Reactions of β-aminopropionic acid *N´*-acylhydrazides with carbonyl compounds

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The reactions of β-aminopropionic acid *N´*-acylhydrazides with aromatic and heterocyclic aldehydes and acetone afford compounds that exist in solutions predominantly as mixtures of 2-substituted 3-acylaminotetrahydropyrimidin-4-ones (ATHP) and tautomeric Schiff´s bases. These compounds in the crystalline state probably have structures of ATHP. The ratio of tautomers depends on the type of substituent in the aromatic ring and solvent. The reactions of 2-aryl-3-benzamidotetrahydropyrimidin-4-ones with carboxylic or sulfonic acid chlorides afford derivatives of 1-acyl- and 1-tosyl-3-benzamidotetrahydropyrimidin-4-ones.

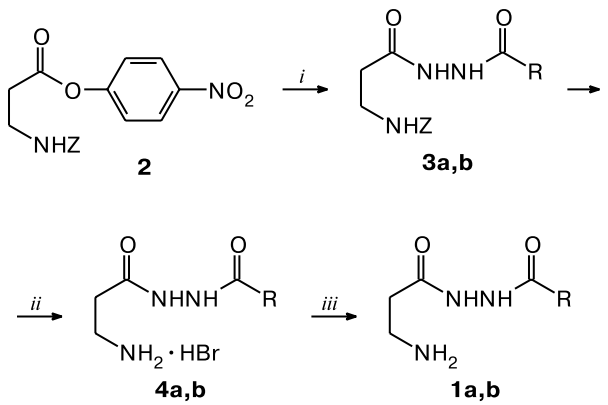
Key words: 3-acylaminotetrahydropyrimidin-4-ones, β-aminopropionic acid *N'*-benzoylhydrazide, β-aminopropionic acid *N'*-acetylhydrazide, ketones, aldehydes, *N*-acylation, *N*-tosylation, Schiff´s bases, tautomeric equilibrium.

Earlier,[1] we have studied the reactions of *N'*-acyl- and *N'*-tosyl-substituted hydrazides of 2-aminobenzoic acid with aliphatic and aromatic aldehydes and aliphatic ketones. These reactions were shown to have a general character and afford 2,3-disubstituted 1,2-dihydroquinazolin-4-ones (DHQ).

To extend this reaction to aliphatic analogs, *viz.*, *N'*-acylhydrazides of β-amino acids, we studied the reactions of β-aminopropionic acid *N'*-acylhydrazides **1a,b** with carbonyl compounds.

Previously undescribed hydrazides **1a,b** were synthesized according to Scheme 1.

Scheme 1

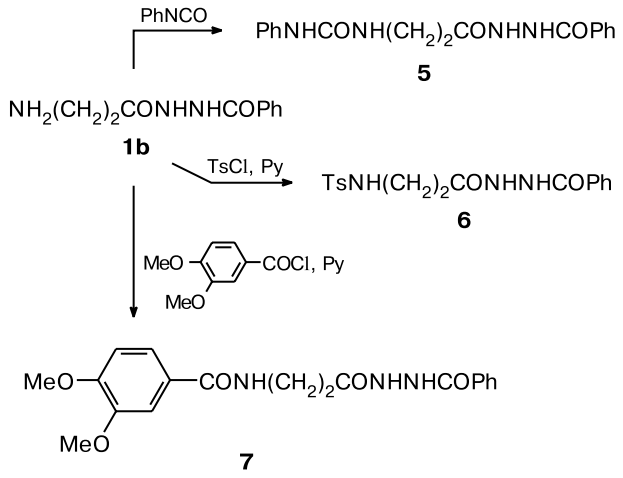


R = Me (**a**), Ph (**b**); Z = $PhCH_2OCO$

Reagents and yields: *i*. $RCONHNH_2$, 70—80%; *ii*. HBr—AcOH, 50—100%; *iii*. MeONa, 100%.

The ^1H NMR spectra of hydrazides **1a,b** clearly exhibit signals of protons of the R substituent and CH_2 groups; however, signals of the amino and hydrazide groups are presented as one broadened singlet. The structures of hydrazides **1a,b** were confirmed by the synthesis of compounds **5—7** using the reactions of hydrazide **1b** with respective electrophiles (Scheme 2).

Scheme 2



Aldehydes and ketones of the aliphatic, aromatic, and aliphatic-aromatic series were used as carbonyl compounds in the reactions with hydrazides **1a,b**. The reactions of **1a,b** with aromatic aldehydes in anhydrous Pr^iOH refluxing for 6—8 h afforded condensation products **8a—i** in 35—85% yields. Products **8a—i** are characterized by rather

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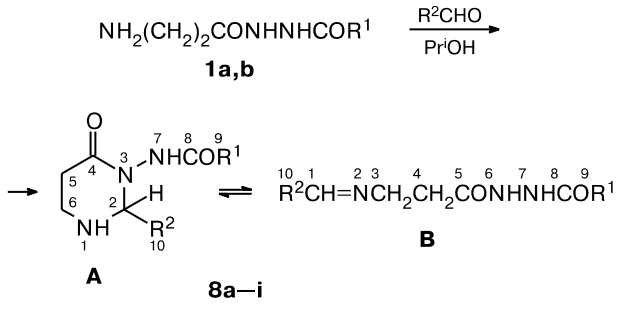
Table 1. Melting points, yields, and elemental analysis data for 2-aryl-substituted 3-acylaminotetrahydropyrimidin-4-ones **8a—i**

