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Some reactions of 2-cyanomethyl-3-methyl-3*H*-imidazo[4,5-*b*]pyridine with isothiocyanates. Antituberculotic activity of the obtained compounds

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Some reactions of 2-cyanomethyl-3-methyl-3*H*-imidazo[4,5-*b*]pyridine with isothiocyanates were carried out. New derivatives of imidazo[4,5-*b*]pyridine with different substituents in 2-position and derivatives of the new pyrido-imidazo-thiazine ring system were synthesized. Most of the obtained compounds were tested for their *in vitro* antituberculotic activity.

1. Introduction

Continuing our interest in the chemistry and biological properties of imidazo[4,5-*b*]pyridine derivatives [1, 2], we synthesized and tested some new derivatives of this heterocycle.

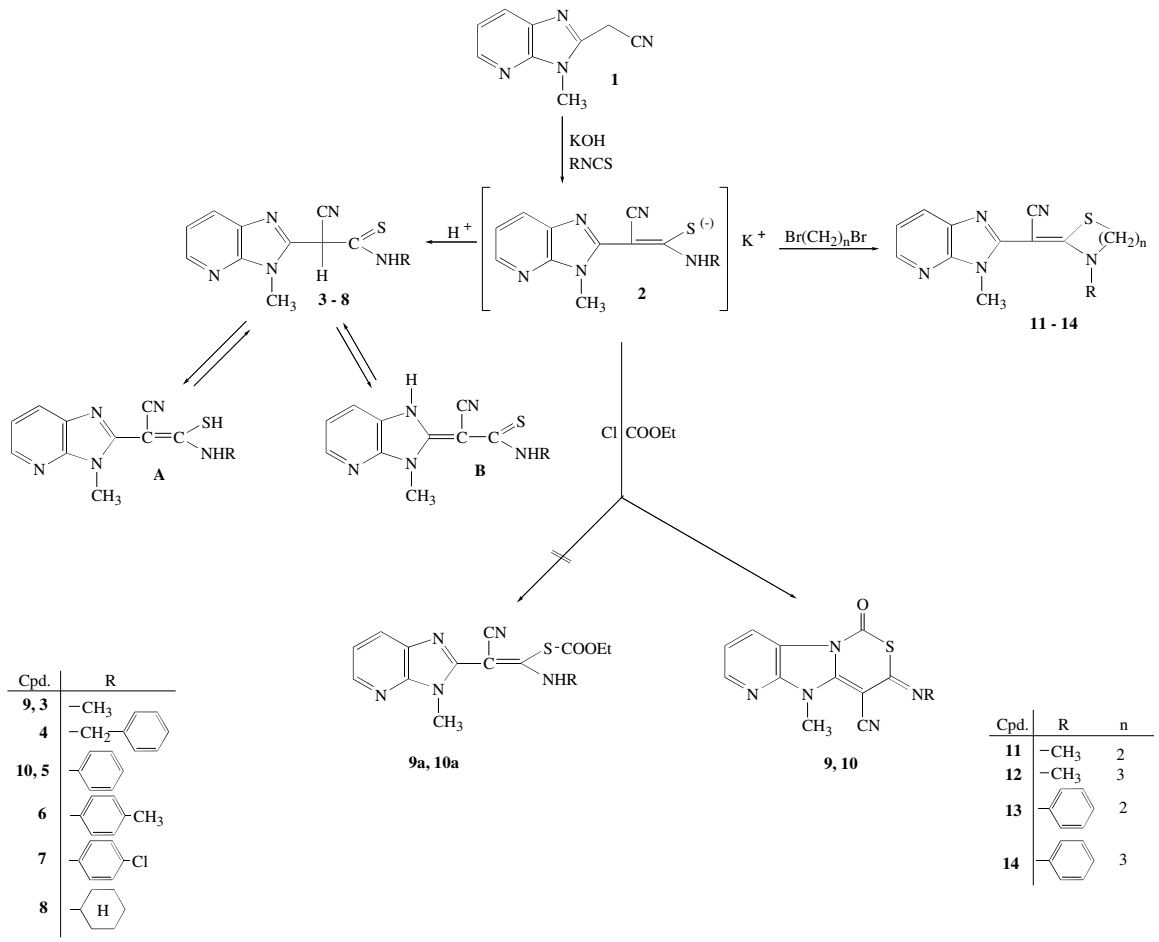
2. Investigations, results and discussion

2.1. Chemistry

As the starting compound for the syntheses, 2-cyanomethyl-3-methyl-3*H*-imidazo[4,5-*b*]pyridine (**1**), reported previously [3], was used. The reactions of this compound with isothiocyanates (in the presence of potassium hydroxide) gave the non-isolated adducts **2** which, upon acidifying with 1 N hydrochloric acid, yielded the N-substituted thiocarboxamides **3**–**8** whereas its reactions with halogenated compounds (ethyl chloroformate, 1,2-dibromoethane, 1,3-dibromopropane) gave the compounds **9**–**14** (Scheme 1).

