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A novel convenient synthesis of 5-acyl-1,2-dihydropyrimidin-2-ones via 4-trichloromethyl-1,2,3,4-tetrahydropyrimidin-2-ones

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ABSTRACT

A novel four-step methodology for the synthesis of 5-acyl-1,2-dihydropyrimidin-2-ones has been developed. The reaction of readily available *N*-[(1-acetoxy-2,2,2-trichloro)ethyl]ureas with Na-enolates of 1,3-diketones or β-oxoesters followed by heterocyclization–dehydration of the oxoalkylureas formed gave 5-acyl-4-trichloromethyl-1,2,3,4-tetrahydropyrimidin-2-ones. The latter, in the presence of NaH, eliminate $CHCl_3$ to give the target compounds.

1. Introduction

1,2-Dihydropyrimidin-2-ones **1a** are of considerable interest due to their wide range of biological activities.[1] These compounds have been extensively studied, and effective methods for their synthesis have been developed.[2] In contrast, 5-acyl-1,2-dihydropyrimidin-2-ones (**1b**, Fig. 1) have been studied less widely. A number of methods including condensations of (C–C–C–N–C–N)-,[3] (C–C–C–N+C–N)-,[4] and (C–C–C+N–C–N)-types,[3b,5] dehydrogenation[6] and oxidation[7] of corresponding 1,2,3,4-tetrahydropyrimidin-2-ones, catalytic acylation of 5-trialkylstannylpyrimidines,[8] and hydrolysis of appropriate 2-functionalized pyrimidines[8,9] has been reported for the synthesis of pyrimidines **1b**. However, the synthetic methods generally efficient in the preparation of **1a** tend to give poor yields in the specific case of **1b**. The lack of reliable synthetic methods severely hampers studies of their potentially diverse biological activities.

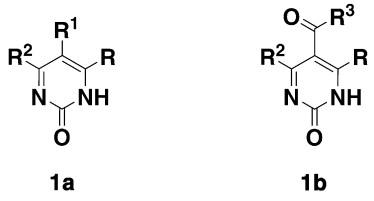
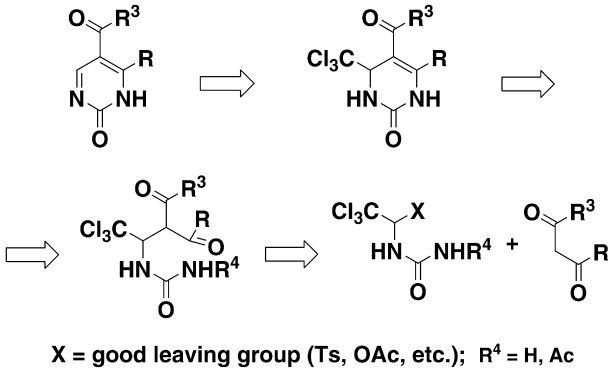


Figure 1. Structures of 1,2-dihydropyrimidin-2-ones **1a** and 5-acyl-1,2-dihydropyrimidin-2-ones **1b**.

Taking into consideration the reported formation of imines from α-trichloromethyl-substituted secondary amines and amides by elimination of chloroform in the presence of bases,[10] we hypothesized that 4-unsubstituted 1,2-dihydropyrimidin-2-ones (**1b** R^2=H) could be obtained starting from corresponding 5-acyl-4-trichloromethyl-1,2,3,4-tetrahydropyrimidin-2-ones. Synthesis of the latter is presented in our retrosynthetic plan (Scheme 1) and includes the ureidoalkylation of sodium enolates of α-substituted ketones.[11a–c]



Scheme 1. Retrosynthesis of 4-unsubstituted 5-acyl-1,2-dihydropyrimidin-2-ones.

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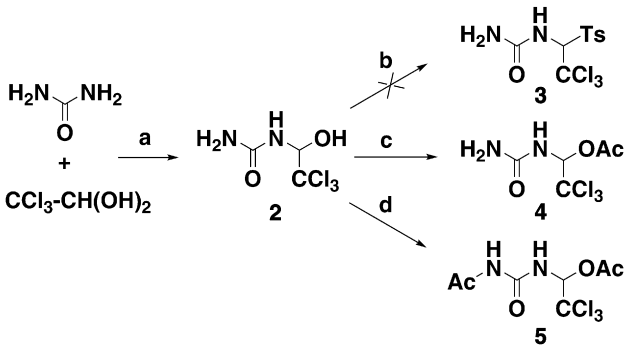
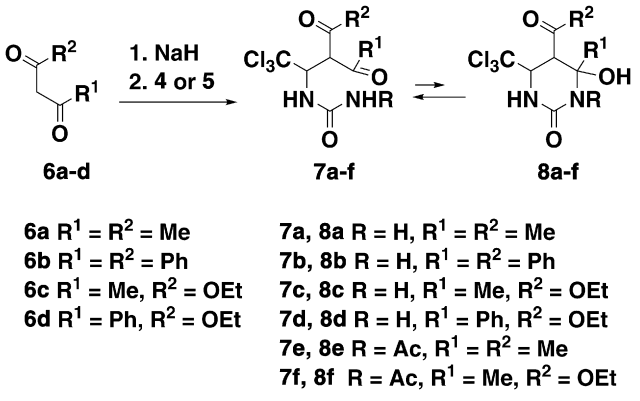
In this article we describe a novel convenient synthesis of 4-unsubstituted 1,2-dihydropyrimidin-2-ones via 5-acyl-4-trichloromethyl-1,2,3,4-tetrahydropyrimidin-2-ones as key intermediates.

2. Results and discussion

In our previous experience, α-tosyl-substituted *N*-alkylureas proved very useful starting materials for the preparation of various 5-acyl-1,2,3,4-tetrahydropyrimidin-2-ones by ureidoalkylation of α-substituted ketones.[11a–c] However, the synthesis of tosyl derivative **3** bearing a trichloromethyl group failed (Scheme 2) while acetoxy derivatives **4** and **5**[12] were conveniently prepared by treatment of the readily available **2**[13] with Ac_2O in pyridine and Ac_2O in the presence of H_2SO_4, respectively. Based on the ability of the acetoxy group to serve as a good leaving group in various reactions of ureidoalkylation,[14,15] we hypothesized that compounds **4** and **5** might also be used in the synthesis of compounds **7** under the conditions similar to those applicable for ureidoalkylation of α-substituted ketones with α-tosyl-substituted *N*-alkylureas.[11a–c]



Scheme 2. Synthesis of ureidoalkylating agents **4** and **5**. Reagents and conditions: (a) H_2O, rt; (b) 4-$MeC_6H_4S(O)OH$, H_2O, rt or heating; (c) Ac_2O, py, rt, 75%; (d) Ac_2O, H_2SO_4, rt, 79%.



Scheme 3. Synthesis of ureas **7a–f** by reaction of sodium enolates of 1,3-diketones **6a**,**b** and β-oxoesters **6c**,**d** with **4** and **5**.

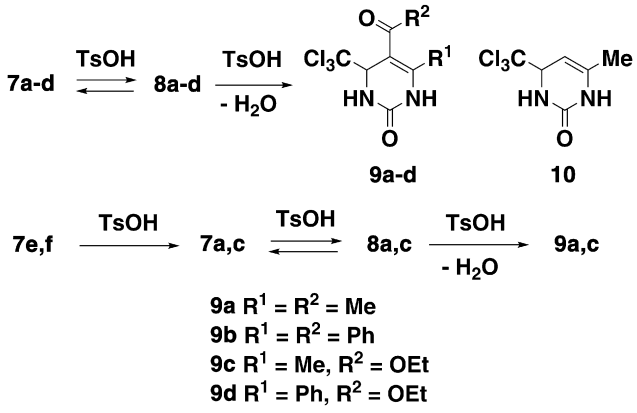
Sodium enolates of 1,3-dicarbonyl compounds **6a**,**b** and β-oxoesters **6c**,**d** generated in situ by treating the corresponding CH-acids with an equivalent amount of NaH reacted with urea **4** for 2.7–4.3 h at rt to give the products of acetoxy group substitution, *N*-oxoalkylureas **7a–d**, in 70–95% yield (Scheme 3, Table 1). Anhydrous MeCN was used as a solvent for preparation of compounds **7a**,**c–d**; however, for compound **7b** anhydrous THF was used because the solubility of the enolate of **6b** in MeCN was very low and the resulting extremely dense suspension hampered the completion of reaction of NaH with **6b**.

