

Table I
R-CO-NH-R₁

No	R	R ₁	M.p. (°C)	Crystallized From	Yield (%)	Formula	Calcd.	Analysis			Found	N	Ms M ⁺
							H	N	C	H			
1	2-Pyridyl	Phenyl	75 (a)	ethanol/water	89	C ₁₂ H ₁₀ N ₂ O	5.09	14.13	72.52	5.08	14.29	198	
2	2-Pyridyl	<i>p</i> -Tolyl	99-101 (b)	ethanol/water	53	C ₁₃ H ₁₂ N ₂ O	5.70	13.20	73.42	5.79	13.23	212	
3	2-Pyridyl	<i>o</i> -Tolyl	105 (c)	ethanol/water	47	C ₁₃ H ₁₂ N ₂ O	5.70	13.20	73.92	5.79	13.07	212	
4	3-Pyridyl	Phenyl	110 (d)	ethanol/water	96	C ₁₂ H ₁₀ N ₂ O	5.09	14.13	72.08	5.60	14.16	198	
5	3-Pyridyl	<i>p</i> -Tolyl	146-147 (e)	ethanol/water	65	C ₁₃ H ₁₂ N ₂ O	5.70	13.20	73.89	5.82	12.95	212	
6	3-Pyridyl	<i>o</i> -Tolyl	105	ethanol/water	63	C ₁₃ H ₁₂ N ₂ O	5.70	13.20	73.84	5.50	12.98		
7	4-Pyridyl	Phenyl	165 (f)	ethanol/water	34	C ₁₂ H ₁₀ N ₂ O	5.09	14.13	72.74	5.27	14.20	198	
8	4-Pyridyl	<i>p</i> -Tolyl	160	ethanol/water	67	C ₁₃ H ₁₂ N ₂ O	5.70	13.20	73.48	5.90	13.46	212	
9	4-Pyridyl	<i>o</i> -Tolyl	194	ethanol/water	66	C ₁₃ H ₁₂ N ₂ O	5.70	13.20	74.01	5.71	13.12		
10	2-Pyrazinyl	Phenyl	127-128 (g)	ethanol	86	C ₁₁ H ₉ N ₃ O	4.55	21.10	66.13	4.61	21.08	199	
11	2-Pyrazinyl	<i>p</i> -Tolyl	150	ethanol	57	C ₁₂ H ₁₁ N ₃ O	5.20	19.71	67.87	5.40	19.91		
12	2-Pyrazinyl	<i>o</i> -Tolyl	204	chloroform/ethanol	87	C ₁₂ H ₁₁ N ₃ O	5.20	19.71	67.93	5.36	19.79		
13	2-Thienyl	Phenyl	138 (h)	chloroform	37	C ₁₁ H ₉ NOS	4.46	6.89	64.94	4.50	6.65		
14	2-Thienyl	<i>p</i> -Tolyl	165 (i)	chloroform	52	C ₁₂ H ₁₁ NOS	5.10	6.45	66.35	4.99	6.27		

(a) Lit. (6) gives m.p. 76°. (b) Lit. (6) gives m.p. 104°. (c) Lit. (6) gives m.p. 64.5°. (d) Lit. (7) gives m.p. 114-115°. (e) Lit. (8) gives m.p. 146-147°. (f) Lit. (9) gives m.p. 170°. (g) Lit. (10) gives m.p. 127-130°. (h) Lit. (11) gives m.p. 140°. (i) Lit. (12) gives m.p. 168°.

2-Pyrazinoyl Azide.

Pyrazine-2-carbohydrazide (0.5 g.) was dissolved in water (50 ml.) and few drops of concentrated hydrochloric acid were added. Upon filtration the solution was cooled on ice and under stirring treated dropwise with aqueous sodium nitrite (0.38 g. in 10 ml. of water). After 2 hours at room temperature the reaction mixture was neutralized with solid sodium bicarbonate and extracted several times with chloroform. The combined extracts were dried and evaporated *in vacuo*. The residue had m.p. 39-41° and the product was used for synthetic purposes without further purification.

p-Toluoyl azide was prepared in the same manner, m.p. 30°, in 51% yield; ir: 2130 cm⁻¹ (N₃).

General Procedure for the Preparation of Amides (2).

A mixture of the corresponding acyl azide (1.1 mmoles), 1,2-dimethoxyethane (2-3 ml.) and the corresponding amine (1.5 mmoles) was left at room temperature for 7-12 days. The progression of the reaction was followed by tlc (DC-Fertigplatten Silikagel, Merck, chloroform and methanol (9:1) as solvent). Upon evaporation of the solvent, the obtained product was crystallized from an appropriate solvent. The obtained amides are listed in Table I.