Surprisingly, the IR spectra of the compounds **3**–**8** showed the presence of a conjugated nitrile group at 2180–2200 cm^{-1}, which suggested that these compounds may exist in two tautomeric forms **A** or **B** (thiol or thione form). This possibility was also confirmed by the ^1H NMR

Scheme 1



spectra of these compounds in which no signal of the methine proton (CH−CN) was observed. The absence of this signal also confirmed the complete conversion of the compounds **3**–**8** into the forms **A** or **B** (or their mixture). Since in the ^{13}C NMR spectrum, recorded for the representative compound **3** the carbon atom signal at 188,21 ppm was observed (this corresponds to the typical chemical shift of a thione carbon atom [4, 5]) one can conclude that compounds **3**–**8** exist in the thione form **B**. It is noteworthy that adducts **2** in reaction with ethyl chloroformate not afforded the acyclic products **9a**, **10a** but the derivatives of a new heterocyclic ring system the pyrido-imidazo-thiazines **9**, **10**. The structure of these compounds was confirmed by their spectral data.

Additionally we studied the reactions of **1** with isothiocyanates (in the presence of sulfur) or with carbon disulphide (in the presence of potassium hydroxide) (Scheme 2).

Using carbon disulphide and potassium hydroxide the non-isolated potassium salt of geminal dithiole (**1a**) was obtained, which was then allowed to react with α,ω-dibromoalcanes (1,2-dibromoethane, 1,3-dibromopropane, 1,4-dibromobutane) to give the 1,3-dithiacycloalkane-imidazo-[4,5-*b*]pyridines **17**–**19**. By reaction with isothiocyanates (methyl- or phenyl-) and sulphur, the thiazolyl-imidazo[4,5-b]pyridines **15**, **16** were prepared.

In the next set of experiments the reactions of the adducts **2a** and **2b** with chloroacetyl chloride were investigated (Schemes 3 and 4). It is known [6] that the chlorine atom attached to the carbonyl group (acid chloride) is far more reactive than the chlorine atom that is held as an alkyl halide. For that reason formation of thiazolidyne-5-on derivatives (compounds **20a** and **22a**) was expected in the above reaction. However, in fact the thiazolidyne-4-on derivatives (compounds **20** and **22**) were obtained. This was confirmed by reaction of the adducts **2a** and **2b** with ethyl chloroacetate. Thus, the adduct **2a** when reacted with ethyl chloroacetate yielded the acyclic ester **21** which on heating in boiling ethanol cyclized to the compound **20**. The adduct **2b** on reaction with ethyl chloroacetate formed the compound **22** directly (the acyclic ester **23** could not be isolated).

In addition, the same compounds **20** and **22** were also obtained as a result of the reaction of the thiocarboxamides **3** or **5** with ethyl bromoacetate. The structures of compounds **20** and **22** were confirmed by their IR, ^{1}H NMR, and MS spectral data. The physical characteristics and yields of the compounds synthesized are summarized in the Table.

2.2. Pharmacological data

Compounds **3**–**22** were tested *in vitro* for their antituberculotic activity. The screening was conducted against *Mycobacterium tuberculosis* strain $H_{37}Rv$ at compound concentration 12.5 μg/ml in BACTEC 12B medium using the BACTEC 460 radiometric system. The results obtained are listed in the Table. The column labeled % Inhibition lists the activity of each compound at the concentration 12.5 μg/ml. Rifampicin was used as a positive control (its MIC was 0.25 μg/ml).