Following the same procedure, urea **5** reacted with the sodium enolate of **6a** and **6c** in MeCN (rt, 4.2–4.4 h) to give oxoalkylureas **7e** and **7f** in 82 and 69% yield, respectively (Scheme 3, Table 1).

IR-, ^{1}H- and ^{13}C NMR spectra indicated that compounds **7a–f** only existed in acyclic form both in solid state and in DMSO-d_6 solution. Their cyclic isomers **8a–f** (Scheme 3) were not detected by any spectroscopic methods.

Compounds **7c**,**d**, and **f** were formed as mixtures of two diastereomers (Table 1). The diastereoselectivity of the product formation depended on the structures of both reagents and was higher with **5** than with **4** (entry 3 vs entry 8) and with **6d** than with **6c** (entry 3 vs entry 4). The reaction time did not affect the ratio of diastereomers (entry 5 vs entry 6). The use of a greater excess of a nucleophile slightly reduced the stereoselectivity (entry 5 vs entry 4), which indicated that these reactions were controlled by both kinetic and thermodynamic factors.

Refluxing solutions of ureas **7a–f** in the presence of TsOH (Scheme 4) led to 4-trichloromethyl-1,2,3,4-tetrahydropyrimidin-2-ones **9a–d**. The dependence of the yields of **9a–d** on the reaction conditions is outlined in Table 2.



Scheme 4. Synthesis of 5-acyl-4-trichloromethyl-1,2,3,4-tetrahydropyrimidin-2-ones **9a–d**.

Table 1
Reaction of ureas **4** and **5** with sodium enolates of **6a–d**[a]

Entry	Starting material		Solvent	Reaction time, h	Molar ratio (**4**/**6** or **5**/**6**)	Product	Diastereomeric ratio[b]	Yield,[c] %
1	**6a**	**4**	MeCN	3.3	1:1	**7a**	—	70
2	**6b**	**4**	THF	4.3	1:1	**7b**	—	89
3	**6c**	**4**	MeCN	4	1.1:1	**7c**	57:43	86
4	**6d**	**4**	MeCN	2.7	1.1:1	**7d**	72:28	95
5	**6d**	**4**	MeCN	5.75	1:1	**7d**	83:17	91
6	**6d**	**4**	MeCN	9.3	1:1	**7d**	84:16	90
7	**6a**	**5**	MeCN	4.4	1:1	**7e**	—	82
8	**6c**	**5**	MeCN	4.2	1.1:1	**7f**	75:25	69

[a] At room temperature.
[b] Established by ^{1}H NMR data of crude product.
[c] All yields refer to isolated material homogeneous spectroscopically and by TLC.

Table 2
Synthesis of pyrimidinones **9a–d** from ureas **7a–f**[a]

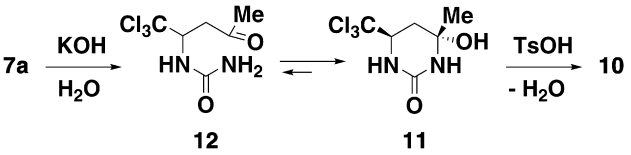
Entry	Starting material	Solvent	Molar ratio of **7**:TsOH	Reaction time, h	Product(s)	Molar ratio of **9a**:**10**[b]	Yield of **9**, %
1	**7a**	MeCN	1:0.3	0.6	**9a**	—	95
2	**7a**	PhMe	1:1.13	1.0	**9a**+**10**	73:27	—
3	**7a**	EtOH	1:1.13	1.0	**9a**+**10**	94:6	—
4	**7a**	EtOH	1:0.5	1.25	**9a**+**10**	94:6	—
5	**7a**	EtOH	1:0.3	0.63	**9a**+**10**	90:10	—
6	**7a**	MeOH	1:0.5	1.75	**9a**+**10**	62:38	—
7	**7b**	MeCN	1:1	2.2	**9b**	—	91
8	**7c**	MeCN	1:0.3	1.0	**9c**	—	93
9	**7c**	PhMe	1:1.1	1.0	**9c**	—	84
10	**7d**	MeCN	1:0.5	33	**9d**	—	81
11	**7d**	MeCN	1:3.0	14.2	**9d**	—	75
12	**7e**	EtOH	1:1.5	2.0	**9a**+**10**	79:21	—
13	**7f**	EtOH	1:2.0	3.0	**9c**	—	77

[a] Boiling in the presence of TsOH.
[b] Based on ^{1}H NMR spectrum of crude product.

Heterocyclization–dehydration of **7a–d** proceeded smoothly in MeCN as a solvent to give **9a–d** in high yields (75–95%, Table 2, entries 1, 7–11). Reaction of **7a**,**c** was complete after 0.5–1 h in the presence of TsOH (0.3 equiv, entries 1, 8). By comparison with compounds **7a**,**c**, their counterparts **7b**,**d**, that possess a less electrophilic carbonyl group, were converted into **9b**,**d** (entries 7, 10–11) using a greater amount of catalyst or/and longer reaction time. Pyrimidine **9c** was also readily synthesized from **7c** using toluene as a solvent (entry 9).

In contrast to the smooth conversion of **7a** into **9a** in MeCN, refluxing **7a** in EtOH, MeOH or toluene in the presence of TsOH led to the formation of **9a** plus the product of its deacetylation, pyrimidine **10** (entries 2–6). Presumably, **10** was obtained as a result of the acid-promoted deacylation of **7a** followed by heterocyclization and dehydration of the intermediate formed. The data listed in Table 2 indicates that the formation of **10** was favored in more polar solvents (entry 4 vs entry 6), at higher reaction temperature (entry 2 vs entry 3), and in protic solvents (entry 1 vs entry 5). The amount of catalyst had no appreciable effect on the ratio of **9a** to **10** (entry 3 vs entry 4 vs entry 5).

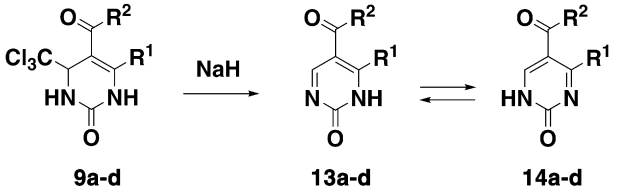
The structure of **10** was confirmed by its independent synthesis from **7a** (Scheme 5). First, compound **7a** was treated with aqueous KOH (rt, 2 h) to give hydroxypyrimidine **11** in 73% yield as a single (4*R**,6*S**)-diastereomer. In the next step, **11** was dehydrated by heating in ethanolic TsOH to give pyrimidine **10** in 83% yield.



Scheme 5. Synthesis of tetrahydropyrimidin-2-one **10**.

Finally, aromatization of tetrahydropyrimidines **9a–d** by NaH (1.2–1.25 equiv) in an aprotic solvent at rt led to formation of the corresponding **13a–d** in good yields (Scheme 6). The reaction proceeded best in THF (for **13a**,**c**,**d**) and, for **13b**, in DME while the more polar MeCN failed to give satisfactory yields even with a prolonged reaction time (24 h) and a greater excess of NaH (up to 1.5 equiv).

