 (br m) (NH), 2247 (vw) (CN), 1693 (s) (amide-I), 1625 (m), 1606 (s) (C═O and C═C), 1576 (w), 1494 (w) (CC_{arom}), 769 (s), 724 (m), 692 (m) (CH_{arom}) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6) δ 8.81 (br d, $^4J = 2.0$ Hz, 1H, $N_{(3)}H$), 7.87 (br doublet of unresolved dd, $^3J = 5.8$, $^4J = 2.0$, $^4J \approx 1.0$ Hz, 1H, $N_{1)}H$), 7.46−7.51 (m, 2H, ArH), 7.19−7.25 (m, 1H, ArH), 7.03−7.15 (m, 7H, ArH), 4.83 (ddd, $^3J = 5.8$, $^3J = 5.0$, $^3J = 3.1$ Hz, 1H, H-7), 3.34 (ddd, $^2J = 15.0$, $^3J = 5.0$, $^4J = 1.0$ Hz, 1H, H_A-6), 2.97 (dd, $^2J = 15.0$, $^3J = 3.1$ Hz, 1H, H_B-6); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 196.8 (C═O in Bz), 154.3 (C-2), 147.5 (C-4), 138.6 (C), 135.8 (C), 131.1 (CH), 130.1 (2CH), 129.6 (CH), 128.9 (2CH), 127.7 (2CH), 127.4 (2CH), 119.3 (CN), 116.9 (C-5), 45.9 (C-7), 32.3 (C-6). Calcd for $C_{19}H_{15}N_3O_2 \times 0.15H_2O$: C, 71.30; H, 4.82; N, 13.13. Found: C, 71.40; H, 4.71; N, 13.10.[30]

Methyl 2-oxo-4-Phenyl-7-phthalimido-2,3,6,7-tetrahydro-1H-1,3-diazepine-5-carboxylate (20a). A suspension of pyrimidine **15b** (0.424 g, 1.25 mmol) and potassium phthalimide (**19**) (0.301 g, 1.63 mmol) in dry MeCN (10 mL) was refluxed under stirring for 30 min, and the solvent was removed under vacuum. The residue was triturated with H_2O (3 mL) until crystallization was complete. The suspension was cooled (0 °C), the precipitate was filtered, washed with ice-cold H_2O, petroleum ether, and dried to give **20a** (0.464 g, 95%) as a light yellow solid. The analytically pure sample (white solid) was obtained by crystallization from EtOH. Mp 222−222.5 °C (decomp, EtOH); IR (Nujol) ν_{max} 3234 (br s), 3172 (br m), 3121 (sh), 3104 (w), 3085 (br m), 3062 (w) (NH), 1780 (s) (amide-I in phthalimide fragment), 1723 (vs) (amide-I in phthalimide fragment and C═O in COOMe), 1678 (br s) (amide-I in urea fragment), 1618 (s) (C═C), 1574 (w), 1562 (w), 1543 (w), 1510 (w) (CC_{arom}), 1284 (s), 1129 (s) (C−O), 766 (s), 720 (s), 694 (s) (CH_{arom}) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6) δ 8.72 (br d, $^4J = 2.0$ Hz, 1H, $N_{(3)}H$), 7.83−7.93 [m, 4H, $C_6H_4(CO)_2N$], 7.27−7.46 (m, 6H, Ph and $N_{(1)}H$), 5.43 (ddd, $^3J = 10.8$, $^3J = 3.3$, $^3J = 1.4$ Hz, 1H, H-7), 3.49 (dd, $^2J = 13.6$, $^3J = 10.8$ Hz, 1H, H_A-6), 3.27 (s, 3H, OCH_3), 3.07 (ddd, $^2J =$

13.6, ^3J = 3.3, ^4J = 1.5 Hz, 1H, H_B-6); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 167.7 (C=O in COOMe), 167.0 [N(C=O)$_2$], 154.6 (C-2), 149.6 (C-4), 136.4 (C), 134.6 (2CH), 131.5 (2C), 129.4 (CH), 129.1 (2CH), 127.7 (2CH), 123.1 (2CH), 108.4 (C-5), 61.9 (C-7), 51.0 (OCH_3), 30.8 (C-6). Anal. Calcd for $C_{21}H_{17}N_3O_5$: C, 64.45; H, 4.38; N, 10.74. Found: C, 64.14; H, 4.48; N, 10.42.

*Methyl 4-Butyl-2-oxo-7-phthalimido-2,3,6,7-tetrahydro-1H-1,3-diazepine-5-carboxylate (**20b**).* A suspension of pyrimidine **15c** (0.493 g, 1.54 mmol) and potassium phthalimide (**19**) (0.371 g, 2.00 mmol) in dry DMSO (3.5 mL) was stirred at room temperature for 2 h, then ice-cold H_2O (12 mL) was added. The obtained suspension was cooled (0 °C), the precipitate was filtered, washed with ice-cold H_2O, petroleum ether, and dried to give **20b** (0.516 g, 90%). Mp 173−174 °C (EtOH) (completely transparent melt at 181 °C); IR (Nujol) ν_{max} 3333 (br s), 3232 (m), 3186 (br m), 3098 (br s) (NH), 1779 (s) (amide-I in phthalimide fragment), 1722 (vs), 1709 (s) (amide-I in phthalimide fragment and C=O in COOMe), 1689 (br s) (amide-I in urea fragment), 1633 (s) (C=C), 1506 (s) (amide-II in urea fragment), 1278 (s), 1124 (s), 1088 (s) (C−O), 720 (s) (CH_{arom}) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 8.55 (br d, ^4J = 2.0 Hz, 1H, $N_{(3)}H$), 7.78−7.91 [m, 4H, $C_6H_4(CO)_2N$], 7.27 (br ddd, ^4J = 2.0, ^4J = 1.6, ^3J = 1.1 Hz, 1H, $N_{(1)}H$), 5.32 (ddd, ^3J = 10.8, ^3J = 3.1, ^3J = 1.1 Hz, 1H, H-7), 3.59 (s, 3H, OCH_3), 3.32 (dd, ^2J = 13.8, ^3J = 10.8 Hz, 1H, H_A-6), 2.92 (ddd, ^2J = 13.8, ^3J = 3.1, ^4J = 1.6 Hz, 1H, H_B-6), 2.80−2.89 (m, 1H, H_A in $\mathit{CH_2}CH_2CH_2CH_3$), 2.29−2.38 (m, 1H, H_B in $\mathit{CH_2}CH_2CH_2CH_3$), 1.23−1.57 (m, 4H, $CH_2\mathit{CH_2CH_2}CH_3$), 0.89 (t, ^3J = 7.2 Hz, 3H, CH_3 in Bu); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 166.93 [N(C=O)$_2$], 166.85 (C=O in COOMe), 154.7 (C-2), 154.2 (C-4), 134.5 (2CH), 131.5 (2C), 123.1 (2CH), 106.7 (C-5), 61.5 (C-7), 51.2 (OCH_3), 32.1 (C-6), 30.4 ($\mathit{CH_2}CH_2CH_2CH_3$), 30.0 ($CH_2\mathit{CH_2}CH_2CH_3$), 21.9 ($CH_2CH_2\mathit{CH_2}CH_3$), 13.8 ($CH_3$ in Bu). Anal. Calcd for $C_{19}H_{21}N_3O_5$: C, 61.45; H, 5.70; N, 11.31. Found: C, 61.41; H, 5.70; N, 11.28.

*Ethyl 2-oxo-4-Phenyl-7-phthalimido-2,3,6,7-tetrahydro-1H-1,3-diazepine-5-carboxylate (**20c**).* Compd **20c** (0.379 g, 96%) as a light yellow solid was prepared from pyrimidine **15f** (0.346 g, 0.98 mmol) and potassium phthalimide (**19**) (0.235 g, 1.27 mmol) in dry MeCN (8 mL) (reflux, 1 h) as described for **20a**. The analytically pure sample (white solid) was obtained by crystallization from EtOH. Mp 213-215 °C (decomp, EtOH); IR (Nujol) ν_{max} 3253 (br s), 3182 (br w), 3135 (br m), 3126 (br m), 3109 (br m) (NH), 1773 (m) (amide-I in phthalimide fragment), 1720 (vs) (amide-I in phthalimide fragment and C=O in COOEt), 1685 (br s) (amide-I in urea fragment), 1626 (s) (C=C), 1578 (w), 1562 (w), 1543 (w), 1499 (w) (CC_{arom}), 1283 (s), 1129 (s) (C−O), 766 (m), 720 (s), 697 (m) (CH_{arom}) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 8.78 (br d, ^4J = 2.0 Hz, 1H, $N_{(3)}H$), 7.83−7.93 [m, 4H, $C_6H_4(CO)_2N$], 7.27−7.47 (m, 6H, ArH and $N_{(1)}H$), 5.42 (ddd, ^3J = 10.6, ^3J = 3.2, ^3J = 1.5 Hz, 1H, H-7), 3.70 (q, ^3J = 7.1 Hz, 2H, OCH_2), 3.46 (dd, ^2J = 13.5, ^3J = 10.6 Hz, 1H, H_A-6), 3.06 (ddd, ^2J = 13.5, ^3J = 3.2, ^4J = 1.4 Hz, 1H, H_B-6), 0.65 (t, ^3J = 7.1 Hz, 3H, CH_3); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 167.5 (C=O in COOEt), 167.1 [N(C=O)$_2$], 154.6 (C-2), 149.6 (C-4), 136.7 (C), 134.6 (2CH), 131.5 (2C), 129.4 (CH), 129.2 (2CH), 127.8 (2CH), 123.2 (2CH), 108.6 (C-5), 62.0 (C-7), 59.6 (OCH_2), 30.8 (C-6), 13.3 (CH_3). Anal. Calcd for $C_{22}H_{19}N_3O_5$: C, 65.18; H, 4.72; N, 10.37. Found: C, 64.87; H, 4.66; N, 10.16.

