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Derivatives of 4-Amino- and 4-Ureido-2-phenyl-1,2,3-triazole-5-carboxylic Acid 1-Oxides

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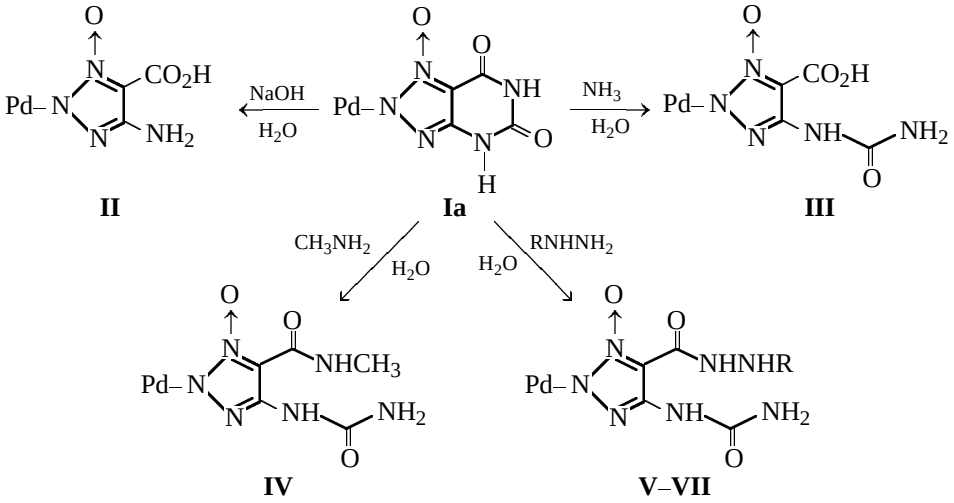
Abstract—4-Amino- and 4-ureido-1,2,3-triazole-5-carboxylic acid oxides, as well as their hydrazides and methylamide, were prepred via pyrimidine ring opening in isomeric 2-phenyl[1.2.3]triazolo[4,5-*d*]pyrimidine-5,7-dione *N*-oxides.

Recyclization of the pyrimidine ring in azolopyrimidines under the action of nucleophiles provides a convenient synthetic approach to heteroaromatic amino acids and their derivatives. This approach has been used to prepare coffeidine [1], previously hardly available 3-amino- and 3-ureido-1,2,5-triazole-5-carboxylic acids and their amides, anilides, and hydrazides [2–4], as well as amino acids of the oxa- and selenadiazole series [5].

The aim of the present work was to extend the above approach to derivatives of 1,2,3-triazole *N*-oxides.

We found that boiling of 2-phenyl[1.2.3]triazolo-[4,5-*d*]pyrimidine-5,7-dione 1-oxide (**Ia**) [6] with aqueous sodium hydroxide and ammonia results in hydrolysis of the pyrimidine ring to form 4-amino- (**II**) and 4-ureido-2-phenyl-1,2,3-triazole-5-carboxylic acid 1-oxides (**III**), respectively. Unlike the reaction with aqueous ammonia, the reaction of compound **Ia** with aqueous methylamine provides *N*-methyl-2-phenyl-4-ureido-1,2,3-triazole-5-carboxamide 1-oxide (**IV**).

Scheme 1.



R = H (**V**), C_3H_7 (**VI**), Ph (**VII**).

The reactions of compound **Ia** with hydrazine and monosubstituted hydrazines occur in a similar way to form hydrazides **V**–**VII** [Scheme (1)].

Position of the N–O bond exerts a strong effect on the reactivity of triazolopyrimidines **Ia** and **Ib**. 3-Oxide **Ib** [7] in almost the same conditions as

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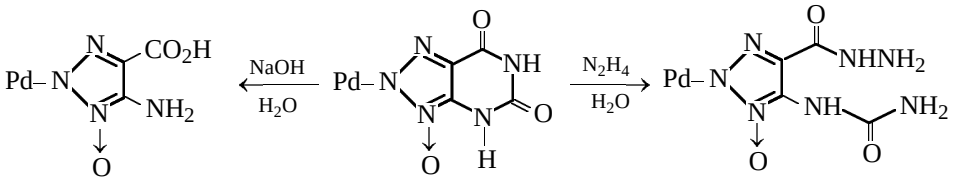
Scheme 2.



