Tetrahedron 66 (2010) 7219–7226

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

New approach to 5-arylsulfonyl-substituted 1,2-dihydropyrimidin-2-ones via base-induced chloroform elimination from 4-trichloromethyl-1,2,3,4-tetrahydropyrimidin-2-ones

Anastasia A. Fesenko, Anatoly D. Shutalev *

Department of Organic Chemistry, Moscow State Academy of Fine Chemical Technology, 86 Vernadsky Avenue, 119571 Moscow, Russian Federation

ARTICLE INFO

Article history:
Received 6 April 2010
Received in revised form 1 June 2010
Accepted 21 June 2010
Available online 25 June 2010

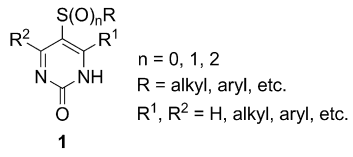
Keywords:
5-Arylsulfonyl-1,2,3,4-tetrahydropyrimidin-2-ones
5-Arylsulfonyl-1,2-dihydropyrimidin-2-ones
Ureidoalkylation
Aromatization

ABSTRACT

A four-step method for the synthesis of 5-arylsulfonyl-substituted 1,2-dihydropyrimidin-2-ones has been developed. The reaction of readily available *N*-[(1-acetoxy-2,2,2-trichloro)ethyl]ureas with sodium enolates of α-arylsulfonylketones followed by heterocyclization–dehydration of the oxoalkylureas formed gave 5-arylsulfonyl-4-trichloromethyl-1,2,3,4-tetrahydropyrimidin-2-ones. The latter, in the presence of strong bases, eliminate $CHCl_3$ to give the target compounds.

1. Introduction

Recently, we have developed a new approach to 5-acyl-1,2-dihydropyrimidin-2-ones via NaH-induced chloroform elimination from the respective 4-trichloromethyl-1,2,3,4-tetrahydropyrimidin-2-ones.[1] Due to the simplicity and efficiency of the synthesis we decided to extend its scope to the preparation of pyrimidin-2-ones with $C_{(5)}$–S bonds (e.g., **1**; Fig. 1). The latter are of considerable interest since some of them possess antibacterial,[2] antiviral,[3] bronchodilator, and antiulcer activities.[4] Nevertheless, compounds **1** remain hitherto practically unknown with few examples described in the literature.[2–5] These examples include hydrolysis of appropriate 2-functionalized pyrimidines,[2,3,5b] condensation reactions of (C–C–C+N–C–N)-type,[4,5b,5c] and oxidation of corresponding 1,2,3,4-tetrahydropyrimidin-2-ones.[5a] The majority of their syntheses are highly specific and suffer from low yields of target products.



1

Figure 1. Structures of 1,2-dihydropyrimidin-2-ones **1** with $C_{(5)}$-S bonds.

Thus, the development of a general approach to the synthesis of compounds **1** particularly 5-arylsulfonyl-substituted 1,2-dihydropyrimidin-2-ones is important. In this article we describe their synthesis using base-induced aromatization of 5-arylsulfonyl-4-trichloromethyl-1,2,3,4-tetrahydropyrimidin-2-ones.

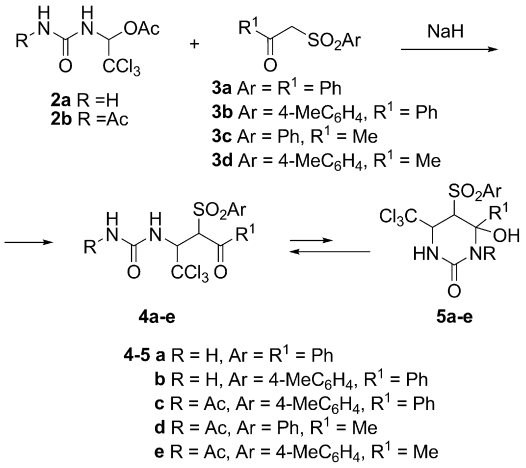
2. Results and discussion

2.1. Synthesis of trichloromethyl-substituted oxoalkylureas

5-Arylsulfonyl-substituted 4-trichloromethyl-1,2,3,4-tetrahydropyrimidin-2-ones were prepared according to our methodology based on the ureidoalkylation of enolates of α-functionalized ketones.[1,6] Readily available α-acetoxy-substituted (trichloroethyl) ureas **2a** and **b** were used as ureidoalkylation reagents.[1] Sodium enolates of ketones bearing the arylsulfonyl group at α-position generated in situ by treating the corresponding CH-acids **3a–d** with an equivalent amount of NaH reacted with ureas **2a** and **b** (MeCN or THF, rt, 4–9 h) to give products of nucleophilic substitution of the acetoxy group, sulfones **4a–e**, in 76–90% yield (Scheme 1, Table 1).

* Corresponding author. E-mail address: shutalev@orc.ru (A.D. Shutalev).

0040-4020/$ – see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2010.06.058



Scheme 1. Synthesis of oxoalkylureas **4a**–**e**.

Table 1
Reaction of ureas **2a** and **b** with sodium enolates of **3a**–**d** at rt

Entry	Starting material		Solvent	Reaction time (h)	Product	Diastereomer ratio[a] (R^*,S^*)-**4**/(R^*,R^*)-**4**	Yield[b] (%)
1	**2a**	**3a**	MeCN	4	**4a**	95:5	88
2	**2a**	**3a**	THF	4.5	**4a**	88:12	76
3	**2a**	**3b**	MeCN	5	**4b**	91:9	85
4	**2b**	**3b**	MeCN	8	**4c**	97:3	88
5	**2b**	**3c**	MeCN	4	**4d**	85:15	85
6	**2b**	**3d**	MeCN	9	**4e**	85:15	86
7	**2b**	**3d**	THF	6.5	**4e**	86:14	90

[a] According to ^{1}H NMR data of crude products.
[b] For isolated compounds.

IR, ^{1}H, and ^{13}C NMR spectra indicated that compounds **4a**–**e** existed only in acyclic form both in solid state and in DMSO-d_6 solution. Their cyclic isomers **5a**–**e** (Scheme 1) were not detected by spectroscopic methods.

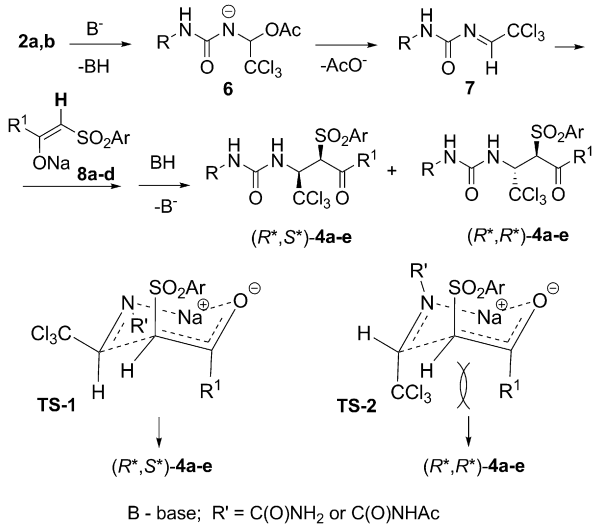
Reactions of **3a**–**d** with **2a** and **b** proceeded with high diastereoselectivity to give sulfones **4a**–**e** in 70–94% diastereomeric excesses (Table 1). The polarity of the solvent had a slight effect on diastereoselectivity (entry 1 vs entry 2; entry 6 vs entry 7). *N*-Acyl-substituted urea **2b** reacted with enolate of **3b** with higher diastereoselectivity compared with urea **2a** (entry 3 vs entry 4).

Based on the values of vicinal couplings of protons in the NH–CH–CH moiety, we have concluded that the minor diastereomers of **4a**–**e** in DMSO-d_6 solution exist in a conformation with an *anti*–*anti* orientation of the named protons ($^3J_{NH,CH}$=10.1–10.8 Hz, $^3J_{CH,CH}$=8.8–9.0 Hz), while the orientation of the protons for major diastereomers is *anti* for NH–CH and *gauche* for CH–CH moieties ($^3J_{NH,CH}$=9.5–9.6 Hz, $^3J_{CH,CH}$=1.5–1.8 Hz).

We optimized the geometry of both isomers for **4a** and **d** using semiempirical methods AM1 and PM6.[7] The data obtained showed that the conformation of (R^*,S^*)-**4a** and **d** with an *anti*–*gauche* orientation of the protons in NH–CH–CH moiety was more stable than that with an *anti*–*anti* orientation and vice versa for (R^*,R^*)-**4a** and **d**. The most stable conformations for (R^*,S^*)- and (R^*,R^*)-**4a** with an *anti* orientation of bulky CCl_3 and $PhSO_2$ groups are shown in Figure 2. In case of major diastereomer formation of intramolecular hydrogen bond between the proton of NH-group and oxygen of carbonyl group becomes possible.

Thus, from quantum mechanical calculations and ^{1}H NMR data we conclude that major diastereomers of **4a** and **d** have the (R^*,S^*)- and minor (R^*,R^*)-configurations. The corresponding diastereomers of compounds **4b**, **c**, and **e** have the same configurations, which is clear from comparison of their ^{1}H NMR spectra with those for **4a** and **d**.

