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α-Aminoazoles in Synthesis of Heterocycles: III.* 4-Trifluoromethylpyrazolo[3,4-*b*]pyridines: Synthesis and Structure

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Abstract—Cyclocondensation of N-substituted 5-aminopyrazoles with fluorinated 1,3-diketones yielded 4-trifluoromethyl-substituted pyrazolo[3,4-*b*]pyridines as the only reaction products. The regiostructure of compounds obtained was proved by ^{1}H and ^{13}C NMR homo- and heteronuclear correlation spectroscopy. Characteristic chemical shifts in the ^{13}C NMR spectra of regioisomeric pyrazolo[3,4-*b*]pyridines were established.

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Cyclocondensations of aminopyrazoles with 1,3-dielectrophiles are extensively used for preparation of bicyclic nitrogen heterocycles that are biologically active substances possessing antioxidant, enzymatic, fungicidal, antibacterial, antiphlogistic, and sedative-hypnotic actions [2–7], some among them have found application in pharmacology [8]. The problem of regiodirection of the reaction is still urgent for the molecules of 3(5)-aminopyrazoles and 1,3-dielectrophiles contain nonequivalent reaction sites.

It is known that in the reaction of N*1*-substituted 5-aminopyrazoles with 1,3-dielectrophiles formed substituted pyrazolo[3,4-*b*]pyridines; as bifunctional reagents 1,3-ketoesters [9, 10], symmetric 1,3-diketones, among them hexafluoroacetylacetone [10–12] were employed. However the application of unsymmetrical 1,3-diketones to the synthesis of pyrazolopyridines is poorly documented evidently because two regioisomeric products may form in the reaction. In this connection a special interest can be attracted by pyrazolopyridines containing a trifluoromethyl group capable of modifying the chemical reactivity and biological action of the heterocycle [13].

The unambiguous establishment of the regiostructure of polycyclic nitrogen heterocycles is a complex problem and as we already have stated before [1] the interpretation of experimental findings may lead to an erroneous conclusion [14, 15].

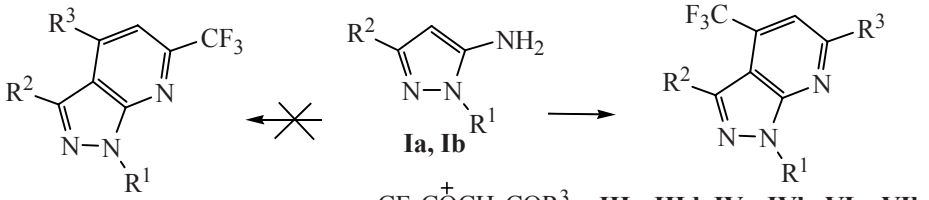
* For communication, II see [1].

The target of this study was the investigation of the direction of reaction between N-substituted aminopyrazoles and trifluoromethyl-containing 1,3-diketones and establishing characteristic spectral distinctions of individual regioisomers.

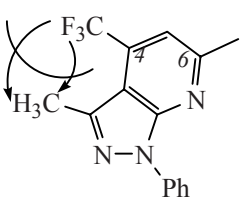
We studied the reactions of N*1*-substituted 5-aminopyrazoles **Ia–Il** with trifluoromethyl-containing 1,3-diketones **IIa–IIf**. It was established that the reactions proceeded regiospecifically giving 4-trifluoromethyl-containing pyrazolo[3,4-*b*]pyridines notwithstanding the character of substituents at the atoms N*1* (CH_2Ph, Ph) and C*3* of aminopyrazole (R^2 = Me, Ar), and the substituent in diketone (R^3 = Me, *t*-Bu, Ar, Ht). Reaction was performed by melting or boiling in acetic acid and resulted in over 90% yield.

The structure of pyrazolo[3,4-*b*]pyridines obtained **III–VI** was proved by means of ^{1}H and ^{13}C NMR spectroscopy. The position of the trifluoromethyl group at the C*4* atom was unambiguously established from the observed long-range coupling constants between the fluorine atoms of the trifluoromethyl group and the protons and carbon atoms of the substituent R^2 (CH_3, C^{o}H) in the position *3* of pyrazolopyridines **IIIa–IIId**.

