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SYNTHESIS OF NEW IMIDAZO-[4,5-*b*]PYRIDINE DERIVATIVES

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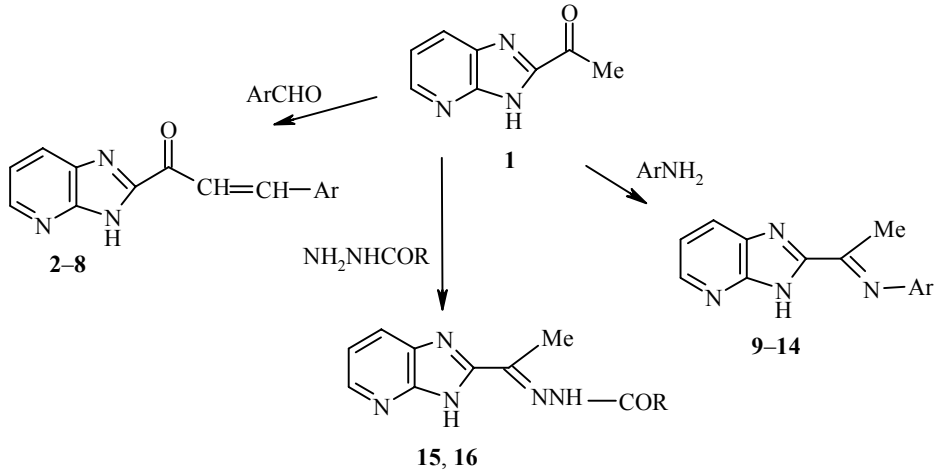
New imidazo[4,5-b]pyridine derivatives with various substituents in the 2-position (α,β-unsaturated ketones, imines, Δ^2-pyrazolines, pyrimidines, 1,2,3,4-tetrahydropyrimidines) and derivatives of the new pyrido[3',2':4,5]imidazo[1,2-d][1,2,4]triazine ring system were synthesized. Biological data for selected compounds are presented.

Keywords: imidazo[4,5-*b*]pyridine, pyrido[3',2':4,5]imidazo[1,2-*d*][1,2,4]triazine, antituberculotic activity.

Imidazo[4,5-*b*]pyridine can be considered as 1-deazapurine or 4(7)-azabenzimidazole. Such an analogy induces interest in the biological activity of this system's derivatives. To date some of them have been applied in pharmacotherapy [1]. As a continuation of our interest in the chemistry and biological properties of imidazo[4,5-*b*]pyridines [2, 3], we synthesized some new derivatives of this heterocycle.

As the starting compound for the syntheses, 2-acetylimidazo[4,5-*b*]pyridine (**1**), reported previously [2], was used. In reactions of this compound with several aromatic aldehydes or aromatic amines, corresponding α,β-unsaturated ketones **2-8** and imines **9-14** were obtained. The reaction of **1** with acetic hydrazide or ethyl carbazate led to the acetylhydrazone **15** and ethoxycarbonylhydrazone **16,** respectively (Scheme 1).

Scheme 1



2 Ar = Ph; **3** Ar = C_6H_4Cl-*p*; **4** Ar = C_6H_4OH-*p*; **5** Ar = C_6H_4CN-*p*; **6** Ar = $C_6H_4CF_3$-*p*; **7** Ar = $C_6H_3(Cl)_2$-2,4; **8** Ar = $C_6H_3Me_2$-2,4; **9** Ar = C_6H_4Cl-*p*; **10** Ar = C_6H_4F-*p*; **11** Ar = C_6H_4CN-*p*; **12** Ar = $C_6H_4Me_2$-*p*; **13** Ar = CH_2Ph; **14** Ar = 4-methylpiperidin-4-yl; **15** R = Me; **16** R = OEt