Scheme 2 illustrates a supposed mechanism, which explains the high diastereoselectivity of the reaction of **2a** and **b** with sodium enolates of **3a**–**d**.



Scheme 2. Probable pathway of reaction between **2a** and **b** and sodium (*Z*)-enolates of **3a**–**d**.

Nucleophilic addition of enolates of α-arylsulfonylketones to *N*-acylimines **7** resulting from the base-induced elimination of AcOH from starting ureas **2a** and **b** according to an E1cB mechanism (via **6**) is the principal stage of this pathway.[8,9] This addition can be considered as an aza-analog of aldol reactions between preformed enolates and acylimines.[10] The enolate also plays the role of base and regenerates

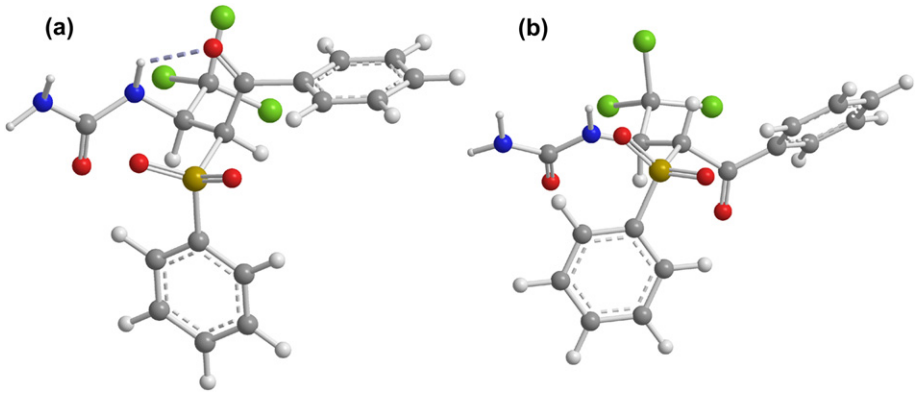
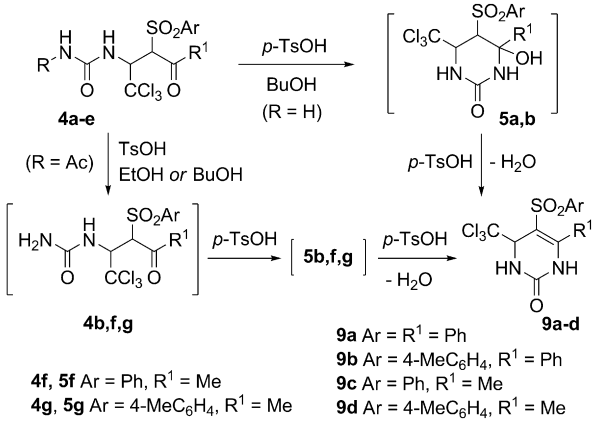


Figure 2. Optimized geometry of (R^*,S^*)-**4a** (a) and (R^*,R^*)-**4a** (b) (PM6, Mopac 2009).

after the addition stage. The reaction of **2a** and **b** with the sodium (*Z*)-enolates of **3a**–**d**[11,12] proceeds similarly to aldol additions via six-member chair-like transition states **TS-1** and **TS-2** resulting from nucleophilic attack of **8a**–**d** on *Si* or *Re* face of *N*-acylimines **7**, respectively. **TS-2** resulting in minor (*R**,*R**)-isomers is less stable than **TS-1** because of a steric 1,3-diaxial repulsion between CCl_3 group and R^1 in **TS-2**. According to the proposed mechanism, the diastereoselectivity of the reaction increases with increasing the steric bulk of R^1, which is confirmed by data presented in Table 1 (entries 4 and 5).

2.2. Synthesis of 5-arylsulfonyl-4-trichloromethyl-1,2,3,4-tetrahydropyrimidin-2-ones

Tetrahydropyrimidines **9a**–**d** were obtained by the reflux of ureas **4a**–**e** in alcohols (EtOH, *n*-BuOH) in the presence of *p*-TsOH (1–4 equiv) (Scheme 3, Table 2).



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

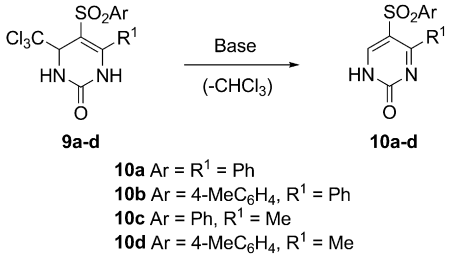
Formation of compounds **9a** and **b** from **4a** and **b** proceeds via heterocyclization of intermediate hydroxypyrimidines **5a** and **b** followed by dehydration. In case of *N*-acetylureas **4c**–**e**, the first step is N-deacylation into corresponding ureas **4b**, **f**, and **g** followed by cyclization into hydroxypyrimidines **5b**, **f**, and **g** and fast dehydration into tetrahydropyrimidines **9b**–**d**. The data presented in Table 2 show that the result of the reaction depends on the structure of the starting compounds and reaction conditions. The rate of pyrimidine **9** formation increases with increasing reaction temperature (entry 7 vs entry 8) and quantity of *p*-TsOH (entry 3 vs entry 4; entry 6 vs entry 7). N-deacylation of **4c**–**e** proceeds much faster than subsequent transformation of obtained **4b**, **f**, and **g** into **9b**–**d** (entry 2 vs entry 4; entries 3, 6, and 7). Benzoyl-containing ureas **4a**–**c** react significantly slower comparing with acetyl-containing ureas **4d** and **e** (entries 1, 2, and 4 vs entries 5and 8). Apparently, cyclization of *N*-deacylated ureas **4a**, **b**, **f**, and **g** into the corresponding hydroxypyrimidines **5**, which is affected by electrophilicity of carbonyl group and steric bulk of R^1, is the rate-determining step of compounds **9a**–**d** formation.

Thus, under optimal conditions reflux of **4a**–**e** in BuOH in the presence of 2–4 equiv of *p*-TsOH led to the smooth formation of pyrimidines **9a**–**d** in 63–93% yields.

The specific feature of ^{1}H NMR spectra of 6-phenyl-substituted compounds **9a** and **b** in DMSO-d_6 solutions is strong broadening of signals of *meta*- and especially *ortho*-protons of 6-Ph ring. The same broadening was observed for *meta*- and *ortho*-carbon atoms in ^{13}C NMR spectra of **9a** and **b**, which can be explained by hindered rotation around $C_{(6)}$–$C_{(1')}$ bond.

2.3. Synthesis of 5-arylsulfonyl-1,2-dihydropyrimidin-2-ones

Treatment of tetrahydropyrimidines **9a**–**d** with strong bases in aprotic solvents resulted in the formation of the corresponding 1,2-dihydropyrimidines **10a**–**d** (Scheme 4).



Scheme 4. Synthesis of 5-arylsulfonyl-1,2-dihydropyrimidin-2-ones **10a**–**d**.

Target pyrimidines **10a**–**d** were obtained by the reaction of **9a**–**d** (rt, MeCN, 1.2–3.3 h) with NaH (1.1 equiv) in 80–98% yields. The rate of elimination decreased with a decrease in the base strength. When compound **9d** was treated with DBU (2.1 equiv) in MeCN, aromatization completed in 5 days and led to formation of **10d** in 96% yield. Reaction of **9c** with sodium malonate in MeCN did not proceed at rt and was complete only after reflux for 1 h, resulting in **10c** in 85% yield. Compound **9d** being treated with NaH (1.1 equiv) in THF (rt, 2 h) gave compound **10d** in 90% yield.

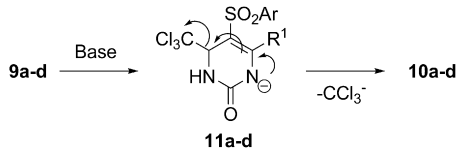
Transformation of **9a**–**d** into **10a**–**d** proceeds via elimination of chloroform from **9a**–**d**. Proton abstraction from the more acidic

Table 2
Transformation of **4a**–**e** into **9a**–**d**[a]

Entry	Starting material	Solvent	Molar ratio of **4**:*p*-TsOH	Reaction time (h)	Product(s)	Molar ratio of products, **9**:**4**[b]	Isolated yield of **9** (%)
1	**4a**	*n*-BuOH	1:4.0	31	**9a**	—	63
2	**4b**	*n*-BuOH	1:4.0	25	**9b**	—	75
3	**4c**	*n*-BuOH	1:3.1	5	**9b**+**4b**[c]	28:72	—
4	**4c**	*n*-BuOH	1:4.0	18	**9b**	—	72
5	**4d**	*n*-BuOH	1:2.0	2	**9c**	—	93
6	**4e**	EtOH	1:1.1	26	**9d**+**4g**[d]	68:32	—
7	**4e**	EtOH	1:2.1	16.5	**9d**+**4g**[d]	80:20	—
8	**4e**	*n*-BuOH	1:2.0	2	**9d**	—	92

[a] Reflux in alcohols in the presence of *p*-TsOH.
[b] According to ^{1}H NMR data.
[c] Diastereomer mixture, 85:15.
[d] Diastereomer mixture, 84:16.