*Ethyl 4-Butyl-2-oxo-7-phthalimido-2,3,6,7-tetrahydro-1H-1,3-diazepine-5-carboxylate (**20d**).* Compd **20d** (0.421 g, 84%) was prepared from pyrimidine **15g** (0.433 g, 1.29 mmol) and potassium phthalimide (**19**) (0.311 g, 1.68 mmol) in dry DMSO (4 mL) (rt, 2 h) as described for **20b**. Mp 177.5−178 °C (MeCN) (completely transparent melt at 183 °C); IR (Nujol) ν_{max} 3297 (br s), 3228 (br s), 3107 (br s) (NH), 1778 (s) (amide-I in phthalimide fragment), 1725 (s), 1715 (vs) (amide-I in phthalimide fragment and C=O in COOEt), 1677 (s), 1666 (s), 1658 (s) (amide-I in urea fragment), 1630 (br s) (C=C), 1511 (m) (CC_{arom}), 1275 (s), 1122 (s) (C−O), 724 (s) (CH_{arom}) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 8.53 (br d, ^4J = 1.9 Hz, 1H, $N_{(3)}H$), 7.77−7.91 [m, 4H, $C_6H_4(CO)_2N$], 7.29 (br ddd, ^4J = 1.9, ^3J = 1.5, ^4J = 1.5 Hz, 1H, $N_{(1)}H$), 5.33 (ddd, ^3J = 10.5, ^3J = 3.0, ^3J = 1.5 Hz, 1H, H-7), 4.03 (q, ^3J = 7.1 Hz, 2H, OCH_2), 3.30 (dd, ^2J = 13.8, ^3J = 10.5 Hz, 1H, H_A-6), 2.90 (ddd, ^2J = 13.8, ^3J = 3.0, ^4J = 1.5 Hz, 1H, H_B-6), 2.74−2.84 (m, 1H, H_A in $\mathit{CH_2}CH_2CH_2CH_3$), 2.32−2.41 (m, 1H, H_B in $\mathit{CH_2}CH_2CH_2CH_3$), 1.22−1.59 (m, 4H, $CH_2\mathit{CH_2CH_2}CH_3$), 1.11 (t, ^3J = 7.1 Hz, 3H, CH_3 in OEt), 0.89 (t, ^3J = 7.2 Hz, 3H, CH_3 in Bu); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 166.9 [N(C=O)$_2$], 166.5 (C=O in COOEt), 154.7 (C-2), 153.8 (C-4), 134.5 (2CH), 131.5 (2C), 123.1 (2CH), 106.9 (C-5), 61.7 (C-7), 59.7 (OCH_2), 32.3 (C-6), 30.4 ($\mathit{CH_2}CH_2CH_2CH_3$), 30.1 ($CH_2\mathit{CH_2}CH_2CH_3$), 22.0 ($CH_2CH_2\mathit{CH_2}CH_3$), 14.0 ($CH_3$ in OEt), 13.8 (CH_3 in Bu). Anal. Calcd for $C_{20}H_{23}N_3O_5$: C, 62.33; H, 6.02; N, 10.90. Found: C, 62.04; H, 5.86; N, 10.77.

*5-Benzoyl-4-methyl-7-phthalimido-2,3,6,7-tetrahydro-1H-1,3-diazepin-2-one (**20e**).* Compd **20e** (0.488 g, 92%) was prepared from pyrimidine **15j** (0.461 g, 1.42 mmol) and potassium phthalimide (**19**) (0.345 g, 1.86 mmol) in dry DMSO (3 mL) (rt, 2 h) as described for **20b**. Mp 234 °C (decomp, EtOH); IR (Nujol) ν_{max} 3264 (sh), 3233 (br s), 3102 (br s) (NH), 1777 (m), 1723 (vs), 1713 (s) (amide-I in phthalimide fragment), 1685 (s) (amide-I in urea fragment), 1645 (m), 1614 (s), 1592 (s) (C=O in Bz and C=C), 1579 (m), 1521 (m) (CC_{arom}), 723 (s), 702 (m) (CH_{arom}) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 8.66 (br d, ^4J = 1.9 Hz, 1H, $N_{(3)}H$), 7.81−7.90 [m, 4H, $C_6H_4(CO)_2N$], 7.42−7.67 (m, 6H, Ph and $N_{(1)}H$), 5.41 (ddd, ^3J = 10.3, ^3J = 2.8, ^3J = 1.6 Hz, 1H, H-7), 3.43 (ddq, ^2J = 14.0, ^3J = 10.3, ^5J = 1.2 Hz, 1H, H_A-6), 2.89 (ddd, ^2J = 14.0, ^3J = 2.8, ^4J = 1.5 Hz, 1H, H_B-6), 1.69 (unresolved d, ^5J ≈ 1.2 Hz, 3H, CH_3); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 196.3 (C=O in Bz), 167.0 [N(C=O)$_2$], 154.4 (C-2), 145.8 (C-4), 139.3 (C), 134.5 (2CH), 132.2 (CH), 131.5 (2C), 128.7 (2CH), 128.5 (2CH), 123.1 (2CH), 115.6 (C-5), 61.1 (C-7), 32.0 (C-6), 20.9 (CH_3). Anal. Calcd for $C_{21}H_{17}N_3O_4$: C, 67.19; H, 4.56; N 11.19. Found: C, 66.96; H, 4.58; N, 11.12.

*Methyl 7-Methoxy-2-oxo-4-phenyl-2,3,6,7-tetrahydro-1H-1,3-diazepine-5-carboxylate (**21a**).* To a solution of Na (0.117 g, 5.10 mmol) in dry MeOH (11 mL) was added pyrimidine **15b** (0.699 g, 2.05 mmol), and the obtained mixture was stirred at room temperature for 1 h 40 min. The resulting suspension was cooled in an ice bath, AcOH (0.180 mL, 3.14 mmol) and $NaHCO_3$ (0.085 g) were subsequently added, and the mixture was stirred in an ice bath for 5 min. The solvent was removed under vacuum (temperature of bath not higher than 30 °C), the residue was triturated with saturated aqueous $NaHCO_3$ (3 mL) and petroleum ether (5 mL) until crystallization was complete. The suspension was cooled (0 °C), the precipitate was filtered, washed with ice-cold H_2O (4 × 3 mL), petroleum ether, and dried to give **21a** (0.530 g, 93%). Mp 184−185.5 °C (decomp, MeCN); IR (Nujol) ν_{max} 3289 (s), 3262 (sh), 3184 (w), 3137 (br m), 3111 (br m) (NH), 3051 (w), 3021 (w), 3005 (w) (CH_{arom}), 1680 (br vs) (amide-I and C=O in COOMe), 1630 (s) (C=C), 1597 (w) (CC_{arom}), 1492 (m) (amide-II), 1298 (s), 1152 (s), 1106 (s), 1078 (s) (C−O), 765 (s), 701 (s) (CH_{arom}) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 8.47 (br d, ^4J = 2.0 Hz, 1H, $N_{(3)}H$), 7.90 (br doublet of unresolved dd, ^3J = 5.2, ^4J = 2.0, ^4J ≈ 0.9 Hz, 1H, $N_{(1)}H$), 7.17−7.42 (m, 5H, ArH), 4.53 (ddd, ^3J = 5.9, ^3J = 5.2, ^3J = 1.7 Hz, 1H, H-7), 3.27 (s, 3H, OCH_3 in COOMe), 3.20 (s, 3H, 7-OCH_3), 3.03 (ddd, ^2J = 14.0, ^3J = 5.9, ^4J = 0.9 Hz, 1H, H_A-6), 2.55 (dd, ^2J = 14.0, ^3J = 1.7 Hz, 1H, H_B-6); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 168.8 (C=O in COOMe), 154.6 (C-2), 146.6 (C-4), 136.9 (C), 129.0 (CH), 128.8 (2CH), 127.7 (2CH), 108.2 (C-5), 84.6 (C-7), 54.1 (7-OCH_3), 50.8 (OCH_3 in COOMe), 32.7 (C-6). Anal. Calcd for $C_{14}H_{16}N_2O_4$: C, 60.86; H, 5.84; N, 10.14. Found: C, 61.07; H, 6.06; N, 10.30.