The structure of compounds **13a–d** was confirmed by ^{1}H- and ^{13}C NMR spectra and by comparing their constants with those reported in literature.[3a,3b,5a,7h] ^{13}C NMR spectra of the solutions of these compounds in DMSO-d_6 revealed an extremely large broadening of the signals of C4, C6, and the carbon atom of group R^1 directly bound to pyrimidine ring, which suggested that the compounds existed as tautomeric mixtures of **13a–d** and **14a–d** (Scheme 6).



13a, 14a $R^1 = R^2 = Me$
13b, 14b $R^1 = R^2 = Ph$
13c, 14c $R^1 = Me$, $R^2 = OEt$
13d, 14d $R^1 = Ph$, $R^2 = OEt$

Scheme 6. Synthesis of 5-acyl-1,2-dihydropyrimidin-2-ones **13a–d**.

3. Conclusion

Thus, we have developed a novel, more general synthesis of 5-acyl-1,2-dihydropyrimidin-2-ones. The four-step procedure involving 4-chloromethyl-1,2,3,4-tetrahydropyrimidin-2-ones as key compounds is very straightforward, giving the yields in a range of 69–95% per step, and uses very inexpensive starting materials. The procedure is versatile in that, in addition to 5-acyl derivatives, it allows one to obtain other 5-functionally substituted 1,2-dihydropyrimidin-2-ones whose preparation will be disclosed in our further publications.

4. Experimental section

4.1. General

MeCN was dried by distillation from P_2O_5 and then from CaH_2. THF and DME were dried over Na-benzophenone followed by distillation. Ethyl acetoacetate and acetylacetone were dried over $MgSO_4$ followed by vacuum distillation. NaH (60% suspension in mineral oil) was washed with dry hexane, and dried in a vacuum desiccator prior to use. All other reagents and solvents were purchased from commercial sources and used without further treatment. IR spectra (in Nujol) were recorded either on a Bruker Equinox 55/S spectrophotometer or on a Bruker Vector 22 spectrophotometer. Bands characteristics in the IR spectra are defined as very strong (vs), strong (s), medium (m), shoulder (sh). NMR spectra were recorded on a Bruker DPX 300 spectrometer at 300.13 (^{1}H) and 75.48 (^{13}C) MHz in DMSO-d_6. ^{1}H NMR chemical shifts are referenced to the residual proton signal for DMSO-d_6 (2.50 ppm). ^{13}C NMR chemical shifts are reported to the carbon signal for DMSO-d_6 (39.50 ppm). Multiplicities are reported as singlet (s), doublet (d), triplet (t), quartet (q), some combination of these, multiplet (m). Thin layer chromatography (TLC) was performed on silica gel plates Silufol UV 254 (Czech Republic) or Kieselgel 60 F_{254} (Merck) in chloroform–methanol (9:1, v/v) as a solvent system. Plates were visualized with iodine vapor or UV light. All yields refer to isolated, spectroscopically and TLC pure material.

4.2. *N*-[(1-Acetoxy-2,2,2-trichloro)ethyl]urea (4)

To a stirred and cooled on cold-water bath mixture of compound **2**[13] (2.020 g, 9.74 mmol) and anhydrous pyridine (4.5 mL) was added Ac_2O (1.511 g, 14.80 mmol). The reaction mixture was stirred for 4 h at rt, the solvent was removed in vacuo, the syrupy residue was triturated with cold H_2O (20 mL) until crystallization, the precipitate was filtered, washed with ice-cold water, ice-cold HCl (3.6%, 15 mL), ice-cold water, and dried to give compound **4** (1.810 g, 74.5%), which was used without further purification. An analytically pure sample was obtained by crystallization from EtOH–benzene (1:6, v/v). Mp 150.5–151.5 °C (decomp., EtOH–

benzene). ^{1}H NMR δ: 7.46 (1H, d, $^3J_{NH,CH}$=10.2 Hz, NH), 6.88 (1H, d, $^3J_{CH,NH}$=10.2 Hz, CH), 6.10 (2H, br s, NH_2), 2.13 ppm (3H, s, CH_3). ^{13}C NMR δ: 168.26 (C=O in Ac), 155.96 [N–C(O)–N], 99.10 (CCl_3), 80.61 (N–CH), 20.49 (CH_3). IR ν, cm^{-1}: 3473 (s), 3341 (s), 3211 (m) (ν NH), 1734 (vs) (ν C=O in OAc), 1677 (vs) (amide-I), 1624 (s), 1525 (vs) (amide-II), 1249 (vs), 1201 (s), 1021 (s) (ν C–O). Anal. Calcd for $C_5H_7Cl_3N_2O_3$: C, 24.07; H, 2.83; N, 11.23%. Found: C, 24.32; H, 2.37; N, 11.58%.

4.3. *N*-[(1-Acetoxy-2,2,2-trichloro)ethyl]-*N*′-acetylurea (5)

Compound **5** was prepared by the procedure briefly described in reference[12] and here we report our detailed method. To a mixture of urea **2**[13] (11.982 g, 57.8 mmol) and Ac_2O (30.075 g, 294.6 mmol) was added three drops of conc. H_2SO_4, and the solid substance rapidly dissolved with heating upon stirring. The resulted solution was cooled to 0 °C until precipitation was complete, then the precipitate was filtered, thoroughly washed with light petrol, and dried to give compound **5** (13.248 g, 78.7%), which was used further without additional purification. Mp 165.5–166 °C (decomp., *i*-PrOH) [Lit.[12] mp 160 °C (decomp.; EtOH–H_2O)]. ^{1}H NMR δ: 10.93 (1H, s, NH in NHAc), 9.67 (1H, d, $^3J_{NH,CH}$=10.0 Hz, NH in NH–CH), 6.96 (1H, d, $^3J_{CH,NH}$=10.0 Hz, CH), 2.18 (3H, s, CH_3 in OAc), 2.07 (3H, s, CH_3 in N–Ac). ^{13}C NMR δ: 173.74 (C=O in NHAc), 168.23 (C=O in OAc), 152.12 [N–C(O)–N], 97.86 (CCl_3), 78.95 (N–CH), 23.69 (CH_3 in NHAc), 20.34 ppm (CH_3 in OAc). IR ν, cm^{-1}: 3235 (s), 3137 (s) (ν NH), 1775 (vs), ~1723 (sh), 1718 (s), 1693 (vs) [ν C=O in OAc, ν C=O in C(O)–NH–C(O)–NH], 1541 (s), 1510 (m) (amide-II), 1258 (s), 1206 (s), 1026 (s) (ν C–O).