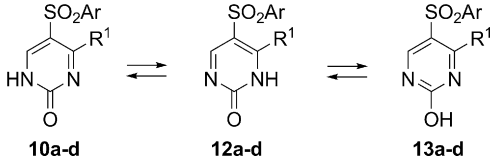
$N_{(1)}$–H group[13] in **9a**–**d** followed by CCl_3-anion elimination from **11a**–**d** leads to formation of **10a**–**d** (Scheme 5).



Scheme 5. Base-induced transformation of **9a**–**d** into **10a**–**d**.

The structure of compounds **10a**–**d** was confirmed by IR, ^{1}H, and ^{13}C NMR spectra. The specific characteristic of the IR spectra of these compounds in solid state is that the NH-stretching vibrations appear as broad and intense bands in an unusual long-wave region (2400–3300 cm^{-1}), which can be explained by formation of strong intermolecular hydrogen bonds of N–H···N=C type.

^{13}C NMR spectra of **10a**–**d** in DMSO-d_6 solutions demonstrated an extreme broadening of the signals of $C_{(4)}$, $C_{(6)}$, and the carbon atom of group R^1 directly bound to pyrimidine ring, suggesting an exchanging process. Presumably, there are three tautomeric forms **10a**–**d**, **12a**–**d**, and **13a**–**d** in DMSO-d_6 (Scheme 6).



Scheme 6. Tautomeric equilibrium of 5-arylsulfonyl-1,2-dihydropyrimidin-2-ones.

To confirm this suggestion we performed ab initio calculations (B3LYP/6-31++G**)[14] for **10a**, **12a**, **13a** and **10c**, **12c**, **13c**. According to these calculations, **13a** is the most stable tautomer in the gas phase, followed by **12a** and **10a** in the order of increasing energy (0.5 and 0.7 kcal/mol, respectively). Analogously, the hydroxy form **13c** is favorable, while the tautomers **10c** and **12c** are less stable (0.4 and 1.4 kcal/mol, respectively). Thus, the computations clearly demonstrate the insignificant difference in energy of all three tautomeric forms **10a**–**d**, **12a**–**d**, and **13a**–**d**.[15]

3. Conclusion

We have developed a new four-step approach to the synthesis of 5-arylsulfonyl-substituted 1,2-dihydropyrimidin-2-ones. Starting trichloromethyl-substituted oxoalkylureas were prepared using ureidoalkylation of sodium enolates of α-arylsulfonyl-substituted ketones with readily available *N*-[(1-acetoxy-2,2,2-trichloro)ethyl] ureas. High diastereoselectivity of this reaction was explained in terms of aza-analog of aldol condensation. Heterocyclization–dehydration of resulted oxoalkylureas in the presence of *p*-TsOH gave 5-arylsulfonyl-4-trichloromethyl-1,2,3,4-tetrahydropyrimidin-2-ones. The key step of the synthesis was the aromatization of the latter compounds induced by strong bases, which proceeds via elimination of chloroform and led to smooth formation of the target 5-arylsulfonyl-substituted dihydropyrimidin-2-ones.

4. Experimental section

4.1. General

Acetonitrile was dried by distillation from P_2O_5 and then from CaH_2. THF was dried over KOH pellets and then over Na. Sodium hydride (60% suspension in mineral oil) was washed with dry hexane, dried in vacuum desiccator prior to use. All other reagents and solvents were purchased from commercial sources and used without additional purification.

IR spectra (in Nujol or hexachlorobut-1,3-diene) were recorded with a Bruker Equinox 55/S or Bruker Vector 22 spectrophotometers. Band characteristics in IR spectra are defined as very strong (vs), strong (s), medium (m), weak (w), and shoulder (sh). NMR spectra were recorded using a Bruker DPX 300 spectrometer at 300.13 (^{1}H) and 75.48 (^{13}C) MHz as solutions 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, and multiplet (m).

Thin-layer chromatography (TLC) was performed on silica gel plates Kieselgel 60 F_{254} (Merck) in chloroform–methanol (9:1, v/v) and chloroform–methanol (5:1, v/v) as solvent systems. Plates were visualized with iodine vapor or UV light.

All yields refer to isolated, spectroscopically and TLC pure material.

4.2. *N*-[(1,1,1-Trichloro-4-oxo-4-phenyl-3-phenylsulphonyl) but-2-yl]urea (4a)

To a mixture of NaH (0.218 g, 9.09 mmol) and phenylsulfonylacetophenone **3a** (2.361 g, 9.07 mmol) was added anhydrous MeCN (16 mL) and the resulted suspension was stirred upon cooling in ice bath for 9 min. To the obtained suspension was added **2a** (2.266 g, 9.08 mmol) and MeCN (4.8 mL) and the reaction mixture was stirred for 4 h 15 min at rt. The solvent was removed under vacuum, to a solid residue was added a saturated aqueous solution of $NaHCO_3$ until a dense suspension formed, and the mixture was left in water bath (temperature of bath 35 °C) for 2 h. Upon cooling to 0 °C, the precipitate was filtered, washed with ice-cold water, light petrol, dried, washed with cold Et_2O (3×10 mL), and dried to give 3.602 g (88.3%) of **4a** as a mixture of (*R**,*S**)- and (*R**,*R**)-diastereomers, 95:5. After three crystallization from EtOH the diastereomeric ratio changed to 98:2. Mp 172.5–173 °C (decomp., EtOH). ^{1}H NMR of major diastereomer (DMSO-d_6) δ: 8.00–8.06 (2H, m, $C_{(2)}$H and $C_{(6)}$H in PhC=O), 7.86–7.92 (2H, m, $C_{(2)}$H and $C_{(6)}$H in $PhSO_2$), 7.69–7.81 (2H, m, $C_{(4)}$H in PhC=O and $PhSO_2$), 7.55–7.66 (4H, m, $C_{(3)}$H and $C_{(5)}$H in PhC=O and $PhSO_2$), 6.89 (1H, d, *J* 9.6 Hz, NH), 6.29 (2H, br s, NH_2), 6.13 (1H, d, *J* 1.7 Hz, CH–SO_2), 5.53 (1H, dd, *J* 9.6, 1.7 Hz, CH–CCl_3). ^{1}H NMR of minor diastereomer (DMSO-d_6) δ: 6.86 (1H, d, *J* 10.6 Hz, NH), 6.17 (2H, br s, NH_2), 5.85 (1H, d, *J* 8.8 Hz, CH–SO_2), 5.75 (1H, dd, *J* 10.6, 8.8 Hz, CH–CCl_3). Signals of other protons overlap with proton signals of major isomer. ^{13}C NMR of major diastereomer (DMSO-d_6) δ: 191.8 (C=O in PhC=O), 157.2 (N–C=O), 137.0 ($C_{(1)}$ in PhC=O), 136.1 ($C_{(1)}$ in $PhSO_2$), 135.0 ($C_{(4)}$ in $PhSO_2$), 134.7 ($C_{(4)}$ in PhC=O), 129.5 ($C_{(2)}$ and $C_{(6)}$ in PhC=O), 129.3 ($C_{(2)}$ and $C_{(6)}$ in $PhSO_2$), 129.2 ($C_{(3)}$ and $C_{(5)}$ in $PhSO_2$), 128.9 ($C_{(3)}$ and $C_{(5)}$ in PhC=O), 102.3 (CCl_3), 64.4 and 63.5 (N–CH–CH–SO_2). IR (Nujol) ν, cm^{-1}: 3503 (s), 3470 (s), 3383 (br s), 3337 (s), 3192 (m) (ν NH), 1711 (s), 1679 (vs), 1662 (s) (amide-I and ν C=O in Bz), 1605 (s) (ν CC in Ph), 1535 (s) (amide-II), 1496 (s) (ν CC in Ph), 1338 (s) (ν_{as} SO_2), 1154 (s) (ν_s SO_2), 751 (vs) (δ CH in Ph). Anal. Calcd for $C_{17}H_{15}Cl_3N_2O_4S$: C, 45.40; H, 3.36; N, 6.23%. Found: C, 45.31; H, 3.34; N, 6.21%.

When THF was used instead of MeCN (rt, 4 h 30 min), **4a** was obtained in 76.4% yield as a mixture of (*R**,*S**)- and (*R**,*R**)-diastereomers, 88:12.