*Methyl 4-Butyl-7-methoxy-2-oxo-2,3,6,7-tetrahydro-1H-1,3-diazepine-5-carboxylate (**21b**).* Compd **21b** (0.890 g, 90%) was obtained from pyrimidine **15c** (1.234 g, 3.85 mmol) and Na (0.214 g, 9.32 mmol) in dry MeOH (20 mL) (rt, 1 h 20 min) as described for **21a**. Mp 145−146.5 °C (decomp, MeCN); IR (Nujol) ν_{max} 3366 (s), 3312 (w), 3232 (s), 3103 (br s) (NH), 1694 (s) (C=O), 1672 (s) (amide-I), 1620 (s) (C=C), 1268 (s), 1188 (s), 1152 (s), 1102 (s), 1070 (s) (C−O) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 8.39 (br d, ^4J = 2.0 Hz, 1H, $N_{(3)}H$), 7.82 (br dd, ^3J = 5.3, ^4J = 2.0 Hz, 1H, $N_{(1)}H$), 4.39 (ddd, ^3J = 6.3, ^3J = 5.3, ^3J = 1.6 Hz, 1H, H-7), 3.60 (s, 3H, OCH_3 in COOMe), 3.15 (s, 3H, 7-OCH_3), 3.00 (dd, ^2J = 14.5, ^3J

= 6.3 Hz, 1H, H$_A$-6), 2.61−2.71 (m, 1H, H$_A$ in $CH_2CH_2CH_2CH_3$), 2.34−2.43 (m, 1H, H$_B$ in $CH_2CH_2CH_2CH_3$), 2.33 (dd, ^2J = 14.5, ^3J = 1.6 Hz, 1H, H$_B$-6), 1.22−1.54 (m, 4H, $CH_2CH_2CH_2CH_3$), 0.87 (t, ^3J = 7.2 Hz, 3H, CH_3 in Bu); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 167.7 (C═O in COOMe), 154.9 (C-2), 151.3 (C-4), 105.1 (C-5), 83.1 (C-7), 53.8 (7-OCH_3), 51.0 (OCH_3 in COOMe), 32.4 (C-6), 31.7 ($CH_2CH_2CH_2CH_3$), 30.7 ($CH_2CH_2CH_2CH_3$), 21.9 ($CH_2CH_2CH_2CH_3$), 13.8 (CH_3 in Bu). Anal. Calcd for $C_{12}H_{20}N_2O_4$: C, 56.24; H, 7.87; N, 10.93. Found: C, 56.31; H, 7.92; N, 11.11.

*Dimethyl 7-Methoxy-2-oxo-2,3,6,7-tetrahydro-1H-1,3-diazepine-4,5-dicarboxylate (**21c**).* Compd **21c** (0.836 g, 75%) was obtained from pyrimidine **15d** (1.388 g, 4.31 mmol) and Na (0.232 g, 10.10 mmol) in dry MeOH (15 mL) (rt, 2 h) as described for **21a**. Mp 152−153 °C (decomp, H_2O); IR (Nujol) ν_{max} 3315 (s), 3266 (m), 3133 (br s) (NH), 1741 (s), 1706 (s) (C═O), 1692 (s) (amide-I), 1624 (s) (C═C), 1541 (m) (amide-II), 1278 (s), 1243 (s), 1235 (s), 1194 (s), 1147 (s), 1102 (s), 1077 (s), 1055 (s) (C−O) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 9.20 (br d, ^4J = 1.9 Hz, 1H, N$_{(3)}$H), 8.23 (br doublet of unresolved dd, ^3J = 6.0, ^4J = 1.9, ^4J ≈ 0.7, 1H, N$_{(1)}$H), 4.42 (ddd, ^3J = 6.0, ^3J = 5.2, ^3J = 1.6 Hz, 1H, H-7), 3.68 (s, 3H, OCH_3 in COOMe), 3.59 (s, 3H, OCH_3 in COOMe), 3.19 (s, 3H, 7-OCH_3), 3.02 (ddd, ^2J = 15.4, ^3J = 5.2, ^4J = 0.7 Hz, 1H, H$_A$-6), 2.40 (dd, ^2J = 15.4, ^3J = 1.6 Hz, 1H, H$_B$-6); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 166.9 (C═O in COOMe), 164.7 (C═O in COOMe), 154.5 (C-2), 139.2 (C-4), 105.0 (C-5), 80.6 (C-7), 54.3 (7-OCH_3), 52.5 (OCH_3 in COOMe), 51.8 (OCH_3 in COOMe), 32.2 (C-6). Anal. Calcd for $C_{10}H_{14}N_2O_6$: C, 46.51; H, 5.46; N, 10.85. Found: C, 46.82; H, 5.51; N, 10.66.

*5-Acetyl-7-methoxy-4-methyl-2,3,6,7-tetrahydro-1H-1,3-diazepin-2-one (**21d**).* To a solution of Na (0.161 g, 7.01 mmol) in dry MeOH (10 mL) was added pyrimidine **15i** (0.705 g, 2.69 mmol), and the obtained mixture was stirred at room temperature for 2 h. The resulting suspension was cooled in an ice bath, AcOH (0.228 mL, 4.33 mmol) and $NaHCO_3$ (0.071 g) were subsequently added, and the mixture was stirred in an ice bath for 5 min. The solvent was removed under vacuum (temperature of bath not higher than 30 °C), the residue was triturated with saturated aqueous $NaHCO_3$ (3 mL) until crystallization was complete. The suspension was cooled (0 °C), the precipitate was filtered on a cold (−10 °C), rapidly washed with ice-cold H_2O (2 × 2 mL), petroleum ether, and dried to give **21d** (0.368 g, 69%). Mp 176.5−178 °C (decomp, MeOH); IR (Nujol) ν_{max} 3223 (br s), 3109 (br s) (NH), 1688 (s) (amide-I), 1662 (s), 1657 (s) (C═O), 1583 (vs) (C═C), 1514 (m) (amide-II), 1156 (s), 1091 (s) (C−O) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 8.44 (br d, ^4J = 2.0 Hz, 1H, N$_{(3)}$H), 7.89 (br ddd, ^3J = 5.3, ^4J = 2.0, ^4J = 0.9 Hz, 1H, N$_{(1)}$H), 4.45 (ddd, ^3J = 6.1, ^3J = 5.3, ^3J = 1.5 Hz, 1H, H-7), 3.17 (s, 3H, OCH_3), 2.95 (ddd, ^2J = 14.5, ^3J = 6.1, ^4J = 0.9 Hz, 1H, H$_A$-6), 2.37 (ddq, ^2J = 14.5, ^3J = 1.5, ^5J = 1.2 Hz, 1H, H$_B$-6), 2.18 (s, 3H, CH_3 in Ac), 2.08 (d, ^5J = 1.2 Hz, 3H, 4-CH_3); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 198.5 (C═O in Ac), 154.6 (C-2), 144.6 (C-4), 115.6 (C-5), 83.3 (C-7), 54.0 (OCH_3), 32.4 (C-6), 30.1 (CH_3 in Ac), 20.5 (4-CH_3). Anal. Calcd for $C_9H_{14}N_2O_3$: C, 54.54; H, 7.12; N, 14.13. Found: C, 54.57; H, 7.31; N, 14.10.

*5-Benzoyl-7-methoxy-4-methyl-2,3,6,7-tetrahydro-1H-1,3-diazepin-2-one (**21e**).* Compd **21e** (1.023 g, 88%) was obtained from pyrimidine **15j** (1.455 g, 4.49 mmol) and Na (0.258 g, 11.20 mmol) in dry MeOH (20 mL) (rt, 3 h) as described for **21a**. Mp 190.5−192 °C (decomp, MeCN); IR (Nujol) ν_{max} 3348 (s), 3225 (br m), 3080 (br m) (NH), 1689 (s) (amide-I), 1639 (m), 1617 (s), 1607 (s) (C═O and C═C), 1576 (w) (CC$_{arom}$), 1515 (m) (amide-II), 1078 (s) (C−O), 727 (m) (CH$_{arom}$) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 8.47 (br d, ^4J = 2.0 Hz, 1H, N$_{(3)}$H), 7.97 (br doublet of unresolved dd, ^3J = 5.6, ^4J = 2.0, ^4J ≈ 1.0 Hz, 1H, N$_{(1)}$H), 7.68−7.74 (m, 2H, ArH), 7.51−7.58 (m, 1H, ArH), 7.43−7.50 (m, 2H, ArH), 4.46 (ddd, ^3J = 5.7, ^3J = 5.6, ^3J = 1.4 Hz, 1H, H-7), 3.18 (s, 3H, OCH_3), 2.86 (ddd, ^2J = 14.4, ^3J = 5.7, ^4J = 1.0 Hz, 1H, H$_A$-6), 2.47 (ddq, ^2J = 14.4, ^3J = 1.4, ^5J = 1.3 Hz, 1H, H$_B$-6), 1.60 (d, ^5J = 1.3 Hz, 3H, 4-CH_3); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 197.5 (C═O in Bz), 154.8 (C-2), 141.9 (C-4), 140.0 (C), 131.8 (CH), 128.6 (2CH), 128.4 (2CH), 114.7 (C-5), 83.0 (C-7), 53.9 (OCH_3), 33.8 (C-6), 21.0 (4-CH_3). Anal. Calcd for $C_{14}H_{16}N_2O_3$: C, 64.60; H, 6.20; N, 10.76. Found: C, 64.64; H, 6.32; N, 10.76.