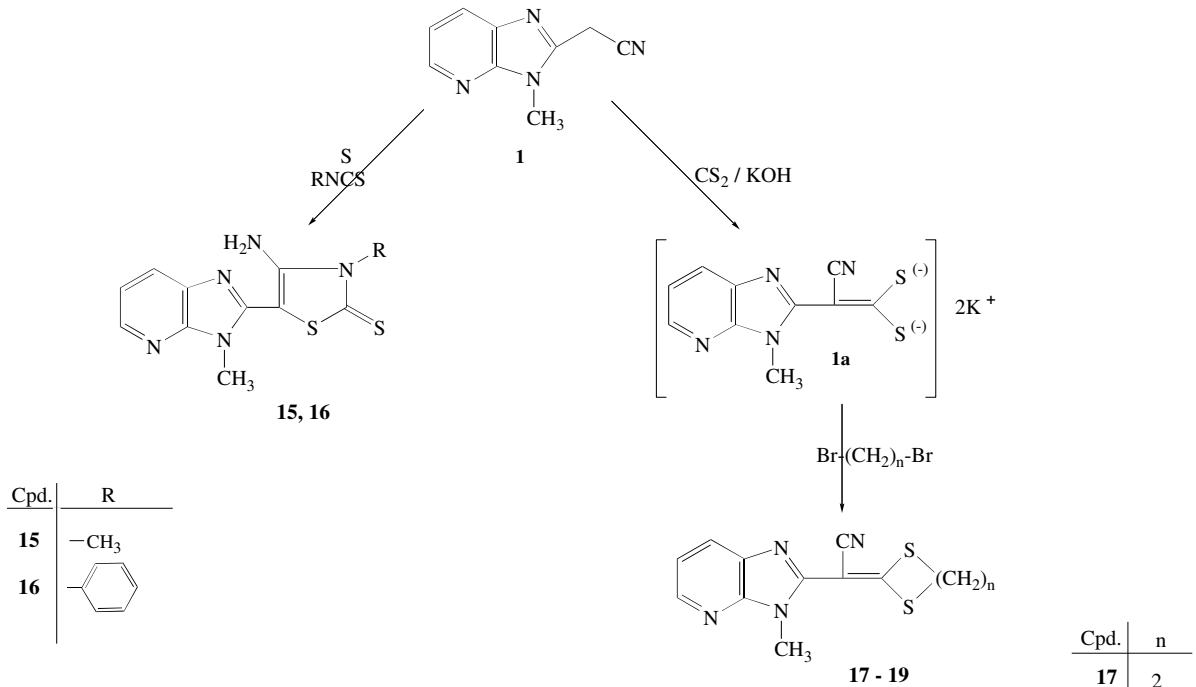
3. Experimental

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. Elementary analyses were carried out in the Department of Physical Chemistry Medical University of Gdańsk. Analytical results were in agreement with calculated values ± 0.4%.

3.1. 2-[(N-Substituted thiocarbamoyl)cyanomethyl]-3-methyl-3H-imidazo[4,5-b]pyridines **3**–8

To a suspension of finely powdered KOH (0.005 mol) in dry DMF (15 ml) at 0 °C the nitrile **1** [3] (0.005 mol) and than the appropriate isothiocyanate

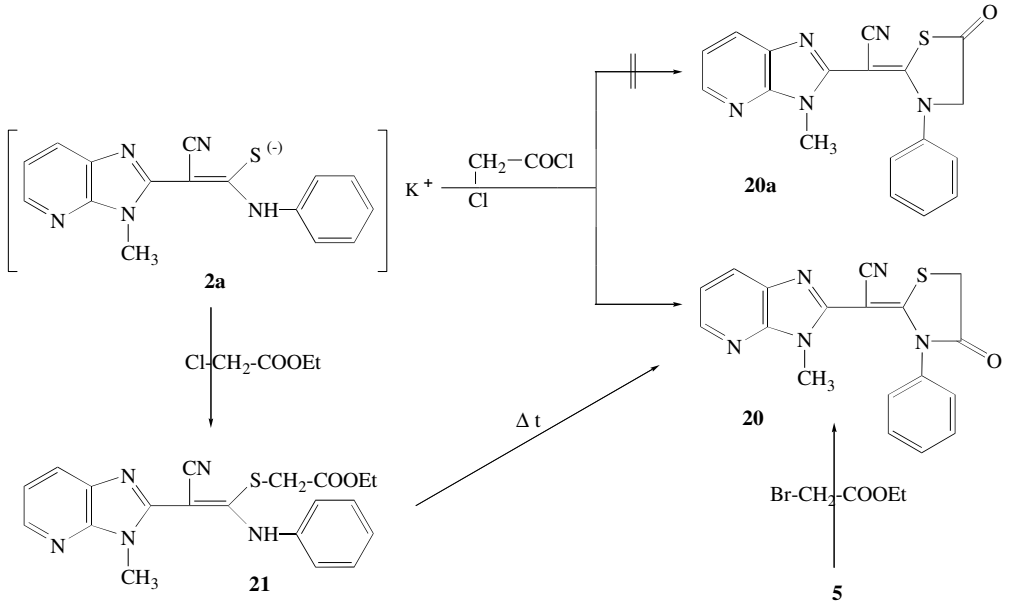
Scheme 2



Cpd.	R
15	−CH_3
16	

Cpd.	n
17	2
18	3
19	4

Scheme 3



(0.005 mol) were added in portions with stirring. The reaction mixture was stirred at room temperature for 3 h, then poured into ice/water and acidified with 0.1 N HCl to a pH 3–4. The resulting precipitate was filtered off, dried and recrystallized from the proper solvent.

3: IR (cm^{-1}): 3340 (NH), 2980, 2860 (CH_3), 2200 (C≡N), 1580, 1540 (CSNH). ^{1}H NMR ($CDCl_3$): 3.23 (s, 3 H, $NHCH_3$), 4.10 (s, 3 H, NCH_3), 7.21–7.23 (m, 1 H, C-6), 7.63 (d, J = 6 Hz, 1 H, C-7), 8.28 (d, J = 4 Hz, 1 H, C-5). ^{13}C NMR ($CDCl_3$): 30.20, 31.92, 64.55, 118.11, 119.16, 119.83, 121.66, 143.36, 144.98, 152.81, 188.21. MS, m/z (%): 247 (2.6), 246 (7), 245 (73) M^+, 213 (10), 212 (100), 199 (5), 172 (5), 171 (7), 92 (9), 78 (6).

