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SYNTHESIS OF 1,3,5-TRISUBSTITUTED 1H-1,2,4-TRIAZOLES CONTAINING HETARYL FRAGMENTS

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N^1-Phenyl- and N^1-(3,5-dichloro-2-pyridyl)amidrazones have been synthesized by the reaction of imino esters of heterocyclic acids with phenyl- or (3,5-dichloro-2-pyridyl)hydrazine. Acylation of the products with acid chlorides leads to 1-phenyl- and 1-(3,5-dichloro-2-pyridyl)-3-hetaryl-5-R^2-1H-1,2,4-triazoles. Compounds of this type are also formed by the condensation of N-acylimino esters of heterocyclic acids with phenyl- or (3,5-dichloro-2-pyridyl)hydrazine.

Keywords: amidrazones, benzothiazole, dichloropyridines, imino esters of acids, indole, 5-nitrofurans, 1,2,4-triazoles, cyclocondensation.

Hetaryl-substituted 1H-1,2,4-triazoles containing, for example, residues of 5-nitrofuran [1, 2], thiophene [2], Δ^2-imidazoline [3], pyridine [2-4], indole [5, 6], pyrazine [3], benzimidazole [7], benzothiazole [8, 9], *sym*-triazine [10, 11], etc. display high antimicrobial, antistaphylococcal, hypotensive, anthelmintic, antiviral, antispasmodic, and antihistamine activity, and also possess various pesticidal actions.

In a continuation of our investigations on the synthesis of azoles with hetaryl substituents [12-14] the preparation is reported in the present work of 1,3,5-trisubstituted 1H-1,2,4-triazoles containing 5-nitro-2-furyl, 2-thienyl, 3-indolylmethyl, 3,5-dichloropyridyl, and 2-benzothiazolylmethyl residues. Heterocyclic systems, combining in one molecule a 1H-1,2,4-triazole residue and the heterocycles indicated above, are of interest as potentially biologically active substances and also as stabilizers and additives for polymeric material, hydrocarbon fuel, and lubricants.

Convenient synthons for obtaining compounds of the 1H-1,2,4-triazole series are imino esters of carboxylic acids and their derivatives [12, 15, 16]. In the present work the methyl imino esters of 5-nitrofuran-2-carboxylic (**1a**), 3-indolylacetic (**1b**), and (2-benzothiazolylthio)acetic acids (**1c**) were used as key compounds for obtaining trisubstituted 1H-1,2,4-triazoles. On interacting compounds **1a-c** with phenyl- (**2a**) and (3,5-dichloro-2-pyridyl)hydrazine (**2b**) in absolute methanol or in dioxane at 30-35°C N^1-phenyl- and N^1-(3,5-dichloro-2-pyridyl)amidrazones of carboxylic acids **3a-e** are formed in high yield (Table 1). By condensing amidrazones **3a-e** with acyl chlorides **4a-f** the 1,3,5-trisubstituted 1H-1,2,4-triazoles **5a-r** were synthesized (method A). On heating (100-120°C) amidrazones **3a-e** with an excess of the appropriate acyl chloride **4a-f** in an inert solvent (toluene, DMF, dioxane) for 8-10 h the yields of the target 1H-1,2,5-triazoles **5a-r** amounted to 63-75% (Table 2).

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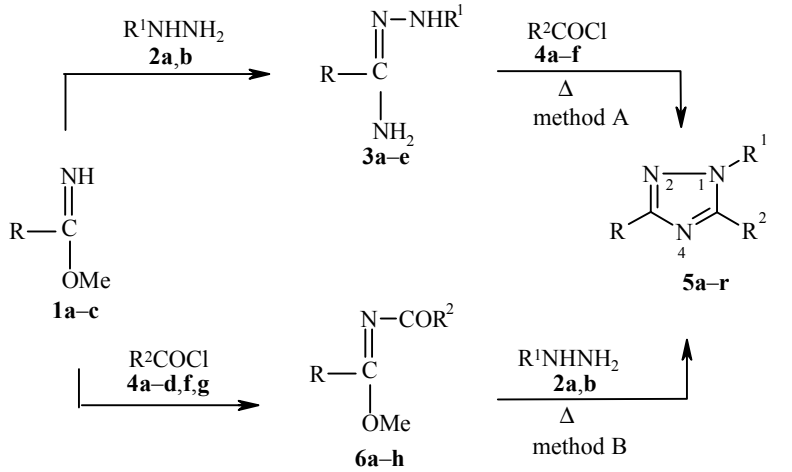
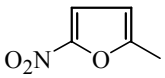
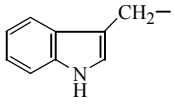
TABLE 1. Characteristics of N^1-Phenyl- and N^1-(3,5-Dichloro-2-pyridyl)amidrazones **3a-e**