4.4. *N*-[(3-Acetyl-1,1,1-trichloro-4-oxo)pent-2-yl]urea (7a)

To a stirred and cooled in ice bath suspension of NaH (0.296 g, 12.33 mmol) in anhydrous MeCN (13.5 mL) was added dropwise the solution of acetylacetone (**6a**) (1.244 g, 12.43 mmol) in MeCN (9 mL) and the resulting suspension was stirred for 16 min. To the formed suspension of the sodium enolate of acetylacetone was added compound **4** (3.079 g, 12.34 mmol). The reaction mixture was stirred for 3 h 20 min at rt and the solvent was removed in vacuo. To the residue was added saturated aqueous solution of $NaHCO_3$ (5 mL), and the obtained suspension was left in a water bath (bath temperature 35 °C) for 30 min. Upon cooling to 0 °C, the precipitate was filtered, washed with ice-cold water, light petrol, cold Et_2O (3×10 mL), and dried to give compound **7a** (2.498 g, 70.0%). Mp >300 °C (decomp., AcOEt). ^{1}H NMR δ: 6.80 (1H, d, $^3J_{NH,CH}$=10.6 Hz, NH), 5.97 (2H, br s, NH_2), 5.58 (1H, dd, $^3J_{CH,NH}$=10.6, $^3J_{CH,CH}$=7.5 Hz, CH–N), 4.37 (1H, d, $^3J_{CH,CH}$=7.5 Hz, CH–C=O), 2.24 (3H, s, CH_3), 2.13 (3H, s, CH_3). ^{13}C NMR δ: 200.71, 200.59 (C=O in Ac), 157.08 (N–C=O), 102.65 (CCl_3), 67.99 (CH in $CHAc_2$), 61.86 (CH–N), 30.22, 29.43 (CH_3). IR ν, cm^{-1}: 3476 (m), 3372 (m), 3214 (s), 3087 (s) (ν NH), 1720 (s) (ν C=O in Ac), 1685 (s) (amide-I), 1618 cm^{-1} (s) (amide-II). Anal. Calcd for $C_8H_{11}Cl_3N_2O_3$: C, 33.19; H, 3.83; N, 9.68%. Found: C, 33.25; H, 3.45; N, 9.33%.

4.5. *N*-[(3-Benzoyl-1,1,1-tricloromethyl-4-oxo-4-phenyl)but-2-yl]urea (7b)

To a stirred and cooled in ice bath suspension of NaH (0.173 g, 7.21 mmol) in anhydrous THF (8 mL) was subsequently added dibenzoylmethane (**6b**) (1.618 g, 7.21 mmol) and THF (3 mL). After 10 min, to the resulting solution was added compound **4** (1.792 g, 7.18 mmol) and then THF (4 mL). The obtained suspension was stirred for 4 h 20 min at rt and solvent was removed in vacuo. The residue was triturated with light petrol, saturated aqueous solution of $NaHCO_3$ (2.5 mL) was added and the obtained mixture was left in a water bath (bath temperature 35 °C) for 30 min. The liquids were decanted, H_2O (5 mL) was added, and the residue was triturated upon cooling to 0 °C until crystallization. The precipitate was filtered, washed with ice-cold water, light petrol, a mixture of Et_2O–light petrol (1:1 v/v; 3×6 mL), and dried to give compound **7b** (2.645 g, 89.0%). Mp 122.5–125.5 °C (decomp., acetone–H_2O, 1:1 v/v). ^{1}H NMR δ: 7.95–8.04 (4H, m, $C_{(2)}$H and $C_{(6)}$H in Ph), 7.62–7.71 (2H, m, $C_{(4)}$H in Ph), 7.48–7.58 (4H, m, $C_{(3)}$H and $C_{(5)}$H in Ph), 6.74 (1H, d, $^3J_{NH,CH}$=10.5 Hz, NH), 6.10 (1H, d, $^3J_{CH,CH}$=6.4 Hz, CH–C=O), 6.01 (1H, dd, $^3J_{CH,NH}$=10.5, $^3J_{CH,CH}$=6.4 Hz, CH–N), 5.89 (2H, br s, NH_2). ^{13}C NMR δ: 192.61, 191.96 (C=O in Bz), 156.91 (N–C=O), 135.89, 135.11 ($C_{(1)}$ in Ph), 134.19, 134.10 ($C_{(4)}$ in Ph), 129.27, 129.19 ($C_{(2)}$ and $C_{(6)}$ in Ph), 128.77, 128.44 ($C_{(3)}$ and $C_{(5)}$ in Ph), 103.10 (CCl_3), 62.52 (CH–N), 56.44 (CH in $CHBz_2$). IR ν, cm^{-1}: 3466 (s), 3357 (s), 3199 (s) (ν NH), 1700 (vs) (ν C=O in Bz), 1675 (s) (amide-I), 1595 (m) (ν CC in Ph), 1555 (s), 1523 (s) (amide-II), 761 (s), 690 cm^{-1} (s) (δ CH in Ph). Anal. Calcd for $C_{18}H_{15}Cl_3N_2O_3$: C, 52.26; H, 3.66; N, 6.77%. Found: C, 52.06; H, 3.52; N, 6.41%.

4.6. *N*-[(1,1,1-Trichloro-3-ethoxycarbonyl-4-oxo)-pent-2-yl]urea (7c)

Compound **7c** (2.827 g, 85.8%) as a mixture of two diastereomers (57:43) was prepared (analogously to **7a**) from **4** (2.572 g, 10.31 mmol), **6c** (1.487 g, 11.43 mmol) and NaH (0.272 g, 11.33 mmol) in MeCN (20 mL) (rt, 4 h). Mp 169.5–170 °C (decomp., AcOEt) (rate of heating 1 °C per 4–11 s) and >250 °C (decomp. without melting) (rate of heating 1 °C per more than 25 s). ^{1}H NMR of major diastereomer δ: 6.71 (1H, d, $^3J_{NH,CH}$=10.5 Hz, NH), 6.07 (2H, br s, NH_2), 5.53 (1H, dd, $^3J_{CH,NH}$=10.5, $^3J_{CH,CH}$=5.1 Hz, CH–N), 4.26 (1H, d, $^3J_{CH,CH}$=5.1 Hz, CH–C=O), 4.06–4.23 (2H, m, signals overlap with signals of analogous protons of minor diastereomer, OCH_2), 2.27 (3H, s, CH_3 in Ac), 1.21 (3H, t, $^3J_{CH3,CH2}$=7.1 Hz, CH_3 in OEt). ^{1}H NMR of minor diastereomer δ: 6.84 (1H, d, $^3J_{NH,CH}$=10.6 Hz, NH), 5.98 (2H, br s, NH_2), 5.53 (1H, dd, $^3J_{CH,NH}$=10.6, $^3J_{CH,CH}$=8.2 Hz, CH–N), 3.93 (1H, d, $^3J_{CH,CH}$=8.2 Hz, CH–C=O), 4.06–4.23 (2H, m, signals overlap with signals of analogous protons of major diastereomer, OCH_2), 2.17 (3H, s, CH_3 in Ac), 1.19 (3H, t, $^3J_{CH3,CH2}$=7.1 Hz, CH_3 in OEt). ^{13}C NMR of major diastereomer δ: 199.13 (C=O in Ac), 166.58 (C=O in COOEt), 156.92 (N–C=O), 102.66 (CCl_3), 61.55 (OCH_2), 61.42 (CH–N), 59.96 (CH in CH–Ac), 28.92 (CH_3 in Ac), 13.75 (CH_3 in OEt). ^{13}C NMR of minor diastereomer δ: 199.33 (C=O in Ac), 167.08 (C=O in COOEt), 157.04 (N–C=O), 102.35 (CCl_3), 62.32 (CH–N), 61.95 (OCH_2), 61.14 (CH in CH–Ac), 28.68 (CH_3 in Ac), 13.73 (CH_3 in OEt). IR ν, cm^{-1}: 3465 (s), 3354 (s), 3281 (s), 3206 (s) (ν NH), 1711 (vs) (ν C=O in Ac and COOEt), 1663 (vs) (amide-I), 1622 (s), 1597 (s), 1546 (vs) (amide-II), 1231 (vs), 1162 (s), 1025 cm^{-1} (s) (ν C–O). Anal. Calcd for $C_9H_{13}Cl_3N_2O_4$: C, 33.83; H, 4.10; N, 8.77%. Found: C, 33.85; H, 3.71; N, 8.53%.