4.3. *N*-[(1,1,1-Trichloro-4-oxo-4-phenyl-3-tosyl)but-2-yl]urea (4b)

Compound **4b** (2.696 g, 85.0%) as a mixture of (*R**,*S**)- and (*R**,*R**)-diastereomers (91:9) was prepared (analogously to **4a**) from **2a**

(1.714 g, 6.87 mmol), *p*-tosylacetophenone **3b** (1.877 g, 6.84 mmol), and NaH (0.164 g, 6.84 mmol) in MeCN (16 mL) (rt, 4 h 45 min). After crystallization from EtOH the diastereomeric ratio changed to 92:8. Mp 205–205.5 °C (decomp., EtOH). ^{1}H NMR of major diastereomer (DMSO-d_6) δ: 7.99–8.05 (2H, m, $C_{(2)}$H and $C_{(6)}$H in Ph), 7.77 (2H, m, AA′ part of AA′XX′ spin system, J_{ortho} 8.3 Hz, $C_{(2)}$H and $C_{(6)}$H in 4-MeC_6H_4), 7.70–7.77 (1H, m, $C_{(4)}$H in Ph), 7.55–7.63 (2H, m, $C_{(3)}$H and $C_{(5)}$H in Ph), 7.43 (2H, m, XX′ part of AA′XX′ spin system, J_{ortho} 8.3 Hz, $C_{(3)}$H and $C_{(5)}$H in 4-MeC_6H_4), 6.89 (1H, d, *J* 9.6 Hz, NH), 6.30 (2H, br s, NH_2), 6.09 (1H, d, *J* 1.7 Hz, CH–SO_2), 5.49 (1H, dd, *J* 9.6, 1.7 Hz, CH–CCl_3), 2.40 (3H, s, CH_3). ^{1}H NMR of minor diastereomer (DMSO-d_6) δ: 7.90–7.95 (2H, m, $C_{(2)}$H and $C_{(6)}$H in Ph), 7.26 (2H, m, XX′ part of AA′XX′ spin system, J_{ortho} 8.3 Hz, $C_{(3)}$H and $C_{(5)}$H in 4-MeC_6H_4), 6.84 (1H, d, *J* 10.1 Hz, NH), 6.18 (2H, br s, NH_2), 5.78 (1H, d, *J* 8.8 Hz, CH–SO_2), 5.73 (1H, dd, *J* 10.1, 8.8 Hz, CH–CCl_3), 2.29 (3H, s, CH_3). Signals of other protons overlap with proton signals of major isomer. ^{13}C NMR of major diastereomer (DMSO-d_6) δ: 191.9 (C=O in PhC=O), 157.2 (N–C=O), 145.8 ($C_{(4)}$ in 4-MeC_6H_4), 137.1 ($C_{(1)}$ in Ph), 134.6 ($C_{(4)}$ in Ph), 133.3 ($C_{(1)}$ in 4-MeC_6H_4), 129.8 ($C_{(3)}$ and $C_{(5)}$ in 4-MeC_6H_4), 129.5 ($C_{(2)}$ and $C_{(6)}$ in Ph), 129.2 ($C_{(2)}$ and $C_{(6)}$ in 4-MeC_6H_4), 128.9 ($C_{(3)}$ and $C_{(5)}$ in Ph), 102.4 (CCl_3), 64.4 and 63.5 (N–CH–CH–SO_2), 21.2 (CH_3 in Ts). IR (Nujol) ν, cm^{-1}: 3437 (s), 3374 (m), 3315 (m), 3248 (w), 3204 (m) (ν NH), 1683 (vs) (amide-I and ν C=O in Bz), 1594 (m) (ν CC in Ph and C_6H_4), 1494 (s) (amide-II), 1335 (m) (ν_{as} SO_2), 1131 (m) (ν_s SO_2), 803 (m) (δ CH in C_6H_4), 742 (s) (δ CH in Ph). Anal. Calcd for $C_{18}H_{17}Cl_3N_2O_4S$: C, 46.62; H, 3.70; N, 6.04%. Found: C, 46.55; H, 4.04; N, 6.18%.

4.4. *N*-Acetyl-*N*′-[(1,1,1-trichloro-4-oxo-4-phenyl-3-tosyl)but-2-yl]urea (4c)

Compound **4c** (3.745 g, 88.1%) as a mixture of (*R**,*S**)- and (*R**,*R**)-diastereomers (97:3) was prepared (analogously to **4a**) from **2b** (2.453 g, 8.41 mmol), *p*-tosylacetophenone **3b** (2.305 g, 8.40 mmol), and NaH (0.202 g, 8.40 mmol) in MeCN (21 mL) (rt, 7 h 44 min). After crystallization from EtOH the diastereomeric ratio changed to 98:2. Mp 233–233.5 °C (decomp., EtOH). ^{1}H NMR of major diastereomer (DMSO-d_6) δ: 10.64 (1H, br s, NH in NH–Ac), 9.90 (1H, br d, *J* 9.5 Hz, NH), 8.02–8.07 (2H, m, $C_{(2)}$H and $C_{(6)}$H in Ph), 7.70–7.76 (1H, m, $C_{(4)}$H in Ph), 7.67 (2H, m, AA′ part of AA′XX′ spin system, J_{ortho} 8.4 Hz, $C_{(2)}$H and $C_{(6)}$H in 4-MeC_6H_4), 7.54–7.61 (2H, m, $C_{(3)}$H and $C_{(5)}$H in Ph), 7.41 (2H, m, XX′ part of AA′XX′ spin system, J_{ortho} 8.4 Hz, $C_{(3)}$H and $C_{(5)}$H in 4-MeC_6H_4), 6.17 (1H, d, *J* 1.8 Hz, CH–SO_2), 5.59 (1H, dd, *J* 9.5, 1.8 Hz, CH–CCl_3), 2.39 (3H, s, CH_3 in Ts), 2.02 (3H, s, CH_3 in NH–Ac). ^{1}H NMR of minor diastereomer (DMSO-d_6) δ: 10.80 (1H, br s, NH in NH–Ac), 9.52 (1H, br d, *J* 10.2 Hz, NH), 7.92–7.97 (2H, m, $C_{(2)}$H and $C_{(6)}$H in Ph), 7.24 (2H, m, XX′ part of AA′XX′ spin system, J_{ortho} 8.3 Hz, $C_{(3)}$H and $C_{(5)}$H in 4-MeC_6H_4), 5.99 (1H, d, *J* 9.0 Hz, CH–SO_2), 5.93 (1H, dd, *J* 10.2, 9.0 Hz, CH–CCl_3), 2.26 (3H, s, CH_3 in Ts), 2.07 (3H, s, CH_3 in NH–Ac). Signals of other protons overlap with proton signals of major isomer. ^{13}C NMR of major diastereomer (DMSO-d_6) δ: 191.3 (C=O in PhC=O), 171.9 (C=O in NH–Ac), 153.3 (C=O in urea), 146.1 ($C_{(4)}$ in 4-MeC_6H_4), 136.9 ($C_{(1)}$ in Ph), 134.7 ($C_{(4)}$ in Ph), 132.9 ($C_{(1)}$ in 4-MeC_6H_4), 129.8 ($C_{(3)}$ and $C_{(5)}$ in 4-MeC_6H_4), 129.3 ($C_{(2)}$ and $C_{(6)}$ in Ph), 129.1 ($C_{(2)}$ and $C_{(6)}$ in 4-MeC_6H_4), 129.0 ($C_{(3)}$ and $C_{(5)}$ in Ph), 100.7 (CCl_3), 63.6 and 63.5 (N–CH–CH–SO_2), 21.2 (CH_3 in Ts). IR (Nujol) ν, cm^{-1}: 3237 (m), 3129 (m) (ν NH), 1692 (vs), 1674 (s) (amide-I and ν C=O in Bz), 1594 (m) (ν CC in Ph and C_6H_4), 1531 (s) (amide-II), 1505 (m) (ν CC in Ph and C_6H_4), 1323 (s) (ν_{as} SO_2), 1130 (m) (ν_s SO_2), 805 (s) (δ CH in C_6H_4), 745 (s) (δ CH in Ph). Anal. Calcd for $C_{20}H_{19}Cl_3N_2O_5S$: C, 47.49; H, 3.79; N, 5.54%. Found: C, 47.27; H, 3.84; N, 5.60%.

4.5. *N*-Acetyl-*N*′-[(1,1,1-trichloro-4-oxo-3-phenylsulfonyl) pent-2-yl]urea (4d)

