Synthesis of substituted pyrido[1,2-*a*]pyrimidines from 2-arylmethylidene-3-fluoroalkyl-3-oxopropionates

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Cyclocondensation of 2-arylmethylidene-3-fluoroalkyl-3-oxopropionates with 2-aminopyridine occurs at both the polyfluoroacylvinyl and alkoxycarbonylvinyl fragments to give alkyl 4-aryl-2-polyfluoroalkyl-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxylates and 4-aryl-2-hydroxy-3-polyfluoroacyl-4*H*-pyrido[1,2-*a*]pyrimidines, respectively. When treated with copper(II) acetate, the pyrido[1,2-*a*]pyrimidines yield metal complexes.

Key words: cyclocondensation, regioisomerism, 2-arylmethylidene-3-fluoroalkyl-3-oxopropionate, 2-aminopyridine, pyrido[1,2-*a*]pyrimidine, complex formation.

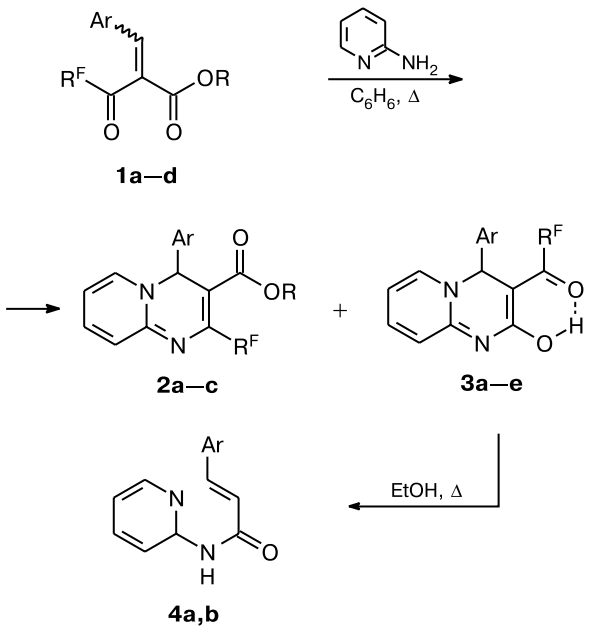
Pyrimidines are essential structural units found in natural compounds (nucleic acids, vitamin B_1), synthetic drugs (barbiturates), and chemotherapeutic preparations (fluorouracil).[1a,2] Interest in the synthesis of pyrimidine derivatives is due to their biological activities. 1,3-Dicarbonyl compounds and their derivatives are widely used as starting reagents for the synthesis of pyrimidines. Earlier,[3] we have found that 2-arylmethylidene-3-fluoroalkyl-3-oxopropionates react with 3-amino-1,2,4-triazole and 5-aminotetrazole to give 6-alkoxycarbonyl-7-alkyl(aryl)-5-fluoroalkyl-1,2,4-tri(tetr)azolo[1,5-*a*]pyrimidines.

In the present work, we studied reactions of 2-arylmethylidene-3-oxo-3-polyfluoroalkylpropionates **1** with 2-aminopyridine with the aim of obtaining heteroannelated pyrimidines.

We found that in contrast to the previous[3] transformations with aminoazoles, the cyclocondensation of esters **1a**—**d** with 2-aminopyridine is not regioselective since products of two types **2a**—**c** and **3a**—**e** were obtained (Scheme 1). The reactions between equimolar amounts of esters **1** and 2-aminopyridine were carried out in boiling anhydrous benzene. Monitoring of the process by TLC revealed the immediate formation of two products. In other solvents (ethanol, diethyl ether, and DMF), the reactions were less selective and yielded difficult-to-separate mixtures of products, the conversions of the starting esters **1** being incomplete. Note that heterocycles **2** and **3** were not obtained by three-component condensation of a 3-oxo ester, an aldehyde, and 2-aminopyridine (in contrast to analogous reactions with aminoazoles).[3]