Compound	M.p. /°C	Yield (%)	Found / Calculated (%)			Molecular formula
			C	H	N	
8a	226—229	35	59.27 59.30	6.44 6.51	16.02 15.96	$C_{13}H_{17}N_3O_3$
8b	222—225	53	51.75 51.80	4.98 5.07	20.24 20.13	$C_{12}H_{14}N_4O_4$
8c	146—148	35	68.85 69.14	5.75 5.80	14.41 14.23	$C_{17}H_{17}N_3O_2$
8d	166—169	36	65.49 65.58	5.44 5.50	13.78 13.50	$C_{17}H_{17}N_3O_3$
8e	162—164	66	66.54 66.65	5.59 5.59	13.02 12.96	$C_{18}H_{19}N_3O_3$
8f	213—215	85	59.52 59.82	4.92 5.02	16.43 16.41	$C_{17}H_{16}N_4O_4$
8g	173—175	76	63.95 64.21	5.95 5.96	11.62 11.82	$C_{19}H_{21}N_3O_4$
8h	177—181	35	47.40 47.45	3.21 3.28	19.78 19.53	$C_{17}H_{14}N_6O_8$
8i	158—160	40	63.00 63.15	5.31 5.30	14.54 14.73	$C_{15}H_{15}N_3O_3$

Scheme 3



R^1 = Me (**1a**), Ph (**1b**)

	R^1	R^2		R^1	R^2
8a	Me	4-MeO-C_6H_4	**8f**	Ph	4-O_2N-C_6H_4
8b	Me	4-O_2N-C_6H_4	**8g**	Ph	(3,4-MeO)$_2$-C_6H_3
8c	Ph	Ph	**8h**	Ph	(2,4,6-O_2N)$_3$-C_6H_2
8d	Ph	3-HO-C_6H_4	**8i**	Ph	
8e	Ph	4-MeO-C_6H_4			

narrow intervals of melting points (Table 1). The NMR spectra of solutions of compounds **8a—i** in $CDCl_3$ and DMSO-d_6 contained a set of signals of two substances.

Table 2. Signals of isomers **A** in the ^{1}H NMR spectra of 2-aryl-substituted 3-acylaminotetrahydropyrimidin-4-ones **8a—i** (atoms are numbered in Scheme 3)

Compound	Solvent	δ, *J*/Hz						
		N(1)H	C(2)H	C(5)H_2	C(6)H_2	N(7)H	R^1(9)	R^2(10)
8a	$CDCl_3$	6.95 (m)	5.55 (s)	2.55 (m)	3.23 (m)	9.80 (s)	1.90 (s, 3 H, CH_3)	4-MeO-C_6H_4: 3.90 (s, 3 H); 6.95 (m, 2 H); 7.25 (m, 2 H)
8b	$CDCl_3$	7.55 (m)	5.75 (s)	2.70 (m)	3.25 (m)	9.90 (s)	1.95 (s, 3 H, CH_3)	4-NO_2-C_6H_4: 7.95, 8.22 (both d, 2 H each, *J* = 7.3)
8c	$CDCl_3$	7.40 (m)	5.70 (s)	2.70 (m)	3.25 (m)	8.60 (br.s)	7.40 (m, 3 H); 7.80 (d, 2 H, *J* = 7.4)	Ph: 7.30 (m, 3 H); 7.45 (d, 2 H, *J* = 7.4)
	DMSO-d_6	7.40 (br.s)	5.32 (s)	2.60 (m)	3.90 (m)	10.0 (br.s)	7.45 (m, 3 H); 7.90 (d, 2 H, *J* = 7.4)	7.45 (m, 3 H); 7.75 (d, 2 H, *J* = 7.4)
8d	DMSO-d_6	7.20 (m)	5.40 (s)	2.60 (m)	3.80 (m)	9.90 (br.s)	7.50 (m, 3 H); 7.65 (d, 2 H, *J* = 7.4)	3-HO-C_6H_4: 6.82 (d, 1 H, *J* = 7.8); 7.20 (m, 2 H); 7.15 (s, 1 H)
8e	$CDCl_3$	7.30 (m)	5.72 (s)	2.70 (m)	3.70 (m)	8.70 (br.s)	7.40 (m, 3 H); 7.70 (d, 2 H, *J* = 7.4)	4-$MeOC_6H_4$: 3.85 (s, 3 H); 6.95, 7.45 (both d, 2 H each, *J* = 7.7)
	DMSO-d_6	7.40 (m)	5.45 (s)	2.55 (m)	3.75 (m)	9.20 (br.s)	7.30 (m, 3 H); 7.75 (d, 2 H, *J* = 7.4)	3.80 (s, 3 H); 6.95, 7.45 (both d, 2 H each, *J* = 7.7)
8f	$CDCl_3$	7.25 (m)	5.85 (s)	2.70 (t, *J* = 7.0)	3.25 (t, *J* = 7.0)	9.22 (br.s)	7.40 (m, 3 H); 7.60 (d, 2 H, *J* = 7.4)	4-NO_2-C_6H_4: 7.80, 8.20 (both d, 2 H each, *J* = 7.3)
	DMSO-d_6	7.45 (m)	5.65 (d, *J* = 8.1)	2.55 (t, *J* = 7.0)	3.1 (t, *J* = 7.0)	10.1 (br.s)	7.40 (m, 3 H); 7.55 (d, 2 H, *J* = 7.4)	7.75, 8.20 (both d, 2 H each, *J* = 7.3)
	CD_3OD	7.45 (m)	5.75 (s)	2.75 (m)	3.25 (m)	9.50 (br.s)	7.45 (m, 3 H); 7.55 (d, 2 H, *J* = 7.4)	7.85, 8.35 (both d, 2 H each, *J* = 7.3)
8g	$CDCl_3$	7.20 (s)	5.70 (s)	2.60 (m)	3.25 (m)	9.80 (br.s)	7.45 (m, 3 H); 7.60 (d, 2 H, *J* = 7.4)	(3,4-MeO)$_2$-C_6H_4: 3.85, 4.00 (both s, 3 H each); 6.90 (m, 2 H); 7.3 (s, 1 H)
8h	$CDCl_3$	7.25 (br.s)	5.75 (s)	2.45 (m)	3.70 (m)	9.55 (s)	7.25 (br.s, 5 H)	(2,4,6-NO_2)$_3$-C_6H_2: 9.35 (br.s, 2 H)
8i	$CDCl_3$	7.45 (m)	5.82 (d, *J* = 7.9)	2.65 (m)	3.25 (m)	8.95 (br.s)	7.45 (m, 3 H); 7.65 (d, 2 H, *J* = 7.4)	C_4H_3O: 6.35, 6.45 (both s, 1 H each); 7.45 (m, 1 H)
	DMSO-d_6	7.45 (br.s)	5.60 (s)	3.0 (m)	3.50 (m)	10.0 (br.s)	7.45 (m, 3 H); 7.75 (d, 2 H, *J* = 7.4)	6.40, 6.50 (both s, 1 H each); 7.50 (br.s, 1 H)