*5-Benzoyl-7-methoxy-4-phenyl-2,3,6,7-tetrahydro-1H-1,3-diazepin-2-one (**21f**).* Compd **21f** (0.645 g, 95%) was obtained from pyrimidine **15k** (0.814 g, 2.11 mmol) and Na (0.144 g, 6.29 mmol) in dry MeOH (9 mL) (rt, 1 h 50 min) as described for **21a**. Mp 203.5−204 °C (decomp, MeCN); IR (Nujol) ν_{max} 3324 (s), 3214 (s), 3099 (br s), 3066 (m) (NH), 3026 (w) (CH$_{arom}$), 1678 (s), 1672 (s) (amide-I), 1640 (w), 1611 (vs) (C═O and C═C), 1597 (w), 1578 (w), 1509 (w), 1492 (m) (CC$_{arom}$), 1186 (s), 1061 (s) (C−O), 764 (s), 693 (s) (CH$_{arom}$) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 8.65 (br d, ^4J = 1.9 Hz, 1H, N$_{(3)}$H), 8.05 (br doublet of unresolved dd, ^3J = 5.3, ^4J = 1.9, ^4J ≈ 1.0 Hz, 1H, N$_{(1)}$H), 7.43−7.49 (m, 2H, ArH), 7.14−7.21 (m, 1H, ArH), 7.01−7.12 (m, 7H, ArH), 4.64 (ddd, ^3J = 5.6, ^3J = 5.3, ^3J = 1.5 Hz, 1H, H-7), 3.18 (s, 3H, OCH_3), 3.13 (ddd, ^2J = 13.7, ^3J = 5.6, ^4J = 1.0 Hz, 1H, H$_A$-6), 2.66 (dd, ^2J = 13.7, ^3J = 1.5 Hz, 1H, H$_B$-6); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 198.1 (C═O in Bz), 155.0 (C-2), 145.2 (C-4), 139.2 (C), 136.0 (C), 130.9 (CH), 130.0 (2CH), 129.4 (CH), 129.0 (2CH), 127.7 (2CH), 127.3 (2CH), 117.9 (C-5), 85.3 (C-7), 53.9 (OCH_3), 34.3 (C-6). Anal. Calcd for $C_{19}H_{18}N_2O_3$: C,70.79; H, 5.63; N, 8.69. Found: C, 70.55; H, 5.61; N, 8.81.

*Methyl 2-oxo-4-phenyl-2,3,6,7-tetrahydro-1H-1,3-diazepine-5-carboxylate (**22**).* The suspension of pyrimidine **15b** (0.615 g, 1.81 mmol) and finely powdered $NaBH_4$ (0.103 g, 2.71 mmol) in dry THF (12 mL) was refluxed under stirring for 2 h, and the solvent was removed under vacuum. The residue was dissolved in $CHCl_3$ (15 mL), washed with saturated aqueous $NaHCO_3$ (10 mL), H_2O (3 × 10 mL), and brine (3 × 10 mL). The solvent was removed under vacuum. The residue was purified using column chromatography on silica gel (20.01 g) eluting with $CHCl_3$/MeOH (from 100:0 to 100:1) to give **22** (0.190 g, 43%). Mp 141.5−143 °C (MeCN); IR (Nujol) ν_{max} 3225 (br s), 3099 (br s) (NH), 1725 (s) (C═O), 1694 (vs) (amide-I), 1641 (s) (C═C), 1601 (w) (CC$_{arom}$), 1510 (s) (amide-II), 1494 (m) (CC$_{arom}$), 1292 (vs), 1155 (s), 1092 (s) (C−O), 763 (s), 695 (s) (CH$_{arom}$) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 7.76 (br d, ^4J = 2.2 Hz, 1H, N$_{(3)}$H), 7.30−7.38 (m, 3H, ArH), 7.31 (br dt, ^3J = 4.6, ^4J = 2.2 Hz, 1H, N$_{(1)}$H, signals partly overlap with signals of aromatic protons), 7.18−7.24 (m, 2H, ArH), 3.23−3.28 (m, 2H, H-7), 3.21 (s, 3H, OCH_3), 2.64−2.68 (m, 2H, H-6); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 169.0 (C═O in COOMe), 156.6 (C-2), 145.7 (C-4), 138.8 (C), 128.5 (CH), 128.2 (2CH), 127.7 (2CH), 109.7 (C-5), 50.7 (OCH_3), 41.3 (C-7), 30.8 (C-6). Anal. Calcd for $C_{13}H_{14}N_2O_3$: C, 63.40; H, 5.73; N, 11.38. Found: C, 63.30; H, 5.78; N, 11.33.

*Methyl 4-Methyl-2-oxo-7-phenylthio-2,3,6,7-tetrahydro-1H-1,3-diazepine-5-carboxylate (**24a**).* To a cooled in an ice bath, stirred suspension of NaH (0.024 g, 1.01 mmol) in dry THF (1 mL) was added a solution of thiophenol (0.112 g, 1.02 mmol) in THF (2 mL) over 2 min. The resulting suspension was stirred at room temperature for 20 min, then pyrimidine **15a** (0.256 g, 0.92 mmol) and THF (2 mL) were added. The obtained mixture was stirred at room temperature for 2 h, and the solvent was removed under vacuum. The oily residue was triturated upon cooling with petroleum ether (2 mL) and saturated aqueous $NaHCO_3$ (2 mL) until crystallization was completed. The suspension was cooled (0 °C), the precipitate was filtered, washed with ice-cold H_2O, petroleum ether, and dried to give **24a** (0.249 g, 93%). Mp 171−173.5 °C (EtOH); IR (Nujol) ν_{max} 3348 (s), 3218 (br m), 3089 (br s) (NH), 1695 (s) (C═O), 1670 (s) (amide-I), 1621 (s) (C═C), 1580 (w), 1510 (w) (CC$_{arom}$), 1271 (s), 1156 (s), 1090 (s) (C−O), 736 (s), 688 (m) (CH$_{arom}$) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 8.60 (br d, ^4J = 2.0 Hz, 1H, N$_{(3)}$H), 8.04 (br doublet of unresolved dd, ^3J = 6.1, ^4J = 2.0, ^4J ≈ 0.9 Hz, 1H, N$_{(1)}$H), 7.24−7.45 (m, 5H, ArH), 5.00 (ddd, ^3J = 6.1, ^3J = 6.1, ^3J = 2.0 Hz, 1H, H-7), 3.57 (s, 3H, OCH_3), 3.21 (ddd, ^2J = 15.1, ^3J = 6.1, ^4J = 0.9 Hz, 1H, H$_A$-6), 2.68 (ddq, ^2J = 15.1, ^3J = 2.0, ^5J = 1.3 Hz, 1H, H$_B$-6), 2.19 (d, ^5J = 1.3 Hz, 3H, 4-CH_3); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 167.9 (C═O in COOMe), 154.1 (C-2), 147.6 (C-4), 133.9 (C), 131.7 (2CH), 128.9 (2CH), 127.1 (CH), 104.6 (C-5), 61.2 (C-7), 51.1 (OCH_3), 34.0 (C-6), 20.7 (4-CH_3). Anal. Calcd for

$C_{14}H_{16}N_2O_3S$: C, 57.52; H, 5.52; N, 9.58. Found: C, 57.60; H, 5.74; N, 9.76.

*Methyl 2-oxo-4-phenyl-7-phenylthio-2,3,6,7-tetrahydro-1H-1,3-diazepine-5-carboxylate (**24b**).* Compd **24b** (0.146 g, 94%) was obtained from pyrimidine **15b** (0.150 g, 0.44 mmol), NaH (0.012 g, 0.51 mmol), and thiophenol (0.061 g, 0.55 mmol) in dry THF (5 mL) (rt, 2 h 25 min) as described for **24a**. Mp 144.5−146 °C (EtOAc); IR (Nujol) ν_{max} 3207 (br s), 3074 (br s), 3059 (br s) (NH), 1680 (vs) (C═O and amide-I), 1631 (s) (C═C), 1600 (w), 1580 (w), 1491 (w) (CC_{arom}), 1293 (vs), 1148 (s), 1089 (s) (C−O), 757 (s), 743 (m), 697 (s) (CH_{arom}) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 8.42 (br d, ^4J = 2.1 Hz, 1H, $N_{(3)}H$), 7.91 (br ddd, ^3J = 5.5, ^4J = 2.1, ^4J = 0.9 Hz, 1H, $N_{(1)}H$), 7.19−7.49 (m, 10H, ArH), 5.07 (ddd, ^3J = 6.2, ^3J = 5.5, ^3J = 2.4 Hz, 1H, H-7), 3.26 (s, 3H, OCH_3), 3.14 (ddd, ^2J = 14.7, ^3J = 6.2, ^4J = 0.9 Hz, 1H, H_A-6), 2.93 (dd, ^2J = 14.7, ^3J = 2.4 Hz, 1H, H_B-6); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 168.4 (C═O in COOMe), 154.0 (C-2), 147.4 (C-4), 137.3 (C), 133.5 (C), 132.1 (2CH), 129.0 (2CH), 128.9 (CH), 128.5 (2CH), 127.7 (2CH), 127.3 (CH), 108.3 (C-5), 63.0 (C-7), 50.8 (OCH_3), 34.6 (C-6). Anal. Calcd for $C_{19}H_{18}N_2O_3S$: C, 64.39; H, 5.12; N, 7.90. Found: C, 64.39; H, 5.25; N, 7.90.