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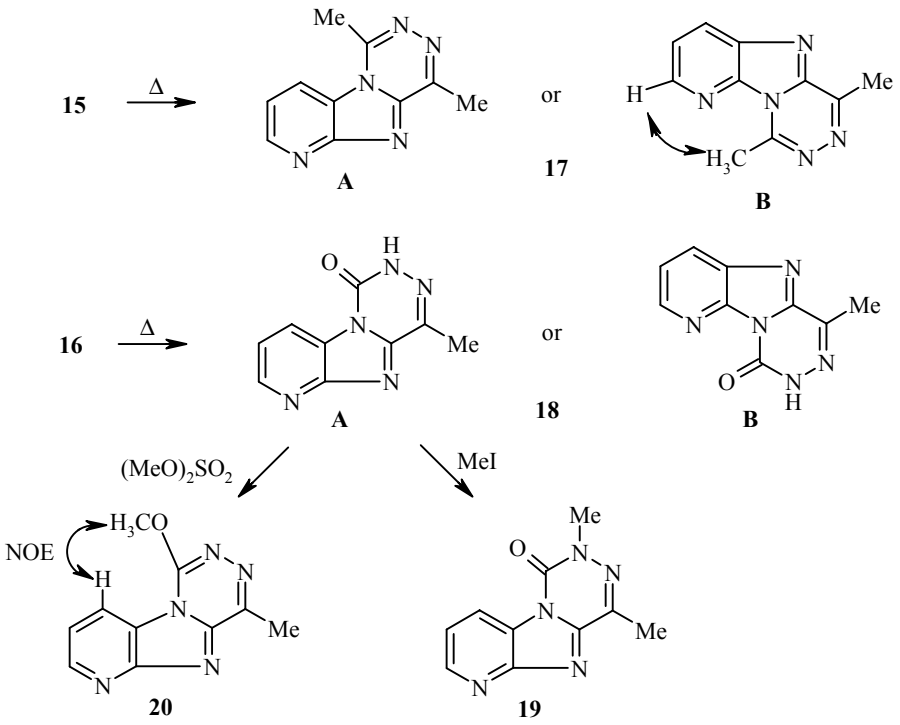
It was found that the compounds **15** and **16** upon heating in boiling N,N-dimethylaniline undergo intramolecular cyclization to the new heterocyclic ring system, pyridoimidazo[1,2,4]triazine (compounds **17** and **18**, Scheme 2). Due to the tautomeric properties of the imidazo[4,5-*b*]pyridine system, compounds **17**, **18** may be of **A** or **B** structure (ring closure with participation of N-1 or N-3 atoms is possible).

Scheme 2



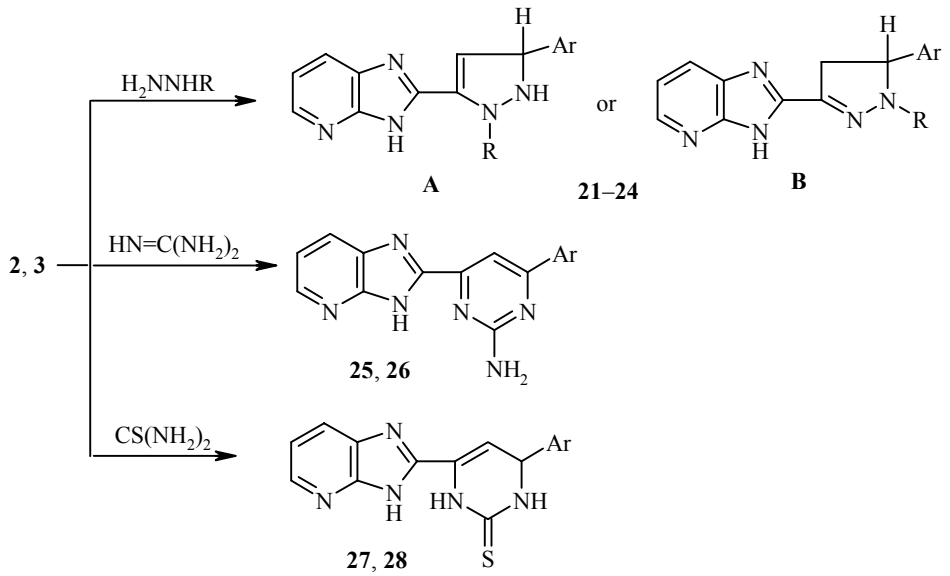
As in NOE investigation of compound **17**, a positive effect between CH_3 group protons of the [1,2,4]triazine ring and α-proton of the pyridine ring was observed; one can thus conclude that compound **17** has in fact the structure **B**.