General Procedure for the Preparation of Ureas (3).

A solution of the corresponding acyl azide (1.1 mmoles), 1,2-dimethoxyethane (5 ml.) (or chloroform) and the corresponding amine (1.3-1.5 mmoles) were heated under reflux for 1-2.5 hours. The progression of the reaction was followed by tlc. The reaction between *o*-toluidine and picolinoyl or pyrazinoyl azide was completed in 20 minutes. Upon cooling the reaction mixture the separated product was filtered (or, if necessary, the solvent was evaporated) and crystallized from an appropriate solvent. The obtained ureas are listed in Table II.

3-(Pyridyl-3')-2,4-dioxo-1,2,3,4-tetrahydropyrido[2,3-*d*]pyrimidine (7).

The general method as described above for the preparation of ureas was followed with the exception that the reaction time was 8 hours at an oil bath temperature of 140°. The bicycle was obtained from nicotinoyl azide and ethyl 2-aminopyridine-3-carboxylate in 39% yield, m.p. over 240° (from ethanol); ms: M⁺ = 240; nmr (DMSO-*d*₆): τ = 1.5-2.2 (m, 4H), 2.3-2.6 (m, 1H), 2.7-3.2 (m, 2H).

Anal. Calcd. for C₁₂H₈N₄O₂: C, 55.99; H, 3.35; N, 23.32. Found: C, 56.12; H, 3.82; N, 23.02.

3-(Pyridyl-3')-2,4-dioxo-1,2,3,4-tetrahydropyrido[3,2-*d*]pyrimidine (8a).

This compound was prepared in a similar manner as described for 7 in 4.5 hours at 120° from ethyl 3-aminopyridine-2-carboxylate and nicotinoyl azide in 40% yield, m.p. over 300° (from *N,N*-dimethylformamide); ms: M⁺ = 240; nmr (DMSO-*d*₆): τ = 1.7-1.95 (m, 3H) and 2.4-2.95 (m, 4H).

Anal. Calcd. for C₁₂H₈N₄O₂: C, 55.99; H, 3.35; N, 23.32. Found: C, 55.84; H, 3.63; N, 23.26.

3-(Pyridyl-2')-2,4-dioxo-1,2,3,4-tetrahydropyrido[3,2-*d*]pyrimidine (8b).

This compound was prepared from picolinoyl azide and ethyl 3-aminopyridine-2-carboxylate in boiling 1,2-dimethoxyethane after 4.5 hours in 72% yield, m.p. 168-170° (from ethanol and water); nmr (DMSO-*d*₆): τ = 2.0-2.2 (m, 2H), 2.6-2.95 (m, 3H) and 3.25-3.60 (m, 2H).