2-Arylmethylidene-3-oxopropionates **1** contain three nonequivalent electrophilic reactive sites (fluoroacyl group, ester fragment, and C=C bond) that can be attacked by a nucleophile. At the same time, 2-aminopyridines in cyclocondensation with 1,3-dicarbonyl compounds and their derivatives can act as N,N- or N,C-dinucleophiles.[4—6] Thus, the reactions under study can theoretically yield eight heterocyclic structures, depending on

Scheme 1



R = Et, Ar = Ph, $R^F = HCF_2$ (**1a**, **2a**, **3a**), CF_3 (**1b**, **2b**, **3b**);
R = Et, Ar = $MeOC_6H_4$, $R^F = CF_3$ (**1c**, **3c**);
R = Me, Ar = Ph, $R^F = H(CF_2)_2$ (**1d**, **2c**, **3d**);
R = Me, Ar = $MeOC_6H_4$, $R^F = H(CF_2)_2$ (**1e**, **3e**);
Ar = Ph (**4a**), 4-$MeOC_6H_4$ (**4b**)

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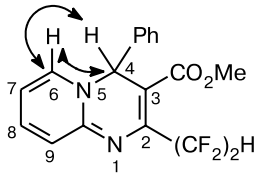
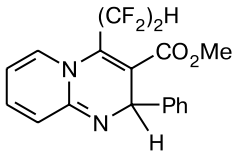
the electrophilic site in ester **1** under an initial attack by the amine and on the nucleophilic site (N or C) in 2-aminopyridine involved in subsequent cyclization.

Elemental analysis data and IR and ^{1}H NMR spectra suggest that products **2a—c** are alkoxycarbonylpyrido[1,2-*a*]pyrimidines formed by cyclocondensation of esters **1** through the polyfluoroacylvinyl fragment with the N,N-sites of 2-aminopyridine. However, the aforementioned data was insufficient for making our choice between two equiprobable structures **2A** and **2B**.



2A



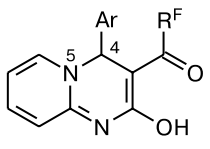
2B

The structures of compounds **2** were determined from the 2D ^{1}H—^{13}C HMBC NMR spectrum of product **2c**. An analysis of the 2D HMBC spectrum revealed that the signal at δ 138.03 (C(6)) shows a cross peak with the signal at δ 6.51 (s, H(4)) and the signal at δ 61.85 (C(4)) shows a cross peak with the signal at δ 8.18 (dd, H(6), $^3J_{H(6),H(7)}$ = 6.8 Hz, $^4J_{H(6),H(8)}$ = 1.7 Hz); this is unambiguous evidence for structure **2A**.

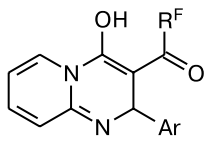
A comparison of the ^{1}H and ^{19}F NMR spectra of compound **2c** with those of products **2a,b** allowed us to assign to the latter the structures of alkyl 4-aryl-2-polyfluoroalkyl-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxylates, which form as the result of the initial addition of the amino group of 2-aminopyridine to the fluoroacyl fragment of ester **1** followed by cyclization *via* addition of the pyridine N atom to the C=C bond (see Scheme 1).

Such a reaction pathway is typical of 2-arylmethylidene-3-fluoroalkyl-3-oxopropionates **1**, which react with phenylhydrazine,[7] 3-amino-1,2,4-triazole, and 5-aminotetrazole[3] to form heterocycles. However, this is not the only reaction pathway for 2-aminopyridine since compounds **3** were also isolated from the reaction products, along with the expected pyrido[1,2-*a*]pyrimidines **2**.

According to elemental analysis data and IR and ^{1}H NMR spectra, products **3** are polyfluoroacylpyrido[1,2-*a*]pyrimidines, whose formation involves the alkoxycarbonylvinyl fragment of ester **1** and the N,N-sites of 2-aminopyrimidine. However, the spectral data were poorly informative, which made it difficult to choose between two alternative regioisomeric structures **3A** and **3B**.