Compound **4d** (3.745 g, 84.6%) as a mixture of (*R**,*S**)- and (*R**,*R**)-diastereomers (85:15) was prepared (analogously to **4a**) from **2b** (2.789 g, 9.67 mmol), phenylsulfonylacetone **3c** (1.896 g, 9.56 mmol), and NaH (0.229 g, 9.56 mmol) in MeCN (19 mL) (rt, 3 h 40 min). Mp 213.5–214 °C (decomp., EtOH). ^{1}H NMR of major diastereomer (DMSO-d_6) δ: 10.58 (1H, br s, NH), 9.73 (1H, br d, *J* 9.5 Hz, NH), 7.61–7.91 (5H, m, Ph), 5.54 (1H, d, *J* 1.5 Hz, CH–SO_2), 5.27 (1H, dd, *J* 9.5, 1.5 Hz, CH–CCl_3), 2.52 (3H, s, CH_3 in CH–Ac), 1.98 (3H, s, CH_3 in NH–Ac). ^{1}H NMR of minor diastereomer (DMSO-d_6) δ: 10.72 (1H, br s, NH), 9.19 (1H, br d, *J* 10.7 Hz, NH), 7.61–7.9 (5H, m, signals overlap with proton signals of major isomer, Ph), 5.65 (1H, dd, *J* 10.7, 8.8 Hz, CH–CCl_3), 5.50 (1H, d, *J* 8.8 Hz, CH–SO_2), 2.38 (3H, s, CH_3 in CH–Ac), 2.01 (3H, s, CH_3 in NH–Ac). ^{13}C NMR of major diastereomer (DMSO-d_6) δ: 199.9 (C=O in CH–Ac), 171.9 (C=O in NH–Ac), 153.4 (C=O in urea), 135.8 ($C_{(1)}$ in Ph), 135.2 ($C_{(4)}$ in Ph), 129.5 ($C_{(2)}$ and $C_{(6)}$ in Ph), 129.2 ($C_{(3)}$ and $C_{(5)}$ in Ph), 100.7 (CCl_3), 68.1 (CH–SO_2), 63.3 (CH–NH), 34.9 (CH_3 in CH–Ac), 23.5 (CH_3 in NH–Ac), 21.2 (CH_3 in Ts). IR (Nujol) ν, cm^{-1}: 3239 (br s), 3139 (br s), 3067 (m) (ν NH), 1718 (s) (ν C=O in CH–Ac), 1694 (vs) (amide-I), 1583 (w) (ν CC in Ph), 1538 (vs) (amide-II), 1496 (m) (ν CC in Ph), 1316 (s) (ν_{as} SO_2), 1155 (vs) (ν_s SO_2), 743 (s), 682 (s) (δ CH in Ph). Anal. Calcd for $C_{14}H_{15}Cl_3N_2O_5S$: C, 39.13; H, 3.52; N, 6.52%. Found: C, 39.44; H, 3.63; N, 6.59%.

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

Compound **4e** (2.250 g, 90.0%) as a mixture of (*R**,*S**)- and (*R**,*R**)-diastereomers (86:14) was prepared (analogously to **4a**) from **2b** (1.746 g, 5.99 mmol), *p*-tosylacetone **3d** (1.196 g, 5.63 mmol), and NaH (0.136 g, 5.65 mmol) in THF (10 mL) (rt, 6 h 28 min). When MeCN was used instead of THF (rt, 8 h 42 min), **4e** was obtained in 85.6% yield as a mixture of (*R**,*S**)- and (*R**,*R**)-diastereomers, 85:15. Mp 224.5–225 °C (decomp., EtOH). ^{1}H NMR of major diastereomer (DMSO-d_6) δ: 10.54 (1H, br s, NH), 9.71 (1H, br d, *J* 9.5 Hz, NH), 7.75 (2H, m, AA′ part of AA′XX′ spin system, J_{ortho} 8.4 Hz, $C_{(2)}$H and $C_{(6)}$H in 4-MeC_6H_4), 7.48 (2H, m, XX′ part of AA′XX′ spin system, J_{ortho} 8.4 Hz, $C_{(3)}$H and $C_{(5)}$H in 4-MeC_6H_4), 5.48 (1H, d, *J* 1.5 Hz, CH–SO_2), 5.25 (1H, dd, *J* 9.5, 1.5 Hz, CH–CCl_3), 2.52 (3H, s, CH_3 in CH–Ac), 2.44 (3H, s, CH_3 in 4-MeC_6H_4), 1.98 (3H, s, CH_3 in N–Ac). ^{1}H NMR of minor diastereomer (DMSO-d_6) δ: 10.70 (1H, br s, NH), 9.21 (1H, br d, *J* 10.8 Hz, NH), 7.69 (2H, m, AA′ part of AA′XX′ spin system, J_{ortho} 8.4 Hz, $C_{(2)}$H and $C_{(6)}$H in 4-MeC_6H_4), 7.45 (2H, m, XX′ part of AA′XX′ spin system, J_{ortho} 8.4 Hz, $C_{(3)}$H and $C_{(5)}$H in 4-MeC_6H_4), 5.63 (1H, dd, *J* 10.8, 8.8 Hz, CH–CCl_3), 5.41 (1H, d, *J* 8.8 Hz, CH–SO_2), 2.41 (3H, s, CH_3 in 4-MeC_6H_4), 2.37 (3H, s, CH_3 in CH–Ac), 2.02 (3H, s, CH_3 in N–Ac). ^{13}C NMR of major diastereomer (DMSO-d_6) δ: 200.0 (C=O in CH–Ac), 171.8 (C=O in NH–Ac), 153.3 (C=O in urea), 146.0 ($C_{(4)}$ in 4-MeC_6H_4), 133.0 ($C_{(1)}$ in 4-MeC_6H_4), 129.8 ($C_{(3)}$ and $C_{(5)}$ in 4-MeC_6H_4), 129.2 ($C_{(2)}$ and $C_{(6)}$ in 4-MeC_6H_4), 100.7 (CCl_3), 68.1 (CH–SO_2), 63.4 (CH–NH), 34.8 (CH_3 in CH–Ac), 23.4 (CH_3 in NH–Ac), 21.2 (CH_3 в Ts). IR (Nujol) ν, cm^{-1}: 3229 (br s), 3141 (br s), 3064 (m) (ν NH), 1719 (s) (ν C=O in CH–Ac), 1696 (s) (amide-I), 1602 (w) (ν CC in C_6H_4), 1536 (s) (amide-II), 1496 (w) (ν CC in C_6H_4), 1325 (s) (ν_{as} SO_2), 1155 (vs) (ν_s SO_2), 797 (s) (δ CH in C_6H_4). Anal. Calcd for $C_{15}H_{17}Cl_3N_2O_5S$: C, 40.60; H, 3.86; N, 6.31%. Found: C, 40.37; H, 3.95; N, 6.32%.

4.7. 4-(Trichloromethyl)-6-phenyl-5-phenylsulphonyl-1,2,3,4-tetrahydropyrimidin-2-one (9a)

A solution of **4a** (3.038 g, 6.18 mmol) and *p*-TsOH·H_2O (4.701 g, 24.72 mmol) in *n*-BuOH (20 mL) was heated to reflux under stirring

for 31 h, and solvent was then removed in vacuum. To a residue was added saturated aqueous solution of $NaHCO_3$ (10 mL) and light petrol (20 mL), and the obtained mixture was neutralized by solid $NaHCO_3$ to pH 8 under stirring. Upon cooling to 0 °C, the precipitate was filtered, washed with ice-cold water, light petrol, dried, washed with cold Et_2O (3×10 mL), and dried to give 1.832 g (62.6%) of **9a**. Mp 278.5 °C (decomp., EtOH). ^{1}H NMR (DMSO-d_6) δ: 10.36 (1H, s, $N_{(1)}H$), 9.05 (1H, d, J 5.2 Hz, $N_{(3)}H$), 7.39–7.47 (2H, m, $C_{(4)}H$ in 6-Ph and $PhSO_2$), 7.20–7.27 (2H, m, $C_{(3)}H$ and $C_{(5)}H$ in $PhSO_2$), 7.04–7.09 (2H, m, $C_{(2)}H$ and $C_{(6)}H$ in $PhSO_2$), 6.70–7.30 (4H, m, very br signals, $C_{(2)}H$ and $C_{(6)}H$, $C_{(3)}H$ and $C_{(5)}H$ in 6-Ph), 5.28 (1H, d, J 5.2 Hz, 4H). ^{13}C NMR (DMSO-d_6) δ: 154.1 ($C_{(2)}$), 151.0 ($C_{(6)}$), 142.5 ($C_{(1)}$ in $PhSO_2$), 132.3 ($C_{(4)}$ in $PhSO_2$), 131.2 ($C_{(4)}$ in 6-Ph), 130.6 ($C_{(1)}$ in 6-Ph), 130.2 (very br, $C_{(2)}$ and $C_{(6)}$ in 6-Ph), 128.5 ($C_{(2)}$ and $C_{(6)}$ in $PhSO_2$), 127.8 (br, $C_{(3)}$ and $C_{(5)}$ in 6-Ph), 126.3 ($C_{(3)}$ and $C_{(5)}$ in $PhSO_2$), 104.8 (CCl_3), 104.6 ($C_{(5)}$), 66.0 ($C_{(4)}$). IR (Nujol) ν, cm^{-1}: 3288 (m), 3234 (m), 3129 (m) (ν NH), 1711 (vs) (amide-I), 1612 (s) (ν C=C), 1294 (s) (ν_{as} SO_2), 1142 (s) (ν_s SO_2), 759 (s), 685 (s) (δ CH in Ph). Anal. Calcd for $C_{17}H_{13}Cl_3N_2O_3S$: C, 47.30; H, 3.04; N, 6.49%. Found: C, 47.32; H, 3.30; N, 6.49%.