*Methyl 4-Butyl-2-oxo-7-phenylthio-2,3,6,7-tetrahydro-1H-1,3-diazepine-5-carboxylate (**24c**).* Compd **24c** (0.333 g, 80%) was obtained from pyrimidine **15c** (0.401 g, 1.25 mmol), NaH (0.033 g, 1.38 mmol), and thiophenol (0.165 g, 1.38 mmol) in dry THF (7 mL) (rt, 2 h) as described for **24a**. The crude product (0.391 g) was purified using column chromatography on silica gel (12.78 g) eluting with $CHCl_3$. Mp 117.5−119 °C (EtOH); IR (Nujol) ν_{max} 3353 (s), 3231 (s), 3122 (sh), 3099 (s) (NH), 1694 (s) (C═O), 1673 (s) (amide-I), 1607 (s) (C═C), 1586 (w), 1510 (w) (CC_{arom}), 1263 (s), 1147 (s), 1083 (s) (C−O), 735 (m), 689 (m) (CH_{arom}) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 8.53 (br d, ^4J = 1.9 Hz, 1H, $N_{(3)}H$), 8.00 (br doublet of unresolved dd, ^3J = 6.0, ^4J = 1.9, ^4J ≈ 0.9 Hz, 1H, $N_{(1)}H$), 7.23−7.44 (m, 5H, ArH), 4.99 (ddd, ^3J = 6.2, ^3J = 6.0, ^3J = 2.0 Hz, 1H, H-7), 3.56 (s, 3H, OCH_3), 3.18 (ddd, ^2J = 15.0, ^3J = 6.2, ^4J = 0.9 Hz, 1H, H_A-6), 2.72−2.82 (m, 1H, H_A in $CH_2CH_2CH_2CH_3$), 2.67 (dd, ^2J = 15.0, ^3J = 2.0 Hz, 1H, H_B-6), 2.33−2.43 (m, 1H, H_B in $CH_2CH_2CH_2CH_3$), 1.27−1.62 (m, 4H, $CH_2CH_2CH_2CH_3$), 0.89 (t, ^3J = 7.2 Hz, 3H, CH_3 in Bu); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 167.6 (C═O in COOMe), 154.5 (C-2), 152.2 (C-4), 134.0 (C), 131.6 (2CH), 129.0 (2CH), 127.1 (CH), 104.9 (C-5), 61.8 (C-7), 51.1 (OCH_3), 33.9 (C-6), 32.7 ($CH_2CH_2CH_2CH_3$), 30.8 ($CH_2CH_2CH_2CH_3$), 22.0 ($CH_2CH_2CH_2CH_3$), 13.9 (CH_3 in Bu). Anal. Calcd for $C_{17}H_{22}N_2O_3S$: C, 61.05; H, 6.63; N, 8.38. Found: C, 61.04; H, 6.87; N, 8.40.

*Ethyl 4-Methyl-2-oxo-7-phenylthio-2,3,6,7-tetrahydro-1H-1,3-diazepine-5-carboxylate (**24d**).* Compd **24d** (0.297 g, 96%) was obtained from pyrimidine **15e** (0.295 g, 1.01 mmol), NaH (0.027 g, 1.11 mmol), and thiophenol (0.124 g, 1.12 mmol) in dry THF (5 mL) (rt, 2 h) as described for **24a**. Mp 169−170 °C (EtOH). (lit.[16] 169−170 °C). ^{1}H and ^{13}C NMR spectra of **24d** in DMSO-d_6 are identical with those reported previously.[16]

*Ethyl 2-oxo-4-Phenyl-7-phenylthio-2,3,6,7-tetrahydro-1H-1,3-diazepine-5-carboxylate (**24e**).* Compd **24e** (0.361 g, 95%) was obtained from pyrimidine **15f** (0.366 g, 1.03 mmol), NaH (0.028 g, 1.18 mmol), and thiophenol (0.138 g, 1.25 mmol) in dry THF (8 mL) (rt, 2 h) as described for **24a**. Mp 103.5−106.5 °C (EtOAc−petroleum ether, 2:5 v/v); IR (Nujol) ν_{max} 3207 (br s), 3082 (sh), 3071 (br s), 3058 (sh) (NH), 1677 (vs) (C═O and amide-I), 1627 (s) (C═C), 1601 (w), 1580 (w), 1492 (w) (CC_{arom}), 1291 (vs), 1150 (s), 1093 (s) (C−O), 755 (s), 741 (s), 701 (s), 691 (s) (CH_{arom}) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 8.45 (br d, ^4J = 2.0 Hz, 1H, $N_{(3)}H$), 7.94 (br dd of unresolved d, ^3J = 5.4, ^4J = 2.0, ^4J ≈ 0.8 Hz, 1H, $N_{(1)}H$), 7.19−7.49 (m, 10H, ArH), 5.06 (ddd, ^3J = 6.2, ^3J = 5.4, ^3J = 2.4 Hz, 1H, H-7), 3.63−3.79 (m, 2H, OCH_2), 3.15 (ddd, ^2J = 14.6, ^3J = 6.2, ^4J = 0.8 Hz, 1H, H_A-6), 2.91 (dd, ^2J = 14.6, ^3J = 2.4 Hz, 1H, H_B-6), 0.70 (t, ^3J = 7.1 Hz, 3H, CH_3); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 168.2 (C═O in COOEt), 154.0 (C-2), 147.3 (C-4), 137.6 (C), 133.6 (C), 132.1 (2CH), 129.0 (2CH), 128.8 (CH), 128.6 (2CH), 127.7 (2CH), 127.3 (CH), 108.5 (C-5), 62.9 (C-7), 59.4 (OCH_2), 34.6 (C-6), 13.3 (CH_3). Anal. Calcd for $C_{20}H_{20}N_2O_3S$: C, 65.20; H, 5.47; N, 7.60. Found: C, 65.21; H, 5.38; N, 7.73.

*Ethyl 4-Butyl-2-oxo-7-phenylthio-2,3,6,7-tetrahydro-1H-1,3-diazepine-5-carboxylate (**24f**).* Compd **24f** (0.334 g, 94%) was prepared from pyrimidine **15g** (0.342 g, 1.02 mmol), NaH (0.027 g, 1.13 mmol), and thiophenol (0.124 g, 1.13 mmol) in dry THF (6 mL) (rt, 2 h) as described for **24a**. Mp 134−135.5 °C (EtOAc); IR (Nujol) ν_{max} 3338 (s), 3235 (br m), 3133 (br m), 3103 (br m) (NH), 1690 (s) (C═O), 1673 (s) (amide-I), 1609 (s) (C═C), 1585 (w), 1510 (w) (CC_{arom}), 1260 (s), 1150 (s), 1085 (s) (C−O), 739 (m), 690 (m) (CH_{arom}) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 8.48 (br d, ^4J = 1.9 Hz, 1H, $N_{(3)}H$), 7.95 (br dd, ^3J = 6.0, ^4J = 1.9 Hz, 1H, $N_{(1)}H$), 7.23−7.44 (m, 5H, ArH), 4.99 (ddd, ^3J = 6.2, ^3J = 6.0, ^3J = 1.9 Hz, 1H, H-7), 4.00−4.15 (m, 2H, OCH_2), 3.17 (dd, ^2J = 14.9, ^3J = 6.2 Hz, 1H, H_A-6), 2.71−2.80 (m, 1H, H_A in $CH_2CH_2CH_2CH_3$), 2.67 (dd, ^2J = 14.9, ^3J = 1.9 Hz, 1H, H_B-6), 2.33−2.42 (m, 1H, H_B in $CH_2CH_2CH_2CH_3$), 1.28−1.63 (m, 4H, $CH_2CH_2CH_2CH_3$), 1.13 (t, ^3J = 7.1 Hz, 3H, CH_3 in OEt), 0.89 (t, ^3J = 7.2 Hz, 3H, CH_3 in Bu); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 167.2 (C═O in COOEt), 154.5 (C-2), 151.8 (C-4), 134.1 (C), 131.4 (2CH), 129.0 (2CH), 127.0 (CH), 105.5 (C-5), 62.0 (C-7), 59.6 (OCH_2), 33.8 (C-6), 32.8 ($CH_2CH_2CH_2CH_3$), 30.8 ($CH_2CH_2CH_2CH_3$), 22.1 ($CH_2CH_2CH_2CH_3$), 14.1 (CH_3 in OEt), 13.9 (CH_3 in Bu). Anal. Calcd for $C_{18}H_{24}N_2O_3S$: C, 62.04; H, 6.94; N, 8.04. Found: C, 62.24; H, 7.25; N, 8.07.