3A



3B

The structures of heterocycles **3** were determined chemically. It was found that compounds **3a—e** are unstable and partially decompose in boiling ethanol to give (*E*)-*N*-(pyridin-2-yl)-3-arylprop-2-enamides **4a,b** (see Scheme 1). Their structures were proven by IR and ^{1}H and ^{13}C NMR spectroscopy. For more exact signal assignments in the ^{1}H and ^{13}C NMR spectra of compounds **4**, the 2D ^{1}H—^{13}C HSQC and 2D ^{1}H—^{13}C HMBC NMR spectra of compound **4b** were recorded. The 2D HSQC data allowed the assignment of the protonated C atoms, which were exactly located in the molecule from the 2D HMBC data (see Experimental and Table 1). Amides **4a,b** can be obtained only from pyrido[1,2-*a*]pyrimidines **3A** *via* their deacylation followed by cleavage of the C(4)—N(5) bond of the heterocycle, because aromatic azaheterocycles, especially with the N atom as a bridgehead, undergoes relatively easy opening.[1b]

Therefore, heterocycles **3a—e** are 4-aryl-2-hydroxy-3-polyfluoroacyl-4*H*-pyrido[1,2-*a*]pyrimidines **3A**. Their formation involves initial addition of the amino group of 2-aminopyridine to the alkoxycarbonyl residue of ester **1** followed by cyclization through the C=C bond and the pyridine N atom (see Scheme 1).

It should be noted that the yields of the products varied with the size of the fluoroalkyl substituent. For instance, with an increase in its size, the yield of 3-polyfluoroacylpyrido[1,2-*a*]pyrimidine **3** increased, while the yield of 3-alkoxycarbonylpyrido[1,2-*a*]pyrimidine **2** decreased. Apparently, this is due to steric hindrances presented by a bulky polyfluoroalkyl substituent to 2-aminopyridine attacking the acyl C atom.

In addition, the yields of the products depend on the structure of the arylmethylidene substituent. For instance, we failed to isolate pyrido[1,2-*a*]pyrimidines **2d,e** (Ar = 4-MeOC$_6$H$_4$; R^F = CF$_3$ and R = Et (**d**) and R^F = H(CF$_2$)$_2$ and R = Me (**e**)) from the reaction products of 4-methoxyphenyl esters **1c,e**, although they were detected by TLC (products **2** and **3** have distinctive features). Apparently, heterocycles **2d,e** cannot be isolated from the reaction mixture in the individual state because of their high solubilities in virtually all the solvents used.

In contrast to 2-arylmethylidene-3-oxo-3-polyfluoroalkylpropionates **1**, the reaction of 2-phenylmethylideneacetoacetate yielded a difficult-to-separate mixture from which no individual products were isolated. Obviously, this is due to the lowered selectivities of these processes.

Pyrido[1,2-*a*]pyrimidines **2** and **3** can exhibit not only potential biological activity but also complexing properties. Indeed, when treated with copper(II) acetate, 2-hydroxy-3-polyfluoroacylpyrido[1,2-*a*]pyrimidines **3d,e** formed copper chelate complexes **5a,b** (Scheme 2) due to the presence of the enolized 1,3-dicarbonyl fragment.

Ethyl 4-phenyl-2-trifluoromethyl-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxylate **2b** reacted with copper(II) acetate to give complex **6**. Apparently, the py-