VIII **Ib** **IX**

1-oxide **Ia** gives isomeric compounds **II** and **V**, amino acid **VIII**, and hydrazide **IX** [Scheme (2)] but fails to react with phenylhydrazine on 6-h boiling.

No reduction of the N–O bond was observed under the above conditions even with excess hydrazine at elevated temperature. The structure and composition of the synthesized compounds were established by elemental analysis, mass spectrometry, and IR spectroscopy (see table).

EXPERIMENTAL

The mass spectra were recorded in a Varian MAT-112 instrument, ionizing energy 70 eV, ion source temperature 220°C. The IR spectra were obtained on a Specord-80 instrument for thin films with mineral oil. Purity control was performed by TLC on Silufol UV-254 plates.

4-Amino-2-phenyl-2*H*-1,2,3-triazole-5-carboxylic acid 1-oxide (II). To a solution of 0.5 g of NaOH in 15 mlof water, 0.5 g of compound **Ia** was added, and the mixture was refluxed until ammonia no longer evolved. The solution was filtered while hot, the filtrate was neutralized with HCl, and the precipitate that formed was recrystallized from alcohol. Yield 0.34 g. Mass spectrum, *m/z* (I_{rel}, %): 220 (33), 204 (2), 175 (8), 105 (23), 91 (8), 77 (100). IR spectrum, ν, cm^{-1}: 3410–3030, 1700, 1690, 1680, 1670, 1600, 1580, 1560, 1540, 1510.

4-Ureido-2-phenyl-2*H*-1,2,3-triazole-5-carboxylic acid 1-oxide (III). Compound **Ia**, 0.5 g, in 20 ml of aqueous ammonia was boiled in an open vessel for 5 h. Fresh portions of ammonia were added every 20 min. The reaction mixture was filtered, and the filtrate was neutralized with HCl. The precipitate (unreacted oxide **Ia**) was separated, and the filtrate was acidified with HCl to pH 3. The precipitate that formed was separated and recrystallized from ethanol. Yield 0.32 g. Mass spectrum, *m/z* (I_{rel}, %): 263 (8), 247 (4), 246 (5), 230 (6), 220 (29), 204 (20), 176 (8), 105 (25), 91 (21), 77 (100). IR spectrum, ν, cm^{-1}: 3370–3000, 1710, 1700, 1680, 1660, 1650, 1640, 1620, 1590, 1560, 1550, 1540.

***N*-Methyl-2-phenyl-4-ureido-1,2,3-triazole-5-carboxamide 1-oxide (IV).** Methylamine hydrochloride, 2 g, and 1 g of sodium carbonate were dissolved in a minimum of water, after which 0.2 g of compound **Ia** was added, and the mixture was heated to boiling. Therewith, compound **Ia** dissolved completely, and the reaction product began to precipitate in a few minutes. When precipitate no longer formed, it was separated and recrystallized from alcohol. Yield 0.16 g. Mass spectrum, *m/z* (I_{rel}, %): 276 (16), 259 (8), 233 (100), 204 (4), 175 (6), 128 (45), 105 (28), 91 (12), 77 (94). IR spectrum, ν, cm^{-1}: 3260–3000, 1700, 1650, 1620, 1570, 1550, 1510.

2-Phenyl-4-ureido-1,2,3-triazole-5-carbohydrazide 1-oxide (V). A solution of compound **Ia** in 50%

Properties of 1,2,3-triazolecarboxylic acid *N*-oxides and their derivatives **II**–**IX**