In the ^{1}H NMR spectra of reaction products obtained from 3-methylaminopyrazoles **Ia–Ie** and trifluoromethyl-containing 1,3-diketones **IIa–IIf** appeared a quartet signal of the protons of methyl group with a coupling constant $^6J(CF_3–CH_3)$ 1.6 Hz, and in the

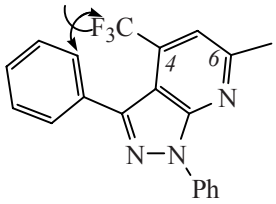


I, R^1 = Ph, R^2 = Me (**a**), 4-XC_6H_4 , X = MeO (**b**), Me (**c**), H (**d**), Cl (**e**); R^1 = Bn, R^2 = 4-$MeOC_6H_4$ (**f**), Ph (**g**); **II**, R^3 = Me (**a**), *t*-Bu (**b**), C_4H_3S (**c**), 4-YC_6H_4, Y = *i*-PrO (**d**), H (**e**), Br (**f**); **III**, R^1 = Ph, R^3 = Me, R^2 = Me (**a**), 4-XC_6H_4 , X = Me (**b**), H (**c**), Cl (**d**); **IV**, R^1 = R^3 = Ph, R^2 = Me (**a**), 4-XC_6H_4 , X = MeO (**b**), Me (**c**), H (**d**), Cl (**e**); R^1 = R^2 = Ph, R^3 = 4-*i*-$PrOC_6H_4$ (**f**); R^1 = Bn, R^2 = R^3 = Ph (**g**); R^2 = 4-$MeOC_6H_4$, R^3 = 4-BrC_6H_4 (**h**); **V**, R^1 = Bn, R^2 = 4-$MeOC_6H_4$, R^3 = *t*-Bu; **VI**, R^1 = Ph, R^3 = C_4H_3S, R^2 = Me (**a**), Ph (**b**).



^{1}H NMR: $^6J(C\underline{F}_3–C\underline{H}_3)$ 1.6 Hz

^{13}C NMR: $^5J(C\underline{F}_3–\underline{C}H_3)$ 3.5 Hz



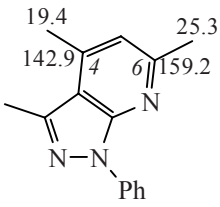
^{1}H NMR: $\delta(H^o)$ 7.64 ppm

^{13}C NMR: $^6J(C\underline{F}_3–\underline{C}^o)$ 1.7 Hz

^{13}C NMR spectra the carbon atom of the methyl gave rise to a quartet with a coupling constant $^5J(CF_3–CH_3)$ 3.5 Hz due to the through-space interaction of closely located CF_3 and CH_3 groups. In the ^{13}C NMR spectra of 3-phenylpyrazolopyridines a quartet signal was observed from the *ortho*-carbon atom of the phenyl group [$^6J(CF_3–C^o)$ 1.7 Hz] also indicating that the trifluoromethyl group was attached to C^4 atom of the pyridine ring.

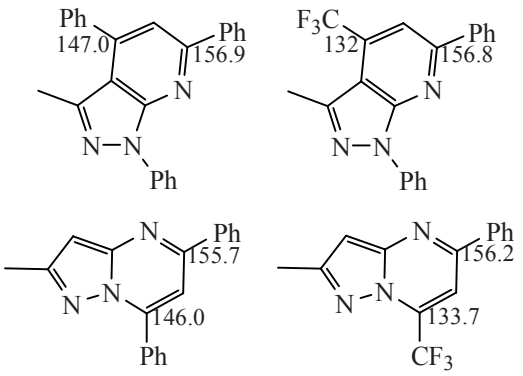
The chemical shift of the carbon atom C^4CF_3 (fragment –C=C–CF_3) is characteristic for the whole series of the trifluoromethyl-containing pyrazolopyridines and equals 132–133 ppm. At the same time the chemical shift of the carbon atom C^6CF_3 [fragment –C(CF_3)=N] revealed in the analysis of the ^{13}C NMR spectrum of methyl-4,6-bis(trifluoromethyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine (**VII**) appears significantly downfield (~147 ppm). It turned out that the chemical shifts of carbons in the fragments –C(CF_3)=N– and –C=C–CF_3 are virtually identical for pyrazolo[3,4-*b*]-pyridines, pyrazolo[1,5-*a*]-pyrimidines [15], and triazolo-[1,5-*a*]pyrimidines [16] and consequently they are sufficiently characteristic and can be used for elucidating the position of the CF_3 group in the heterocyclic compounds containing the mentioned fragments.