Table 3. Signals of isomers **B** in the ^{1}H NMR spectra of Schiff´s bases **8a—i** (atoms are numbered in Scheme 3)

Compound	Solvent	δ, *J*/Hz					
		C(1)H=N	C(3)H_2N	C(4)H_2CO	N(6)H—N(7)H	R^1(9)	R^2(10)
8a	$CDCl_3$	8.25 (s)	3.80 (t, *J* = 7.0)	2.65 (t, *J* = 7.0)	9.90 (s)	2.1 (s, 3 H, CH_3)	4-MeO-C_6H_4: 3.95 (s, 3 H); 6.95, 7.75 (both m, 2 H each)
	DMSO-d_6	8.25 (s)	3.75 (t, *J* = 7.0)	2.32(t, *J* = 7.0)	9.50 (br.s)	1.75 (s, 3 H, CH_3)	3.75 (s, 3 H); 6.95, 7.65 (both d, 2 H each, *J* = 7.1)
8b	$CDCl_3$	8.40 (s)	3.95 (m)	2.70 (m)	9.90 (s)	2.05 (s, 3 H, CH_3)	4-NO_2-C_6H_4: 8.00, 8.25 (both d, 2 H each, *J* = 7.3)
	DMSO-d_6	8.50 (t)	3.85 (m)	2.40 (m)	9.50 (br.s)	1.75 (s, 3 H, CH_3)	8.00, 8.25 (both d, 2 H each, *J* = 7.3)
8c	$CDCl_3$	8.30 (s)	3.90 (m)	2.70 (m)	9.60 (br.s)	7.40 (m, 3 H); 7.80 (d, 2 H, *J* = 7.4)	Ph: 7.30 (m, 3 H); 7.45 (d, 2 H, *J* = 7.4)
	DMSO-d_6	8.45 (s)	3.85 (br.s)	2.60 (br.s)	10.0 (br.s)	7.45 (m 3 H); 7.90 (d, 2 H, *J* = 7.4)	7.45 (m, 3 H); 7.75 (d, 2 H, *J* = 7.4)
8d	DMSO-d_6	8.30 (s)	3.80 (m)	2.60 (m)	9.95 (br.s)	7.50 (m, 3 H); 7.95 (d, 2 H, *J* = 7.4)	3-HO-C_6H_4: 6.90 (d, 1 H, *J* = 7.8); 7.20 (m, 2 H); 9.95 (br.s, 1 H)
8e	$CDCl_3$	8.23 (s)	3.80 (m)	2.70 (m)	9.90 (br.s)	7.40 (m, 3 H); 7.80 (d, 2 H, *J* = 7.4)	4-$MeOC_6H_4$: 3.85 (s, 3 H); 6.95, 7.45 (both d, 2 H each, *J* = 7.7)
	DMSO-d_6	8.30 (s)	3.70 (m)	2.60 (m)	10.00 (br.s)	7.45 (m, 3 H); 7.95 (d, 2 H, *J* = 7.4)	3.80 (s, 3 H); 6.95, 7.45 (both d, 2 H each, *J* = 7.7)
8f	$CDCl_3$	8.40 (s)	3.95 (t, *J* = 7.0)	2.70 (t, *J* = 7.0)	9.75 (br.s)	7.45 (m, 3 H); 7.65 (d, 2 H, *J* = 7.4)	4-NO_2-C_6H_4: 7.80, 8.20 (both d, 2 H each, *J* = 7.3)
	DMSO-d_6	8.55 (s)	3.95 (m)	2.65 (m)	10.05 (br.s)	7.40 (m, 3 H); 7.65 (d, 2 H, *J* = 7.4)	7.75, 8.20 (both d, 2 H each, *J* = 7.3)
	CD_3OD	8.53 (s)	4.00 (t, *J* = 7.0)	2.75 (t, *J* = 7.0)	9.60 (br.s)	7.45 (m, 3 H); 7.75 (d, 2 H, *J* = 7.4)	7.85, 8.35 (both d, 2 H each, *J* = 7.3)
8g	$CDCl_3$	8.25 (s)	3.85 (m)	2.70 (m)	10.00 (br.s)	7.45 (m, 3 H); 7.80 (d, 2 H, *J* = 7.4)	(3,4-$MeO)_2$-C_6H_4: 3.85, 4.00 (both s, 3 H each); 6.90 (m, 2 H); 7.30 (s, 1 H)
	DMSO-d_6	8.30 (s)	3.80 (m)	2.60 (m)	9.90 (br.s)	7.50 (m, 3 H); 7.85 (d, 2 H, *J* = 7.4)	3.80 (s, 6 H); 7.00, 7.25 (both m, 1 H each); 7.40 (s, 1 H)
8h	$CDCl_3$	9.15 (s)	4.05 (m)	3.65 (m)	9.55 (s)	7.25 (br.s, 5 H)	(2,4,6-$NO_2)_3$-C_6H_2: 9.35 (br.s, 2 H)
8i	$CDCl_3$	8.10 (s)	3.85 (t, *J* = 6.8)	2.70 (t, *J* = 6.8)	9.00 (br.s)	7.45 (m, 3 H); 7.80 (d, 2 H, *J* = 7.4)	C_4H_3O: 6.50, 6.90 (both s, 1 H each); 7.45 (m, 1 H)
	DMSO-d_6	8.25 (s)	3.85 (m)	2.60 (m)	10.00 (br.s)	7.45 (m, 3 H); 7.85 (m, 2 H, *J* = 7.4)	6.60, 6.90 (both s, 1 H each); 7.50 (m, 1 H)