In order to find the correct structure of the compound **18**, synthesis of its O-methyl derivative was attempted. However, probably due to its "amide" character, on reaction of **18** with CH_3I as alkylating agent (in alkaline medium) the N-methyl derivative **19** was obtained. Finally, the desired O-methyl derivative **20** was synthesized by the reaction of **18** with dimethyl sulfate in nitrobenzene. Compound **20** was then examined by the NOE method. Since in this investigation a positive effect between O-methyl group protons of 1,2,4-triazine ring and □-proton of pyridine ring was found, one can conclude that compound **18** has in fact the structure **A**.

In the next set of experiments the reactions of α,β-unsaturated ketones **2**, **3** with hydrazine, methylhydrazine, guanidine, as well as thiourea were investigated. New imidazo[4,5-*b*]pyridine derivatives with various substituents in the 2-position (Δ^2-pyrazolines **21**-**24**, pyrimidines **25**, **26**, and 1,2,3,4-tetrahydropyrimidines **27**, **28**) were obtained from these reactions (Scheme 3).

According to the literature data [4-7], reaction of α,β-enones with hyd-razines can lead to two different pyrazolines (1,4 or 1,2 addition). The type of product obtained from these reactions depends mainly on the catalyst used.

Scheme 3



21, 22 R = H; **23, 24** R = Me; **21**, **23, 25, 27** Ar = Ph; **22**, **24, 26**, **28** Ar = *p*-ClC_6H_4

Thus, the compounds **21-24** prepared in our work can be of **A** or **B** structure (our reactions were carried out without a catalyst). Because in the ^{1}H NMR spectra of compounds **21-24** signals of the CH_2–CH fragment of the pyrazoline ring were present (CH_2 protons as two doublets of doublets at δ 3.02-3.12 and 3.62-3.74 as well as CH proton as a triplet at δ 4.75-5.16 ppm), it can be concluded that they have in fact the structure **B**.

Compounds **3**, **6**, **8**, **10**, **11**, **21**, **25**, **27** chosen as examples were tested *in vitro* for their antituberculotic activity against *Mycobacterium tuberculosis* H_{37}Rv and two strains isolated from a tuberculosis patient: the 210 strain, resistant to isoniazide, ethambutol, and rifampicine, as well as the 192 strain, fully susceptible towards isoniazide, ethambutol, and rifampicine. The antibacterial activity of the compounds was determined in liquid Youmans medium containing 10% bovine serum using the method previously described [2]. The lowest concentration of the investigated compound at which no growth of strains could be observed was taken as the MIC. The results obtained are given in Table 1. Pyrazinamide was used as a positive control (its MIC was 30-60 μg/ml).

TABLE 1. Antituberculotic Activity, MIC Values (μg/ml)

Compound	*Mycobacterium*		
	H_{37}Rv	192	210
3	25	50	50
8	25	25	12.5
11	25	50	50
21	12.5	50	50
25	100	50	100
27	12.5	25	50