The ^{13}C NMR spectrum of 3,6-dimethyl-4-trifluoromethyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine (**IIIa**) was registered without decoupling from protons, and it permitted the assignment of signals from all carbon atoms and unambiguous establishment of the location of two methyl (C^3CH_3, C^6CH_3) and a trifluoromethyl (C^4CF_3) groups. The signal of atom C^3CH_3 at 14.77 ppm appeared as a quartet of quartets with a coupling constant $^5J_{C–F}$ 3.6, $^1J_{C–H}$ 128.6 Hz, and the signal of the carbon C^6CH_3 at 25.47 ppm was observed as a quartet of doublets ($^1J_{C–H}$ 127.9, $^3J_{C–H}$ 4.4 Hz). The observed long-range coupling constants $^3J(CF_3–C)$ for atoms C^{3a} (109.64 ppm, $^3J_{C–F}$ ~3 Hz) and C^5 (114.15 ppm, $^3J_{C-F}$ 4.4 Hz) confirm the position of the trifluoromethyl froup at the atom C^4 of the pyridine ring.



The chemical shifts of proton and carbon signals of groups C^4CH_3 [fragment –C=C–CH_3] and C^6CH_3 [fragment –C(CH_3)=N] were unambiguously established by an example of 3,4,6-trimethylpyrazolo-[3,4-*b*]pyridine (**VIII**) by using COLOC pulse sequence. The analysis of spectra obtained demonstrated that the CH_3 group whose signals appeared in the ^{1}H and ^{13}C NMR spectra at δ_H 2.65 and δ_C 25.3 ppm was located at the atom C^6 (δ_C 159.2 ppm), and the CH_3 group having chemical shifts of signals δ_H 2.75 and δ_C 19.4 ppm, at the atom C^4 (δ_C 142.9 ppm). It was revealed from the ^{13}C NMR spectra of pyrazolo-pyridines **IIIa–IIId** that the chemical shifts of carbon signals of methyl groups and pyridine ring (C^6CH_3) were virtually constant for all compounds **III** and coincided with the corresponding values of the C^6CH_3 group of 3,4,6-trimethylpyrazolo[3,4-*b*]pyridine (**VIII**).

Thus the above reasoning permitted unambiguous establishing of the position of the trifluoromethyl group in compounds **III–VI** at the atom C^4, and therefore the phenyl group of compounds **IVa–IVh** and the thienyl



group of compounds **VIa** and **VIb** were attached to atom C^6.

In the spectra of compounds **IVa–IVh** the chemical shift of the atom C^6 [fragment $-C^6(C_6H_5)=N$] is virtually identical and coincides with the chemical shift of the C^6 in the spectrun of 3-methyl-1,4,6-triphenyl-1*H*-pyrazolo-[3,4-*b*]pyridine (**IX**) and also with the characteristic chemical shifts of the fragment C–C(Ph)=N of a series of pyrazolo[1,5-*a*]pyrimidines [15].

At the same time the value of the chemical shift of the carbon atom C^4Ph [147.0 ppm, fragment C–C(Ph)=C] obtained from the ^{13}C NMR spectrum of compound **VIII** differed by 10 ppm from the chemical shift of the carbon atom $C^6C_6H_5$ [156.9 ppm, fragment C–C(Ph)=N].

The characteristic chemical shifts of the carbon atoms of the regioisomeric pyrazolopyridines make it possible to establish unambiguously the structure of regioisomers (see the table).

Thus by cyclocondensation of N-substituted 5-aminopyrazoles with fluorinated 1,3-diketones we synthesized 4-trifluoromethyl-substituted pyrazolo[3,4-*b*]pyridines as the only reaction products. The characteristic chemical shifts of carbon signals in the ^{13}C NMR spectra of substituted pyrazolo[3,4-*b*]pyridines were estimated permitting establishing the regioisomeric structure of the compounds.