Table 4. Ratio of tautomers **A** and **B** of compounds **8a—i** in solutions according to the ^{1}H NMR spectroscopic data

Compound	**A** : **B** ratio	
	$CDCl_3$	DMSO-d_6
8a	27 : 73	<1 : 99
8b	50 : 50	<1 : 99
8c	50 : 50	7 : 93
8d	—	12 : 88
8e	31 : 69	5 : 95
8f	50 : 50	23 : 77
8g	18 : 82	<1 : 99
8h	70 : 30	—
8i	33 : 66	8 : 92

Taking into account the results of elemental analysis of compounds **8a—i**, we can assume that these substances are mixtures of 3-acylaminotetrahydropyrimidin-4-one derivatives (**A**), whose NMR spectra are characterized by signals at 5.4—5.9 ppm for protons at the C(2) atom, and the corresponding tautomeric Schiff´s bases (**B**), whose NMR spectra contain signals at 8.2—9.1 ppm for protons at the C(1) atom (Scheme 3, Tables 2 and 3). The ratio of tautomers **A** and **B** depended on the nature of solvent and substituents R^1 and R^2 (Table 4).

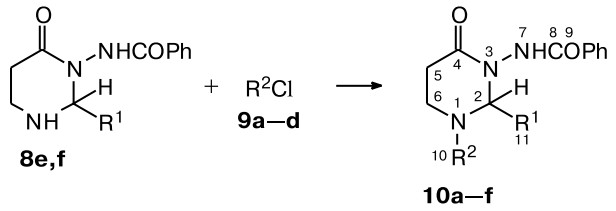
In solutions of compounds **8a—i** in DMSO-d_6, linear tautomer **B** was predominant. In $CDCl_3$, the fraction of heterocycle **A** increased, which was especially noticeable for the compounds containing electron-withdrawing substituents in the aromatic ring of R^2. Trinitrophenyl de-

rivative **8h** existed in a $CDCl_3$ solution predominantly in cyclic form **A**.

Although compounds **8a—i** are characterized by rather high melting points, they are partially decomposed being recrystallized and chromatographed on silica gel, which did not allow us to obtain a sample appropriate for establishing the structures of compounds **8a—i** in the crystalline state by X-ray diffraction analysis.

Compounds **8e,f** react with carboxylic and sulfonic acid chlorides **9a—d** to form 1-acyl- and 1-tosyl-3-acylaminotetrahydropyrimidin-4-one derivatives **10a—f** (Scheme 4).

Scheme 4



8: R^1 = 4-MeO-C_6H_4 (**e**), 4-O_2N-C_6H_4 (**f**)

9: R^2 = Ac (**a**), Bz (**b**), (3,4-MeO)$_2$-C_6H_3CO (**c**), Ts (**d**)

	R^1	R^2		R^1	R^2
10a	4-MeO-C_6H_4	Ac	**10d**	4-O_2N-C_6H_4	Bz
10b	4-MeO-C_6H_4	Bz	**10e**	4-O_2N-C_6H_4	(3,4-MeO)$_2$-C_6H_3CO
10c	4-O_2N-C_6H_4	Ac	**10f**	4-O_2N-C_6H_4	Ts

The structures of compounds **10a—f** were established from the data of elemental analysis and ^1H NMR spectra (Tables 5 and 6). The latter contained signals of protons at the C(2) atom in a region of δ 6.45—7.05 characteristic of ATHP.

A specific feature of the IR spectra of compounds **10c,d,f** in KBr pellets is the presence of a band with the frequency ~1600 cm^{-1} and two bands at 1648—1656 and 1696—1704 cm^{-1} with the ratio of intensities ~1 : 5 : 3, which correspond to the CONNHCO fragment.[2] A similar spectrum in a region of 1600—1700 cm^{-1} is characteristic of compound **8f** in the crystalline state. At the same time, the IR spectrum of compound **6** having the CONHNHCO fragment differs substantially in this region. In our opinion, this comparison suggests that crystals of compound **8f** and, perhaps, other condensation products **8** in the crystalline state have the structure of cyclic tautomer **A** rather than Schiff´s base **B**.