TABLE 2. Physical and Analytical Data of the Compounds **2-28**

Compound	mp, °C, solvent	Empirical formula	Found, % / Calculated, %			Yield, %
			C	H	N	
2	248-250 Toluene	$C_{15}H_{11}N_3O$	72.08 / 72.27	4.52 / 4.45	17.14 / 16.86	80
3	270-272 DMF	$C_{15}H_{10}ClN_3O$	63.27 / 63.50	3.60 / 3.55	14.96 / 14.81	76
4	309-311 DMF–H_2O	$C_{15}H_{11}N_3O_2$	67.82 / 67.91	4.26 / 4.18	16.12 / 15.84	80
5	292-294 Dioxane	$C_{16}H_{10}N_4O$	69.85 / 70.06	3.92 / 3.68	20.67 / 20.43	59
6	251-253 EtOH	$C_{16}H_{10}F_3N_3O$	60.42 / 60.56	3.26 / 3.17	13.47 / 13.24	22
7	280-282 DMF	$C_{15}H_9Cl_2N_3O$	56.48 / 56.62	3.07 / 2.85	13.46 / 13.20	63
8	255-257 DMF	$C_{17}H_{15}N_3O$	73.38 / 73.63	5.53 / 5.45	15.46 / 15.15	70
9	258-260 Toluene	$C_{14}H_{11}ClN_4$	61.93 / 62.11	4.18 / 4.09	20.84 / 20.69	80
10	224-226 Toluene	$C_{14}H_{11}FN_4$	66.04 / 66.12	4.52 / 4.36	22.34 / 22.03	70
11	233-235 Toluene	$C_{15}H_{11}N_5$	68.72 / 68.95	4.16 / 4.24	27.06 / 26.81	56
12	295-298 Toluene	$C_{16}H_{17}N_5$	68.64 / 68.79	6.18 / 6.13	25.32 / 25.07	71
13	202-204 Benzene	$C_{15}H_{14}N_4$	71.73 / 71.97	5.81 / 5.64	22.76 / 22.39	70
14	282-dec. Dioxane	$C_{14}H_{19}N_5$	65.26 / 65.34	7.51 / 7.44	27.46 / 27.22	76
15	281-283 DMF–H_2O	$C_{10}H_{11}N_5O$	55.18 / 55.29	5.12 / 5.10	32.50 / 32.24	73
16	248-250 Dioxane	$C_{11}H_{13}N_5O_2$	53.36 / 53.43	5.38 / 5.30	28.48 / 28.33	75
17	181-183 Cyclohexane	$C_{10}H_9N_5$	60.17 / 60.29	4.60 / 4.55	35.24 / 35.16	40
18	320-322 DMF–H_2O	$C_9H_7N_5O$	53.66 / 53.73	3.58 / 3.51	34.97 / 34.81	72
19	174-176 EtOH–H_2O	$C_{10}H_9N_5O$	55.60 / 55.81	4.28 / 4.22	32.72 / 32.54	50
20	252-254 EtOH–H_2O	$C_{10}H_9N_5O$	55.72 / 55.81	4.30 / 4.22	32.80 / 32.54	46
21	205-207 DMF–H_2O	$C_{15}H_{13}N_5$	68.34 / 68.42	5.04 / 4.98	26.83 / 26.60	63
22	231-233 DMF–H_2O	$C_{15}H_{12}ClN_5$	60.45 / 60.50	4.12 / 4.06	23.64 / 23.52	70
23	280-282 DMF–H_2O	$C_{16}H_{15}N_5$	69.21 / 69.29	5.52 / 5.45	25.34 / 25.26	65
24	308-310 DMF	$C_{16}H_{14}ClN_5$	61.46 / 61.63	4.64 / 4.52	22.60 / 22.46	70
25	307-309 DMF–H_2O	$C_{16}H_{12}N_6$	66.53 / 66.65	4.30 / 4.19	29.36 / 29.15	65
26	312-314 DMF–H_2O	$C_{16}H_{11}ClN_6$	59.46 / 59.53	3.58 / 3.43	26.31 / 26.04	70
27	341-344 DMF–H_2O	$C_{16}H_{13}N_5S$	62.47 / 62.53	4.31 / 4.26	22.93 / 22.79	70
28	337-340 DMF–H_2O	$C_{16}H_{12}ClN_5S$	56.18 / 56.21	3.67 / 3.54	20.72 / 20.49	65