EXPERIMENTAL

^1H and ^{13}C NMR spectra were registered on a spectrometer Bruker DPX-300 (300.13 and 75.47 MHz respectively) at 22°C. Chemical shifts were measured from the signals of deuterated solvent [$CDCl_3$ (7.28 and 76.90 ppm), DMCO-d_6 (2.50 and 39.50 ppm)]. A Bruker program package for pulse sequence COLOC was used with optimization on 8 Hz.

Characteristic chemical shifts of carbon atoms in ^{13}C NMR spectra of pyrazolo[3,4-*b*]pyridines, δ, ppm

Fragment	C^6	CH_3	Fragment	C^4	CH_3
$C^6(Me)=N$	~159.5	25–26	$C^4(Me)=C$	~143.5	19–20
$C^6(Ph)=N$	~157.0		$C^4(Ph)=C$	~147.5	
$C^6(CF_3)=N$	~147.5		$C^4(CF_3)=C$	~132–133	

3(5)-Aminopyrazoles **Ia–Ih** were prepared as described in [17, 18], fluorocontaining 1,3-diketones **IIa–IIc** were synthesized by procedure [19].

Pyrazolo[3,4-*b*]pyridines. *a*. Equimolar amounts of compounds **I** and **II** dissolved in acetic acid were mixed at 18–20°C, then the mixture was boiled for 2–4 h, the acetic acid was distilled off at a reduced pressure, and the residue was recrystallized from ethanol.

b. Equimolar amounts of compounds **I** and **II** were mixed and heated at 120–140°C for 10–30 min. Compounds obtained were recrystallized from ethanol.

3,6-Dimethyl-4-trifluoromethyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine (IIIa). Yield 90%, mp 61.5°C. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.71 d (3H, C^6CH_3, $^4J_{H-H}$ 1.0 Hz), 2.78 s (3H, C^3CH_3), 7.32 c (1H, C^5H), 7.30–8.26 m (5H, C_6H_5). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm (reported coupling constants were obtained from the ^{13}C NMR spectrum registered without decoupling from protons): 14.77 q.q (C^3CH_3, $^1J_{C-H}$ 128.6, $^5J_{C-F}$ 3.6 Hz), 25.47 q.d (C^6CH_3, $^1J_{C-H}$ 127.9, $^3J_{C-H}$ 4.4 Hz), 109.64 q (C^{3a}, $^3J_{C-F}$ ~3 Hz), 114.15 d.q.q (C^5, $^1J_{C-H}$ 164.9, $^3J_{C-H}$ 4.3, $^3J_{C-F}$ 4.4 Hz), 122.70 q.d (CF_3, $^1J_{C-F}$ 273.2, $^3J_{C-H}$ 5.1 Hz), 131.84 q (C^4CF_3, $^2J_{C-F}$ 34.9 Hz), 141.36 q (C^3, $^2J_{C-H}$ 7.5 Hz), 152.21 s (C^{7a}), 159.48 q.d (C^6, $^2J_{C-H}$ 5.8, $^2J_{C-H}$ 2.2 Hz), 121.07, 126.47, 129.40, 139.49 (Ph). Found, %: C 55.30; H 3.30. $C_{15}H_{12}F_3N_3$. Calculated, %: C 61.85; H 4.15.

6-Methyl-3-(*p*-tolyl)-4-trifluoromethyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine (IIIb). Yield 93%, mp 145°C. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.48 s (3H, CH_3), 2.83 s (3H, C^6CH_3), 7.39 s (1H, C^5H), 7.30–7.60, 8.30–8.33 m (9H, Ph, Ar). ^{13}C NMR spectrum, δ, ppm: 21.80 (CH_3), 25.46 (C^6CH_3), 109.25 (C^{3a}), 115.40 q (C^5, $^3J_{C-F}$ 5.0 Hz), 122.89 q (CF_3, $^1J_{C-F}$ 273.7 Hz), 132.47 q (C^4CF_3, $^2J_{C-F}$ 34.8 Hz), 145.43 (C^3), 151.96 (C^{7a}), 159.68 (C^6), 122.38, 126.85, 129.03, 129.40, 130.08, 138.97, 139.45 (Ph, Ar). Found, %: C 68.43; H 4.59. $C_{21}H_{16}F_3N_3$. Calculated, %: C 68.66; H 4.39.