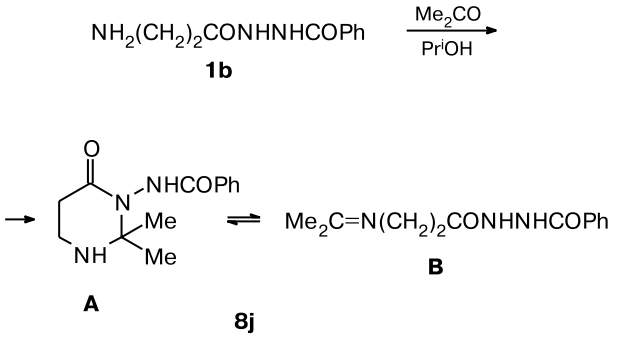
Of aliphatic carbonyl compounds, we studied formaldehyde, acetaldehyde, acetone, cyclopentanone, and cyclohexanone in the reactions with **1b**. As previously, the reactions were carried out in boiling Pr^iOH. We succeeded to isolate the individual reaction product **8j** only when acetone was used, but its yield was only 10% (Scheme 5). As follows from the data of elemental analysis, IR spectrum, and ^{13}C NMR spectrum of compound **8j** (which exhibits signals of the C(2) atom corresponding to the cyclic form of 3-acylamino-2,2-dimethyltetrahydropyrimidin-4-one (δ 76.47) and C=N group of isomeric Schiff´s base (δ 165.43)), this compound in solution is also a mixture of tautomeric cyclic (**A**) and linear (**B**) forms (see Table 4).

Table 5. Melting points, yields, and elemental analysis data for 1-acyl(1-tosyl)-3-benzoylaminotetrahydropyrimidin-4-ones **10a—f**

Compound	M.p. /°C	Yield (%)	Found / Calculated (%)			Molecular formula
			C	H	N	
10a	179—182	54	65.24 65.38	5.79 5.76	11.22 11.44	$C_{20}H_{21}N_3O_4$
10b	185—187	62	69.79 69.92	5.50 5.40	10.02 9.78	$C_{25}H_{23}N_3O_4$
10c	268—269	80	59.61 59.68	4.70 4.76	14.62 14.65	$C_{19}H_{18}N_4O_5$
10d	158—160	55	64.60 64.80	4.54 4.54	12.49 12.61	$C_{24}H_{20}N_4O_5$
10e	137—140	50	61.73 61.90	4.73 4.80	10.90 11.10	$C_{26}H_{24}N_4O_7$
10f*	211—213	60	58.35 58.29	4.45 4.48	11.38 11.33	$C_{24}H_{22}N_4O_6S$

* Found: S, 6.26%; calculated: S, 6.48%.

Scheme 5



N-Benzoylhydrazone of acetophenone **11** turned out to be the main product of the reaction of hydrazide **1b** with acetophenone (a representative of aliphatic-aromatic ketones) under similar conditions (Scheme 6).

Scheme 6

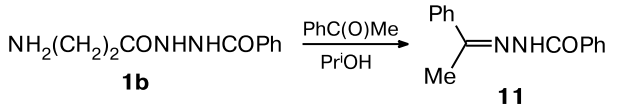


Table 6. ^{1}H NMR spectroscopic data for 2-aryl-substituted 1-acyl(1-tosyl)-3-benzoylaminotetrahydropyrimidin-4-ones **10a—f***

Compound	Solvent	δ, *J*/Hz					
		C(2)H	$C(4)H_2$, $C(5)H_2$ (m, 1 H)	N(7)H (s)	Ph(9)	R^2(10)	R^1(11)
10a	DMSO-d_6	6.90 (s)	2.35, 2.60, 2.75, 3.40	10.65	7.50 (m, 3 H); 7.85 (d, 2 H, *J* = 7.4)	$COCH_3$ 2.15 (s, 3 H)	4-MeO-C_6H_4: 3.80 (s, 3 H); 6.95 (d, 2 H, *J* = 7.7); 7.50 (m, 2 H)
10b	DMSO-d_6	6.80 (br.s)	2.60, 2.75; 3.40 (2 H)	10.75	7.50 (m, 3 H); 7.82 (d, 2 H, *J* = 7.4)	COPh 7.50 (m, 5 H)	4-MeO-C_6H_4: 3.78 (s, 3 H); 7.00 (d, 2 H, *J* = 7.7); 7.50 (m, 2 H)
10c	DMSO-d_6	7.05 (s)	2.60, 2.83, 3.45, 3.90	10.75	7.50 (m, 3 H); 7.75 (d, 2 H, *J* = 7.4)	$COCH_3$ 2.20 (s, 3 H)	4-NO_2-C_6H_4: 7.90, 8.25 (both d, 2 H each, *J* = 9.0)
10d	DMSO-d_6	7.00 (s)	2.60, 2.80, 3.45, 3.80	10.85	7.50 (m, 3 H); 7.80 (d, 2 H, *J* = 7.4)	COPh 7.50 (m, 5 H)	4-NO_2-C_6H_4: 7.90, 8.30 (both d, 2 H each, *J* = 9.0)
10e	$CDCl_3$	6.85 (s)	2.65, 2.90, 3.35, 4.10	9.70	7.40 (m, 3 H); 7.75 (m, 2 H)	(3,4-MeO)$_2$-C_6H_4 3.90 (s, 6 H); 7.12 (m, 2 H); 7.25 (m, 1 H)	4-NO_2-C_6H_4: 7.75, 8.20 (both d, 2 H each, *J* = 9.0)
10f	$CDCl_3$	7.05 (s)	2.20, 2.45, 3.25, 3.75	8.70	7.35 (t, 3 H, *J* = 7.7); 7.70 (m, 2 H)	4-CH_3-$C_6H_4SO_2$ 2.45 (c, 3 H); 7.45 (d, *J* = 8.5); 7.70 (m, 2 H)	4-NO_2-C_6H_4: 8.15, 8.35 (both d, 2 H each, *J* = 9.0)

* Atoms are numbered in Scheme 4.