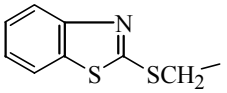
Compound	Empirical formula	Found, % / Calculated, %			mp, °C*	R_f*[2]	^{1}H NMR spectrum, δ, ppm. (J, Hz)	Yield, %
		C	H	N				
3a	$C_{11}H_{10}N_4O_3$	53.77 / 53.66	3.95 / 4.06	22.90 / 22.76	136-137	0.42	6.50 (2H, br. s, NH_2); 6.94 (1H, d, 3-H furan, J_{34} = 3.6); 7.20-7.28 (5H, m, Ph); 7.37 (1H, d, 4-H furan, J_{34} = 3.6); 8.10 (1H, br. s, NH)	84
3b	$C_{10}H_7Cl_2N_5O_3$	38.11 / 37.97	2.30 / 2.21	22.04 / 22.15	165-167	0.62	6.42 (2H, br. s, NH_2); 6.80 (1H, d, 3-H furan, J_{34} = 3.5); 7.18 (1H, d, 4-H furan, J_{34} = 3.5); 7.78 (1H, d, 4-H pyridine, J_{46} = 1.7); 8.04 (1H, d, 6-H pyridine, J_{46} = 1.7); 8.18 (1H, br. s, NH)	77
3c	$C_{16}H_{16}N_4$	72.61 / 72.73	5.94 / 6.06	21.45 / 21.21	85-86	0.34	3.78 (2H, s, CH_2); 6.52 (2H, br. s, NH_2); 6.92–7.18 (9H, m, H arom.); 7.34 (1H, d, 2-H indole, J_{12} = 2.5); 8.04 (1H, br. s, NH); 8.20 (1H, br. s, NH indole)	78
3d	$C_{15}H_{14}N_4S_2$	57.23 / 57.32	4.52 / 4.46	17.96 / 17.83	89-90.5	0.48	3.82 (2H, s, CH_2S); 6.18 (2H, br. s, NH_2); 7.10-7.42 (9H, m, H arom.); 8.02 (1H, br. s, NH)	74
3e	$C_{14}H_{11}Cl_2N_5S_2$	43.67 / 43.57	3.02 / 2.86	18.04 / 18.23	170-172	0.46	3.46 (2H, s, CH_2S); 6.26 (2H, br. s, NH_2); 7.28-7.40 (4H, m, H arom.); 7.79 (1H, d, 4-H pyridine, J_{46} = 1.8); 8.02 (1H, br. s, NH); 8.12 (1H, d, 6-H pyridine, J_{46} = 1.8)	85

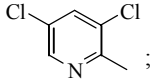
* Compounds were recrystallized: **3a,e** from 2-propanol–water, 3:1; **3b** from ethanol; **3c** from ethanol–water, 2:1; **3d** from dioxane–water, 1:2.

*[2] Solvent systems: benzene–methanol, 30:1 (compounds **3a,c,e**); chloroform–methanol, 40:1 (compounds **3b,d**).

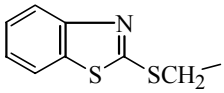


1a, **3a**,**b**, **5a**,**b**, **6a** R =  ; **1b**, **3c**, **5c–f**, **6b**,**c** R =  ;

1c, **3d**,**e**, **5g–q**, **6d–h** R =  ; **2a**, **3a**,**c**,**d**, **5a**,**c**,**d**,**g–k**,**q** R^1 = Ph;

2b, **3b**,**e**, **5d**,**e**,**f**,**l–p**,**r** R^1 =  ; **4a**, **5a**,**b**,**e**,**g**,**l**, **6a**,**b**,**e** R^2 = Ph;