6-Methyl-4-trifluoromethyl-1,3-diphenyl-1*H*-pyrazolo[3,4-*b*]pyridine (IIIc). Yield 95%, mp 125°C.

^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.83 s (3H, C^6CH_3), 7.39 s (1H, C^{5}H), 7.34–8.33 m (9H, Ph, Ar). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 25.48 (C^6CH_3), 109.19 (C^{3a}), 115.52 q (C^5, $^3J_{C–F}$ 5.0 Hz), 122.73 q (CF_3, $^1J_{C–F}$ 273.7 Hz), 132.44 q (C^4CF_3, $^2J_{C–F}$ 34.7 Hz), 145.33 (C^3), 151.95 (C^{7a}), 159.82 (C^6), 122.44, 126.95, 128.32, 129.16, 129.42, 130.25, 133.87, 139.40 (Ph, Ar). Found, %: C 68.10; H 4.20. $C_{20}H_{14}F_3N_3$. Calculated, %: C 67.98; H 3.99.

6-Methyl-4-trifluoromethyl-1-phenyl-3-(4-chlorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine (IIId). Yield 95%, mp 122°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.83 s (3H, C^6CH_3), 7.44 s (1H, C^{5}H), 7.32–8.30 m (9H, 2Ar). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 25.50 (C^6CH_3), 100.98 (C^{3a}), 115.68 q (C^5, $^3J_{C–F}$ 5.0 Hz), 122.85 q (CF_3, $^1J_{C–F}$ 273.7 Hz), 132.23 q (C^4CF_3, $^2J_{C–F}$ 34.4 Hz), 144.08 (C^3), 151.93 (C^{7a}), 160.04 (C^6), 122.44, 127.12, 128.63, 129.47, 131.58, 132.05, 135.36, 139.25 (Ph, Ar). Found, %: C 62.10; H 3.60. $C_{20}H_{13}ClF_3N_3$. Calculated, %: C 61.95; H 3.38.

3-Methyl-4-trifluoromethyl-1,6-diphenyl-1*H*-pyrazolo[3,4-*b*]pyridine (IVa). Yield 91%, mp 151°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.76 s (3H, CH_3), 7.91 s (1H, C^{5}H), 7.31–8.36 m (10H, 2Ph). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.85 (CH_3), 110.44 (C^{3a}), 111.14 q (C^5, $^3J_{C–F}$ 4.4 Hz), 123.22 q (CF_3, $^1J_{C–F}$ 273.1 Hz), 132.53 q (C^4CF_3, $^2J_{C–F}$ 34.3 Hz), 141.55 (C^3), 152.37 (C^{7a}), 157.26 (C^6), 121.75, 126.45, 127.95, 129.42, 130.59, 138.31, 139.54 (2Ph). Found, %: C 67.69; H 4.15. $C_{20}H_{14}F_3N_3$. Calculated, %: C 67.98; H 3.99.

3-(4-Methoxyphenyl)-4-trifluoromethyl-1,6-diphenyl-1*H*-pyrazolo[3,4-*b*]pyridine (IVb). Yield 95%, mp 166°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.92 s (3H, CH_3O), 7.99 s (1H, C^{5}H), 7.04–8.44 m (14H, 2Ph, Ar). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 55.73 (CH_3O), 110.08 (C^{3a}), 112.42 q (C^5, ^3J_F 5.1 Hz), 122.86 q (CF_3, ^1J_F 273.0 Hz), 133.19 q (C^4CF_3, $^2J_{C–F}$ 34.3 Hz), 145.30 (C^3), 152.17 (C^{7a}), 157.47 (C^6), 113.88, 128.02, 131.56, 160.54 (Ar), 122.27, 126.84, 129.47, 139.48 (N^1 Ph), 125.80, 130.72, 138.24 (C^{6}Ph). Found, %: C 69.90; H 4.29. $C_{26}H_{18}F_3N_3O$. Calculated, %: C 70.11; H 4.07.