TABLE 3. IR and MS Data for Compounds **2-28**

Com-pound	IR, cm^{-1}	*m/z* (*I*, %)
1	2	3
2	3600-2400 (NH), 1680 (C=O), 1610 (C=C), 980 (*trans* C=C)	M^+ 249 (36), 221 (18), 220 (100), 119 (22), 103 (20), 77 (18)
3	3600-2400 (NH), 1670 (C=O), 1590 (C=C), 980 (*trans* C=C), 820 (1,4-disubst. arom.)	M^+ 285 (11), 283 (27), 256 (36), 255 (20), 254 (100), 137 (12), 119 (34), 102 (19), 101 (23), 75 (11), 44 (10)
4	3600-2400 (NH, OH), 1680 (C=O), 1600 (C=C), 1260 (C–O), 980 (*trans* C=C), 840 (1,4-disubst. arom.)	M^+ 265 (25), 237 (10), 236 (58), 161 (86), 146 (16), 133 (37), 120 (12), 119 (100), 118 (15), 92 (47), 91 (20), 73 (22), 65 (18), 64 (19), 57 (11), 45 (13), 44 (24), 43 (87), 42 (14), 41 (17), 39 (18), 38 (12)
5	3600-2400 (NH), 2220 (C≡N), 1670 (C=O), 1600 (C=C), 980 (*trans* C=C), 840 (1,4-disubst. arom.)	M^+ 274 (38), 246 (16), 245 (100), 128 (18), 119 (36), 101 (10)
6	3600-2400 (NH), 1660 (C=O), 1610 (C=C), 980 (*trans* C=C), 830 (1,4-disubst.arom.)	M^+ 317 (56), 289 (24), 288 (100), 171 (13), 151 (23), 119 (56), 41 (10)
7	3500-2400 (NH), 1670 (C=O), 1580 (C=C), 980 (*trans* C=C), 870, 805 (1,2,4-trisubst. arom.)	M^+ 318 (7), 320 (5), 317 (32), 290 (17), 289 (10), 288 (27), 284 (12), 282 (45), 256 (30), 255 (16), 254 (100), 171 (14), 137 (15), 136 (29), 135 (28), 119 (62), 99 (24), 92 (19), 64 (20)
8	3500-2200 (NH), 1670 (C=O), 1600 (C=C), 980 (*trans* C=C), 880, 820 (1,2,4-trisubst. arom.)	M^+ 277 (11), 262 (10), 250 (15), 249 (90), 248 (87), 234 (90), 130 (21), 129 (32), 128 (37), 119 (64), 116 (37), 115 (100), 91 (70), 64 (45), 51 (18)
9	3200-2400 (NH), 1650 (C=N)	M^+ 270 (52), 272 (14), 269 (100), 255 (21), 229 (17), 111 (28), 92 (9), 75 (16), 57 (10)
10	3200-2400 (NH), 1640 (C=N)	M^+ 254 (100), 253 (97), 239 (84), 213 (50), 212 (34), 186 (28), 145 (10), 136 (33), 127 (11), 95 (99), 92 (16), 91 (15), 75 (47)
11	3200-2400 (NH), 2230 (C≡N), 1660 (C=N)	M^+ 261 (44), 260 (100), 246 (22), 220 (18), 219 (16), 193 (16), 143 (12), 102 (56), 92 (13), 91 (11), 75 (12), 64 (11), 51 (11), 39 (10)
12	3400-2400 (NH), 1610 (C=N)	M^+ 279 (100), 278 (40), 264 (19), 145 (14), 119 (12), 92 (17), 91 (17), 77 (14), 65 (12), 64 (11), 42 (16), 39 (11)
13	3600-2600 (NH), 1630 (C=N)	M^+ 250 (79), 234 (16), 208 (12), 173 (14), 146 (11), 131 (23), 130 (14), 120 (15), 91 (100), 90 (11), 65 (24), 39 (10)
14	3500-2400 (NH), 1600 (C=N)	M^+ 257 (2), 161 (22), 160 (31), 159 (18), 148 (25), 147 (100), 146 (97), 144 (14), 133 (18), 120 (34), 119 (43), 96 (23), 93 (26), 92 (30), 82 (26), 66 (21), 56 (46), 42 (36), 39 (44), 38 (20)
15	3600-2600, 1690, 1630, 1280	M^+ 217 (9), 175 (46), 174 (80), 146 (100), 145 (19), 144 (16), 93 (17), 66 (10), 43 (31), 39 (10)
16	3600-2400 (NH), 1720 (C=O), 1270, 1060 (C–O)	M^+ 247 (54), 175 (11), 174 (100), 147 (16), 146 (99), 145 (13), 144 (15), 119 (12), 93 (27), 66 (17)
17	3080, 2970, 1580, 1520, 1420	M^+ 199 (100), 170 (15), 159 (45), 117 (18), 65 (10)
18	3300-2400, 1730, 1610, 1560, 1410, 1370, 1140	M^+ 201 (100), 145 (31), 144 (63), 120 (12), 119 (66), 117 (14), 92 (20), 91 (62), 65 (20), 64 (30), 56 (24), 40 (18), 39 (15), 38 (19)
19	2960, 1720, 1610, 1410	M^+ 215 (100), 173 (17), 172 (19), 158 (12), 146 (10), 145 (25), 144 (30), 120 (12), 119 (65), 91 (50), 70 (35), 69 (13), 64 (24), 44 (17), 43 (47), 42 (23), 40 (16), 38 (15)
20	3050, 2960, 1650, 1610, 1550, 1480, 1430, 1320, 1130	M^+ 215 (100), 201 (61), 173 (11), 160 (22), 159 (35), 158 (28), 145 (12), 144 (22), 133 (39), 119 (33), 118 (68), 105 (12), 91 (44), 79 (11), 78 (13), 64 (28), 44 (74), 43 (30), 42 (26), 40 (17), 39 (23)