4b, **5c**,**h**, **6c** R^2 = 4-$NO_2C_6H_4$; **4c**, **5d**,**i**,**n**, **6g** R^2 = 3,4,5-$(MeO)_3C_6H_2$; **4d**, **5m**, **6f** R^2 = $PhCH_2$; **4e**, **5j**,**o** R^2 = 2-thienyl;

4f, **5f**,**k**,**p**, **6h** R^2 =  ; **4g**, **5q**,**r**, **6d** R^2 = Me

Acylation of methyl imino esters **1a-c** with acid chlorides **4a-d,f,g** in anhydrous ether or benzene in the presence of triethylamine leads to the carboxylic acid methyl N-acylimino esters **6a-h** in 68-80% yield (Table 3). By condensing the N-acylimino esters **6a-h** with hydrazines **2a,b** (molar ratio 1:1.1) in anhydrous dioxane or DMF at 35-40°C (3-4 h) the 1,3,5-trisubstituted 1H-1,2,4-triazoles **5a-c,e,g,i,k-n,p-r** are formed in 80-90% yield (method B).

In the IR spectra of amidrazones **3a-e** two absorption bands are observed at 1600-1700 cm^{-1}. The intense absorption maxima at 1660-1670 cm^{-1} correspond to the stretching vibrations of the C=N group and those at 1640-1650 cm^{-1} to the N–H deformation vibration in the primary amino group, which is characteristic of amidrazones [17, 18]. The NH stretching vibrations in NH_2 and N^1H groups of the amidrazone fragment are superimposed and are displayed as a broad absorption band at 3180-3320 cm^{-1} with a weakly expressed separation of the maxima. Compounds **3a-e** must therefore be assigned to an amidrazone structure and not to the hydrazinoimine structure [RC(C=NH)NHNHR^1] tautomeric with it [18].

In the spectra of the N-acylimino esters **6a-h** the bands at 1685-1710 and 1640-1655 cm^{-1} correspond to the stretching vibrations of the carbonyl and C=N groups respectively.

In the spectra of 1H-1,2,4-triazoles **5a-r** the stretching vibrations of the C=N and C=C fragments of the heteroaromatic nuclei are characterized by absorption bands of varying intensity at 1615-1630, 1575-1600, 1555-1565, and 1460-1475 cm^{-1}. The group of bands at 1460-1475 cm^{-1} is characteristic of the 1,2,4-triazole ring [19]. The presence of this ring is also confirmed by absorption bands for the stretching (1500-1510 and 1100-1125 cm^{-1}) and deformation (950-1055 cm^{-1}) vibrations of the 1,2,4-triazole ring [20, 21], and also by a