3-(*p*-Tolyl)-4-trifluoromethyl-1,6-diphenyl-1*H*-pyrazolo[3,4-*b*]pyridine (IVc). Yield 91%, mp 131°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.50 s (3H, CH_3), 8.00 s (1H, C^{5}H), 7.34–8.45 m (14H, 2Ph, Ar). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 21.85 (4-CH_3), 110.02 (C^{3a}), 112.40 q (C^5, $^3J_{C–F}$ 4.6 Hz), 122.96 q (CF_3, $^1J_{C–F}$ 273.5 Hz), 133.18 q (C^4CF_3, $^2J_{C–F}$ 34.4 Hz), 145.57 (C^3), 152.17 (C^{7a}), 157.47 (C^6), 126.84, 128.01, 129.12, 129.47, 130.54, 130.71, 138.24, 139.10, 139.52 (2Ph, Ar). Found, %: C 72.47; H 4.46. $C_{26}H_{18}F_3N_3$. Calculated, %: C 72.72; H 4.22.

4-Trifluoromethyl-1,3,6-triphenyl-1*H*-pyrazolo[3,4-*b*]pyridine (IVd). Yield 96%, mp 164°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 8.00 s (1H, C^{5}H), 7.37–8.44 m (15H, 3Ar). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 109.18 (C^{3a}), 111.74 q (C^5, $^3J_{C–F}$ 5.1 Hz), 122.17 q (CF_3, $^1J_{C–F}$ 273.0 Hz), 132.44 q (C^4CF_3, $^2J_{C–F}$ 34.7 Hz), 144.75 (C^3), 151.38 (C^{7a}), 156.82 (C^6), 126.18, 127.27, 127.63, 127.84, 128.73, 128.50, 129.51, 130.00, 132.68, 138.64, 137.44 (3Ph). Found, %: C 55.30; H 3.30. $C_{20}H_{13}BrF_3N_3$. Calculated, %: C 55.57; H 3.03.

4-Trifluoromethyl-3-(4-chlorophenyl)-1,6-diphenyl-1*H*-pyrazolo[3,4-*b*]pyridine (IVe). Yield 93%, mp 161–162°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 8.00 s (1H, C^{5}H), 7.36–8.41 m (14H, 2Ph, Ar). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 109.72 (C^{3a}), 12.67 q (C^5, $^3J_{C–F}$ 5.1 Hz), 122.86 q (CF_3, $^1J_{C–F}$ 273.0 Hz), 133.02 q (C^4CF_3, $^2J_{C–F}$ 34.3 Hz), 144.26 (C^3), 152.14 (C^{7a}), 159.82 (C^6), 122.33, 127.10, 128.03, 128.70, 129.52, 130.86, 131.60, 131.95, 135.47, 138.07, 139.31 (2Ph, Ar). Found, %: C 66.46; H 3.52. $C_{25}H_{15}ClF_3N_3$. Calculated, %: C 66.75; H 3.36.

6-(4-Isopropoxyphenyl)-4-trifluoromethyl-1,3-diphenyl-1*H*-pyrazolo[3,4-*b*]pyridine (IVf). Yield 94%, mp 152°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.45 d [9H, $(CH_3)_2$, $J_{H–H}$ 5.5 Hz], 4.69 septet [1H, $CH(CH_3)_2$, $J_{H–H}$ 5.5 Hz], 7.92 s (1H, C^{5}H), 7.28–8.08 m (13H, 2Ph, Ar). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 21.94 (CH_3), 70.00 (OCH), 108.86 (C^{3a}), 111.40 q (C^5, $^3J_{C–F}$ 5.6 Hz), 122.54 q (CF_3, $^1J_{C–F}$ 273.8 Hz), 132.50 q (C^4CF_3, $^2J_{C–F}$ 31.9 Hz), 145.02 (C^3), 151.74 (C^{7a}), 158.85 (C^6), 116.02, 120.71, 121.79, 126.30, 127.87, 128.71, 128.95, 129.01, 129.80, 133.14, 139.08, 160.00 (2Ph, Ar). Found, %: C 72.51; H 4.43. $C_{28}H_{22}F_3N_3O$. Calculated, %: C 71.03; H 4.68.