4: IR (cm^{-1}): 3310 (NH), 2196 (C≡N), 1590, 1530 (CSNH). ^{1}H NMR ($CDCl_3$): 4.11 (s, 3 H, NCH_3), 4.95 (s, 2 H, $-CH_2-$), 7.23–7.42 (m, 6 H, ar, C-6), 7.64 (s, 1 H, C-7), 8.29 (s, 1 H, C-5). MS, m/z (%): 323 (2), 322 (7), 321 (43) M^+, 288 (10), 230 (8), 215 (6), 183 (8), 173 (6), 172 (7), 171 (4), 132 (4), 106 (7), 92 (12), 91 (100), 79 (5), 78 (6), 65 (14), 51 (5), 39 (6).

5: IR (cm^{-1}): 3335 (NH), 3050 (CH ar), 2920 (CH_3), 2180 (C≡N), 1580, 1530 (CSNH). ^{1}H NMR (DMSO-d_6): 3.36 (s, 3 H, NCH_3), 7.11–7.35 (m, 6 H, ar, C-6), 7.85 (s, 1 H, C-7), 8.09 (s, 1 H, C-5). MS, m/z (%): 309 (9), 308 (30), 307 (100) M^+, 275 (13), 274 (61), 215 (24), 172 (29), 171 (19), 135 (28), 132 (12), 93 (29), 79 (10), 78 (19), 77 (42), 65 (22), 64 (12), 52 (16), 51 (44), 39 (23), 28 (12).

6: IR (cm^{-1}): 3150 (NH), 3060 (CH ar), 2930 (CH_3), 2190 (C≡N), 1560 (CSNH). ^{1}H NMR (DMSO-d_6): 2.28 (s, 3 H, CH_3), 3.34 (s, 3 H, NCH_3), 7.13 (d, J = 6 Hz, 2 H, ar), 7.22 (m, 1 H, C-6), 7.65 (br.s, 2 H, ar), 7.83 (s, 1 H, C-7), 8.08 (s, 1 H, C-5). MS, m/z (%): 323 (4), 322 (16), 321 (68) M^+, 307 (14), 289 (21), 288 (100), 274 (24), 215 (41), 298 (12), 172 (37), 171 (45), 149 (20), 144 (11), 132 (16), 107 (76), 106 (14), 105 (11), 103 (12), 93 (15), 91 (34), 79 (18), 78 (25), 77 (18), 65 (26), 51 (19), 44 (11), 39 (18), 32 (13), 28 (57).

7: IR (cm^{-1}): 3370 (NH), 2200 (C≡N), 1630, 1580 (CSNH). ^{1}H NMR ($CDCl_3$): 4.18 (s, 3 H, NCH_3), 7.40 (m, 4 H, ar), 7.69 (d, J = 7.6 Hz, 1 H, C-6), 8.34 (d, J = 5 Hz, 1 H, C-7), 8.56 (s, 1 H, C-5). MS, m/z (%): 343 (26), 342 (15), 341 (77) M^+, 310 (30), 308 (100), 220 (24), 216 (11), 215 (96), 172 (8), 171 (67), 169 (78), 153 (26), 132 (27), 127 (45), 113 (11), 111 (36), 104 (13), 103 (19), 92 (10), 79 (18), 78 (26), 77 (12), 75 (26), 64 (11), 52 (12), 51 (19), 50 (14), 39 (14).