Comp. no.	Yield, %	mp, °C	Found, %			Formula	Calculated, %		
			C	H	N		C	H	N
II	75	154	49.00	3.65	25.45	$C_9H_8N_4O_3$	49.09	3.64	25.45
III	60	207–210	45.65	3.40	26.60	$C_{10}H_9N_5O_4$	45.63	3.42	26.62
IV	70	230–235	47.80	4.40	30.40	$C_{11}H_{12}N_6O_3$	47.83	4.35	30.43
V	66	200	43.30	3.95	35.40	$C_{10}H_{11}N_7O_3$	43.32	3.97	35.38
VI	55	193	48.90	5.35	30.70	$C_{13}H_{17}N_7O_3$	48.90	5.33	30.72
VII	68	220	54.40	4.20	27.80	$C_{16}H_{15}N_7O_3$	54.39	4.25	27.76
VIII	70	223	49.20	3.60	25.50	$C_9H_8N_4O_3$	49.09	3.64	25.45
IX	50	>230	43.35	3.98	35.40	$C_{10}H_{11}N_7O_3$	43.32	3.97	35.38

ethanolic hydrazine hydrate was refluxed for 1 h. The precipitate that formed was recrystallized from alcohol. Yield 0.15 g. Mass spectrum, *m/z* (I_{rel}, %): 277 (13), 261 (5), 244 (9), 230 (28), 213 (24), 205 (8), 187 (13), 171 (6), 160 (6), 129 (14), 105 (16), 91 (17), 77 (100). IR spectrum, ν, cm^{-1}: 3410–3020, 1720, 1710, 1700, 1650, 1620, 1600, 1590, 1560, 1550, 1530, 1510.

***N'*-Propyl-2-phenyl-4-ureido-1,2,3-triazole-5-carbohydrazide 1-oxide (VI).** A mixture of 0.3 g of compound **Ia** and 1.5 ml of propylhydrazine in 10 ml of 70% ethanol was refluxed for 4 h. The precipitate that formed upon cooling was recrystallized from alcohol–chloroform, 1 : 3. Yield 0.2 g. Mass spectrum, *m/z* (I_{rel}, %): 319 (6), 303 (2), 248 (4), 230 (60), 213 (39), 187 (34), 160 (8), 119 (7), 105 (15), 91 (18), 77 (100). IR spectrum, ν, cm^{-1}: 3410–3000, 1700, 1680, 1670, 1640, 1610, 1600, 1590, 1580, 1570, 1530, 1500.

***N'*-Phenyl-2-phenyl-4-ureido-1,2,3-triazole-5-carbohydrazide 1-oxide (VII).** A mixture of 0.3 g of compound **Ia**, 2 ml of phenylhydrazine, 2 ml of water, and 6 ml of alcohol was refluxed for 3 h. The precipitate that formed upon cooling was recrystallized from alcohol–chloroform, 1 : 3. Yield 0.29 g. Mass spectrum, *m/z* (I_{rel}, %): 353 (6), 337 (4), 320 (57), 278 (4), 230 (38), 213 (66), 203 (13), 187 (51), 160 (6), 107 (48), 91 (62), 78 (48), 65 (44), 51 (100). IR spectrum, ν, cm^{-1}: 3350–3020, 1640, 1630, 1610, 1590, 1560, 1550, 1530, 1510.

4-Amino-2-phenyl-2*H*-1,2,3-triazole-5-carboxylic acid 3-oxide (VIII) was prepared like compound **II**. Mass spectrum, *m/z* (I_{rel}, %): 220 (3), 204 (22), 186 (8), 175 (4), 105 (12), 90 (34), 77 (100). IR spectrum, ν, cm^{-1}: 3380–3000, 1710, 1690, 1670, 1650, 1640, 1610, 1550, 1510.

2-Phenyl-4-ureido-1,2,3-triazole-5-carbohydrazide 3-oxide (IX). A solution of 0.5 g of compound **Ib** in 30 ml of 50% ethanolic hydrazine hydrate was refluxed for 1.5 h and then filtered while hot. The filtrate was cooled to 0°C. The precipitate that formed was separated, washed with ethanol, and dried in air. Yield 0.28 g. Mass spectrum, *m/z* (I_{rel}, %): 277 (1), 261 (2), 244 (21), 229 (5), 213 (35), 187 (4), 105 (15), 91 (15), 77 (100). IR spectrum, ν, cm^{-1}: 3320–3300, 1720, 1710, 1680, 1670, 1660, 1600, 1580, 1560, 1530.

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