1-Benzyl-4-trifluoromethyl-3,6-diphenyl-1*H*-pyrazolo[3,4-*b*]pyridine (IVg). Yield 95%, mp 160°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 5.89 s (2H, CH_2), 7.94 s (1H, C^{5}H), 7.30–7.42, 7.45–7.61, 8.21–8.23 m (14H, 3Ph). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 51.63 (CH_2), 112.11 d.q (C^5), 108.22 (C^{3a}, $J_{C–H}$ 165.0, $^3J_{C–F}$ 5.0 Hz), 123.06 q (CF_3, $^1J_{C–F}$ 274.2 Hz), 132.99 q (C^4CF_3, $^2J_{C–F}$ 34.8 Hz), 144.32 (C^3), 152.44 (C^{7a}), 157.15 (C^6), 127.96, 128.34, 128.83, 129.08, 129.00, 129.44, 130.25,

130.62, 133.80, 137.11, 138.39 (3Ph). Found, %: C 72.51; H 4.43. $C_{26}H_{18}F_3N_3$. Calculated, %: C 72.72; H 4.22.

1-Benzyl-6-(4-bromophenyl)-3-(4-methoxyphenyl)-4-trifluoromethyl-1*H*-pyrazolo[3,4-*b*]pyridine (IVh). Yield 92%, mp 158°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.89 s (3H, OCH_3), 5.86 s (2H, CH_2,), 7.85 s (1H, C^5H), 7.28–8.08 m (13H, 3Ar). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 51.15 (CH_2), 55.21 (OCH_3), 108.05 (C^{3a}), 110.98 q (C^5, $^3J_{C–F}$ 5.0 Hz), 122.51 q (CF_3, $^1J_{C–F}$ 272.8 Hz), 132.32 q (C^4CF_3, $^2J_{C–F}$ 34.8 Hz), 143.72 (C^3), 151.88 (C^{7a}), 155.30 (C^6), 113.82, 124.79, 126.04, 128.33, 128.73, 129.06, 129.39, 131.43, 132.59, 137.03, 137.25, 159.93 (Ph, 2Ar). Found, %: C 72.51; H 4.43. $C_{27}H_{19}BrF_3N_3O$. Calculated, %: C 60.24; H 3.56.

1-Benzyl-6-*tert*-butyl-3-(4-methoxyphenyl)-4-trifluoromethyl-1*H*-pyrazolo[3,4-*b*]pyridine (V). Yield 91%, mp 113°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.54 s [1H, $(CH_3)_3$], 3.87 s (3H, OCH_3), 5.78 s (2H, CH_2), 7.50 s (1H, C^5H), 7.30–8.26 m (9H, Ph, Ar). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 30.11 [$(CH_3)_3$], 38.32 [$C(CH_3)_3$], 51.08 (CH_2), 55.18 (OCH_3), 106.94 q (C^{3a}, $^3J_{C–F}$ ~3 Hz), 110.47 (C^5, $^3J_{C–F}$ 5.0 Hz), 122.78 q (CF_3, $^1J_{C–F}$ 273.2 Hz), 131.72 q (C^4CF_3, $^2J_{C–F}$ 34.9 Hz), 143.17 (C^3), 169.49 (C^6), 113.26, 126.01, 127.75, 128.46, 128.59, 130.94, 136.76, 159.73 (Ph, Ar). Found, %: C 72.51; H 4.43. $C_{25}H_{24}F_3N_3O$. Calculated, %: C 68.32; H 5.50.

3-Methyl-6-(2-thienyl)-4-trifluoromethyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine (VIa). Yield 92%, mp 157°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.71 s (3H, CH_3), 7.16 m, 7.37 t ($J_{H–H}$ 7.0 Hz), 7.49 d (3H, C_3H_3S, $J_{H–H}$ 4.8 Hz), 7.50–8.03 (5H, Ph), 7.74 c (1H, C^5H). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.35 q (CH_3, $^3J_{C–F}$ 3.3 Hz), 109.43 q (C^5, $J_{C–F}$ 5.5 Hz), 109.80 (C^{3a}), 122.65 q (CF_3, $^1J_{C–F}$ 274.76 Hz), 132.02 q (C^4, $^2J_{C–F}$ 34.3 Hz), 141.23 (C^3), 151.38 (C^{7a}), 151.77 (C^6), 120.92, 128.94, 129.48, 139.06 (Ph), 125.88, 126.82, 128.30, 143.74 (C_4H_3S). Found, %: C 59.90; H 3.55. $C_{18}H_{12}F_3N_3S$. Calculated, %: C 60.16; H 3.37.