Scheme 4

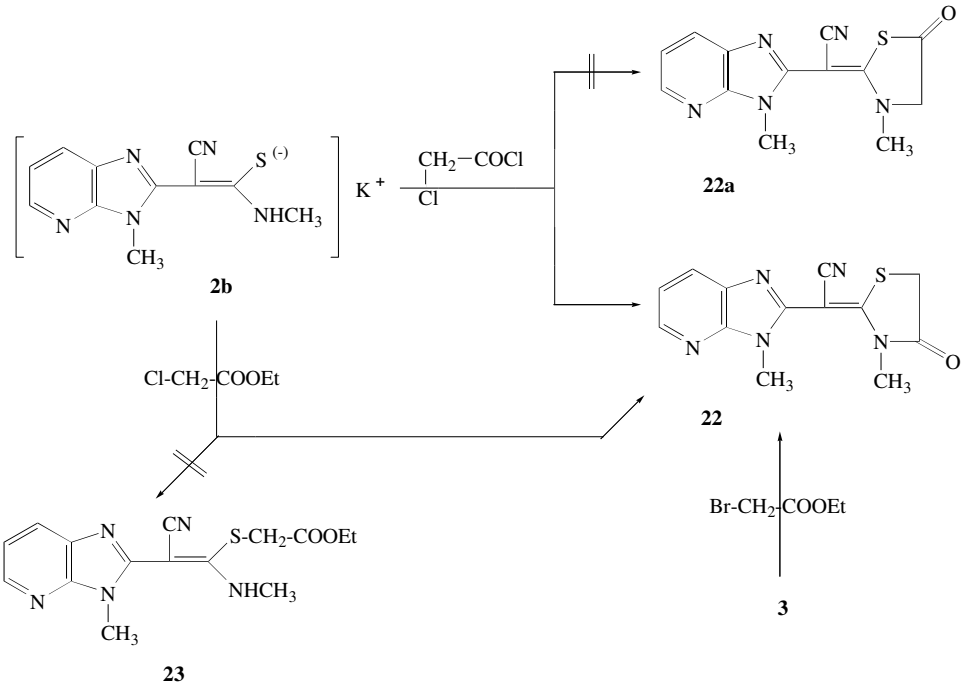


Table: Physicochemical data and antituberculotic activity of compounds 3–22

Compd.	M.p. (°C) Solvent	Yield (%)	Mol. formula M.wt.	% Inhibition (concentration 12.5 μg/ml)
3	238–240 T	84	$C_{11}H_{11}N_5S$ 245.3	58
4	228–230 T	81	$C_{17}H_{15}N_5S$ 321.3	5
5	195–196 DMF	84	$C_{16}H_{13}N_5S$ 307.3	42
6	192–193 DMF/H_2O	80	$C_{17}H_{15}N_5S$ 321.3	73
7	200–201 T	87	$C_{16}H_{12}ClN_5S$ 341.8	58
8	186–187 DMF/H_2O	64	$C_{16}H_{19}N_5S$ 313.4	72
9	330–332 DMF	84	$C_{12}H_9N_5OS$ 271.3	13
10	343–345 DMF	34	$C_{17}H_{11}N_5OS$ 333.3	0
11	236–238 DMF	40	$C_{13}H_{13}N_5S$ 271.3	0
12	234–236 DMF	30	$C_{14}H_{15}N_5S$ 285.4	0
13	182–184 B	26	$C_{18}H_{15}N_5S$ 333.4	0
14	223–225 B	31	$C_{19}H_{17}N_5S$ 347.4	0
15	293–295 DMF/H_2O	60	$C_{11}H_{11}N_5S_2$ 277.4	0
16	285–287 B	68	$C_{16}H_{13}N_5S_2$ 339.4	7
17	209–211 T	60	$C_{12}H_{10}N_4S_2$ 274.4	0
18	140–142 DMF/H_2O	80	$C_{13}H_{12}N_4S_2$ 288.4	45
19	158–160 T	30	$C_{14}H_{14}N_4S_2$ 302.4	0
20	258–260 T	50	$C_{18}H_{13}N_5OS$ 347.4	0
21	152–154 EtOH	76	$C_{20}H_{19}N_5O_2S$ 393.4	
22	238–240 T	62	$C_{13}H_{11}N_5OS$ 285.3	2

* T – toluene; B – benzene

8: IR (cm^{-1}): 3290 (NH), 2930, 2840 (CH_2), 2190 (C≡N), 1560, 1530 (CSNH). ^{1}H NMR (DMSO-d_6): 1.14–1.89 (m, 10 H, $-CH_2-$), 3.88 (s, 3 H, NCH_3), 4.34 (br.s, 1 H, NCH, cyclo), 7.28 (m, 1 H, C-6), 7.72 (d, J = 7 Hz, 1 H, NH), 7.99 (d, J = 7.6 Hz, 1 H, C-7), 8.24 (d, J = 4.5 Hz, 1 H, C-5). MS, m/z (%): 315 (6), 314 (18), 313 (85) M^+, 280 (10), 258 (35), 215 (13), 199 (11), 198 (100), 197 (11), 183 (13), 173 (12), 172 (18), 171 (15), 98 (14), 78 (10), 55 (17), 41 (19), 28 (31).

3.2. 4-Cyano-5-methyl-3-methylimino-pyrido[2′,3′ : 4,5]imidazo[1,2-c][1,3] thiazin-1-on (**9**)

4-Cyano-5-methyl-3-phenylimino-pyrido[2′,3′ : 4,5]imidazo[1,2-c][1,3] thiazin-1-on (**10**)

To a stirred suspension of finely powdered KOH (0.005 mol) in dry DMF (15 ml) cooled to 0 °C the nitrile **1** [3] (0.005 mol) and next the proper isothiocyanate (0.005 mol) were added gradually. The reaction mixture was stirred at room temperature for 3 h then cooled again to 0 °C, treated dropwise with ethyl chloroformate and heated at 70–80 °C (temperature of a bath) with continuous stirring for 1–2 h. The solid precipitated after cooling (**9**) or after pouring into ice/water (**10**), was filtered off, and recrystallized.

The same compounds **9**, **10**, are also obtained when after addition of ethyl chloroacetate the reaction is carried out at room temperature for 5 h.

9: IR (cm^{-1}): 2980, 2950 (CH_3), 2220 (C≡N), 1720 (C=O), 1630, 1610 (C=N). ^{1}H NMR (DMSO-d_6): 3.73 (s, 3 H, NCH_3), 4.02 (s, 3 H, NCH_3), 7.65–7.48 (m, 1 H, C-5), 8.52 (s, 1 H, C-7), 8.61 (s, 1 H, C-5). ^{13}C NMR (DMSO-d_6): 31.04, 32.67, 40.80, 64.49, 119.86, 120.20, 120.26, 122.88, 143.47, 145.44, 153.16, 188.48. MS, m/z (%): 273 (5.5), 272 (14), 271 (100) M^+, 215 (19), 214 (58), 213 (22), 79 (18), 78 (24), 64 (17), 52 (15), 28 (69).