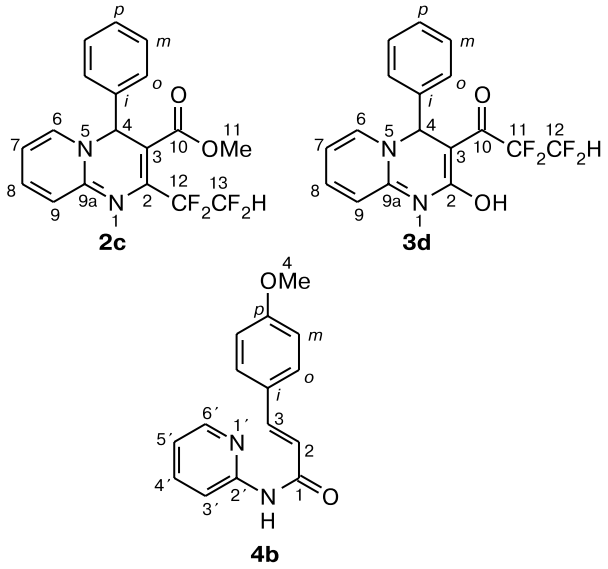
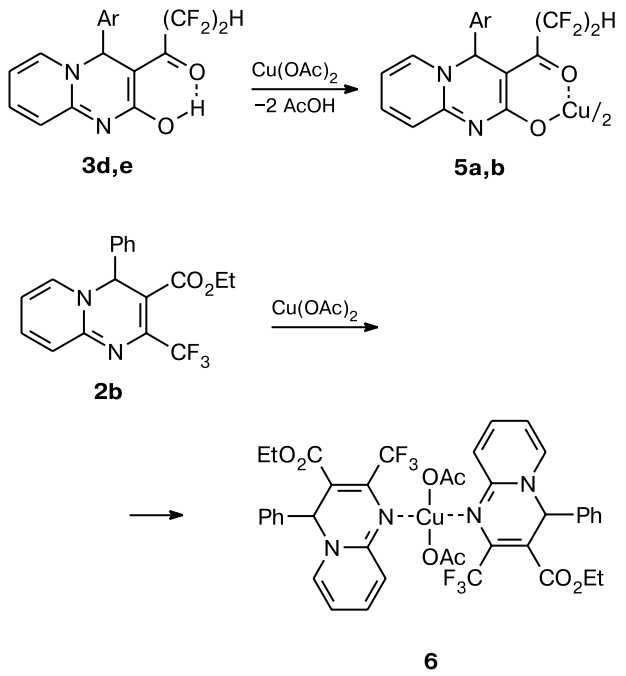


Table 1. ^{13}C NMR spectra of compounds **2c**, **3d**, and **4b** in DMSO-d_6

Atom	δ ($J_{C,F}$/Hz)		
	2c	**3d**	**4b**
C(1)	—	—	164.39
C(2)	147.13 (t, $^2J_{C,F}$ = 25.4)	160.22	119.33
C(3)	96.66	86.44	140.69
C(4)	61.85	64.84	55.30
C(6)	138.03	140.00	—
C(7)	115.27	114.61	—
C(8)	139.58	144.37	—
C(9)	122.49	117.68	—
C(9a)	150.81 (dd, $^4J_{C,F}$ = 3.0, $^4J_{C,F}$ = 1.4)	148.48	—
C(10)	164.13	170.98 (t, ^2J = 24.8)	—
C(11)	51.44	110.9 (tt, ^1J = 248.2, ^2J = 29.5)	—
C(12)	113.25 (dddd, $^1J_{C,F}$ = 253.5, $^1J_{C,F}$ = 250.8, $^2J_{C,F}$ = 26.8, $^2J_{C,F}$ = 22.8)	112.9 (tt, ^1J = 251.4, ^2J = 29.4)	—
C(13)	110.20 (dddd, ^1J = 249.8, ^1J = 247.8, ^2J = 34.1, ^2J = 27.2)	—	—
C_i	140.79	140.66	127.19
C_o	125.98	125.41	129.43
C_m	128.87	128.72	114.45
C_p	128.70	128.02	160.70
C(2′)	—	—	152.27
C(3′)	—	—	113.57
C(4′)	—	—	138.07
C(5′)	—	—	119.25
C(6′)	—	—	148.00

Scheme 2



Ar = Ph (**3d**, **5a**), 4-$MeOC_6H_4$ (**3e**, **5b**)

ridine N atom is involved in the coordination with the metal.

Thus, we demonstrated that the cyclization of 2-arylmethylidene-3-fluoroalkyl-3-oxopropionates **1** with 2-aminopyridine occurs at both the fluoroacylvinyl and alkoxycarbonylvinyl fragments to give alkyl 4-aryl-2-polyfluoroalkyl-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxylates **2** and 4-aryl-2-hydroxy-3-polyfluoroacetyl-4*H*-pyrido[1,2-*a*]pyrimidines **3**, respectively. Compounds **2** and **3** form complexes with transition metal ions.