6-(2-Thienyl)-4-trifluoromethyl-1,3-diphenyl-1*H*-pyrazolo[3,4-*b*]pyridine (VIb). Yield 93%, mp 187°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 7.86 s (1H, C^5H), 7.20–7.67 m (13H, 2Ph, C_3H_3S). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 109.33 (C^{3a}), 110.83 q (C^5, $^3J_{C–F}$ 4.4 Hz), 122.30 q (CF_3, $^1J_{C–F}$ 275.32 Hz), 132.68 q (C^4, $^2J_{C–F}$ 33.7 Hz), 145.20 (C^3), 151.18 (C^{7a}), 152.12 (C^6), 121.54, 127.94, 128.84, 129.00, 129.80, 132.92, 138.98 (2Ph), 126.41, 127.14, 128.44, 143.62 (C_4H_3S). Found, %: C 65.25; H 3.57. $C_{23}H_{14}F_3N_3S$. Calculated, %: C 65.55; H 3.35.

3-Methyl-4,6-bis(trifluoromethyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine (VII). Yield 89%, mp 78–79°C [10]. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.79 s (3H, CH_3), 7.82 s (1H, C^5H), 7.40–8.27 m (5H, Ph). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.27 (CH_3), 109.57 (C^5, $^3J_{H–F}$ 2.8 Hz), 113.09 (C^{3a}), 120.00 q (CF_3, $^1J_{H–F}$ 273.7 Hz), 120.92 (CF_3, $^1J_{H–F}$ 273.6 Hz), 133.30 q (C^4CF_3, $^2J_{H–F}$ 36.0 Hz), 141.31 (C^3), 146.90 (C^6CF_3, ^2J_F 36.0 Hz), 150.33 (C^{7a}), 121.18, 126.71, 129.12, 138.28 (Ph).

3,4,6-Trimethyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine (VIII). Yield 87%, mp 127–128°C [9]. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.65 s (3H, C^6CH_3), 2.68 s (3H, C^3CH_3), 2.75 s (3H, C^4CH_3), 7.23–8.31 m (5H, C_6H_5). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm (reported coupling constants were obtained from the ^{13}C NMR spectrum registered without decoupling from protons): 15.76 q (C^3CH_3, $^1J_{C–H}$ 128.8 Hz), 19.36 q.d (C^4CH_3, $^1J_{C–H}$ 127.1, $^3J_{C–H}$ 4.1 Hz), 25.28 q.d (C^6CH_3, $^1J_{C–H}$ 127.1, $^3J_{C–H}$ 2.1 Hz), 114.99 s (C^{3a}), 119.02 m (C^5), 142.83 q (C^3, $^2J_{C–H}$ 8.7 Hz), 142.93 q (C^4, $^2J_{C–H}$ 8.0 Hz), 151.75 C (C^{7a}), 159.20 q (C^6, $^2J_{C–H}$ 8.0 Hz), 122.20, 125.57, 129.32, 140.22 (Ph).

3-Methyl-1,4,6-triphenyl-1*H*-pyrazolo[3,4-*b*]pyridine (IX). Yield 70%, mp 148°C. ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 15.80 (CH_3), 114.22 (C^5), 115.72(C^{3a}), 142.90 (C^3), 146.99 (C^4), 152.07 (C^{7a}), 156.86 (C^6), 121.37, 125.75, 128.01, 128.76, 129.14, 129.20, 129.37, 129.47, 129.85, 138.27, 139.58, 140.24 (3Ph). Found, %: C 82.91; H 5.47. $C_{25}H_{19}N_3$. Calculated, %: C 83.08; H 5.30.

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