10: IR (cm^{-1}): 3020 (CH ar), 2900 (CH_3), 2210 (C≡N), 1720 (C=O), 1620 (C=N). ^{1}H NMR (DMSO-d_6): 4.04 (s, 3 H, NCH_3), 7.26 (d, J = 8 Hz, 2 H, ar), 7.45 (t, J_1J_2 = 7 Hz, 1 H, C-5), 7.51–7.54 (m, 3 H, ar), 8.43 (d, J = 8 Hz, 1 H, C-7), 8.55 (d, J = 5 Hz, 1 H, C-5). MS, m/z (%): 335 (3), 334 (13), 333 (57) M^+, 332 (100), 214 (12), 213 (7), 166 (6), 159 (5), 119 (4), 79 (4), 78 (6), 77 (5), 51 (5), 44 (8), 32 (12), 28 (68).

3.3. 2-[(3-Methylthiazolidin-2-ylidene)cyanomethyl]-3-methyl-3H-imidazo[4,5-b]pyridine (**11**)

2-[(3-Methyl[1,3]thiazin-2-ylidene)cyanomethyl]-3-methyl-3H-imidazo[4,5-b]pyridine (**12**)

2-[(3-Phenylthiazolidin-2-ylidene)cyanomethyl]-3-methyl-3H-imidazo[4,5-b]pyridine (**13**)

2-[(3-Phenyl[1,3]thiazin-2-ylidene)cyanomethyl]-3-methyl-3H-imidazo[4,5-b]pyridine (**14**)

To a cooled (0 °C) suspension of finely powdered KOH (0.005 mol) in dry DMF (15 ml) the nitrile **1** [3] (0.005 mol) and than methyl- or phenyl isothiocyanate were added in portions with stirring. The reaction mixture was stirred at room temperature for 3 h, then cooled again to 0 °C treated with an appropriate halogenated compound (0.005 mol) and stirred at RT for additional 3–5 h. After that time the reaction mixture was poured into ice/water, the resulting product was filtered off, dried and recrystallized from the proper solvent.

11: IR (cm^{-1}): 2980, 2900 (CH_3), 2220 (C≡N), 1610 (C=C). ^{1}H NMR ($CDCl_3$): 3.37 (s, 4 H, CH_2), 3.47 (s, 3 H, NCH_3), 4.00 (s, 3 H, NCH_3), 7.18 (m, 1 H, C-6), 7.81 (d, J = 8 Hz, 1 H, C-7), 8.28 (d, J = 5 Hz, 1 H, C-5). MS, m/z (%): 273 (1), 272 (3), 271 (6) M^+, 246 (10), 245 (37), 213 (12), 212 (100), 211 (38), 197 (20), 196 (17), 78 (11), 44 (17), 28 (12).

12: IR (cm^{-1}): 2940, 2870 (CH_3), 2220 (C≡N), 1600 (C=C). ^{1}H NMR ($CDCl_3$): 2.17 (m, 2 H, CH_2), 3.35 (m, 7 H, CH_2, NCH_3), 4.00 (s, 3 H, NCH_3), 7.06 (d, d, J_1, J_2 = 5 Hz, 1 H, C-6), 7.66 (d, J = 7 Hz, 1 H, C-7), 8.17 (d, J = 4 Hz, 1 H, C-5). MS, m/z (%): 287 (2), 286 (3), 285 (13) M^+, 213 (29), 212 (100), 211 (59), 210 (11), 197 (18), 196 (21), 183 (10), 79 (8), 78 (11).

13: IR (cm^{-1}): 2940 (CH_3), 2220 (C≡N), 1620 (C=C). ^{1}H NMR ($CDCl_3$): 3.26 (t, J = 7 Hz, 2 H, CH_2), 3.88 (s, 1 H, NCH_3), 4.27 (t, J = 8 Hz, 2 H, CH_2), 7.19 (d, d, J_1J_2 = 5 Hz, 1 H, C-6), 7.42–7.53 (m, 5 H, ar), 7.96 (d, J = 7 Hz, 1 H, C-5), 8.32 (d, J = 5 Hz, 1 H, C-5). MS, m/z (%): 335 (4), 334 (15), 333 (100) M^+, 332 (14), 305 (23), 286 (25), 273 (22), 256 (25), 78 (90), 77 (26), 52 (12), 51 (15).