Experimental

IR spectra were recorded on a Perkin—Elmer Spectrum One spectrometer (Nujol, 400—4000 cm^{-1}). NMR spectra were recorded on Bruker DRX-400 (400 (^1H) and 100 MHz (^{13}C), $SiMe_4$ as the standard; 376 MHz (^{19}F), C_6F_6 as the standard) and Tesla BS-587A spectrometers (75.3 MHz (^{19}F), C_6F_6 as the standard). Elemental analysis was carried out on a Perkin—Elmer PE 2400 II CHNS-O analyzer. Mass spectra were recorded on a Varian MAT-311A instrument.

The starting 2-arylmethylidene-3-fluoroalkyl-3-oxopropionates **1a—e** were prepared according to known procedures.[8,9]

Reactions of 2-arylmethylidene-3-fluoroalkyl-3-oxopropionates 1 with 2-aminopyridine (general procedure). A mixture of ester **1** (0.01 mol) and 2-aminopyridine (0.01 mol, 0.94 g) in dry benzene (20 mL) was refluxed for 4—6 days. The precipitate that formed was filtered off and washed with boiling chloroform (for compounds **b,c**, with diethyl ether) to give compounds **3a—e**. The filtrate was concentrated and chromatographed on silica gel with chloroform as an eluent to give compounds **2a—c**.

Ethyl 2-difluoromethyl-4-phenyl-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxylate (2a). The yield was 42%, m.p. 236—238 °C. Found (%): C, 65.54; H, 4.93; F, 11.36; N, 8.29. $C_{18}H_{16}F_2N_2O_2$. Calculated (%): C, 65.45; H, 4.88; F, 11.50; N, 8.48. IR, ν/cm^{-1}: 3067, 3030 (C—H); 1684 (C=O); 1637, 1591 (C=C, C=N); 1131—1022 (C—F). ^{1}H NMR (DMSO-d$_6$), δ: 1.16 (t, 3 H, $CH_2C\underline{H}_3$, $^3J_{H,H}$ = 7.1 Hz); 4.08, 4.07 (both dq, 1 H each, $C\underline{H}_2CH_3$, $^2J_{H,H}$ = 10.8 Hz, $^3J_{H,H}$ = 7.1 Hz); 6.47 (d, 1 H, H(4), $J_{H,H}$ = 1.4 Hz); 6.77 (td, 1 H, H(7), $^3J_{H(7),H(6)}$ = $^3J_{H(7),H(8)}$ = 6.7 Hz, $^4J_{H(7),H(9)}$ = 1.0 Hz); 7.0 (dd, 1 H, H(9), $^3J_{H(9),H(8)}$ = 8.8 Hz, $^4J_{H(9),H(7)}$ = 1.0 Hz); 7.28—7.37 (m, 5 H, Ph); 7.38 (t, 1 H, $\underline{H}CF_2$, $^2J_{H,F}$ = 54.5 Hz); 7.57 (ddd, 1 H, H(8), $^3J_{H(8),H(7)}$ = 6.7 Hz, $^3J_{H(8),H(9)}$ = 8.8 Hz, $^4J_{H(8),H(6)}$ = 1.4 Hz); 8.06 (dd, 1 H, H(6), $^3J_{H(6),H(7)}$ = 6.7 Hz, $^4J_{H(6),H(8)}$ = 1.4 Hz). ^{19}F NMR (DMSO-d$_6$), δ: 41.83 (m, HCF_2, midpoint of the AB system).