TABLE 2. Characteristics of Trisubstituted 1H-1,2,4-Triazoles **5a-r**

Compound	Empirical formula	Found, % / Calculated, %				mp, °C*	R_f*[2]	^{1}H NMR spectrum, δ, ppm (J, Hz)	Yield, % (method of preparation)
		C	H	N	S				
1	2	3	4	5	6	7	8	9	10
5a	$C_{18}H_{12}N_4O_3$	65.17 / 65.06	3.52 / 3.61	16.98 / 16.87		147-148.5	0.58	7.24 (1H, d, 3-H furan, J_{34} = 4.0); 6.94-7.14 (10H, m, 2Ph); 7.64 (1H, d, 4-H furan, J_{34} = 4.0)	70 (A) 82 (B)
5b	$C_{17}H_9Cl_2N_5O_3$	50.62 / 50.75	2.37 / 2.24	8.05 / 8.19		152-154 (dec.)	0.44	6.90-7.02 (5H, m, Ph); 7.20 (1H, d, 3-H furan, J_{34} = 3.7); 7.52 (1H, d, 4-H furan, J_{34} = 3.7); 7.88 (1H, d, 4-H pyridine, J_{46} = 1.8); 8.08 (1H, d, 6-H pyridine, J_{46} = 1.8)	63 (A) 81 (B)
5c	$C_{23}H_{17}N_5O_2$	70.04 / 69.87	4.21 / 4.30	17.86 / 17.72		137-138	0.74	3.65 (2H, s, CH_2); 6.92-7.10 (9H, m, H arom.); 7.30 (1H, d, 2-H indole, J_{12} = 3.1); 7.48-7.58 (4H, m, H arom.); 8.20 (1H, br. s, NH indole)	67 (A) 85 (B)
5d	$C_{26}H_{24}N_4O_3$	70.79 / 70.91	5.53 / 5.45	12.90 / 12.73		158-159	0.56	3.22 (9H, br. s, 3MeO); 3.80 (2H, s, CH_2); 6.84-7.18 (9H, m, H arom.); 7.27 (2H, s, H arom.); 7.45 (1H, d, 2-H indole, J_{12} = 3.7); 8.08 (1H, br. s, NH indole)	74 (A)
5e	$C_{22}H_{15}Cl_2N_5$	63.02 / 62.86	3.46 / 3.57	16.81 / 16.67		175-176.5	0.50	4.04 (2H, s, CH_2); 7.08-7.19 (9H, m, H arom.); 7.48 (1H, d, 2-H indole, J_{12} = 3.8); 7.82 (1H, d, 4-H pyridine, J_{46} = 1.7); 8.10 (1H, d, 6-H pyridine, J_{46} = 1.7); 8.20 (1H, br. s, NH indole)	65 (A) 80 (B)
5f	$C_{24}H_{16}Cl_2N_6S_2$	54.92 / 55.07	3.13 / 3.06	16.21 / 16.06	12.08 / 12.23	128-130	0.64	3.54 (2H, s, CH_2); 3.93 (2H, s, CH_2); 7.15-7.42 (8H, m, H arom.); 7.48 (1H, d, 2-H indole, J_{12} = 2.5); 7.75 (1H, d, 4-H pyridine, J_{46} = 2.0); 8.05 (1H, d, 6-H pyridine, J_{46} = 2.0); 8.18 (1H, br. s, NH indole)	68 (A)
5g	$C_{22}H_{17}N_4S_2$	66.03 / 65.84	4.29 / 4.24	13.82 / 13.96	15.86 / 15.96	115-116.5	0.58	3.68 (2H, s, CH_2S); 6.88-7.04 (10H, m, 2Ph); 7.58-7.69 (4H, m, H arom.)	66 (A) 84 (B)
5h	$C_{22}H_{16}N_5O_2S_2$	59.02 / 59.19	3.66 / 3.59	15.81 / 15.69	14.18 / 14.35	146-147	0.63	3.81 (2H, s, CH_2S); 6.69 (2H, m, H arom.); 6.84-7.01 (5H, m, Ph); 7.18 (2H, m, H arom.); 7.74-7.82 (4H, m, H arom.)	64 (A)
5i	$C_{25}H_{22}N_4O_3S_2$	61.05 / 61.22	4.38 / 4.49	11.41 / 11.23	12.95 / 13.06	134-135	0.70	3.33 (9H, s, 3MeO); 3.95 (2H, s, CH_2S); 6.92-7.05 (5H, m, Ph); 7.22 (2H, s, H arom.); 7.84-7.91 (4H, m, H arom.)	75 (A) 80 (B)

TABLE 2 (continued)