4.7. *N*-[(1,1,1-Trichloro-3-ethoxycarbonyl-4-oxo-4-phenyl)but-2-yl]urea (7d)

Compound **7d** (1.913 g, 94.5%) as a mixture of two diastereomers (72:28) was prepared (analogously to **7a** with the exception that it was washed with Et_2O–light petrol, 1:1, instead of Et_2O) from **4** (1.323 g, 5.30 mmol), **6d** (1.122 g, 5.84 mmol), and NaH (0.139 g, 5.79 mmol) in MeCN (10 mL) (rt, 2 h 40 min). Mp 82.5–85 °C (EtOH–H_2O, 1:1 v/v). ^{1}H NMR of major diastereomer δ: 7.54–8.02 (5H, m, signals overlap with signals of analogous protons of minor diastereomer, Ph), 6.83 (1H, d, $^3J_{NH,CH}$=10.7 Hz, NH), 6.03 (br s, 2H, NH_2), 5.87 (1H, dd, $^3J_{CH,NH}$=10.7, $^3J_{CH,CH}$=6.7 Hz, CH–N), 4.97 (1H, d, $^3J_{CH,CH}$=6.7 Hz, CH–C=O), 3.95–4.17 (2H, m, signals overlap with signals of analogous protons of minor diastereomer, OCH_2), 1.10 (3H, t, $^3J_{CH3,CH2}$=7.1 Hz, CH_3 in OEt). ^{1}H NMR of minor diastereomer δ: 7.54–8.02 (5H, m, signals overlap with signals of

analogous protons of major diastereomer, Ph), 6.81 (1H, d, $^3J_{NH,CH}$=10.2 Hz, NH), 5.94 (2H, br s, NH_2), 5.65 (1H, dd, $^3J_{CH,NH}$=10.2, $^3J_{CH,CH}$=6.1 Hz, CH–N), 5.15 (1H, d, $^3J_{CH,CH}$=6.1 Hz, CH–C=O), 3.95–4.17 (2H, m, signals overlap with signals of analogous protons of major diastereomer, OCH_2), 1.05 (3H, t, $^3J_{CH3,CH2}$=7.1 Hz, CH_3 in OEt). ^{13}C NMR of major diastereomer δ: 190.48 (C=O in Bz), 165.90 (C=O in COOEt), 156.86 (N–C=O), 134.96 ($C_{(1)}$ in Ph), 134.35 ($C_{(4)}$ in Ph), 129.35 ($C_{(2)}$ and $C_{(6)}$ in Ph), 128.29 ($C_{(3)}$ and $C_{(5)}$ in Ph), 102.72 (CCl_3), 61.87 (OCH_2), 61.13 (CH–N), 56.27 (CH in CH–Bz), 13.69 (CH_3 in OEt). ^{13}C NMR of minor diastereomer δ: 192.94 (C=O in Bz), 166.99 (C=O in COOEt), 156.92 (N–C=O), 136.28 ($C_{(1)}$ in Ph), 134.09 ($C_{(4)}$ in Ph), 129.09 ($C_{(2)}$ and $C_{(6)}$ in Ph), 128.61 ($C_{(3)}$ and $C_{(5)}$ in Ph), 102.89 (CCl_3), 63.61 (CH–N), 61.87 (OCH_2), 53.22 (CH in CH–Bz), 13.67 (CH_3 in OEt). IR ν, cm^{-1}: 3442 (s), 3383 (s), 3196 (s) (ν NH), 1734 (s) (ν C=O in COOEt), 1670 (vs) (amide-I and ν C=O in Bz), 1596 (m) (ν CC in Ph), 1511 (s) (amide-II), 1223 (s), 1169 (s), 1023 (s) (ν C–O), 728 (s), 687 cm^{-1} (s) (δ CH in Ph). Anal. Calcd for $C_{14}H_{15}Cl_3N_2O_4$: C, 44.06; H, 3.96; N, 7.34%. Found: C, 44.02; H, 3.75; N, 7.46%.

4.8. *N*-Acetyl-*N*′-[(3-acetyl-1,1,1-trichloro-4-oxo) pent-2-yl]urea (7e)

Compound **7e** (1.826 g, 82.1%) was prepared (analogously to **7a**) from **5** (1.956 g, 6.71 mmol), **6a** (0.690 g, 6.89 mmol), and NaH (0.161 g, 6.71 mmol) in MeCN (8 mL) (rt, 4 h 25 min). Mp 162.5–164 °C (BuOH). ^{1}H NMR δ: 10.72 (1H, s, NH in NHAc), 9.41 (1H, d, $^3J_{NH,CH}$=10.5 Hz, NH in NH–CH), 5.66 (1H, dd, $^3J_{CH,NH}$=10.5, $^3J_{CH,CH}$=6.2 Hz, CH–N), 4.67 (1H, d, $^3J_{CH,CH}$=6.2 Hz, CH–C=O), 2.26 (3H, s, CH_3 in $CHAc_2$), 2.25 (3H, s, CH_3 in $CHAc_2$), 2.04 (3H, s, CH_3 in N–Ac). ^{13}C NMR δ: 201.24, 199.91 (C=O in $CHAc_2$), 173.11 (C=O in NHAc), 152.92 [N–C(O)–N], 101.32 (CCl_3), 65.75 (CH in $CHAc_2$), 61.60 (CH–N), 31.32, 29.91 (CH_3 in $CHAc_2$), 23.57 (CH_3 in NHAc). IR ν, cm^{-1}: 3240 (s), 3127 (s) (ν NH), 1734 (s), 1710 (s) (ν C=O in Ac), 1690 (vs) (amide-I), 1529 (vs), 1501 cm^{-1} (s) (amide-II). Anal. Calcd for $C_{10}H_{13}Cl_3N_2O_4$: C, 36.22; H, 3.95; N, 8.45%. Found: C, 36.35; H, 3.73; N, 8.34%.

4.9. *N*-Acetyl-*N*′-[(1,1,1-trichloro-3-ethoxycarbonyl-4-oxo)pent-2-yl]urea (7f)

Compound **7f** (1.258 g, 68.8%) as a mixture of two diastereomers (75:25) was prepared (analogously to **9a**) from **5** (1.475 g, 5.06 mmol), **6c** (0.738 g, 5.67 mmol), and NaH (0.134 g, 5.57 mmol) in MeCN (16 mL) (rt, 4 h 14 min). Mp 123–129 °C (EtOH–H_2O, 1:1 v/v). ^{1}H NMR of major diastereomer δ: 10.72 (1H, s, NH in NHAc), 9.55 (1H, d, $^3J_{NH,CH}$=10.3 Hz, NH in NH–CH), 5.64 (1H, dd, $^3J_{CH,NH}$=10.3, $^3J_{CH,CH}$=4.5 Hz, CH–N), 4.44 (1H, d, $^3J_{CH,CH}$=4.5 Hz, CH–C=O), 4–4.24 (2H, m, signals overlap with signals of analogous protons of minor diastereomer, OCH_2), 2.26 (3H, s, CH_3 in Ac), 2.03 (3H, s, CH_3 in N–Ac), 1.21 (3H, t, $^3J_{CH3,CH2}$=7.1 Hz, CH_3 in OEt). ^{1}H NMR of minor diastereomer δ: 10.74 (1H, s, NH in NHAc), 9.50 (1H, d, $^3J_{NH,CH}$=10.3 Hz, NH in NH–CH), 5.57 (1H, dd, $^3J_{CH,NH}$=10.3, $^3J_{CH,CH}$=6.1 Hz, CH–N), 4.38 (1H, d, $^3J_{CH,CH}$=6.1 Hz, CH–C=O), 4.06–4.24 (2H, m, signals overlap with signals of analogous protons of major diastereomer, OCH_2), 2.26 (3H, s, CH_3 in Ac), 2.04 (3H, s, CH_3 in N–Ac), 1.19 (3H, t, $^3J_{CH3,CH2}$=7.3 Hz, CH_3 in OEt). ^{13}C NMR of major diastereomer δ: 198.60 (C=O in Ac), 172.98 (C=O in NHAc), 166.58 (C=O in COOEt), 152.90 [N–C(O)–N], 101.31 (CCl_3), 62.00 (OCH_2), 60.81 (CH–N), 59.23 (CH in CH–Ac), 28.83 (CH_3 in Ac), 23.58 (CH_3 in NHAc), 13.59 (CH_3 in OEt). ^{13}C NMR of minor diastereomer δ: 200.42 (C=O in Ac), 172.99 (C=O in NHAc), 166.65 (C=O in COOEt), 153.00 [N–C(O)–N], 101.05 (CCl_3), 62.63 (CH–N), 62.14 (OCH_2), 58.07 (CH in CH–Ac), 30.95 (CH_3 in Ac), 23.62 (CH_3 in NHAc), 13.75 (CH_3 in OEt). IR ν, cm^{-1}: 3258 (s), 3200 (m) (ν NH), 1748 (s), 1727 (vs) (ν C=O in COOEt and Ac), 1673 (s) (amide-I), 1535 (s), 1501 (s) (amide-II), 1213 (s), 1147 (s), 1033 cm^{-1} (s) (ν C–O). Anal. Calcd for $C_{11}H_{15}Cl_3N_2O_5$: C, 36.54; H, 4.18; N, 7.75%. Found: C, 36.47; H, 3.91; N, 7.85%.