4.8. 4-(Trichloromethyl)-6-phenyl-5-tosyl-1,2,3,4-tetrahydropyrimidin-2-one (9b)

Method A: A solution of **4b** (2.328 g, 4.60 mmol) and p-TsOH·H_2O (3.498 g, 18.39 mmol) in n-BuOH (17 mL) was heated to reflux under stirring for 25 h, and solvent was then removed in vacuum. To an oily residue was added saturated aqueous solution of $NaHCO_3$ (pH 8), and the resulting mixture was stirred until complete crystallization. Upon cooling to 0 °C, the precipitate was filtered, thoroughly washed with ice-cold water, light petrol, dried, washed with cold Et_2O (3×5 mL), and dried to give 1.530 g (74.8%) of **9b**. Mp 234–234.5 °C (decomp., AcOEt). ^{1}H NMR (DMSO-d_6) δ: 10.31 (1H, s, $N_{(1)}H$), 9.00 (1H, d, J 5.2 Hz, $N_{(3)}H$), 7.40–7.47 (1H, m, $C_{(4)}H$ in 6-Ph), 7.18–7.31 (2H, m, br signals, $C_{(3)}H$ and $C_{(5)}H$ in 6-Ph), 6.85–7.17 (2H, m, very br signals, $C_{(2)}H$ and $C_{(6)}H$ in 6-Ph), 7.03 (2H, m, AA′ part of AA′XX′ spin system, J_{ortho} 8.3 Hz, $C_{(2)}H$ and $C_{(6)}H$ in 4-MeC_6H_4), 6.93 (2H, m, XX′ part of AA′XX′ spin system, J_{ortho} 8.3 Hz, $C_{(3)}H$ and $C_{(5)}H$ in 4-MeC_6H_4), 5.27 (1H, d, J 5.2 Hz, 4H), 2.28 (3H, s, CH_3 in 4-MeC_6H_4). ^{13}C NMR (DMSO-d_6) δ: 153.9 ($C_{(2)}$), 151.0 ($C_{(6)}$), 142.5 ($C_{(4)}$ in 4-MeC_6H_4), 139.8 ($C_{(1)}$ in 4-MeC_6H_4), 131.1 ($C_{(4)}$ in Ph), 130.7 ($C_{(1)}$ in Ph), 130.1 (very br, $C_{(2)}$ and $C_{(6)}$ in Ph), 128.9 ($C_{(3)}$ and $C_{(5)}$ in 4-MeC_6H_4), 127.7 (br, $C_{(3)}$ and $C_{(5)}$ in Ph), 126.3 ($C_{(2)}$ and $C_{(6)}$ in 4-MeC_6H_4), 104.9 ($C_{(5)}$), 104.8 (CCl_3), 66.0 ($C_{(4)}$), 20.9 (CH_3 в Ts). IR (Nujol) ν, cm^{-1}: 3399 (s), 3293 (sh), 3239 (br s), 3128 (s) (ν NH), 1712 (vs) (amide-I), 1612 (s) (ν C=C), 1597 (m), 1494 (m) (ν CC in Ph and C_6H_4), 1301 (s) (ν_{as} SO_2), 1145 (s) (ν_s SO_2), 821 (s) (δ CH in C_6H_4), 763 (s), 695 (s) (δ CH in Ph). Anal. Calcd for $C_{18}H_{15}Cl_3N_2O_3S$: C, 48.50; H, 3.39; N, 6.29%. Found: C, 48.47; H, 3.26; N, 6.26%.

Method B: A solution of **4c** (4.909 g, 9.70 mmol) and p-TsOH·H_2O (7.386 g, 38.82 mmol) in n-BuOH (30 mL) was heated to reflux under stirring for 18 h and then solvent was removed in vacuum. To an oily residue was added saturated aqueous solution of $NaHCO_3$ (10 mL) and H_2O (40 mL), the resulted mixture was triturated upon cooling, and the aqueous layer was decanted. To the obtained residue was added saturated aqueous solution of $NaHCO_3$ (5 mL) and the mixture was allowed to stand overnight at rt. The resulted solid was triturated until fine suspension formed, upon cooling to 0 °C, the precipitate was filtered, thoroughly washed with ice-cold water, light petrol, dried, washed with cold Et_2O (2×10 mL), and dried to give 3.183 g (72.0%) of **9b**.

4.9. 4-(Trichloromethyl)-6-methyl-5-phenylsulphonyl-1,2,3,4-tetrahydropyrimidin-2-one (9c)

A solution of **4d** (8.558 g, 19.92 mmol) and p-TsOH·H_2O (7.574 g, 39.82 mmol) in n-BuOH (50 mL) was heated to reflux upon stirring for 2 h and then solvent was removed in vacuum. The obtained residue was triturated with light petrol (2×20 mL), the liquid layer was decanted and saturated aqueous solution of $NaHCO_3$ was added (to pH 8), to the obtained suspension was added light petrol (10 mL). 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 6.939 g (92.9%) of **9c**. Mp 251.5 °C (decomp., EtOH). ^{1}H NMR (DMSO-d_6) δ: 10.21 (1H, s, $N_{(1)}H$), 8.93 (1H, d, J 5.0 Hz, $N_{(3)}H$), 7.58–7.71 (5H, m, Ph), 5.06 (1H, d, J 5.0 Hz, 4H), 1.89 (3H, s, 6-CH_3). ^{13}C NMR (DMSO-d_6) δ: 153.4 ($C_{(2)}$), 151.2 ($C_{(6)}$), 143.7 ($C_{(1)}$ in Ph), 132.9 ($C_{(4)}$ in Ph), 129.4 ($C_{(2)}$ and $C_{(6)}$ in Ph), 126.1 ($C_{(3)}$ and $C_{(5)}$ in Ph), 104.9 (CCl_3), 102.6 ($C_{(5)}$), 66.3 ($C_{(4)}$), 17.6 (6-CH_3). IR (Nujol) ν, cm^{-1}: 3284 (br s), 3168 (m) (ν NH), 3087 (w), 3063 (w) (ν CH in Ph), 1718 (s), 1685 (s) (amide-I), 1618 (s) (ν C=C), 1289 (s) (ν_{as} SO_2), 1137 (s) (ν_s SO_2), 758 (s), 689 (s) (δ CH in Ph).

4.10. 4-(Trichloromethyl)-6-methyl-5-tosyl-1,2,3,4-tetrahydropyrimidin-2-one (9d)

Compound **9d** (2.346 g 92.3%) was prepared (analogously to **9c**) from **4e** (3.051 g, 6.79 mmol) and p-TsOH·H_2O (2.619 g, 13.77 mmol) in n-BuOH (26 mL) (reflux, 2 h). Mp 256–256.5 °C (decomp., EtOH). ^{1}H NMR (DMSO-d_6) δ: 10.17 (1H, d, J 1.8 Hz, $N_{(1)}H$), 8.91 (1H, dd, J 5.0, 1.8 Hz, $N_{(3)}H$), 7.66 (2H, m, AA′ part of AA′XX′ spin system, J_{ortho} 8.3 Hz, $C_{(2)}H$ and $C_{(6)}H$ in 4-MeC_6H_4), 7.41 (2H, m, XX′ part of AA′XX′ spin system, J_{ortho} 8.3 Hz, $C_{(3)}H$ and $C_{(5)}H$ in 4-MeC_6H_4), 5.04 (1H, d, J 5.0 Hz, 4H), 2.38 (3H, s, CH_3 in 4-MeC_6H_4), 1.89 (3H, s, 6-CH_3). ^{13}C NMR (DMSO-d_6) δ: 153.1 ($C_{(2)}$), 151.3 ($C_{(6)}$), 143.3 ($C_{(4)}$ in 4-MeC_6H_4), 141.0 ($C_{(1)}$ in 4-MeC_6H_4), 129.8 ($C_{(3)}$ and $C_{(5)}$ in 4-MeC_6H_4), 126.2 ($C_{(2)}$ and $C_{(6)}$ in 4-MeC_6H_4), 104.9 (CCl_3), 103.0 ($C_{(5)}$), 66.3 ($C_{(4)}$), 21.0 (CH_3 в Ts), 17.6 (6-CH_3). IR (Nujol) ν, cm^{-1}: 3222 (br s), 3084 (br s) (ν NH), 1726 (s) (amide-I), 1625 (s) (ν C=C), 1598 (w), 1491 (w) (ν CC in C_6H_4), 1293 (s) (ν_{as} SO_2), 1146 (s) (ν_s SO_2), 809 (s) (δ CH in C_6H_4). Anal. Calcd for $C_{13}H_{13}Cl_3N_2O_3S$: C, 40.70; H, 3.42; N, 7.30%. Found: C, 40.92; H, 3.51; N, 7.54%.