1	2	3	4	5	6	7	8	9	10
5j	$C_{20}H_{14}N_4S_3$	59.03 59.11	3.37 3.45	14.03 13.79	23.57 23.64	101-102	0.50	3.70 (2H, s, CH_2S); 6.74-6.82 (5H, m, Ph); 7.54-7.83 (7H, m, H arom.)	72 (A)
5k	$C_{24}H_{17}N_5S_4$	57.09 57.26	3.44 3.38	13.81 13.22	25.66 25.45	96-97	0.72	3.68 (2H, s, CH_2S); 3.76 (2H, s, CH_2S); 6.78-6.90 (5H, m, Ph); 7.72-7.94 (8H, m, H arom.)	68 (A) 90 (B)
5l	$C_{21}H_{13}Cl_2N_5S_2$	53.71 53.62	2.84 2.76	15.01 14.89	13.54 13.62	164-165.5	0.74	3.86 (2H, s, CH_2S); 6.88-6.96 (5H, m, Ph); 3.34-7.58 (4H, m, H arom.); 7.77 (1H, d, 4-H pyridine, J_{46} = 3.0); 8.03 (1H, d, 6-H pyridine, J_{46} = 3.0)	74 (A) 90 (B)
5m	$C_{22}H_{15}Cl_2N_5S_2$	54.42 54.54	2.92 3.00	14.62 14.46	13.08 13.22	134-136	0.59	3.65 (2H, s, CH_2Ph); 3.95 (2H, s, CH_2S); 6.69-6.74 (5H, m, Ph); 7.28-7.48 (4H, m, H arom.); 7.70 (1H, d, 4-H pyridine, J_{46} = 2.7); 7.92 (1H, d, 6-H pyridine, J_{46} = 2.7)	65 (A) 83 (B)
5n	$C_{24}H_{19}Cl_2N_5O_3S_2$	51.57 51.43	3.28 3.39	12.37 12.50	11.59 11.43	188-190	0.67	3.38 (9H, s, 3MeO); 3.80 (2H, s, CH_2S); 7.08 (2H, s, H arom.); 7.38-7.56 (4H, m, H arom.); 7.88 (1H, d, 4-H pyridine, J_{46} = 2.7); 8.16 (1H, d, 6-H pyridine, J_{46} = 2.7)	70 (A) 82 (B)
5o	$C_{19}H_{11}Cl_2N_5S_3$	47.81 47.90	2.43 2.31	14.54 14.70	20.30 20.17	156-157.5	0.50	4.04 (2H, s, CH_2S); 7.28-7.47 (7H, m, H arom.); 7.72 (1H, d, 4-H pyridine, J_{46} = 1.7); 8.05 (1H, d, 6-H pyridine, J_{46} = 1.7)	67 (A)
5p	$C_{23}H_{14}Cl_2N_6S_4$	48.25 48.17	2.35 2.44	14.81 14.66	22.20 22.34	120-122	0.77	3.84 (2H, s, CH_2S); 3.95 (2H, s, CH_2S); 7.49-7.62 (8H, m, H arom.); 7.85 (1H, d, 4-H pyridine, J_{46} = 2.6); 8.18 (1H, d, 6-H pyridine, J_{46} = 2.6)	72 (A) 88 (B)
5q	$C_{17}H_{14}N_4S_2$	60.22 60.35	4.22 4.14	16.45 16.57	19.11 18.93	145-146	0.80	2.38 (3H, s, Me); 3.94 (2H, s, CH_2S); 6.88-7.03 (5H, m, Ph); 7.66-7.74 (4H, m, H arom.)	84 (B)
5r	$C_{16}H_{11}Cl_2N_5S_2$	46.92 47.06	2.81 2.70	17.01 17.16	15.85 15.68	139-140	0.64	2.65 (3H, s, Me); 3.87 (2H, s, CH_2S); 7.52-7.66 (4H, m, H arom.); 7.74 (1H, d, 4-H pyridine, J_{46} = 2.1); 7.90 (1H, d, 6-H pyridine, J_{46} = 2.1)	87 (B)

* Compounds were recrystallized, **5a,b,e,f,h,l,q** from 2-propanol, **5c,d,g,i** from 2-propanol–water, 1:1, **5j** from benzene–hexane, 5:1, **5k,m,r** from 2-propanol–water, 2:1, **5n** from methyl cellosolve, **5o** from toluene–ethanol, 5:1, **5p** from 2-propanol–water, 4:1.

*[2] Solvent systems: benzene–methanol, 30:1 (compounds **5a,b,e,l,n,r**); chloroform–methanol, 40:1 (compounds **5c,d,j,k,m,o,p**); benzene–methanol, 20:1 (compounds **5f-i,q**).

