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Synthesis of N^3-substituted amidrazones

Synteza N^3-podstawionych amidrazonów

Amidrazones are hypothetical hydrazites of imide acids used to obtain the heterocyclic systems. They are also applied in industry and medicine (pesticides, bacterio- and virusostatic) [1–4]. They react with the reagents of various composition. The nitrogen atoms of the amidrazone group are the potential places of the electrophilic reagent attack. The most tractable is the first free nitrogen.

Amidrazones are used as substrates to form the five-membered systems (1,2,4-triazoles; 1,3,4-thiadiazoles; 1,3,4-oxadiazoles; tetrazoles, pyrazoles, imidazoles) [5–7], the six-membered systems (1,2,4-triazines) [3,8,9], the seven-membered systems (1,2,4-triazepines) [10] and the bisheterocyclic systems [11,12].

The significant limitation of the amidrazone application in the syntheses is their not always easy availability, among others their low yield, instability, cyclization to the derivatives of 1,2,4,5-tetrazine systems and possible decomposition [12,13,17,18].

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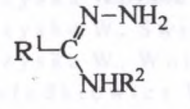
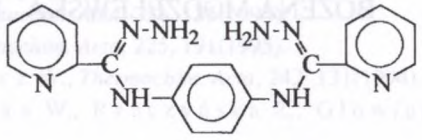
The subject of our interest were amidrazones (I–X), which were used in reactions of addition (first step) and cyclization (second step) with e.g. isothiocyanates or DMAD (dimethyl acethylenedicarboxylate) leading to formation of 5- or 6- membered heterocyclic systems [7,11,12].

N^3-substituted amidrazones are the compounds of the generalized formula:



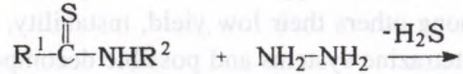
(I - IX)



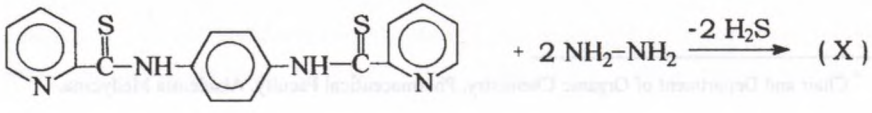
(X)

No	R	R^2
I	C_6H_5	C_6H_5
II	C_6H_5	p-CH_3–C_6H_4
III	C_6H_5	p-NO_2–C_6H_4
IV	2-C_5H_4N	C_6H_5
V	2-C_5H_4N	p-CH_3–C_6H_4
VI	2-C_5H_4N	p-NO_2–C_6H_4
VII	2-C_5H_4N	2-C_5H_4N
VIII	4-C_5H_4N	C_6H_5
IX	4-C_5H_4N	p-CH_3–C_6H_4

The preparation method of N^3-substituted amidrazones is based on the condensation of N-arylsubstituted acid thioamides with hydrazine hydrate.



(I - IX)



(X)

Amidrazones (I–IV,X) were prepared according to the literature [4,19–21].

Preparation of N^3-p-tolyl-2-picolinamidrazone (V) and N^3-p-tolyl-4-picolinamidrazone (IX)

The general method: 1.0g of N-*p*-tolyl-thioamide of 2 or 4-picolinic acid [22] was suspended in 5cm^3 of ethanol. 3cm^3 of 80% hydrazine hydrate was added and slightly heated (till dissolved). After 24h 10cm^3 of water was added and the precipitate filtered and purified by dissolving in methanol in room temperature. The contaminations were filtered, water added up to turbidity and left for 24h. Then the product was filtered.

Preparation of N^3-p-nitrophenyl-2-picolinamidrazone (VI)

1.0g of N^3-*p*-nitrophenyl-thioamide of 2-picolic acid [22] was suspended in 5cm^3 of ethanol and then 3cm^3 of 100 hydrazine hydrate was added. The content was kept boiling in a flask under the reflux condenser for 3min. and left for 12h. The dark-yellow, brilliant precipitate was purified by crystallization from ethanol.