4.11. 4-Phenyl-5-phenylsulphonyl-1,2-dihydropyrimidin-2-one (10a)

To a mixture of NaH (0.037 g, 1.54 mmol) and **9a** (0.665 g, 1.40 mmol) was added anhydrous MeCN (10 mL) and the resulted suspension was stirred in an ice bath for 3 min. The obtained solution was stirred for 7 min at rt and then precipitation occurred. The resultant suspension was stirred for additional 1 h 45 min at rt, and solvent was removed in vacuum. To a dry residue was added H_2O (2 mL), the obtained suspension was neutralized with 2% aqueous solution of HCl to pH 7. Upon cooling to 0 °C, the precipitate was filtered, washed with ice-cold water, light petrol, and dried to give 0.406 g (92.5%) of **10a**. Mp 245.5–246.5 °C (EtOH). ^{1}H NMR (DMSO-d_6) δ: 13.04 (1H, br s, NH), 8.85 (1H, s, 6H), 7.53–7.61 (1H, m, $C_{(4)}H$ in $PhSO_2$), 7.40–7.47 (1H, m, $C_{(4)}H$ in 4-Ph), 7.35–7.40 (4H, m, $C_{(2)}H$ and $C_{(6)}H$, $C_{(3)}H$ and $C_{(5)}H$ in $PhSO_2$), 7.25–7.31 (2H, m, $C_{(3)}H$ and $C_{(5)}H$ in 4-Ph), 7.04–7.08 (2H, m, $C_{(2)}H$ and $C_{(6)}H$ in 4-Ph). ^{13}C NMR (DMSO-d_6) δ: 170.7 (very br, $C_{(4)}$), 155.0 ($C_{(2)}$), 154.5 (very br, $C_{(6)}$), 140.4 ($C_{(1)}$ in $PhSO_2$), 134.9 (very br, $C_{(1)}$ in 6-Ph), 133.4 ($C_{(4)}$ in $PhSO_2$), 129.9 (br, $C_{(4)}$ in 4-Ph), 129.0 ($C_{(2)}$ and $C_{(6)}$ in $PhSO_2$), 128.1 (br, $C_{(2)}$ and $C_{(6)}$ in 4-Ph), 127.5 ($C_{(3)}$ and $C_{(5)}$ in 4-Ph), 127.1 ($C_{(3)}$ and $C_{(5)}$ in $PhSO_2$), 117.2 ($C_{(5)}$). IR (Nujol) ν, cm^{-1}: 3064 (m), 2725 (m), 2661 (m), 2626 (m) (ν NH), 1687 (vs) (amide-I), 1596 (vs) (ν C=C, ν C=N), 1517 (s) (amide-II), 1308 (s) (ν_{as} SO_2), 1147 (vs) (ν_s SO_2), 766 (s), 691 (s) (δ CH in Ph). Anal. Calcd for $C_{16}H_{12}N_2O_3S$: C, 61.53; H, 3.87; N, 8.97%. Found: C, 61.47; H, 3.85; N, 8.91%.

4.12. 4-Phenyl-5-tosyl-1,2-dihydropyrimidin-2-one (10b)

Compound **10b** (0.353 g, 79.6%) was prepared (analogously to **10a**) from **9b** (0.620 g, 1.36 mmol) and NaH (0.037 g, 1.54 mmol) in

MeCN (4.6 mL) (rt, 1 h 30 min). Mp 225.5–226 °C (MeCN). ^{1}H NMR (DMSO-d_6) δ: 12.99 (1H, br s, NH), 8.82 (1H, s, 6H), 7.42–7.48 (1H, m, $C_{(4)}$H in Ph), 7.27–7.33 (2H, m, $C_{(3)}$H and $C_{(5)}$H in Ph), 7.25 (2H, m, AA′ part of AA′XX′ spin system, J_{ortho} 8.5 Hz, $C_{(2)}$H and $C_{(6)}$H in 4-MeC_6H_4), 7.19 (2H, m, XX′ part of AA′XX′ spin system, J_{ortho} 8.5 Hz, $C_{(3)}$H and $C_{(5)}$H in 4-MeC_6H_4), 7.06–7.11 (2H, m, $C_{(2)}$H and $C_{(6)}$H in Ph), 2.32 (3H, s, CH_3). ^{13}C NMR (DMSO-d_6) δ: 170.2 (very br, $C_{(4)}$), 155.0 ($C_{(2)}$), ~154.7 (very br, $C_{(6)}$), 144.0 ($C_{(4)}$ in 4-MeC_6H_4), 137.6 ($C_{(1)}$ in 4-MeC_6H_4), 134.8 (very br, $C_{(1)}$ in 6-Ph), 129.8 (br, $C_{(4)}$ in 4-Ph), 129.4 ($C_{(3)}$ and $C_{(5)}$ in 4-MeC_6H_4), 128.1 (br, $C_{(2)}$ and $C_{(6)}$ in 4-Ph), 127.4 (br, $C_{(3)}$ and $C_{(5)}$ in 4-Ph), 127.2 ($C_{(2)}$ and $C_{(6)}$ in 4-MeC_6H_4), 117.6 ($C_{(5)}$), 21.0 (CH_3). IR (Nujol) ν, cm^{-1}: 3157 (br s), 3064 (br s), 2730 (br s), 2669 (br s) (ν NH), 1700 (vs) (amide-I), 1657 (vs) (ν C=C), 1609 (vs) (ν C=N), 1514 (s) (amide-II), 1492 (m) (ν CC in C_6H_4 and Ph), 1315 (s) (ν_{as} SO_2), 1154 (vs) (ν_s SO_2), 816 (s) (δ CH in C_6H_4), 768 (s), 698 (s) (δ CH in Ph). IR (hexachlorobut-1,3-diene) ν, cm^{-1}: 3158 (br s), 3067 (vs), 3007 (br s), 2951 (br s), 2921 (s), 2866 (br s), 2743 (br s), 2673 (br s) (ν NH). Anal. Calcd for $C_{17}H_{14}N_2O_3S$: C, 62.56; H, 4.32; N, 8.58%. Found: C, 62.25; H, 4.44; N, 8.67%.

4.13. 4-Methyl-5-phenylsulphonyl-1,2-dihydropyrimidin-2-one (10c)

Compound **10c** (0.618 g, 97.9%) was prepared (analogously to **10a**) from **9c** (1.038 g, 2.81 mmol) and NaH (0.074 g, 3.09 mmol) in MeCN (10 mL) (rt, 3 h 20 min). Mp 247 °C (decomp., EtOH). ^{1}H NMR (DMSO-d_6) δ: 12.81 (1H, very br s, NH), 8.75 (1H, s, 6H), 7.94–7.99 (2H, m, $C_{(2)}$H and $C_{(6)}$H in Ph), 7.70–7.76 (1H, m, $C_{(4)}$H in Ph), 7.60–7.68 (2H, m, $C_{(3)}$H and $C_{(5)}$H in Ph), 2.33 (3H, s, 4-CH_3). ^{13}C NMR (DMSO-d_6) δ: 167.4 (very br, $C_{(4)}$), 158.0 (very br, $C_{(6)}$), 155.1 ($C_{(2)}$), 140.9 ($C_{(1)}$ in Ph), 133.8 ($C_{(4)}$ in Ph), 129.7 ($C_{(2)}$ and $C_{(6)}$ in Ph), 127.1 ($C_{(3)}$ and $C_{(5)}$ in Ph), 116.0 ($C_{(5)}$), 21.0 (br, 4-CH_3). IR (Nujol) ν, cm^{-1}: 3164 (m), 3083 (sh), 3064 (s), 2774 (br s), 2687 (br s), 2574 (m) (ν NH), 1713 (vs) (amide-I), 1664 (s) (ν C=C, ν C=N), 1589 (s), 1578 (s) (amide-II), 1314 (s) (ν_{as} SO_2), 1165 (vs) (ν_s SO_2), 735 (s), 688 (s) (δ CH in Ph). Anal. Calcd for $C_{11}H_{10}N_2O_3S$: C, 52.79; H, 4.03; N, 11.19%. Found: C, 52.82; H, 4.12; N, 10.96%.

4.14. 4-Methyl-5-tosyl-1,2-dihydropyrimidin-2-one (10d)

Compound **10d** (0.901 g, 97.8%) was prepared (analogously to **10a**) from **9d** (1.338 g, 3.49 mmol) and NaH (0.092 g, 3.84 mmol) in MeCN (20 mL) (rt, 1 h 15 min). Mp 265–265.5 °C (decomp., EtOH). ^{1}H NMR (DMSO-d_6) δ: 12.78 (1H, very br s, NH), 8.72 (1H, s, 6H), 7.84 (2H, m, AA′ part of AA′XX′ spin system, J_{ortho} 8.3 Hz, $C_{(2)}$H and $C_{(6)}$H in 4-MeC_6H_4), 7.44 (2H, m, XX′ part of AA′XX′ spin system, J_{ortho} 8.3 Hz, $C_{(3)}$H and $C_{(5)}$H in 4-MeC_6H_4), 2.39 (3H, s, CH_3 in Ts), 2.32 (3H, s, 4-CH_3). ^{13}C NMR (DMSO-d_6) δ: 167.3 (br, $C_{(4)}$), 157.7 (br, $C_{(6)}$), 155.3 ($C_{(2)}$), 144.3 ($C_{(4)}$ in 4-MeC_6H_4), 138.1 ($C_{(1)}$ in 4-MeC_6H_4), 130.1 ($C_{(3)}$ and $C_{(5)}$ in 4-MeC_6H_4), 127.1 ($C_{(2)}$ and $C_{(6)}$ in 4-MeC_6H_4), 116.3 ($C_{(5)}$), 21.0 (CH_3 in Ts), 21.0 (br, 4-CH_3). IR (Nujol) ν, cm^{-1}: 3090 (m), 3064 (m), 3022 (m), 3006 (m), 2746 (s), 2689 (s), 2646 (m) (ν NH), 1708 (s), 1695 (vs) (amide-I), 1672 (s) (ν C=C), 1612 (s) (ν C=N), 1545 (s) (amide-II), 1316 (s) (ν_{as} SO_2), 1156 (vs) (ν_s SO_2), 818 (s) (δ CH in C_6H_4). IR (hexachlorobut-1,3-diene) ν, cm^{-1}: 3092 (m), 3066 (m), 3026 (m), 3009 (w), 2971 (m), 2950 (m), 2926 (m), 2846 (br vs), 2830 (s), 2755 (br vs), 2693 (br vs), 2649 (m) (ν NH). Anal. Calcd for $C_{12}H_{12}N_2O_3S$: C, 54.53; H, 4.58; N, 10.60%. Found: C, 54.44; H, 4.52; N, 10.39%.