TABLE 3 (continued)

1	2	3
21	3600-2400 (NH), 1630 (C=N)	M^+ 263 (100), 262 (22), 234 (26), 186 (59), 145 (13), 144 (15), 115 (10), 77 (10)
22	3400-2400 (NH), 1630 (C=N), 860(1,4-disubst. arom.)	M^+ 297 (100), 299 (29), 296 (29), 268 (19), 233 (11), 232 (11), 186 (78), 145 (21), 144 (24), 117 (15), 83 (10), 71 (12), 69 (11), 57 (21), 44 (13), 43 (16), 41 (11)
23	3400-2400 (NH), 1620 (C=N)	M^+ 277 (84), 276 (17), 234 (15), 200 (100), 115 (10), 104 (16), 28 (20)
24	3200-2200 (NH), 1630 (C=N), 815 (1,4-disubst. arom.)	M^+ 311 (74), 313 (21), 310 (18), 233 (12), 232 (12), 200 (100), 138 (16), 93 (10)
25	3500, 3300, 1640, 1590	M^+ 288 (100), 287 (12), 144 (12), 57 (14), 43 (11)
26	3520, 3360, 1650, 1600, 850	M^+ 322 (100), 324 (30), 321 (12), 161 (10), 144 (11)
27	3500-2400, 1620, 1520	M^+ 307 (5), 306 (16), 305 (100), 304 (29), 247 (23), 144 (20)
28	3600-2600, 1600, 1520	M^+ 341 (32), 340 (26), 339 (100), 338 (31), 281 (24), 145 (10), 144 (45), 119 (17), 92 (11), 65 (11), 44 (12)