Experimental

^{1}H NMR spectra were recorded on Bruker AC-200 (200.13 MHz) and Bruker AM-300 (300.13 MHz) spectrometers. ^{13}C NMR spectra were measured on a Bruker AM-250 spectrometer (62.9 MHz). Signals of protons, whose multiplicity is not given, are strongly broadened (perhaps, due to dynamic processes). IR spectra were recorded on a Specord M80 spectrometer in KBr pellets. Melting points were measured on a Boetius hot-stage apparatus and were uncorrected. A $CHCl_3$—MeOH (16 : 1) mixture was used for TLC. Compound **2** was synthesized by a described procedure.[3]

***N*-Benzyloxycarbonyl-β-aminopropionic acid *N′*-acetyl- (3a) and *N′*-benzoylhydrazides (3b).** Hydrazide of acetic (benzoic) acid (0.05 mol) was added to a solution of ester **2** (17.2 g, 0.05 mol) in DMF (80 mL). The resulting solution was stirred for 5 h at 100 °C and cooled to ~20 °C. The solvent was evaporated *in vacuo*, and the residue was first crystallized twice from ethyl acetate (50 mL) and then twice from ethanol (50 mL). Compound **3a** was obtained in 65% yield (9.06 g, m.p. 174—176 °C) or compound **3b** was obtained in 70% yield (11.9 g, m.p. 164—166 °C). **Compound 3a.** Found (%): C, 56.05; H, 6.08; N, 14.71. $C_{13}H_{17}N_3O_4$. Calculated (%): C, 55.91; H, 6.14; N, 14.94. ^{1}H NMR (DMSO-d_6), δ: 1.87 (s, 3 H, CH_3); 2.30 (t, 2 H, CH_2C, *J* = 6.0 Hz); 3.25 (m, 2 H, CH_2N, *J* = 6.0); 5.00 (s, 2 H, CH_2O); 7.17 (br.s, 1 H, $NHCO_2$); 7.35 (m, 5 H, Ph); 9.70 (br.s, 2 H, NHNH). **Compound 3b.** Found (%): C, 63.35; H, 5.64; N, 12.25. $C_{18}H_{19}N_3O_4$. Calculated (%): C, 63.33; H, 5.61; N, 12.31. ^{1}H NMR (DMSO-d_6), δ: 2.40 (t, 2 H, C$\underline{H}_2$C, *J* = 6.1 Hz); 3.35 (m, 2 H, CH_2N); 5.05 (s, 2 H, CH_2O); 7.20 (br.s, 1 H, $NHCO_2$); 7.35 (m, 5 H, $\underline{Ph}CH_2$); 7.55 (m, 3 H, PhCO); 7.90 (d, 2 H, PhCO, *J* = 7.4 Hz); 9.95, 10.30 (both br.s, 1 H each, NHCO).

Hydrobromides of β-aminopropionic acid *N′*-acetyl- (4a) and *N′*-benzoylhydrazide (4b). A 0.3 *M* solution of HBr in AcOH (15 mL) was added to a solution of compound **3a** (**3b**) (0.02 mol) in AcOH (15 mL). The reaction mixture was stirred for 0.5—1.5 h at ~20 °C (TLC monitoring), and anhydrous Et_2O (160 mL) was added. The precipitate that formed was filtered off, dried in air, recrystallized from a mixture of EtOH (15 mL) and Et_2O (40 mL), successively washed with mixtures of EtOH (10 mL)/Et_2O (40 mL) and EtOH (3 mL)/Et_2O (30 mL), and dried in air. Compound **4a** was obtained in 94% yield (4.2 g, m.p. 207—210 °C) and compound **4b** was obtained in 83% yield (4.78 g, m.p. 132—134 °C). **Compound 4a.** Found (%): C, 26.76; H, 5.34; N, 18.53; Br, 35.48. $C_5H_{12}BrN_3O_2$. Calculated (%): C, 26.56; H, 5.35; N, 18.59; Br, 35.34. ^{1}H NMR (DMSO-d_6), δ: 1.85 (s, 3 H, CH_3); 2.45 (t, 2 H, CH_2C, *J* = 7.1 Hz); 3.00 (m, 2 H, CH_2N, *J* = 7.1 Hz); 7.87 (br.s, 3 H, $NH_3^+Br^-$); 9.70, 9.85 (both s, 1 H each, CONH). **Compound 4b.** Found (%): C, 41.58; H, 5.01; N, 14.56; Br, 27.23. $C_{10}H_{14}BrN_3O_2$. Calculated (%): C, 41.46; H, 4.89; N, 14.57; Br, 27.43. ^{1}H NMR (DMSO-d_6), δ: 2.60 (t, 2 H, CH_2C, *J* = 6.9 Hz); 3.05 (m, 2 H, CH_2N, *J* = 6.9 Hz); 7.50 (m, 3 H, PhC); 7.80—7.95 (m, 2 H, PhC + $NH_3^+Br^-$); 10.10, 10.30 (both s, 1 H each, NHCO).