Acknowledgements

We thank Dr. Andrei Guzaev (AM Chemicals LLC, Oceanside, CA, USA) for helpful discussions. We are also grateful to Dmitry A. Cheshkov for ^{1}H NMR NOE difference experiments.

Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2010.06.058.

References and notes

1. Fesenko, A. A.; Solovyev, P. A.; Shutalev, A. D. *Tetrahedron* **2010**, *66*, 940–946.
2. Caldwell, W. T.; Sayin, A. N. *J. Am. Chem. Soc.* **1952**, *74*, 4314–4317.
3. Schroeder, A. C.; Bardos, T. J. *J. Med. Chem.* **1981**, *24*, 109–112.
4. Lipinski, C. A.; Stam, J. G.; Pereira, J. N.; Ackerman, N. R.; Hess, H.-J. *J. Med. Chem.* **1980**, *23*, 1026–1031.
5. (a) Mamaev, V. P.; Dubovenko, Z. D. *Khim. Geterotsikl. Soedin.* **1970**, *6*, 541–545 [*Chem. Heterocycl. Compd.* (Engl. Transl.) **1970**, *6*, pp 501–504]; (b) Arukwe, J.; Keilen, G.; Undheim, K. *Acta Chem. Scand., Ser. B* **1988**, *42*, 530–536; (c) Hafez, A. A. A. *Collect. Czech. Chem. Commun.* **1993**, *58*, 2222–2226.
6. (a) Shutalev, A. D.; Kuksa, V. A. *Khim. Geterotsikl. Soedin.* **1997**, *33*, 105–109 [*Chem. Heterocycl. Compd.* (Engl. Transl.) **1997**, *33*, pp 91–95]; (b) Shutalev, A. D. *Khim. Geterotsikl. Soedin.* **1997**, *33*, 1696–1697 [*Chem. Heterocycl. Compd.* (Engl. Transl.) **1997**, *33*, pp 1469–1470]; (c) Shutalev, A. D.; Kishko, E. A.; Sivova, N. V.; Kuznetsov, A. Y. *Molecules* **1998**, *3*, 100–106; (d) Fesenko, A. A.; Shutalev, A. D. *Tetrahedron Lett.* **2007**, *48*, 8420–8423; (e) Fesenko, A. A.; Cheshkov, D. A.; Shutalev, A. D. *Mendeleev Commun.* **2008**, *18*, 51–53.
7. The PM6 and AM1 calculations were carried out using the Mopac 2009 (James J.P. Stewart, Stewart Computational Chemistry, Version 9.211W, http://openmopac.net/index.html) and WinMopac programs (Version 7.21, http://www.psu.ru/science/soft/winmopac/index_e.html), respectively.
8. It was stated,[16] that *N*-acylimines form as an intermediate in the reactions of amidoalkylation of various nucleophiles in basic media with amidoalkylating reagents derived from primary amides.
9. For reviews on α-halogenated imino compounds, see: (a) De Kimpe, N.; Schamp, N. *Org. Prep. Proced. Int.* **1979**, *11*, 115–199; (b) De Kimpe, N.; Verhé, R.; De Buyck, L.; Schamp, N. *Org. Prep. Proced. Int.* **1980**, *12*, 49–180.
10. For reviews on aldol reactions, see: (a) Mahrwald, R. *Aldol Reactions*; Springer: Dordrecht, 2009; (b) *Modern Aldol Reactions*; Mahrwald, R., Ed.; Wiley-VCH: Weinheim, 2004; Vols. 1 and 2.
11. The preference of sodium (*Z*)-enolates formation from **3a**–**d** in MeCN was demonstrated by NMR spectroscopy as followed. A solution of **3c** (13.5 mg, 0.0636 mmol) in MeCN-d_3 (0.5 mL) was added to a 5 mm NMR tube charged with NaH (2.3 mg, 0.0958 mmol). The obtained mixture was shaken carefully until the evolution of gas ceased. Assignment of the (*Z*)-configuration of the generated Na-enolate was based on the NOE effect observed between the α-proton (3.3% enhancement after irradiation of the vicinal CH_3) and the methyl protons in its ^{1}H NMR NOE difference spectrum. (*Z*)-Configuration of the enolate of **3c** was also confirmed by the value of vicinal coupling constant of ^{13}C–^{1}H in $^{13}CH_3$–C=C–H moiety, which equals 2.0 Hz in proton coupled ^{13}C NMR spectra. The expected constant value for (*E*)-enolate is 5 Hz.[17]
12. Semiempirical calculations using PM6[7] method demonstrated that (*Z*)-enolates of compounds **3a**–**d** are thermodynamically more stable than (*E*)-enolates.
13. According to ab initio calculations (B3LYP/6-31++G**)[14] the anion **11c** is more stable (10.0 kcal/mol) than the anion resulted from $N_{(3)}$-H deprotonation in the gas phase.
14. The ab initio calculations were carried out using the Gaussian 03 program Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03, Revision E.01*; Gaussian: Wallingford, CT, 2004.
15. For the prototropic tautomerism of six-membered heterocycles, see (a) Katritzky, A. R.; Lagowski, J. M. In *Adv. Heterocycl. Chem.*; Katritzky, A. R., Ed.; Academic: New York, 1963; Vol. 1, pp 339–437; (b) Elguero, J.; Katritzky, A. R.; Denisko, O. V. In *Adv. Heterocycl. Chem.*; Katritzky, A. R., Ed.; Academic: San Diego, 2000; Vol. 76, pp 1–84; (c) Rauhut, G. In *Adv. Heterocycl. Chem.*; Katritzky, A. R., Ed.; Academic: San Diego, 2001; Vol. 81, pp 1–105; (d) Stanovnik, B.; Tišler, M.; Katritzky, A. R.; Denisko, O. V. In *Adv. Heterocycl. Chem.*; Katritzky, A. R., Ed.; Academic: San Diego, 2001; Vol. 81, pp 253–303; (e) Stanovnik, B.; Tišler, M.; Katritzky, A. R.; Denisko, O. V. In *Adv. Heterocycl. Chem.*; Katritzky, A. R., Ed.; Elsevier: Amsterdam, 2006; Vol. 91, pp 1–134.

16. (a) Zaugg, H. E. *Synthesis* **1970**, 49–73; (b) De Kimpe, N.; Verhé, R.; De Buyck, L.; Dejonghe, W.; Schamp, N. *Bull. Soc. Chim. Belg.* **1976**, *85*, 763–779; (c) Kobayashi, T.; Ishida, N.; Hiraoka, T. *J. Chem. Soc., Chem. Commun.* **1980**, 736–737; (d) Zaugg, H. E. *Synthesis* **1984**, 85–110; (e) Zaugg, H. E. *Synthesis* **1984**, 181–212; (f) Hamon, D. P. G.; Massy-Westropp, R. A.; Razzino, P. *Tetrahedron* **1992**, *48*, 5163–5178; (g) Petrini, M.; Torregiani, E. *Synthesis* **2007**, 159–186; (h) Pizzuti, M. G.; Minnaard, A. J.; Feringa, B. L. *J. Org. Chem.* **2008**, *73*, 940–947; (i) Mazurkiewicz, R.; Pazdźierniok-Holewa, A.; Orlińska, B.; Stecko, S. *Tetrahedron Lett.* **2009**, *50*, 4606–4609.

17. Mixture of stereoisomeric Na-enolates **3c** (in 86:14 ratio) was prepared as described above[11] by the reaction of **3c** (16.2 mg, 0.0763 mmol) with NaH (2.7 mg, 0.1125 mmol) in DMSO-d_6 (0.5 mL). The values of vicinal coupling constants $^{13}C-^{1}H$ of $^{13}CH_3-C=C-H$ moiety of obtained enolates in proton coupled ^{13}C NMR spectra were 1.7 and 4.9 Hz correspondingly. Based on the relationship between this constant and dihedral angle C–C=C–H we conclude that major stereoisomer has (*Z*)-configuration and minor (*E*)-configuration.[18] Assignment of the (*Z*)-configuration of the major stereoisomer was also based on the NOE effect observed between the α-proton (5.1% enhancement after irradiation of the vicinal CH_3) and the methyl protons in its ^{1}H NMR NOE difference spectrum.

18. Pretsch, E.; Büllmann, P.; Affolter, C. *Structure Determination of Organic Compounds*; Springer: Berlin, Heidelberg, 2000.