14: IR (cm^{-1}): 2960 (CH_3), 2220 (C≡N), 1630 (C=C). ^{1}H NMR ($CDCl_3$): 2.28–2.33 (m, 2 H, CH_2), 3.19 (s, 2 H, CH_2), 3.55 (s, 2 H, CH_2), 3.89 (s, 3 H, NCH_3), 6.61 (s, 1 H, C-6), 6.94 (s, 5 H, ar), 7.71 (s, 1 H, C-7), 8.15 (s, 1 H, C-5). MS, m/z (%): 349 (4), 348 (16), 347 (100) M^+, 319 (11), 318 (14), 300 (16), 291 (22), 286 (29), 273 (12), 214 (55), 78 (13), 77 (25).

3.4. 2-(4-Amino-3-methylthiazol-2-(3H)-thion-5-yl)-3-methyl-3H-imidazo[4,5-b]pyridine (**15**)

2-(4-Amino-3-phenylthiazol-2-(3H)-thion-5-yl)-3-methyl-3H-imidazo[4,5-b]pyridine (**16**)

A mixture of nitrile **1** [3] (0.005 mol), finely powdered S_8 (0.005 mol) and triethylamine (0.005 mol) in abs. EtOH (15 ml) was stirred at room temperature for 30 min. The proper isothiocyanate (0.005 mol) was then added gradually and stirring was continued for 20 min. Next, the reaction mixture was refluxed with constant stirring for 2 h. After cooling the resultant precipitate was filtered off, washed with ether, dried and recrystallized.

15: IR (cm^{-1}): 3600–3300, 2970, 1620, 1120. ^{1}H NMR (DMSO-d_6): 3.64 (s, 3 H, NCH_3), 3.88 (s, 3 H, NCH_3), (d, d, J_1J_2 = 5 Hz, 1 H, C-6), 7.89 (d, J = 8 Hz, 1 H, C-7), 8.01 (s, 2 H, NH_2), 8.20 (d, J = 4 Hz, 1 H, C-5). MS, m/z (%): 279 (6), 278 (10), 277 (100) M^+, 204 (11), 178 (7), 177 (76), 176 (32), 135 (3), 44 (4), 28 (3).

16: IR (cm^{-1}): 3600–3300, 2920, 1620, 1500, 1460, 1260. ^{1}H NMR (DMSO-d_6): 3.95 (s, 3 H, NCH_3), 7.21 (d, d, J_1J_2 = 5 Hz, 1 H, C-6), 7.43 (s, 5 H, ar), 7.63 (br.s, 2 H, NH_2), 7.90 (d, J = 8 Hz, 1 H, C-7), 8.23 (d, J = 4 Hz, 1 H, C-5). MS, m/z (%): 341 (7), 340 (14), 339 (100) M^+, 204 (21), 178 (8), 177 (94), 176 (31), 135 (5), 77 (8), 51 (4).

3.5. 2-[(1,3-Dithiacyclopentan-2-ylidene)cyanomethyl]-3-methyl-3H-imidazo[4,5-b]pyridine (**17**)

2-[(1,3-Dithiacyclohexan-2-ylidene)cyanomethyl]-3-methyl-3H-imidazo[4,5-b]pyridine (**18**)

2-[(1,3-Dithiacycloheptan-2-ylidene)cyanomethyl]-3-methyl-3H-imidazo[4,5-b]pyridine (**19**)

To a stirred suspension of finely powdered KOH (0.01 mol) in dry DMF (15 ml) cooled to 0 °C the nitrile **1** [3] (0.005 mol) and next CS_2 (0.006 mol) were added gradually. The reaction mixture was stirred at room temperature for 3 h, then cooled again to 0 °C, treated with the ap-

propiate α,ω-dibromo compound (0.005 mol) and stirred at room temperature for additional 6–12 h. Then, it was poured into ice/water, the resulting precipitate was filtered off, dried and recrystallized.
17: IR (cm^{-1}): 2960 (CH alifat), 2220 (C≡N), 1664 (C=C). ^{1}H NMR ($CDCl_3$): 3.62 (s, 4 H, CH_2), 4.07 (s, 3 H, NCH_3), 7.15–7.35 (m, 1 H, C-6), 8.02 (d, J = 6 Hz, 1 H, C-7), 8.40 (d, J = 3 Hz, 1 H, C-5). MS, m/z (%): 276 (3), 275 (4), 274 (30) M^+, 248 (7), 247 (10), 246 (100), 170 (32), 143 (7), 119 (6), 78 (8), 57 (7), 55 (5), 43 (6).
18: IR (cm^{-1}): 2940 (CH alifat), 2220 (C≡N), 1650 (C=C). ^{1}H NMR ($CDCl_3$): 2.30–2.35 (m, 2 H, CH_2), 3.01 (t, J = 6 Hz, 2 H, CH_2), 3.21 (t, J = 7 Hz, 2 H, CH_2), 4.00 (s, 3 H, NCH_3), 7.26 (d, d, J_1J_2 = 5 Hz, 1 H, C-6), 8.06 (d, J = 7 Hz, 1 H, C-7), 8.42 (d, J = 5 Hz, 1 H, C-5). MS, m/z (%): 290 (7), 289 (12), 288 (100) M^+, 255 (9), 246 (19), 243 (8), 242 (47), 241 (98), 214 (15), 213 (10), 196 (24), 170 (17), 78 (16).
19: IR (cm^{-1}): 2940 (CH alifat), 2220 (C≡N), 1660 (C=C). ^{1}H NMR ($CDCl_3$): 2.11 (s, 4 H, CH_2), 3.10 (t, J = 4 Hz, 2 H, CH_2), 3.22 (t, J = 4 Hz, 2 H, CH_2), 3.95 (s, 3 H, NCH_3), 7,26 (d, d, J_1J_2 = 4 Hz, 1 H, C-6), 8.07 (d, J = 6 Hz, 1 H, C-7), 8.43 (d, J = 3 Hz, 1 H, C-5). MS, m/z (%): 304 (2), 303 (4), 302 (26) M^+, 246 (8), 216 (11), 215 (58), 214 (100), 213 (11), 170 (11), 92 (8), 91 (11), 78 (11), 55 (7), 41 (7).