β-Aminopropionic acid *N′*-acetyl- (1a) and *N′*-benzoylhydrazides (1b). A solution of MeONa (0.030 mol) in anhydrous MeOH (15 mL) was added dropwise to a solution of compound **4a** or **4b** (0.025 mol) in anhydrous MeOH (20 mL). The resulting mixture was stirred for 1 h at ~20 °C. The solvent was evaporated, and the residue was dissolved in anhydrous Pr^iOH (40 mL). A precipitate of NaBr was filtered off and washed with anhydrous Pr^iOH (30 mL). The mother liquor was concentrated to dryness, and the resulting product was dried and stored *in vacuo*. Compound **1a** was obtained in 100% yield (3.62 g, m.p. 69—72 °C) and compound **1b** was obtained in 100% yield (5.17 g,

m.p. 104—106 °C). **Compound 1a.** Found (%): C, 41.65; H, 7.77; N, 28.79. $C_5H_{11}N_3O_2$. Calculated (%): C, 41.37; H, 7.64; N, 28.95. ^{1}H NMR (DMSO-d_6), δ: 1.72 (s, 3 H, CH_3); 2.12 (t, 2 H, CH_2C, J = 6.2 Hz); 2.70 (m, 2 H, CH_2N 6.2), 4.50 (br.s, 4 H, NHNH + NH_2). **Compound 1b.** Found (%): C, 57.85; H, 6.29; N, 20.17. $C_{10}H_{13}N_3O_2$. Calculated (%): C, 57.96; H, 6.32; N, 20.28. ^{1}H NMR (DMSO-d_6), δ: 2.30 (t, 2 H, CH_2C, J = 6.0 Hz); 2.82 (m, 2 H, CH_2N, J = 6.0 Hz); 6.00 (br.s, 4 H, NHNH + NH_2); 7.50 (m, 3 H, PhCO); 7.90 (d, 2 H, PhCO, J = 7.4 Hz).

***N*-Phenylcarbamoyl-β-aminopropionic acid *N′*-benzoylhydrazide (5).** Phenyl isocyanate (0.26 mL, 0.29 g, 2.4 mmol) was added to a solution of hydrazide **1b** (0.5 g, 2.4 mmol) in pyridine (4.7 mL). The resulting solution was stirred for 3.5 h at 20 °C and poured into a 5% solution of HCl (110 mL). The precipitate that formed was filtered off and crystallized from an EtOH—EtOAc (1 : 4) mixture. Compound **5** was obtained in 50% yield (0.37 g, m.p. 215—218 °C). Found (%): C, 62.73; H, 5.49; N, 16.92. $C_{17}H_{18}N_4O_3$. Calculated (%): C, 62.57; H, 5.56; N, 17.17. ^{1}H NMR (DMSO-d_6), δ: 2.40 (t, 2 H, CH_2C, J = 6.5 Hz); 3.35 (m, 2 H, CH_2N); 6.20 (t, 1 H, NH, J = 5.8 Hz); 6.95, 7.20 (both t, 2 H each, PhN, J = 8.8 Hz); 7.40 (d, 2 H, PhN, J = 7.8 Hz); 7.55 (m, 3 H, PhC); 7.90 (d, 2 H, PhC, J = 6.9 Hz); 8.55 (s, 1 H, NH); 9.95, 10.30 (both br.s, 1 H each, NH).

***N*-Tosyl- (6) and *N*-(3,4-dimethoxybenzoyl)-β-aminopropionic acid *N′*-benzoylhydrazides (7).** Pyridine (2.9 mmol) and the corresponding acid chloride (2.4 mmol) were successively added to a solution of hydrazide **1b** (0.5 g, 2.4 mmol) in anhydrous dioxane (10 mL). The resulting solution was stirred for 4 h at ~20 °C, the solvent was evaporated, and the residue was crystallized from a water—EtOH (1 : 1) mixture. Compound **6** was obtained in 46% yield (0.4 g, m.p. 139—142 °C) and compound **7** was obtained in 50% yield (0.44 g, m.p. 187—188 °C). **Compound 6.** Found (%): C, 56.54; H, 5.34; N, 11.69, S, 8.78. $C_{17}H_{19}N_3O_4S$. Calculated (%): C, 56.50; H, 5.30; N, 11.63; S, 8.87. ^{1}H NMR (DMSO-d_6), δ: 2.30 (s, 3 H, CH_3); 2.35 (t, 2 H, CH_2C, J = 6.6 Hz); 2.95 (m, 2 H, CH_2N); 7.50 (m, 8 H, $SO_2N\underline{H}$ + Ph + C_6H_4S); 7.90 (d, 2 H, Ph J = 6.9 Hz); 9.95, 10.35 (both s, 1 H each, NHCO). **Compound 7.** Found (%): C, 61.22; H, 5.57; N, 11.05. $C_{19}H_{21}N_3O_5$. Calculated (%): C, 61.45; H, 5.70; N, 11.31. ^{1}H NMR (DMSO-d_6), δ: 2.50 (t, 2 H, $C\underline{H_2}C$, J = 6.4 Hz); 3.50 (m, 2 H, CH_2N); 3.85 (s, 6 H, 2 CH_3O); 7.00 (d, 1 H, (3,4-MeO)$_2$-$C_6\underline{H}_3$, J = 8 Hz); 7.50 (m, 5 H, Ph + (3,4-MeO)$_2$-$C_6\underline{H}_3$); 7.90 (d, 2 H, Ph, J = 7.4 Hz); 8.30, 9.90, 10.30 (all s, 1 H each, NH).