4.10. 5-Acetyl-4-(trichloromethyl)-6-methyl-1,2,3,4-tetrahydropyrimidin-2-one (9a)

A suspension of compound **7a** (2.377 g, 8.21 mmol) and TsOH·H_2O (0.461 g, 2.42 mmol) in MeCN (20 mL) was refluxed for 36 min under stirring and then the solvent was removed in vacuo. To the dry residue was added saturated aqueous solution of $NaHCO_3$ (5 mL), and the mixture was triturated until crystallization. Upon cooling to 0 °C, the precipitate was filtered, washed with ice-cold water, light petrol, and dried to give compound **9a** (2.115 g, 94.9%). Mp >300 °C (decomp., EtOH). ^{1}H NMR δ: 9.66 (1H, d, $^4J_{N(1)H,N(3)H}$=1.7 Hz, $N_{(1)}H$), 8.57 (1H, dd, $^3J_{N(3)H,4\text{-}H}$=4.7, $^4J_{N(3)H,N(1)H}$=1.7 Hz, $N_{(3)}H$), 5.07 (1H, d, $^3J_{4\text{-}H,N(3)H}$=4.7 Hz, 4-H), 2.31 (3H, s, CH_3 in Ac), 2.21 (3H, s, 6-CH_3). ^{13}C NMR δ: 195.33 (C=O in Ac), 151.70 ($C_{(2)}$), 149.34 ($C_{(6)}$), 105.96 (CCl_3), 105.01 ($C_{(5)}$), 65.95 ($C_{(4)}$), 30.12 (CH_3 in Ac), 18.56 (6-CH_3). IR ν, cm^{-1}: 3206 (s), 3106 (s) (ν NH), 1710 (vs) (ν C=O in Ac), 1663 (s) (amide-I), 1601 cm^{-1} (s) (ν C=C). Anal. Calcd for $C_8H_9Cl_3N_2O_2$: C, 35.39; H, 3.34; N, 10.32%. Found: C, 35.51; H, 2.97; N, 10.51%.

4.11. 5-Benzoyl-4-(trichloromethyl)-6-phenyl-1,2,3,4-tetrahydropyrimidin-2-one (9b)

Compound **9b** (2.291 g, 90.7%) was prepared (analogously to **9a**) from **7b** (2.641 g, 6.38 mmol) and TsOH·H_2O (1.213 g, 6.38 mmol) in MeCN (18 mL) (reflux, 2 h 10 min). Mp 222–223 °C (MeCN). ^{1}H NMR δ: 9.77 (1H, s, $N_{(1)}H$), 8.68 (1H, d, $^3J_{N(3)H,4\text{-}H}$=4.5 Hz, $N_{(3)}H$), 7.41–7.46 (2H, m, $C_{(2)}H$ and $C_{(6)}H$ in Bz), 7.20–7.26 (2H, m, $C_{(4)}H$ in Bz), 7.03–7.15 (7H, m, $C_{(3)}H$ and $C_{(5)}H$ in Bz, CH in 6-Ph), 5.22 (1H, d, $^3J_{4\text{-}H,N(3)H}$=4.5 Hz, 4-H). ^{13}C NMR δ: 194.42 (C=O in Bz), 152.04 ($C_{(2)}$), 149.08 ($C_{(6)}$), 138.11 ($C_{(1)}$ in Bz), 132.99 ($C_{(1)}$ in 6-Ph), 131.55 ($C_{(4)}$ in Bz), 129.21 ($C_{(4)}$ in 6-Ph), 129.06 ($C_{(2)}$ and $C_{(6)}$ in Bz), 128.59 ($C_{(2)}$ and $C_{(6)}$ in 6-Ph), 127.74 ($C_{(3)}$ and $C_{(5)}$ in Bz), 127.62 ($C_{(3)}$ and $C_{(5)}$ in 6-Ph), 105.36 (CCl_3), 105.00 ($C_{(5)}$), 67.74 ($C_{(4)}$). IR ν, cm^{-1}: 3212 (s), 3134 (s) (ν NH), 1711 (vs), ~1694 (sh) (amide-I and ν C=O in Bz), 1627 (s) (ν C=C), 1597 (m), 1578 (m), 1496 (m) (ν CC in Ph), 732 (s), 699 cm^{-1} (s) (δ CH in Ph). Anal. Calcd for $C_{18}H_{13}Cl_3N_2O_2$: C, 54.64; H, 3.31; N, 7.08%. Found: C, 54.60; H, 3.12; N, 7.18%.

4.12. Ethyl 4-(trichloromethyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (9c)

Method A: Compound **9c** (2.423 g, 93.4%) was prepared (analogously to **9a**) from **7c** (2.749 g, 8.60 mmol) and TsOH·H_2O (0.491 g, 2.58 mmol) in MeCN (16 mL) (reflux, 58 min).

Method B: Compound **9c** (0.335 g, 76.7%) was prepared (analogously to **9a**) from **7f** (0.524 g, 1.45 mmol) and TsOH·H_2O (0.557 g, 2.93 mmol) in EtOH (5 mL) (reflux, 3 h). Mp 257.5–258 °C (decomp., toluene) (rate of heating 1 °C per 12–32 s) and Mp >258 °C (decomp. without melting) (rate of heating 1 °C per more than 58 s). ^{1}H NMR δ: 9.74 (1H, d, $^4J_{N(1)H,N(3)H}$=1.9 Hz, $N_{(1)}H$), 8.54 (1H, dd, $^3J_{N(3)H,4\text{-}H}$=4.8, $^4J_{N(3)H,N(1)H}$=1.9 Hz, $N_{(3)}H$), 4.91 (1H, d, $^3J_{4\text{-}H,N(3)H}$=4.8 Hz, 4-H), 4.12 (1H, dq, $^2J_{CH(A),CH(B)}$=10.8, $^3J_{CH(A),CH3}$=7.1 Hz, A part of ABX_3 spin system, CH(A) in OCH_2), 4.10 (1H, dq, $^2J_{CH(B),CH(A)}$=10.8, $^3J_{CH(B),CH3}$=7.1 Hz, B part in ABX_3 spin system, CH(B) в OCH_2), 2.23 (3H, s, 6-CH_3), 1.20 (3H, t, $^3J_{CH3,CH(A)}$=$^3J_{CH3,CH(B)}$=7.1 Hz, X part of ABX_3 spin system, CH_3 в OEt). ^{13}C NMR δ: 165.57 (C=O in COOEt), 151.76 ($C_{(2)}$), 151.41 ($C_{(6)}$), 105.70 (CCl_3), 94.14 ($C_{(5)}$), 65.96 ($C_{(4)}$), 59.80 (OCH_2), 17.75 (6-CH_3), 14.15 (CH_3 in OEt). IR ν, cm^{-1}: 3225 (s), 3108 (s) (ν NH), 1726 (s) (ν C=O in COOEt), 1709 (s) (amide-I), 1644 (s) (ν C=C), 1229 (s), 1098 cm^{-1} (s) (ν C–O). Anal. Calcd for $C_9H_{11}Cl_3N_2O_3$: C, 35.85; H, 3.68; N, 9.29%. Found: C, 35.59; H, 2.95; N, 9.24%.