TABLE 3. Characteristics of Methyl N-Acyliminoesters **6a-h**

Compound	Empirical formula	Found, % / Calculated, %			mp, °C*	R_f*[2]	^{1}H NMR spectrum, δ, ppm (J, Hz)	Yield, %
		C	H	N				
6a	$C_{13}H_{10}N_2O_5$	57.10 / 56.93	3.57 / 3.65	10.11 / 10.22	127-128	0.55	3.38 (3H, s, MeO); 6.80 (1H, d, 3-H furan, J_{34} = 3.5); 6.94-7.04 (5H, m, Ph); 7.42 (1H, d, 4-H furan, J_{34} = 3.5)	74
6b	$C_{18}H_{16}N_2O_2$	74.09 / 73.97	5.37 / 5.48	9.68 / 9.59	152-153.5	0.40	3.30 (3H, s, MeO); 3.84 (2H, s, CH_2); 7.08-7.22 (9H, m, H arom.); 7.44 (1H, d, 2-H indole, J_{12} = 3.0); 8.14 (1H, br. s, NH indole)	68
6c	$C_{18}H_{15}N_3O_4$	63.93 / 64.09	4.53 / 4.45	12.31 / 12.46	164-165	0.52	3.25 (3H, s, MeO); 4.02 (2H, s, CH_2); 7.16-7.30 (8H, m, H arom.); 7.37 (1H, d, 2-H indole, J_{12} = 2.7); 8.24 (1H, br. s, NH indole)	78
6d	$C_{12}H_{12}N_2O_2S_2$	51.30 / 51.43	4.37 / 4.28	9.83 / 10.00	98-99	0.42	3.27 (3H, s, MeO); 3.59 (3H, s, MeO); 4.00 (2H, s, CH_2S); 7.52-7.60 (4H, m, H arom.)	68
6e	$C_{17}H_{14}N_2O_2S_2$	59.54 / 59.65	4.01 / 4.09	8.05 / 8.19	144-145.5	0.32	3.20 (3H, s, MeO); 3.82 (2H, s, CH_2S); 7.12-7.35 (9H, m, H arom.)	77
6f	$C_{18}H_{16}N_2O_2S_2$	60.79 / 60.67	4.56 / 4.49	8.02 / 7.86	108-109.5	0.48	3.26 (3H, s, MeO); 3.48 (2H, s, CH_2Ph); 3.96 (2H, s, CH_2S); 6.94-7.05 (5H, m, Ph); 7.32-7.41 (4H, m, H arom.)	72
6g	$C_{20}H_{20}N_2O_5S_2$	55.42 / 55.55	4.73 / 4.62	6.33 / 6.48	Oil (n_D^{20} 1.5874)	0.56	3.04 (3H, s, MeO); 3.28 (9H, s, 3MeO); 4.10 (2H, s, CH_2S); 7.12 (2H, s, H arom.); 7.64-7.71 (4H, m, H arom.)	72
6h	$C_{19}H_{15}N_3O_2S_4$	51.04 / 51.23	3.31 / 3.37	6.08 / 6.29	Oil	0.63	3.15 (3H, s, MeO); 3.92 (2H, s, CH_2S); 4.14 (2H, s, CH_2S); 7.44-7.62 (8H, m, H arom.)	71

* Compounds were recrystallized: **6a,b,e** from ethanol–water, 1:1; **6c** from ethanol; **6d,f** from acetonitrile.

*[2] Solvent systems: benzene–methanol, 20:1 (compounds **6a,d,g,h**); benzene–methanol, 30:1 (compounds **6b,c,e,f**).

group of intense absorption bands at 1270-1290 cm^{-1} characteristic of the stretching vibrations of C–N bonds in substituted 1,2,4-triazoles [21].

In the ^1H NMR spectra (Tables 1-3) of amidrazones **3a,b**, N-acylimino ester **6a**, and 1-R^1-3-(5-nitro-2-furyl)-5-R^2-1H-1,2,4-triazoles **5a,b** the signals of the 3- and 4-H protons of the furan ring are observed as doublets at 6.80-7.24 and 7.10-7.64 ppm (J_{34} = 3.5-4.0 Hz) respectively [22]. It should be noted that in the spectra of 1,2,4-triazoles **5a,b** the signals of these protons are displaced towards low field compared with the spectra of amidrazones **3a,b** and N-acylimino ester **6a**.