2-Substituted 3-acylaminotetrahydropyrimidin-4-ones (8a—i) (general procedure). An equimolar amount of aldehyde was added to a solution of the corresponding hydrazide (**1a** or **1b**) (2.5 mmol) in anhydrous Pr^{i}OH (10 mL). The mixture was refluxed for 6 h in the case of compounds **8a—g,i** and for 8 h in the case of **8h**. When synthesizing compounds **8b**, **8f**, and **8h**, the precipitate that formed was filtered off, washed with a mixture of Pr^{i}OH (6 mL) and hexane (6 mL), and dried. For compounds **8a**, **8c**, **8e**, **8g**, and **8i**, the solvent was evaporated, and the residue was recrystallized from a Pr^{i}OH—hexane mixture. For compound **8d**, the solvent was evaporated, and the residue was recrystallized from a $CHCl_3$—Et_2O (1 : 4) mixture. The yields, melting points, and ^{1}H NMR spectroscopic and elemental analysis data for the synthesized compounds are presented in Tables 1—3.

IR spectra (ν/cm^{-1}) of compounds **8a**: 1608 (C<u>O</u>NH), 1648 (<u>CO</u>CH_2); **8b**: 1348 (NO_2), 1528 (NO_2), 1604 (C<u>O</u>NH), 1644 (<u>CO</u>CH_2); **8d**: 1648 (C<u>O</u>NH), 1696 (<u>CO</u>CH_2); **8e**: 1648 (C<u>O</u>NH), 1668 (<u>CO</u>CH_2); **8f**: 1348 (NO_2), 1516 (NO_2), 1656 (C<u>O</u>NH), 1696 (<u>CO</u>CH_2); **8g**: 1644 (C<u>O</u>NH), 1688 (<u>CO</u>CH_2); **8j**: 1644 (C<u>O</u>NH), 1692 (<u>CO</u>CH_2).

3-Benzoylamino-2,2-dimethyltetrahydropyrimidin-4-one (8j). Anhydrous acetone (5 mL) was added to a solution of hydrazide **1b** (0.51 g, 2.5 mmol) in anhydrous Pr^{i}OH (5 mL). The resulting mixture was refluxed for 6 h and cooled. The solvent was evaporated, and the residue was recrystallized from a $CHCl_3$—Et_2O (1 : 4) mixture. Compound **8j** was obtained in 10% yield (0.06 g, m.p. 243—246 °C). Found (%): C, 63.01; H, 7.05; N, 16.75. $C_{13}H_{17}N_3O_2$. Calculated (%): C, 63.14; H, 6.93; N, 16.99. ^{1}H NMR (DMSO-d_6), δ: <u>isomer **A**</u>: 1.80, 1.82 (both s, 3 H each, CH_3); 2.45, 3.45 (both m, 2 H each, CH_2); 7.20 (s, 1 H, NH); 7.30 (br.s, 3 H, Ph); 7.90 (br.s, 2 H, Ph); 9.20 (br.s, 1 H, NH); <u>isomer **B**</u>: 1.80, 1.95 (both s, 3 H each, CH_3); 3.10, 3.40 (both t, 2 H each, CH_2, J = 7.0 Hz); 7.30 (br.s, 3 H, Ph); 7.90 (br.s, 2 H, Ph); 9.20 (br.s, 2 H, NHNH). ^{13}C NMR ($CDCl_3$), δ: <u>isomer **A**</u>: 25.31 (CH_3), 26.27 (CH_3), 34.18 (CH_2N), 36.43 ($\underline{C}H_2C$), 76.47 ($\underline{C}(CH_3)_2$), 127.42, 128.37, 131.83 (Ph), 167.21 ($CH_2\underline{C}O$), 168.86 (NHCO); <u>isomer **B**</u>: 25.51 (CH_3), 30.90 (CH_3), 37.88 ($\underline{C}H_2C$); 64.10 (CH_2N), 127.64, 131.37, 131.96 (Ph), 165.43 ($\underline{C}Me_2$), 168.86 (NHCO), 171.10 ($CH_2\underline{C}O$). IR, ν/cm^{-1}: 1636 (C<u>O</u>NH), 1696 (<u>CO</u>CH_2).

2-Aryl-substituted 1-acyl- and 1-tosyl-3-benzoylaminotetrahydropyrimidin-4-ones (10a—f) (general procedure). Pyridine (0.11 mL, 1.2 mmol) and the corresponding acid chloride **9a—d** (1 mmol) were successively added to a solution of compound **8e** (or **8f**) (1.0 mmol) in anhydrous dioxane (10 mL). The resulting mixture was stirred for 6 h at ~20 °C, the solvent was evaporated, and the residue was recrystallized from a water—EtOH (1 : 1) mixture. The yields, melting points, and ^{1}H NMR spectroscopic and elemental analysis data for the products are presented in Tables 5 and 6.

***N*-Benzoylhydrazone of acetophenone (11).** Acetophenone (0.29 g, 2.4 mmol) was added to a solution of hydrazide **1b** (0.5 g, 2.4 mmol) in anhydrous Pr^{i}OH (10 mL). The residue was treated with a mixture of Pr^{i}OH (6 mL) and EtOAc (10 mL), and the undissolved residue was filtered off. The solvent was evaporated from the mother liquor, and the residue was twice recrystallized from Pr^{i}OH (6 mL). Compound **11** was obtained in 41% yield (0.24 g, m.p. 155—157 °C). Found (%): C, 75.44; H, 5.91; N, 11.52. $C_{15}H_{14}N_2O$. Calculated (%): C, 75.60; H, 5.92; N, 11.76. ^{1}H NMR (DMSO-d_6), δ: 2.30 (s, 3 H, CH_3); 7.50 (m, 6 H, PhC + PhCO); 7.85 (m, 4 H, PhCO); 10.22 (s, 1 H, NH).

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