TABLE 4. ^{1}H NMR Data for Compounds **15-26**

Compound	Solvent	Chemical shifts, δ, ppm (*J*, Hz)
15	DMSO-d_6	2.18 (3H, s, CH_3); 3.30 (3H, s, $COCH_3$); 7.05-7.22 (1H, m, C(6)H); 7.80 (1H, d, *J* = 6.0, C(7)H); 8.25 (1H, d, *J* = 5.0, C(5)H)
16	CD_3OD	1.37 (3H, t, *J* = 7.0, –CH_2CH_3); 2.39 (3H, s, CH_3); 4.34 (2H, q, *J* = 7.0, –CH_2CH_3); 7.27-7.36 (1H, m, C(6)H); 8.00 (1H, d, *J* = 7.0, C(7)H); 8.37 (1H, d, *J* = 4.0, C(5)H)
17	DMSO-d-$_6$	2.81 (3H, s, CH_3); 3.20 (3H, s, CH_3); 7.49 (1H, dd, *J* = 4.0, C(3)H); 8.50 (1H, d, *J* = 7.0, C(4)H); 8.74 (1H, d, *J* = 6.0, C(2)H)
18	DMSO-d_6	2.56 (3H, s, CH_3); 7.56 (1H, dd, *J* = 4.7, C(3)H); 8.63 (1H, d, *J* = 6.0, C(4)H); 8.76 (1H, d, *J* = 7.0, C(2)H)
19	DMSO-d_6	2.56 (3H, s, CH_3); 3.71 (3H, s, –NCH_3); 7.57 (1H, dd, J_1 = 5.0, J_2 = 4.0, C(3)H); 8.63 (1H, d, *J* = 6.0, C(4)H); 8.76 (1H, d, *J* = 3, C(2)H)
20	DMSO-d_6 + TFA	2.64 (3H, s, CH_3); 4.41 (3H, s, OCH_3); 7.74 (1H, dd, *J* = 6.0, C(3)H); 8.86 (1H, d, *J* = 7.0, C(4)H); 9.18 (1H, d, *J* = 8.0, C(2)H)
21	DMSO-d_6 + TFA	3.05 (1H, dd, *J* = 2.0, CH_2CH); 3.62 (1H, dd, *J* = 10, CH_2CH); 5.15 (1H, t, *J* = 10, CH_2CH); 7.20-7.31 (5H, m, Ar–H); 7.46 (1H, dd, *J* = 6.0, C(6)H); 8.20 (1H, d, *J* = 8.0, C(7)H); 8.37 (1H, d, *J* = 5.0, C(5)H)
22	DMSO-d_6 + TFA	3.02 (1H, dd, *J* = 10, CH_2CH); 3.62 (1H, dd, *J* = 12, CH_2CH); 5.16 (1H, t, *J* = 10, CH_2CH); 7.19 (4H, s, Ar–H); 7.31 (1H, dd, *J* = 6, C(6)H); 8.21 (1H, d, *J* = 8, C(7)H); 8.40 (1H, d, *J* = 6, C(5)H)
23	DMSO-d_6 + TFA	2.96 (3H, s, NCH_3); 3.12 (1H, dd, *J* = 13, CH_2CH); 3.73 (1H, dd, *J* = 11, CH_2CH); 4.75 (1H, t, *J* = 13, CH_2CH); 7.31-7.45 (5H, m, Ar–H); 7.57 (1H, dd, *J* = 6, C(6)H); 8.30 (1H, d, *J* = 8, C(7)H); 8.50 (1H, d, *J* = 5, C(5)H)
24	DMSO-d_6 + TFA	2.95 (3H, s, NCH_3); 3.10 (1H, dd, *J* = 15, CH_2CH); 3.74 (1H, dd, *J* = 12, CH_2CH); 4.75 (1H, t, *J* = 12, CH_2CH); 7.42 (4H, m, Ar–H); 7.58 (1H, dd, *J* = 6, C(6)H); 8.33 (1H, d, *J* = 7, C(7)H); 8.52 (1H, d, *J* = 6, C(5)H)
25	DMSO-d_6 + TFA	7.48-7.56 (3H, m, NH_2, C(5)H pyrimidine); 7.70 (1H, dd, *J* = 6, C(6)H); 8.02-8.08 (5H, m, Ar–H); 8.57 (1H, d, *J* = 8, C(7)H); 8.66 (1H, d, *J* = 5, C(5)H)
26	DMSO-d_6	6.89 (2H, br. s, NH_2); 7.31 (1H, dd, *J* = 5, C(6)H); 7.60 (2H, d, *J* = 9, Ar–H); 7.97 (1H, s, C(5)H pyrimidine); 8.04 (1H, d, *J* = 5, C(7)H); 8.20 (2H, d, *J* = 9, Ar–H); 8.44 (1H, d, *J* = 4, C(5)H)

EXPERIMENTAL

Melting points are uncorrected. IR spectra: Specord 75 spectrophotometer (pellets in KBr). ^{1}H NMR: 80 MHz Tesla 478 or Varian Unity 500 Plus spectrometers with TMS as internal standard; chemical shifts in δ ppm. MS spectra: LKS 9000 S apparatus with direct inlet, ionization energy 70 eV. The characteristics of the synthesized compounds are given in Tables 2-4.

The biological tests were performed in the Institute of Tuberculosis and Pulmonary Diseases in Warsaw.

1-(Imidazo[4,5-*b*]pyridin-2-yl)-3-aryl-2-propen-1-ones (2-8). To a suspension of ketone **1** [2] (0.002 mol) and an appropriate aldehyde (0.003 mol) in anhydrous ethanol (10 ml) 0.2 ml of piperidine was added and the mixture was refluxed with stirring for 1-2 h. The solid that precipitated after cooling was filtered off and recrystallized.

2-(1-Aryliminoethyl)imidazo[4,5-*b*]pyridines (9-14). Compound **1** [2] (0.002 mol) and an appropriate amine (0.003 mol) were heated at 155-165°C with stirring for 20 min. After cooling, the solid obtained was washed with ether and recrystallized. Compound **13** was obtained by refluxing of **1** and benzylamine in anhydrous xylene (5 ml) for 3 h. The precipitate obtained after cooling was filtered off and recrystallized.