In the spectra of 1,2,4-triazoles **5c-r** the singlet signals at 3.65-4.10 ppm correspond to the methylene group proton at position 3 (and also in position 5 in the spectra of compounds **5f,k,m,p**). In the spectra of compounds **3c**, **5c-f**, and **6b,c** the signal of the 2-H proton of the pyrrole ring is displayed as a doublet at 7.30-7.48 ppm (J_{12} = 2.5-3.8 Hz) and in comparison with the unsubstituted indole and 3-phenylindole (6.68 and 7.03 ppm respectively [23]) is displaced towards low field. Multiplet signals at 7.36-7.82 ppm correspond to the protons of the benzothiazole residues in the spectra of amidrazones **3d,e**, N-acylimino esters **6d-h**, and 1,2,4-triazoles **5f-r**. The proton signals of the 3,5-dichloropyridine residues in the spectra of compounds **3b,e** and **5b,e,f,l-p,r** are observed as two doublets at low field at 7.75-7.95 (4-H) and 8.04-8.16 ppm (6-H) (J_{46} = 1.7-2.5 Hz).

EXPERIMENTAL

The IR spectra were obtained on a Perkin-Elmer 993 instrument in KBr disks or in nujol suspensions. The ^1H NMR spectra were recorded on a Bruker WP-250 (250 MHz) spectrometer for 10-15% solutions in DMSO-d_6, internal standard was TMS. A check on the progress of reactions and the purity of the compounds obtained was carried out by TLC on plates with a bound layer of Al_2O_3 Merck LU-074, visualization was with iodine vapor.

The initial methyl imino esters of 5-nitrofuran-2-carboxylic (**1a**) [24], 3-indolylacetic (**1b**) [25], and (2-benzothiazolyl)thioacetic acids (**1c**) [26], and also (3,5-dichloro-2-pyridyl)hydrazine (**2b**) [27] were obtained by known methods.

N^1-Phenyl- and N^1-(3,5-Dichloro-2-pyridyl)amidrazones of Carboxylic Acids (3a-e). A mixture of methyl imino ester **1a-c** (15 mmol) and hydrazine **2a,b** (15 mmol) in absolute methanol (45 ml) (when making compounds **3a,c,d**) or anhydrous dioxane was stirred at 30-35°C for 4 h, cooled to 10°C, and poured into ice water (200 ml). The solid which separated was filtered off, washed on the filter with water, dried, and crystallized from a suitable solvent (Table 1). N^1-Substituted amidrazones **3a-e** were obtained.

Carboxylic Acid N-Acylimino Esters (6a-h). A solution of acyl chloride **4a-d,f,g** (10 mmol) in the corresponding solvent (25 ml) was added dropwise to a stirred mixture of methyl imino ester **1a-c** (10 mmol) and dry triethylamine (1.01 g, 10 mmol) in anhydrous ether (10 ml) (when making compounds **6a-c**) or anhydrous benzene at 0°C. The reaction mixture was stirred at 30-35°C for 4-6 h, cooled to 20°C, and poured into 3% $NaHCO_3$ solution (70 ml). The organic layer was separated, washed with water (2 × 20 ml), dried over Na_2SO_4, and evaporated to dryness at reduced pressure. The residue was either crystallized from a suitable solvent (Table 3), or chromatographed on a column (40 × 4.5 cm) of Al_2O_3 (when obtaining compounds **6g,h**), eluting with benzene–2-propanol, 10:1. After removing the solvent N-acylimino esters **6g,h** were obtained as viscous dark yellow uncrystallizing oils.

1,3,5-Trisubstituted 1H-1,2,4-Triazoles (5a-r). A. A mixture of amidrazone **3a-e** (4 mmol) and acyl chloride **4a-f** (10 mmol) in anhydrous solvent (30 ml) (toluene when making **5a,d,g,i-k**; dioxane when making **5c,h**; DMF when making **5b,e,f,l-r**) was stirred at 110-120°C for 10 h. The solvent was removed at reduced pressure, and the residue treated with 5% NaOH solution (30 ml). The isolated solid was filtered off, washed on the filter with water, dried, and crystallized from a suitable solvent (Table 2). 1H-1,2,4-Triazoles **5a-r** were obtained.

B. A mixture of N-acylimino ester **6a-h** (10 mmol) and hydrazine **2a,b** (11 mmol) in anhydrous dioxane (45 ml) or anhydrous DMF (when making **5b,e,l-n,p,r**) was stirred at 35-40°C for 4 h, then evaporated to dryness at reduced pressure. The residue was crystallized from a suitable solvent (Table 2) and 1H-1,2,4-triazoles **5a-c,e,g,i,k-n,p,r** were obtained.

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