*5-Acetyl-4-methyl-7-phenylthio-2,3,6,7-tetrahydro-1H-1,3-diazepin-2-one (**24g**).* Compd **24g** (0.244 g, 80%) was prepared from pyrimidine **15i** (0.290 g, 1.11 mmol), NaH (0.029 g, 1.22 mmol), and thiophenol (0.134 g, 1.22 mmol) in dry MeCN (6 mL) (rt, 2 h) as described for **24a**. Mp 160−164 °C (decomp, MeCN); IR (Nujol) ν_{max} 3325 (br s), 3216 (s), 3102 (s), 3072 (sh), 3063 (s) (NH), 1684 (s) (amide-I), 1651 (s) (C═O), 1577 (s) (C═C), 1506 (m) (CC_{arom}), 740 (s), 690 (s) (CH_{arom}) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 8.53 (br d, ^4J = 1.9 Hz, 1H, $N_{(3)}H$), 8.03 (br doublet of unresolved dd, ^3J = 6.0, ^4J = 1.9, ^4J ≈ 0.7 Hz, 1H, $N_{(1)}H$), 7.24−7.46 (m, 5H, ArH), 5.04 (ddd, ^3J = 6.2, ^3J = 6.0, ^3J = 1.9 Hz, 1H, H-7), 3.15 (dd of unresolved d, ^2J = 14.9, ^3J = 6.2, ^4J ≈ 0.7 Hz, 1H, H_A-6), 2.75 (ddq, ^2J = 14.9, ^3J = 1.9, ^5J = 1.2 Hz, 1H, H_B-6), 2.17 (s, 3H, CH_3 in Ac), 2.12 (d, ^5J = 1.2 Hz, 3H, 4-CH_3); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 198.2 (C═O in Ac), 154.1 (C-2), 145.7 (C-4), 134.0 (C), 131.5 (2CH), 129.0 (2CH), 127.1 (CH), 115.3 (C-5), 61.9 (C-7), 34.7 (C-6), 30.0 (CH_3 in Ac), 20.9 (4-CH_3). Anal. Calcd for $C_{14}H_{16}N_2O_2S$: C, 60.85; H, 5.84; N, 10.14. Found: C, 60.70; H, 5.98; N, 9.94.

*5-Benzoyl-4-methyl-7-phenylthio-2,3,6,7-tetrahydro-1H-1,3-diazepin-2-one (**24h**).* Compd **24h** (0.367 g, 88%) was prepared from pyrimidine **15j** (0.401 g, 1.24 mmol), NaH (0.033 g, 1.36 mmol), and thiophenol (0.150 g, 1.36 mmol) in dry THF (8 mL) (2 h, rt) as described for **24a**. The crude product was purified using column chromatography on silica gel 60 (13.41 g) eluting with $CHCl_3$/MeOH (from 100:0.75 to 100:1). Mp 86−99 °C (EtOH); IR (Nujol) ν_{max} 3233 (br s), 3100 (br s), 3058 (sh) (NH), 1688 (vs) (amide-I), 1658 (m), 1623 (sh), 1603 (vs) (C═O and C═C), 1577 (w), 1510 (w) (CC_{arom}), 749 (s), 721 (s), 692 (s) (CH_{arom}) cm^{-1}; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 8.63 (br d, ^4J = 2.1 Hz, 1H, $N_{(3)}H$), 8.07 (br doublet of unresolved dd, ^3J = 6.3, ^4J = 2.1, ^4J ≈ 0.8 Hz, 1H, $N_{(1)}H$), 7.74−7.80 (m, 2H, ArH), 7.22−7.59 (m, 8H, ArH), 5.04 (ddd, ^3J = 6.3, ^3J = 5.4, ^3J = 2.3 Hz, 1H, H-7), 2.99 (ddd, ^2J = 14.9, ^3J = 5.4, ^4J = 0.8 Hz, 1H, H_A-6), 2.87 (ddq, ^2J = 14.9, ^3J = 2.3, ^5J = 1.3 Hz, 1H, H_B-6), 1.72 (d, ^5J = 1.3 Hz, 3H, CH_3); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 196.8 (C═O in Bz), 154.4 (C-2), 143.8 (C-4), 139.9 (C), 133.9 (C), 131.9 (CH), 131.7 (2CH), 129.0 (2CH), 128.7 (2CH), 128.5 (2CH), 127.2 (CH), 114.3 (C-5), 62.4 (C-7), 35.9 (C-6), 21.4 (CH_3). Anal. Calcd for $C_{19}H_{18}N_2O_2S$ × $0.15C_2H_5OH$: C, 67.13; H, 5.52; N, 8.11. Found: C, 66.93; H, 5.64; N, 8.08.[31]

*5-Benzoyl-4-phenyl-7-phenylthio-2,3,6,7-tetrahydro-1H-1,3-diazepin-2-one (**24i**).* Compd **24i** (0.532 g, 80%) was prepared from pyrimidine **15k** (0.644 g, 1.67 mmol), NaH (0.044 g, 1.85 mmol), and thiophenol (0.204 g, 1.85 mmol) in dry THF (10 mL) (rt, 2 h) as described for **24a**. The crude product (0.665 g) was purified using column chromatography on silica gel (22.97 g) eluting with $CHCl_3$/petroleum ether (from 20:5 to 85:15). Mp 200.5−201.5 °C (decomp, EtOH); IR (Nujol) ν_{max} 3280 (br s), 3233 (sh), 3201 (sh), 3089 (sh), 3057 (s) (NH), 1669 (s) (amide-I), 1609 (br vs) (C═O and C═C), 1579 (m), 1489 (w) (CC_{arom}), 763 (s), 751 (s), 722 (m), 694 (s) (CH_{arom}) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6) δ 8.68 (br d, ^4J = 2.0 Hz, 1H, $N_{(3)}H$), 8.01 (br ddd, ^3J = 5.4, ^4J = 2.0, ^4J = 0.8 Hz, 1H, $N_{(1)}H$), 7.53−7.59 (m, 2H, ArH), 7.03−7.41 (m, 13H, ArH), 5.15 (ddd, ^3J = 5.7, ^3J = 5.4, ^3J = 2.5 Hz, 1H, H-7), 3.25 (ddd, ^2J = 14.3, ^3J = 5.7, ^4J = 0.8 Hz, 1H, H_A-6), 3.06 (dd, ^2J = 14.3, ^3J = 2.5 Hz, 1H, H_B-6); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 197.0 (C═O in Bz), 154.5 (C-2), 147.0 (C-4), 138.7 (C), 136.0 (C), 133.4 (C), 132.2 (2CH), 131.0 (CH), 130.1 (2CH), 129.5 (CH), 129.2 (2CH), 129.1 (2CH), 127.7 (2CH), 127.5 (CH), 127.4 (2CH), 117.7 (C-5), 65.3 (C-7), 35.7 (C-6). Anal. Calcd for $C_{24}H_{20}N_2O_2S$: C, 71.98; H, 5.03; N, 7.00. Found: C, 71.87; H, 5.12; N, 6.96.

*Methyl 1-Carbamoyl-2-phenyl-1H-pyrrole-3-carboxylate (**33a**).* A suspension of compd **24b** (0.511 g, 1.44 mmol) and $TsOH\cdot H_2O$ (0.027 g, 0.14 mmol) in MeCN (8 mL) was refluxed under stirring for 30 min, and the solvent was removed under vacuum. The oily residue was triturated with saturated aqueous $NaHCO_3$ (2 mL) and petroleum ether (5 mL) until crystallization was completed. The suspension was cooled (0 °C), the precipitate was filtered, washed with ice-cold H_2O, petroleum ether, and dried to give **33a** (0.310 g, 88%). Mp 125.5−127 °C (EtOH); IR (Nujol) ν_{max} 3461 (s), 3332 (m), 3257 (br s), 3184 (m), 3140 (m), 3118 (m) (NH), 3064 (w), 3050 (w), 3007 (w) (CH_{arom}), 1736 (vs) (C═O), 1705 (vs) (amide-I), 1607 (s) (amide-II), 1562 (m), 1509 (w) (CC_{arom}), 1328 (vs), 1235 (s), 1185 (s) (C−O), 751 (s), 699 (s) (CH_{arom}) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6) δ 7.68 (br s, 2H, NH_2), 7.27−7.39 (m, 5H, ArH), 7.24 (d, ^3J = 3.3 Hz, 1H, H-5), 6.59 (d, ^3J = 3.3 Hz, 1H, H-4), 3.57 (s, 3H, CH_3); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 163.7 (C═O in COOMe), 151.4 (NH_2C═O), 137.0 (C-2), 131.5 (C), 130.0 (2CH), 127.8 (CH), 127.2 (2CH), 121.2 (C-5), 115.0 (C-3), 110.3 (C-4), 50.8 (CH_3). Anal. Calcd for $C_{13}H_{12}N_2O_3$: C, 63.93; H, 4.95; N, 11.47. Found: C, 63.87; H, 5.01; N, 11.42.