4.13. Ethyl 4-(trichloromethyl)-2-oxo-6-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (9d)

Compound **9d** (0.918 g, 75.2%) was prepared (analogously to **9a**) from **7d** (1.282 g, 3.36 mmol) and TsOH·H_2O (1.920 g, 10.09 mmol) in MeCN (10 mL) (reflux, 14 h 11 min). Mp 201.5–210 °C (EtOH). ^{1}H NMR δ: 9.89 (1H, unresolved d, $^4J_{N(1)H,N(3)H}$=1.2 Hz, $N_{(1)}H$), 8.65 (1H, dd, $^3J_{N(3)H,4\text{-}H}$=4.8, $^4J_{N(3)H,N(1)H}$=1.2 Hz, $N_{(3)}H$), 7.28–7.48 (5H, m, Ph), 5.03 (1H, d, $^3J_{4\text{-}H,N(3)H}$=4.8 Hz, 4-H), 3.81 (2H, q, $^3J_{CH2,CH3}$=7.1 Hz, OCH_2), 0.81 (3H, t, $^3J_{CH3,CH2}$=7.1 Hz, CH_3). ^{13}C NMR δ: 165.08 (C=O in COOEt), 152.08 ($C_{(2)}$), 151.50 ($C_{(6)}$), 134.20 ($C_{(1)}$ in Ph), 129.29 ($C_{(4)}$ in Ph), 128.44 ($C_{(2)}$ and $C_{(6)}$ in Ph), 127.68 ($C_{(3)}$ and $C_{(5)}$ in Ph), 105.55 (CCl_3), 95.28 ($C_{(5)}$), 66.08 ($C_{(4)}$), 59.69 (OCH_2), 13.49 (CH_3). IR ν, cm^{-1}: 3272 (s), 3223 (s), 3112 (s) (ν NH), 1709 (s) (ν C=O in COOEt), 1674 (s) (amide-I), 1645 (s) (ν C=C), 1599 (m) (ν CC in Ph), 1254 (s), 1196 (s), 1106 (s) (ν C–O), 765 (s), 705 cm^{-1} (s) (δ CH in Ph). Anal. Calcd for $C_{14}H_{13}Cl_3N_2O_3$: C, 46.24; H, 3.60; N, 7.70%. Found: C, 46.36; H, 3.55; N, 7.82%.

4.14. 4-(Trichloromethyl)-6-methyl-1,2,3,4-tetrahydropyrimidin-2-one (10)

A solution of compound **11** (0.259 g, 1.05 mmol) and TsOH·H_2O (0.033 g, 0.17 mmol) in EtOH (8 mL) was refluxed for 1 h and the solvent was removed in vacuo. The resulting residue was triturated until crystallization with saturated aqueous solution of $NaHCO_3$ (1 mL). Upon cooling to 0 °C, the precipitate was filtered, washed with ice-cold water, light petrol, and dried to give compound **10** (0.200 g, 83.3%). Mp 201.5 °C (decomp., toluene). ^{1}H NMR δ: 8.74 (1H, dd, $^4J_{N(1)H,N(3)H}$=$^4J_{N(1)H,5\text{-}H}$=1.8 Hz, $N_{(1)}H$), 7.68 (1H, ddd, $^3J_{N(3)H,4\text{-}H}$=3.8, $^4J_{N(3)H,N(1)H}$=$^4J_{N(3)H,5\text{-}H}$=1.8 Hz, $N_{(3)}H$), 4.71 (1H, dddd, $^3J_{5\text{-}H,4\text{-}H}$=4.6, $^4J_{5\text{-}H,N(1)H}$=$^4J_{5\text{-}H,N(3)H}$=1.8, $^4J_{5\text{-}H,6\text{-}CH3}$=1.3 Hz, 5-H), 4.48 (1H, ddq, $^3J_{4\text{-}H,5\text{-}H}$=4.6, $^3J_{4\text{-}H,N(3)H}$=3.8, $^5J_{4\text{-}H,6\text{-}CH3}$=1.0 Hz, 4-H), 1.78 (3H, dd, $^4J_{6\text{-}CH3,5\text{-}H}$=1.3, $^5J_{6\text{-}CH3,4\text{-}H}$=1.0 Hz, CH_3). ^{13}C NMR δ: 152.59 ($C_{(2)}$), 138.97 ($C_{(6)}$), 105.95 (CCl_3), 83.38 ($C_{(5)}$), 67.23 ($C_{(4)}$), 18.17 (CH_3). IR ν, cm^{-1}: 3218 (s), 3089 (s) (ν NH), 1714 (sh), 1696 (s), 1672 cm^{-1} (sh) (amide-I and ν C=C). Anal. Calcd for $C_6H_7Cl_3N_2O$: C, 31.40; H, 3.07; N, 12.21%. Found: C, 31.09; H, 2.79; N, 11.85%.

4.15. (4*R**,6*S**)-6-(Trichloromethyl)-4-hydroxy-4-methylhexahydropyrimidin-2-one (11)

To a solution of KOH (0.072 g, 1.28 mmol) in H_2O (3.5 mL) was added compound **7a** (0.231 g, 0.80 mmol) and the obtained suspension was stirred for 2 h at rt. Upon cooling to 0 °C, the precipitate was filtered, washed with ice-cold water, light petrol, and dried to give compound **11** (0.144 g, 72.9%) as a single diastereomer. Mp 204.5 °C (decomp., EtOH). ^{1}H NMR δ: 7.34 (1H, dd, $^4J_{N(3)H,N(1)H}$=1.6, $^4J_{N(3)H,5\text{-}He}$=1.5 Hz, $N_{(3)}H$), 6.55 (1H, ddd, $^4J_{N(1)H,5\text{-}He}$=1.9, $^4J_{N(1)H,N(3)H}$=1.6, $^4J_{N(1)H,6\text{-}H}$=1.0 Hz, $N_{(1)}H$), 5.68 (1H, d, $^4J_{OH,5\text{-}Ha}$=0.9 Hz, OH), 4.24 (1H, ddd, $^3J_{6\text{-}H,5\text{-}Ha}$=11.3, $^3J_{6\text{-}H,5\text{-}He}$=4.4, $^4J_{6\text{-}H,N(1)H}$=1.0 Hz, 6-H), 2.26 (1H, dddd, $^2J_{5\text{-}He,5\text{-}Ha}$=12.6, $^3J_{5\text{-}He,6\text{-}H}$=4.4, $^4J_{5\text{-}He,N(1)H}$=1.9, $^4J_{5\text{-}He,N(3)H}$=1.5 Hz, 5-He), 1.67 (1H, ddd, $^2J_{5\text{-}Ha,5\text{-}He}$=12.6, $^3J_{5\text{-}Ha,6\text{-}H}$=11.3, $^4J_{5\text{-}Ha,OH}$=0.9 Hz, 5-Ha), 1.39 (3H, s, CH_3). ^{13}C NMR δ: 154.93 ($C_{(2)}$), 102.09 (CCl_3), 77.24 ($C_{(4)}$), 63.39 ($C_{(6)}$), 37.27 ($C_{(5)}$), 28.56 (CH_3). IR ν, cm^{-1}: 3274 (s), 3107 (s) (ν OH, ν NH), 1666 (vs) (amide-I), 1500 (s) (amide-II), 1131 cm^{-1} (s) (ν C–O). Anal. Calcd for $C_6H_9Cl_3N_2O_2$: C, 29.12; H, 3.67; N, 11.32%. Found: C, 29.25; H, 3.45; N, 10.96%.