Table II
R-NH-CO-NH-R₁

No.	R	R ₁	M.p. (°C)	Crystallized From	Yield (%)	Formula	C	H	Analysis			M ⁺	
									Calcd.	N	C		Found
1	2-Pyridyl	Phenyl	175	ethanol/water	38	C ₁₂ H ₁₁ N ₃ O	67.59	5.20	19.71	67.78	5.37	19.86	213
2	2-Pyridyl	<i>p</i> -Tolyl	170 (a)	ethanol/water	44	C ₁₃ H ₁₃ N ₃ O	68.70	5.77	18.49	69.07	5.83	18.35	227
3	2-Pyridyl	<i>o</i> -Tolyl	>300	ethanol/water	86	C ₁₃ H ₁₃ N ₃ O	68.70	5.77	18.49	68.69	5.87	18.51	
4	2-Pyridyl	3-Pyridyl	157-159	ethanol	47	C ₁₁ H ₁₀ N ₄ O	61.67	4.71	26.16	61.64	4.94	25.82	
5	3-Carboethoxy-2-pyridyl	3-Pyridyl	146-150	ethanol	43	C ₁₄ H ₁₄ N ₄ O ₃	58.73	4.93	19.57	58.89	5.00	19.95	286
6	2-Pyrazinyl	2-Pyrazinyl	197	ethanol	30	C ₁₀ H ₉ N ₅ O	55.81	4.22	32.54	56.17	4.21	32.33	
7	3-Pyridyl	Phenyl	164-165	ethanol/water	60	C ₁₂ H ₁₁ N ₃ O	67.59	5.20	19.71	67.89	5.37	19.91	
8	3-Pyridyl	<i>p</i> -Tolyl	180	ethanol/water	47	C ₁₃ H ₁₃ N ₃ O	68.70	5.77	18.49	68.54	5.91	18.54	
9	3-Pyridyl	<i>o</i> -Tolyl	140	ethanol/water	87	C ₁₃ H ₁₃ N ₃ O	68.70	5.77	18.49	68.71	5.85	18.61	
10	3-Pyridyl	3-Pyridyl	224-226 (b)	ethanol	69	C ₁₁ H ₁₀ N ₄ O	61.67	4.71	26.16	61.68	4.64	25.94	
11	3-Pyridyl	2-Pyrazinyl	210-213	ethanol	50	C ₁₀ H ₉ N ₅ O	55.81	4.22	32.54	55.70	4.28	32.29	
12	4-Pyridyl	Phenyl	150	ethanol/water	48	C ₁₂ H ₁₁ N ₃ O	67.59	5.20	19.71	67.41	5.08	19.65	
13	4-Pyridyl	<i>p</i> -Tolyl	180	ethanol/water	46	C ₁₃ H ₁₃ N ₃ O	68.70	5.77	18.49	68.56	5.85	18.27	
14	4-Pyridyl	<i>o</i> -Tolyl	>210	ethanol/water	26	C ₁₃ H ₁₃ N ₃ O	68.70	5.77	18.49	68.45	5.83	18.56	
15	3-Pyridazinyl	Phenyl	180 (c)	methanol/water	11	C ₁₁ H ₁₀ N ₄ O	61.67	4.71	26.16	62.01	4.78	—	214
16	3-Pyridazinyl	<i>p</i> -Tolyl	210	methanol/water	14	C ₁₂ H ₁₂ N ₄ O	63.14	5.30	24.55	63.36	5.67	24.38	238
17	2-Pyrazinyl	Phenyl	220	ethanol/chloroform	57	C ₁₁ H ₁₀ N ₄ O	61.67	4.71	26.16	61.88	4.73	26.24	
18	2-Pyrazinyl	<i>p</i> -Tolyl	201-202	ethanol	65	C ₁₂ H ₁₂ N ₄ O	63.14	5.30	24.55	63.24	5.45	25.40	
19	2-Thienyl	Phenyl	210-215	chloroform	49	C ₁₁ H ₁₀ N ₂ OS	60.54	4.62	12.84	60.30	4.56	12.70	
20	2-Thienyl	<i>p</i> -Tolyl	185-190	ethanol	97	C ₁₂ H ₁₂ N ₂ OS	62.06	5.21	12.06	62.63	5.29	12.20	
21	2-Thienyl	<i>o</i> -Tolyl	>300	DMF/ethanol	61	C ₁₂ H ₁₂ N ₂ OS	62.06	5.21	12.06	61.80	5.18	12.16	
22	2-Thienyl	2-Carboethoxy-3-pyridyl	173-175	ethanol	81	C ₁₃ H ₁₃ N ₃ O ₃ S	53.61	4.50	14.43	53.73	4.65	14.33	291
23	2-Thienyl	2-Pyridyl	188-190	ethanol	67	C ₁₀ H ₉ N ₃ OS	54.79	4.14	19.17	54.95	4.24	19.06	
24	2-Thienyl	2-Pyrimidinyl	247-249	ethanol	52	C ₉ H ₈ N ₄ OS	49.09	3.66	25.45	48.79	3.58	25.66	
25	2-Thienyl	2-Pyrazinyl	236-239	ethanol	43	C ₉ H ₈ N ₄ OS	49.09	3.66	25.45	49.25	3.70	—	

(a) Lit. (13) gives m.p. 172-173°. (b) Lit. (14) gives m.p. 217-225°. (c) Lit. (15) gives m.p. 180°.

Anal. Calcd. for $C_{12}H_8N_4O_2$: C, 55.99; H, 3.35; N, 23.32. Found: C, 56.50; H, 3.80; N, 22.86.

3-Phenyl-2,4-dioxo-1,2,3,4-tetrahydropyrido[3,2-*d*]pyrimidine (**8c**).

A mixture of phenyl isocyanate (0.15 g.), ethyl 3-aminopyridine-2-carboxylate (0.122 g.) and 1,2-dimethoxyethane (2 ml.) was heated under reflux for 4 hours. Upon cooling the separated product was filtered and crystallized from ethanol (yield 0.084 g., 48%), m.p. over 275°; ms: M^+ = 239; nmr (DMSO-*d*₆): τ = 1.75-1.85 (m, 1H), 2.7-3.5 (m, 7H).

Anal. Calcd. for $C_{13}H_9N_3O_2$: C, 65.26; H, 3.79; N, 17.57. Found: C, 64.82; H, 4.04; N, 17.54.

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