*Ethyl 1-Carbamoyl-2-phenyl-1H-pyrrole-3-carboxylate (**33b**).* Compd **33b** (0.244 g, 94%) was obtained from diazepine **24e** (0.369 g, 1.00 mmol) and $TsOH\cdot H_2O$ (0.020 g, 0.10 mmol) in MeCN (8 mL) (reflux, 30 min) as described for **33a**. Mp 151.5−152.5 °C (EtOH); IR (Nujol) ν_{max} 3450 (s), 3349 (m), 3315 (m), 3276 (br s), 3188 (s), 3149 (w), 3128 (w) (NH), 3086 (w), 3064 (w), 3035 (w) (CH_{arom}), 1737 (s) (C═O), 1712 (s), 1682 (vs) (amide-I), 1598 (s) (amide-II), 1557 (m), 1506 (w), 1481 (s) (CC_{arom}), 1305 (vs), 1199 (vs) (C−O), 737 (s), 707 (s) (CH_{arom}) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6) δ 7.65 (br s, 2H, NH_2), 7.27−7.38 (m, 5H, Ph), 7.24 (d, ^3J = 3.3 Hz, 1H, H-5), 6.58 (d, ^3J = 3.3 Hz, 1H, H-4), 4.01 (q, ^3J = 7.1 Hz, 2H, OCH_2), 1.04 (t, ^3J = 7.1 Hz, 3H, CH_3); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 163.4 (C═O in COOEt), 151.4 (NH_2C═O), 136.8 (C-2), 131.8 (C), 130.0 (2CH), 127.7 (CH), 127.2 (2CH), 121.1 (C-5), 115.6 (C-3), 110.3 (C-4), 59.2 (OCH_2), 13.9 (CH_3). Anal. Calcd for $C_{14}H_{14}N_2O_3$: C, 65.11; H, 5.46; N, 10.85. Found: C, 65.15; H, 5.48; N, 10.82.

*Ethyl 2-Butyl-1-carbamoyl-1H-pyrrole-3-carboxylate (**33c**).* Compd **33c** (0.204 g, 93%) was obtained from diazepine **24f** (0.322 g, 0.92 mmol) and $TsOH\cdot H_2O$ (0.018 g, 0.09 mmol) in MeCN (4 mL) (reflux, 30 min) as described for **33a**. Mp 150.5−151.5 °C (EtOH); IR (Nujol) ν_{max} 3428 (s), 3342 (m), 3248 (s), 3202 (s), 3150 (w), 3128 (w) (NH), 1722 (s) (C═O), 1680 (s) (amide-I), 1619 (s) (amide-II), 1577 (w), 1563 (m), 1511 (m) (CC_{arom}), 1308 (s), 1203 (s) (C−O) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6) δ 7.74 (br s, 2H, NH_2), 7.09 (d, ^3J = 3.4 Hz, 1H, H-5), 6.42 (d, ^3J = 3.4 Hz, 1H, H-4), 4.18 (q, ^3J = 7.1 Hz, 2H, OCH_2), 3.18−3.25 (m, 2H, $\mathit{CH_2}CH_2CH_2CH_3$), 1.43−1.53 (m, 2H, $CH_2\mathit{CH_2}CH_2CH_3$), 1.21−1.34 (m, 2H, $CH_2CH_2\mathit{CH_2}CH_3$), 1.25 (t, ^3J = 7.1 Hz, 3H, CH_3 in OEt), 0.86 (t, ^3J = 7.3 Hz, 3H, CH_3 in Bu); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 164.0 (C═O in COOEt), 152.1 (NH_2C═O), 141.5 (C-2), 119.6 (C-5), 114.1 (C-3), 109.9 (C-4), 59.2 (OCH_2), 31.8 ($\mathit{CH_2}CH_2CH_2CH_3$), 25.0 ($CH_2\mathit{CH_2}CH_2CH_3$), 22.1 ($CH_2CH_2\mathit{CH_2}CH_3$), 14.2 ($CH_3$ in OEt), 13.7 (CH_3 in Bu). Anal. Calcd for $C_{12}H_{18}N_2O_3$: C, 60.49; H, 7.61; N, 11.76. Found: C, 60.48; H, 7.62; N, 11.70.

*Methyl 2-Butyl-1-carbamoyl-1H-pyrrole-3-carboxylate (**33d**).* Compd **33d** (0.336 g, 94%) was obtained from diazepine **21b** (0.408 g, 1.59 mmol) and $TsOH\cdot H_2O$ (0.030 g, 0.16 mmol) in MeCN (8 mL) (reflux, 30 min) as described for **33a**. The analytically pure sample (0.224 g, white solid) was obtained from the crude product (0.398 g) using column chromatography on silica gel 60 (16 g) eluting with petroleum ether/$CHCl_3$ (from 3:1 to 1:2) followed by crystallization from EtOH (2 mL). Mp 148−149 °C (EtOH); IR (Nujol) ν_{max} 3431 (s), 3339 (m), 3242 (s), 3201 (s), 3156 (m), 3137 (m) (NH), 3011 (w) (CH_{arom}), 1725 (vs) (C═O), 1689 (s) (amide-I), 1620 (s) (amide-II), 1578 (m), 1563 (m), 1514 (m) (CC_{arom}), 1309 (s), 1209 (vs) (C−O) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6) δ 7.75 (br s, 2H, NH_2), 7.09 (d, ^3J = 3.4 Hz, 1H, H-5), 6.42 (d, ^3J = 3.4 Hz, 1H, H-4), 3.71 (s, 3H, OCH_3), 3.18−3.26 (m, 2H, $\mathit{CH_2}CH_2CH_2CH_3$), 1.43−1.53 (m, 2H, $CH_2\mathit{CH_2}CH_2CH_3$), 1.21−1.33 (m, 2H, $CH_2CH_2\mathit{CH_2}CH_3$), 0.86 (t, ^3J = 7.3 Hz, 3H, CH_3 in Bu); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 164.4 (C═O in COOMe), 152.1 (NH_2C═O), 141.7 (C-2), 119.7 (C-5), 113.7 (C-3), 109.7 (C-4), 50.8 (OCH_3), 31.7 ($\mathit{CH_2}CH_2CH_2CH_3$), 24.9 ($CH_2\mathit{CH_2}CH_2CH_3$), 22.0 ($CH_2CH_2\mathit{CH_2}CH_3$), 13.6 ($CH_3$ in Bu). Anal. Calcd for $C_{11}H_{16}N_2O_3$: C, 58.91; H, 7.19; N, 12.49. Found: C, 58.82; H, 7.29; N, 12.36.

*Dimethyl 1-Carbamoyl-1H-pyrrole-2,3-dicarboxylate (**33e**).* Compd **33e** (0.383 g, 87%) was obtained from diazepinone **21c** (0.505 g, 1.96 mmol) and $TsOH\cdot H_2O$ (0.037 g, 0.19 mmol) in MeCN (8 mL) (reflux, 30 min) as described for **33a**. Mp 149.5−151.5 °C (EtOAc); IR (Nujol) ν_{max} 3423 (s), 3365 (m), 3328 (br m), 3300 (s), 3196 (m), 3142 (w), 3124 (w) (NH), 1722 (sh), 1713 (vs) (C═O and amide-I), 1604 (m), 1586 (w), 1570 (m), 1486 (m) (CC_{arom}), 1331 (s), 1279 (s), 1227 (s) (C−O) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6) δ 8.07 (br s, 1H, NH), 7.98 (br s, 1H, NH), 7.41 (d, ^3J = 3.3 Hz, 1H, H-5), 6.56 (d, ^3J = 3.3 Hz, 1H, H-4), 3.76 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 162.7 (C═O in COOMe), 162.4 (C═O in COOMe), 149.9 (NH_2C═O), 128.8 (C-2), 120.3 (C-5), 116.2 (C-3), 110.4 (C-4), 52.5 (OCH_3), 51.6 (OCH_3). Anal. Calcd for $C_9H_{10}N_2O_5$: C, 47.79; H, 4.46; N, 12.39. Found: C, 47.65; H, 4.51; N, 12.28.

*3-Acetyl-1-carbamoyl-2-methyl-1H-pyrrole (**33f**).* Method A: Compd **33f** (0.243 g, 79%) as a light yellow solid was obtained from diazepine **21d** (0.366 g, 1.85 mmol) and $TsOH\cdot H_2O$ (0.035 g, 0.18 mmol) in MeCN (5 mL) (reflux, 30 min) as described for **33a**.