3.6. 2-[(3-Phenyl-4-oxothiazolidin-2-ylidene)cyanomethyl]-3-methyl-3H-imidazo[4,5-b]pyridine (**20**)

2-(3-Methyl-3H-imidazo[4,5-b]pyridine-2-yl)-3-anilino-3-ethoxycarbonylmethylenothiocrylonitrile (**21**)

2-[(3-Methyl-4-oxothiazolidin-2-ylidene)cyanomethyl]-3-methyl-3H-imidazo[4,5-b]pyridine (**22**)

Method A: The same procedure as for **11**–**14** was carried out using chloroacetic chloride (for **20** and **22**) or ethyl chloroacetate (for **21**) as the halogenated compounds.
Method B: To a suspension of **3** or **5** (0.001 mol) in abs. EtOH (10 ml) ethyl bromoacetate (0.001 mol) was added. The reaction mixture was heated under reflux for 8 h and then cooled. The resulting precipitate was filtered off and recrystallized. Compound **20** was also obtained when **21** (0.001 mol) in EtOH (10 ml) was heated under reflux for 8 h.
20: IR (cm^{-1}): 2220 (C≡N), 1750 (C=O), 1560 (C=C). ^{1}H NMR (DMSO-d_6): 3.78 (s, 3 H, NCH_3), 4.12 (s, 2 H, CH_2), 7.33 (d, d, J_1J_2 = 5 Hz, 1 H, C-6), 7.62 (s, 5 H, ar), 8.08 (d, J = 7 Hz, 1 H, C-7), 8.39 (d, J = 4 Hz, 1 H, C-5). MS m/z (%): 349 (6), 348 (25), 347 (100) M^+, 319 (62), 300 (37), 275 (71), 274 (38), 273 (24), 272 (10), 171 (12), 78 (24), 77 (81), 51 (43).
21: IR (cm^{-1}): 3430 (NH), 2220 (C≡N), 1730 (C=O), 1580 (C=C), 1310 (C–O–C). ^{1}H NMR (DMSO-d_6): 1.15 (t, J = 7 Hz, 3 H, CH_3), 3.71 (s, 3 H, NCH_3), 3.77 (s, 2 H, S–CH_2), 4.07 (q, J = 7 Hz, 2 H, O–CH_2), 6.92 (t, J = 6 Hz, 1 H, C-6), 7.10–7.20 (m, 5 H, ar), 7.91 (d, J = 7 Hz, 1 H, C-7), 8.22 (d, J = 4 Hz, 1 H, C-5). Ms, m/z (%): 395 (1), 394 (3), 393 (15) M^+, 275 (44), 274 (100), 273 (10), 203 (5), 197 (5), 171 (23), 170 (5), 103 (8), 93 (6), 78 (12), 77 (29), 51 (15), 47 (8).
22: IR (cm^{-1}): 2960, 2910 (CH_3, CH alifat), 2220 (C≡N), 1730 (C=O), 1610 (C=C). ^{1}H NMR ($CDCl_3$ + TFA): 3.82 (s, 3 H, NCH_3), 4.08 (s, 2 H, CH_2–), 4.22 (s, 3 H, NCH_3), 7.78 (d, d, J_1J_2 = 5 Hz, 1 H, C-6), 8.49 (d, J = 8 Hz, 1 H, C-7), 8.82 (d, J = 4 Hz, 1 H, C-5). MS, m/z (%): 287 (4), 286 (11), 285 (100) M^+, 243 (53), 242 (10), 212 (11), 211 (10), 210 (11), 197 (13), 196 (11), 146 (10), 78 (11).

Acknowledgements: Antimycobacterial data were provided by the U. S. Tuberculosis Antimicrobial Acquisition and Coordinating Facility (TAACF), NIAID/NIH Contract No. N01-AI-45246. The author is grateful to Dr. Joseph A. Maddry, manager of the TAACF, for his help in screening of the compounds under study and to Dr. Pawel Sowiński, a head of the Inter-University NMR Laboratory in Gdańsk for helpful discussion.

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Received April 17, 2000
Accepted May 25, 2000

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