N-[1-(Imidazo[4,5-*b*]pyridin-2-yl)ethylidene]acetohydrazide (15), Ethyl 2-[1-(Imidazo[4,5-*b*]-pyridin-2-yl)ethylidene]hydrazine-1-carboxylate (16). To a suspension of ketone **1** [2] (0.003 mol) and acetohydrazide or ethyl carbazate (0.004 mol) in anhydrous ethanol (10 ml) glacial acetic acid (5 drops) was added and the mixture was refluxed with stirring for 5 h. The solid that precipitated after cooling (**16**) or after evaporation of the solvent (**15**) was filtered off and recrystallized.

6,9-Dimethylpyrido[3',2':4,5]imidazo[1,2-*d*][1,2,4]triazine (17), 9-methylpyrido[2',3':4,5]imidazo-[1,2-*d*][1,2,4]triazin-6(7H)-one (18). Compound **15** (0.003 mol) or **16** (0.002 mol) was refluxed in N,N-dimethylaniline (10 ml) for 20 h (**15**) or 10 h (**16**). The solid that precipitated after cooling (**18**) or after evaporation of the solvent (**17**) was filtered off and recrystallized.

7,9-Dimethylpyrido[2',3':4,5]imidazo[1,2-*d*][1,2,4]triazin-6-one (19). To a stirred suspension of finely powdered KOH (0.003 mol) in dry DMF (15 ml) cooled to about 5°C compound **18** was added in portions. The reaction mixture was stirred for 1 h, then a cooled solution of methyl iodide (0.0035 mol) in DMF (1 ml) was added dropwise during 10 min and stirring was continued for 3 h. After that time the solvent was evaporated in vacuo and the remaining product was triturated with a small amount of H_2O, filtered off, and recrystallized.

6-Methoxy-9-methylpyrido[2',3':4,5]imidazo[1,2-*d*][1,2,4]triazine (20). To a stirred solution of compound **18** (0.002 mol) in nitrobenzene (15 ml) (heated at 135-140°C) a solution of dimethyl sulfate (0.003 mol) in nitrobenzene (1 ml) was added dropwise during 10 min. The stirring was then continued at the same temperature for 4 h. After cooling, the solid formed was filtered off, washed with ether and then dissolved in a small amount of H_2O, and alkalized with NH_3. The resultant yellow precipitate was filtered off and recrystallized.

2-(5-Aryl-Δ^2-pyrazolin-3-yl)imidazo[4,5-*b*]pyridines (21, **22), 2-(1-Methyl-5-aryl-Δ^2-pyrazolin-3-yl)imidazo[4,5-*b*]pyridines (23**, **24).** To a suspension of compound **2** or **3** (0.002 mol) in anhydrous ethanol (15 ml) hydrazine hydrate (100%) or methylhydrazine (0.0025 mol) was added and the mixture was refluxed with stirring for 2-3 h. The resulting solid was filtered off and recrystallized.

2-(2-Amino-6-arylpyrimidin-4-yl)imidazo[4,5-*b*]pyridines (25, **26).** To a refluxing mixture of compound **2** or **3** (0.002 mol) and guanidine carbonate (0.002 mol) in ethanol (15 ml) a water solution of sodium hydroxide (40%, 1 ml) was added portionwise during 30 min and refluxing was continued for 7-8 h. After cooling, the separated solid was filtered off and the filtrate was concentrated to half of its volume and poured into H_2O. The precipitated solid was filtered off and recrystallized.

2-(4-Aryl-2-thioxo-1,2,3,4-tetrahydropyrimidin-6-yl)imidazo[4,5-*b*]pyridines (27, 28). To a suspension of compound **2** or **3** (0.002 mol) and thiourea (0.002 mol) in ethanol (20 ml) a water solution of sodium hydroxide (40%, 1 ml) was added and the resulting mixture was refluxed for 15 h. Then, the solvent was completely removed and the remaining product was dissolved in 10 ml of water. The solution was filtered and the filtrate was acidified with acetic acid to pH 3-4. The precipitated solid was filtered off and recrystallized.

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