Method B: To a solution of Na (0.134 g, 5.82 mmol) in dry MeOH (10 mL) was added pyrimidine **15i** (0.600 g, 2.29 mmol), the obtained mixture was stirred at room temperature for 2 h, then $TsOH\cdot H_2O$ (0.799 g, 4.20 mmol) was added, and the suspension was refluxed under stirring for 30 min. The solvent was removed under vacuum. The oily residue was triturated with saturated aqueous $NaHCO_3$ (3 mL) and petroleum ether (5 mL) until crystallization was complete. The obtained suspension was cooled (0 °C), the precipitate was filtered, washed with ice-cold H_2O, petroleum ether, and dried to give **33f** (0.209 g, 55%) as a light yellow solid. The analytically pure sample (white solid) was obtained using column chromatography on silica gel 60 (5 g) eluting with $CHCl_3$/MeOH (from 100:0 to 110:1) followed by crystallization from EtOH. Mp 179.5−181 °C (decomp, EtOH); IR (Nujol) ν_{max} 3411 (s), 3337 (m), 3238 (m), 3195 (br s), 3143 (m), 3123 (m) (NH), 1716 (vs) (amide-I), 1653 (s) (C═O), 1621 (s) (amide-II), 1574 (m), 1550 (s), 1515 (s) (CC_{arom}) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6) δ 7.75 (br s, 2H, NH_2), 7.12 (d, ^3J = 3.5 Hz, 1H, H-5), 6.59 (d, ^3J = 3.5 Hz, 1H, H-4), 2.65 (s, 3H, 2-CH_3), 2.34 (s, 3H, CH_3 in Ac); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 194.7 (C═O on Ac), 152.2 (NH_2C═O), 135.4 (C-2), 122.9 (C-3), 119.2 (C-5), 110.7 (C-4), 29.2 (CH_3 in Ac), 13.1 (2-CH_3). Anal. Calcd for $C_8H_{10}N_2O_2$: C, 57.82; H, 6.07; N, 16.86. Found: C, 57.84; H, 6.09; N, 16.90.

*3-Benzoyl-1-carbamoyl-2-methyl-1H-pyrrole (**33g**).* Method A: Compd **33g** (0.430 g, 96%) as a light yellow solid was obtained from diazepine **21e** (0.512 g, 1.97 mmol) and $TsOH\cdot H_2O$ (0.037 g, 0.19 mmol) in MeCN (8 mL) (reflux, 30 min) as described for **33a**. The analytically pure sample (0.187 g, white solid) was obtained from the crude product (0.412 g) using column chromatography on silica gel 60 (13 g) eluting with $CHCl_3$/MeOH (from 100:0 to 75:1) followed by crystallization from EtOH (7 mL). Mp 191−192.5 °C (EtOH); IR (Nujol) ν_{max} 3398 (s), 3345 (m), 3250 (m), 3196 (br s), 3150 (m), 3121 (w) (NH), 3083 (w), 3059 (w), 3026 (w), 3003 (w) (CH_{arom}), 1728 (vs) (amide-I), 1636 (m), 1622 (s) (C═O and amide-II), 1597 (m), 1577 (m), 1546 (m), 1509 (m) (CC_{arom}), 731 (s), 706 (s) (CH_{arom}) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6) δ 7.81 (br s, 2H, NH_2), 7.47−7.72 (m, 5H, ArH), 7.20 (d, ^3J = 3.5 Hz, 1H, H-5), 6.30 (d, ^3J = 3.5 Hz, 1H, H-4), 2.61 (s, 3H, CH_3); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 191.5 (C═O in Bz), 152.1 (NH_2C═O), 139.6 (C), 136.8 (C-2), 131.8 (CH), 128.7 (2CH), 128.3 (2CH), 122.1 (C-3), 119.2 (C-5), 111.6 (C-4), 13.5 (CH_3). Anal. Calcd for $C_{13}H_{12}N_2O_2$: C, 68.41; H, 5.30; N, 12.27. Found: C, 68.34; H, 5.27; N, 12.28.

Method B: Compd **33g** (0.267 g, 92%) was obtained from diazepine **21e** (0.331 g, 1.27 mmol) and TsOH·H_2O (0.024 g, 0.13 mmol) in EtOH (5 mL) (reflux, 30 min) as described for **33a**.

3-Benzoyl-1-carbamoyl-2-phenyl-1H-pyrrole ***(33h)***. Method A: Compd **33h** (0.114 g, 96%) as a light yellow solid was obtained from diazepine **24i** (0.163 g, 0.41 mmol) and TsOH·H_2O (0.008 g, 0.04 mmol) in MeCN (3 mL) (reflux, 45 min) as described for **33a**.

Method B: Compd **33h** (0.248 g, 94%) as a light yellow solid was obtained from diazepine **21f** (0.292 g, 0.91 mmol) and TsOH·H_2O (0.017 g, 0.09 mmol) in MeCN (6 mL) (reflux, 25 min) as described for **33a**. The analytically pure sample (0.276 g, white solid) was obtained from the crude product (0.382 g) using column chromatography on silica gel 60 (11 g) eluting with petroleum ether/$CHCl_3$ (from 3:1 to 1:1) followed by crystallization from EtOH (1.5 mL). Mp 136−137 °C (EtOH); IR (Nujol) ν_{max} 3356 (br s), 3275 (s), 3189 (br s), 3138 (w), 3113 (m) (NH), 3057 (m), 3023 (w) (CH_{arom}), 1706 (vs) (amide-I), 1633 (s), 1628 (sh) (C═O and amide-II), 1600 (m), 1579 (m), 1541 (m), 1504 (m), 1492 (m) (CC_{arom}), 763 (m), 725 (s), 698 (s) (CH_{arom}) cm^{-1}; ^1H NMR (300.13 MHz, DMSO-d_6) δ 7.77 (br s, 2H, NH_2), 7.31−7.62 (m, 5H, ArH), 7.32 (d, ^3J = 3.3 Hz, 1H, H-5), 7.20−7.23 (m, 5H, ArH), 6.48 (d, ^3J = 3.3 Hz, 1H, H-4); ^{13}C NMR (75.48 MHz, DMSO-d_6) δ 191.4 (C═O in Bz), 151.6 (NH_2C═O), 138.4 (C), 136.0 (C-2), 132.0 (CH), 131.4 (C), 129.9 (2CH), 128.9 (2CH), 128.0 (2CH), 127.5 (CH), 127.4 (2CH), 123.7 (C-3), 121.2 (C-5), 111.3 (C-4). Anal. Calcd for $C_{18}H_{14}N_2O_2$: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.37; H, 4.87; N, 9.66.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b01348.

> Copies of ^1H, ^{13}C NMR, and IR spectra of all the synthesized compounds; X-ray diffraction data for **18b**, **20b**, **21a**,**b**, and **33a**,**f**; and results of DFT calculations for ring expansion of **26** (PDF)
>
> X-ray crystallographic data for compounds **18b**, **20b**, **21a**,**b**, and **33a**,**f** (CIF)

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Notes

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■ ACKNOWLEDGMENTS

This research was financially supported by the Russian Foundation for Basic Research (Grant No. 15-03-07564). The X-ray diffraction experiments were carried out in the Shared Facilities Center of IPCE RAS.

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(12) ^{1}H NMR spectrum of ureide **12** (300.13 MHz, DMSO-d_6) δ 10.78 (s, 1H, N*H*Bz), 9.07 (d, ^3J = 8.6 Hz, 1H, N*H*CH), 4.74−4.85 (m, 1H, CHN), 3.58 (dd, ^2J = 17.5, ^3J = 6.2 Hz, 1H, H_A in BzC*H*$_2$), 3.53 (dd, ^2J = 17.5, ^3J = 6.4 Hz, 1H, H_B in BzC*H*$_2$), signals of other protons overlap with signals of analogous protons of urea **9g**.

(13) Previously[33] we described base-promoted cleavage of the C4-C5 bond in 5-acyl-4-hydroxyhexahydropyrimidine-2-thiones.

(14) ^{1}H NMR spectrum of lactone **14a** (300.13 MHz, DMSO-d_6) δ 9.72 (s, 1H, NH), 7.63 (s, 1H, NH), 7.39−7.60 (m, 5H, ArH), 4.88 (dd, $^2J_{H(A),H(B)}$ = 8.0, $^3J_{H(A),CHN}$ = 7.9 Hz, 1H, H_A in OCH_2), 4.53 (dd, $^3J_{CHN,H(B)}$ = 8.6, $^3J_{CHN,H(A)}$ = 7.9 Hz, 1H, CHN), 3.89 (dd, $^2J_{H(B),H(A)}$ = 8.0, $^3J_{H(B),CHN}$ = 8.6 Hz, 1H, H_B in OCH_2). ^{13}C NMR spectrum of lactone **14a** (75.48 MHz, DMSO-d_6) δ 166.47 (O-C=O), 153.43 (N-C=O), 148.40 (N-C=C), 130.89 (CH), 129.83 (2CH), 127.68 (2CH), 93.07 (N-C=C), 70.42 (OCH_2), 50.37 (CHN).

(15) ^{1}H NMR spectrum of 4-methylene-5-phenyl-1,2,3,4,7,7a-hexahydrofuro[3,4-*d*]pyrimidin-2-one (300.13 MHz, DMSO-d_6) δ 8.88 (s, 1H, NH), 7.11 (s, 1H, NH), 4.81 (dd, $^2J_{H(A),H(B)}$ = 7.5, $^3J_{H(A),CHN}$ = 8.5 Hz, 1H, H_A in OCH_2), 4.59 (dd, $^3J_{CHN,H(B)}$ = 9.7, $^3J_{CHN,H(A)}$ = 8.5 Hz, 1H, CHN), 4.25 (s, 1H, C=CH), 4.10 (dd, $^2J_{H(B),H(A)}$ = 7.5, $^3J_{H(B),CHN}$ = 9.7 Hz, 1H, H_B in OCH_2), 4.02 (s, 1H, C=CH), signals of aromatic protons overlap with signals of analogous protons of diazepine **20e**.

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