Preparation of N^3-2-pyridil-2-picolinamidrazone (VII)

1.0g of N-2-pyridil-thioamide -2-picolinic acid [21] was suspended in 6cm^3 of ethanol; 1cm^3 of 100% hydrazine was added and heated in a flask under the reflux condenser in water bath till dissolved. The flask content was left for 12h. Then some water was added. The creamy, brilliant precipitate formed was filtered and purified by crystallization from water.

Preparation of N^3-phenyl-4-picolinamidrazone (VIII)

Mixture of 2.0g N-phenyl-thioamide-4-picolinic acid [22] and 6cm^3 - of 100% hydrazine hydrate was left for 24 h at room temperature. Then 10cm^3 of water was added, the fluffy, slightly creamy precipitate formed was purified by crystallization from water-methanol solution (1:1).

The data relating to IR and ^{1}H NMR spectra are listed in Table 1. N-aryl-substituted acid thioamides for amidrazones (I–IV, X) were prepared according to literature [22-25].

Table 1. Analytical data

Compound No.	Formula Molecular Weight	M.p., [°C]	Yield, [%]	Analysis %			IR (cm^{-1}) KBr			^{1}H-NMR (ppm) DMSO
				Element	Calculated	Found				
V	$C_{13}H_{14}N_4S$ 258.06	95	35	C H N	60.45 5.42 21.70	60.14 4.92 22.00	3307 3030 2990 1516	NH arom. alif. C=N		2.1(s,3H,CH_3) 6.3–8.1(m,8H arom. + + 2H $2NH_2$ + 1H NH)
VI	$C_{12}H_{11}N_5O_2$ 257.12	127	40	C H N	56.03 4.28 27.23	56.20 4.30 27.00	3300 3052 1520 1320	NH CH C=N NO_2	arom.	6.7–8.1(m,8H arom. + 2H NH_2 + + 1H NH)
VII	$C_{11}H_{11}N_5$ 213.11	112	35	C H N	61.97 4.75 32.86	61.55 4.52 32.50	3340 3070 1517	NH CH C=N	arom.	7.0–8.3(m,8H arom. + 2H NH_2 + + 1H NH)
VIII	$C_{12}H_{12}N_4$ 212.12	124	38	C H N	67.97 5.66 26.41	67.72 5.25 26.30	3280 3030 1520	NH CH C=N	Arom .	6.4–8.3(m,8H arom. + 2H NH_2 + + 1H NH)
IX	$C_{13}H_{14}S$ 258,06	120	38	C H N	60.45 5.42 21.70	60.00 4.90 22.03	3130 3024 2290 1540	NH CH CH C=N	arom. alif.	2.1(s,3H,$2CH_3$) 6.6–8.5(m,8H arom. + 2H NH_2 + + 1H NH)

For N-*p*-tolyl-thioamide of 2-picolinic acid, N-*p*-tolyl-thioamide of 4-picolinic acid and 4-*p*-nitrophenyl-thioamide of 2-picolinic acid we take a try to modify their synthesis by changing reaction conditions. Physicochemical properties of obtained in modified conditions compounds were similar to previously obtained but reaction time was much shorter.

The general method:
50g of 2- or 4-picoline
30g of *p*-toluidine or *p*-nitroaniline
50g of sulfur

The mixture was heated in a flask under the reflux condenser for 24h till boiling. After cooling, 50cm^3 of 15% hydrochloric acid was added and 2h later the precipitate was filtered off and placed in ammonia. To be purified, it was extracted with hot methanol. The solution was condensed and filtered.

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STRESZCZENIE

Zbadano N^3-podstawione amidrazony, które wykorzystano do syntezy układów heterocyklicznych 5- i 6-członowych.

Amidrazony (I-IV, X) zostały opisane w piśmiennictwie, pozostałe (V-IX) otrzymano przy wykorzystaniu wskazówek literaturowych.