4.16. 5-Acetyl-6-methyl-1,2-dihydropyrimidin-2-one (13a)

To a mixture of NaH (0.147 g, 6.13 mmol) and compound **9a** (1.389 g, 5.12 mmol) was added anhydrous THF (8.5 mL), the resulted suspension was stirred for 9 h 12 min at rt and neutralized with 11.6 M HCl (0.528 mL, 6.14 mmol). The solvent was removed in vacuo and the residue was dried to constant weight in a desiccator over P_2O_5. The resulting solid was extracted with boiling EtOH (6×10 mL) and the combined extracts were concentrated in vacuo. The dry residue was triturated with Et_2O until crystallization, upon cooling to 0 °C, the precipitate was filtered, washed with cold Et_2O, and dried to give compound **13a** (0.561 g, 72.0%). Mp 215–217 °C (decomp., MeOH) (Lit.[3b] mp 204–205 °C). ^{1}H NMR δ: 12.36 (1H, very br s, NH), 8.83 (1H, s, 4-H), 2.50 (3H, s, 6-CH_3), 2.43 (3H, s, CH_3 in Ac). ^{13}C NMR δ: 194.54 (C=O in Ac), 169.10 (very br, $C_{(6)}$), 160.79 (very br, $C_{(4)}$), 154.49 ($C_{(2)}$), 114.20 ($C_{(5)}$), 28.37 (CH_3 in Ac), 22.22 (br, 4-CH_3).

4.17. 5-Benzoyl-6-phenyl-1,2-dihydropyrimidin-2-one (13b)

To a mixture of NaH (0.038 g, 1.58 mmol) and compound **9b** (0.502 g, 1.27 mmol) was added anhydrous DME (4.6 mL). The obtained solution was stirred for 25 min and then precipitation occurred. The reaction mixture was stirred for additional 2 h 23 min at rt. The solvent was removed in vacuo, to the dry residue was added H_2O (2 mL) and the obtained suspension was neutralized with HCl (2%) to pH 7 (indicator paper). Upon cooling to 0 °C, the precipitate was filtered, washed with ice-cold water, hexane, and dried to give compound **13b** (0.310 g, 88.4%). Mp 237.5–238 °C (EtOH) [Lit.[5a] mp 228 °C (*i*-PrOH)]. ^{1}H NMR δ: 12.57 (1H, br s, NH), 8.33 (1H, s, 4-H), 7.69–7.74 (2H, m, $C_{(2)}$H and $C_{(6)}$H in Bz), 7.49–7.56 (1H, m, $C_{(4)}$H in Bz), 7.25–7.42 (7H, m, $C_{(3)}$H and $C_{(5)}$H in Bz, CH in 4-Ph). ^{13}C NMR δ: 192.37 (C=O in Bz), 171.19 (very br, $C_{(6)}$), 155.62 ($C_{(2)}$), 152.07 (very br, $C_{(4)}$), 136.99 ($C_{(1)}$ in Bz), 136.40 (very br, $C_{(1)}$ in 6-Ph), 133.17 ($C_{(4)}$ in Bz), 130.51 ($C_{(4)}$ in 6-Ph), 129.55 ($C_{(2)}$ and $C_{(6)}$ in Bz), 128.64 ($C_{(2)}$ and $C_{(6)}$ in 6-Ph), 128.51 ($C_{(3)}$ and $C_{(5)}$ in 6-Ph), 128.17 ($C_{(3)}$ and $C_{(5)}$ in Bz), 115.66 ($C_{(5)}$).

4.18. Ethyl 6-methyl-2-oxo-1,2-dihydropyrimidine-5-carboxylate (13c)

To a mixture of NaH (0.129 g, 5.38 mmol) and compound **9c** (1.356 g, 4.50 mmol) was added anhydrous THF (8.5 mL) and the resulted suspension was stirred for 3 min in an ice bath and for 1 h 33 min at rt. The solvent was removed in vacuo, to the dry residue was added H_2O (3 mL), and the resulting suspension was neutralized with HCl (2%) to pH 7 (indicator paper). Upon cooling to 0 °C, the precipitate was filtered, washed with ice-cold H_2O, light petrol, and dried to give compound **13c** (0.720 g, 87.9%). Mp 250 °C (decomp., EtOH) [Lit.[3a] mp 248–250 °C (decomp., H_2O)]. ^{1}H NMR δ: 12.46 (1H, br s, NH), 8.74 (1H, s, 4-H), 4.22 (2H, q, $^3J_{CH2,CH3}$=7.1 Hz, OCH_2), 2.53 (3H, s, 6-CH_3), 1.28 (3H, t, $^3J_{CH3,CH2}$=7.1 Hz, CH_3 in OEt). ^{13}C NMR δ: 167.10 (very br, $C_{(6)}$), 163.51 (C=O in COOEt), 162.47 (very br, $C_{(4)}$), 155.66 ($C_{(2)}$), 106.11 ($C_{(5)}$), 60.45 (OCH_2), 20.70 (br, 6-CH_3), 14.11 (CH_3 in OEt).

4.19. Ethyl 2-oxo-6-phenyl-1,2-dihydropyrimidine-5-carboxylate (13d)

To a mixture of NaH (0.071 g, 2.96 mmol) and compound **9d** (0.895 g, 2.46 mmol) was added anhydrous THF (8.2 mL) and the obtained suspension was stirred in an ice bath for 3 min. The resulting solution was stirred for 1 h 57 min at rt. After the reaction was complete the solvent was removed in vacuo, the residue was dried to constant weight, extracted with boiling EtOH (10 mL), and then with EtOH at rt (2×5 mL). The combined extracts were concentrated in vacuo, the dry residue was dissolved in $CHCl_3$ (30 mL), the solution was refluxed with silica gel (100–400 μm) for 5 min and filtered. The $CHCl_3$ was removed in vacuo, the resulted residue was triturated with light petrol until crystallization, the precipitate was filtered, washed with light petrol, and dried to give compound **13d** (0.419 g, 69.6%). Mp 124.5–125.5 °C (EtOAc-hexane, 7:4 v/v) (Lit.[7h] mp 130–132 °C). ^{1}H NMR δ: 12.60 (1H, br s, NH), 8.62 (1H, s,

4-H), 7.41–7.56 (5H, m, Ph), 4.03 (2H, q, $^{3}J_{CH2,CH3}$=7.1 Hz, OCH_2), 1.00 (3H, t, $^{3}J_{CH3,CH2}$=7.1 Hz, CH_3).^{13}C NMR δ: 170.73 (very br, $C_{(6)}$), 163.84 (C=O in COOEt), 155.34 ($C_{(2)}$), 154.86 (very br, $C_{(4)}$), 136.52 (very br, $C_{(1)}$ in Ph), 130.13 ($C_{(4)}$ in Ph), 128.25 ($C_{(2)}$ and $C_{(6)}$ in Ph), 127.79 ($C_{(3)}$ and $C_{(5)}$ in Ph), 107.36 ($C_{(5)}$), 60.55 (OCH_2), 13.61 (CH_3).

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