Ethyl 4-phenyl-2-trifluoromethyl-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxylate (2b). The yield was 38%, m.p. 145—146 °C. Found (%): C, 62.33; H, 4.46; F, 16.14; N, 8.17. $C_{18}H_{15}F_3N_2O_2$. Calculated (%): C, 62.07; H, 4.34; F, 16.36; N, 8.04. IR, ν/cm^{-1}: 3031 (C—H); 1714 (C=O); 1636, 1583, 1530 (C=C, C=N); 1171—1085 (C—F). ^{1}H NMR (DMSO-d$_6$), δ: 1.17 (t, 3 H, $CH_2C\underline{H}_3$, $^3J_{H,H}$ = 7.1 Hz); 4.09 (q, 2 H, $C\underline{H}_2CH_3$, $^3J_{H,H}$ = 7.1 Hz); 6.53 (s, 1 H, H(4)); 6.89 (td, 1 H, H(7), $^3J_{H(7),H(6)}$ = $^3J_{H(7),H(8)}$ = 6.8 Hz, $^4J_{H(7),H(9)}$ = 1.1 Hz); 7.07 (dd, 1 H, H(9), $^3J_{H(9),H(8)}$ = 8.2 Hz, $^4J_{H(9),H(7)}$ = 1.1 Hz); 7.24—7.37 (m, 5 H, Ph); 7.65 (ddd, 1 H, H(8), $^3J_{H(8),H(9)}$ = 8.2 Hz, $^2J_{H(8),H(7)}$ = 6.8 Hz, $^4J_{H(8),H(6)}$ = 1.6 Hz); 8.16 (dd, 1 H, H(6), $^3J_{H(6),H(7)}$ = 6.8 Hz, $^4J_{H(6),H(8)}$ = 1.6 Hz). ^{19}F NMR (DMSO-d$_6$), δ: 105.49 (s, CF_3).

Methyl 4-phenyl-2-(2,2,3,3-tetrafluoroethyl)-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxylate (2c). The yield was 30%, m.p. 126—128 °C. Found (%): C, 58.89; H, 3.71; F, 20.55; N, 7.78. $C_{18}H_{14}F_4N_2O_2$. Calculated (%): C, 59.03; H, 3.85; F, 20.74; N, 7.65. IR, ν/cm^{-1}: 3037 (C—H); 1696 (C=O); 1635, 1569 (C=C, C=N); 1120—1077 (C—F). ^{1}H NMR (DMSO-d$_6$), δ: 3.63 (s, 3 H, OMe); 6.51 (s, 1 H, H(4)); 6.89 (ddd, 1 H, H(7), $^3J_{H(7),H(8)}$ = $^3J_{H(7),H(6)}$ = 6.8 Hz, $^4J_{H(7),H(9)}$ = 1.3 Hz); 6.92 (dddd, 1 H, $H(CF_2)_2$, $^2J_{H,F(2)B}$ = 54.3 Hz, $^2J_{H,F(2)A}$ = 52.1 Hz, $^3J_{H,F(1)A}$ = 8.8 Hz, $^3J_{H,F(1)B}$ = 2.3 Hz); 7.01 (dd, 1 H, H(9), $^3J_{H(9),H(8)}$ = 9.0 Hz, $^4J_{H(9),H(7)}$ = 1.3 Hz); 7.26—7.37 (m, 5 H, Ph); 7.64 (ddd, 1 H, H(8), $^3J_{H(8),H(9)}$ = 9.0 Hz, $^3J_{H(8),H(7)}$ = 6.8 Hz, $^4J_{H(8),H(6)}$ = 1.7 Hz); 8.18 (dd, 1 H, H(6), $^3J_{H(6),H(7)}$ = 6.8 Hz, $^4J_{H(6),H(8)}$ = 1.7 Hz). ^{19}F NMR (DMSO-d$_6$), δ: 26.53 (m, 2 F, $HC\underline{F}_2CF_2$, AB system, Δ_{2AB} = 3.78, J_{2AB} = 291.3 Hz, $^2J_{F(2B),H}$ = 54.3 Hz, $^2J_{F(2A),H}$ = 52.1 Hz, $^3J_{F(2A),F(1B)}$ = 15.3 Hz, $^3J_{F(2B),F(1A)}$ = 14.5 Hz, $^2J_{F(2B),F(1B)}$ = 8.2 Hz); 41.46 (dddd, 1 F, $HCF_2C\underline{F}_2$, J_{1AB} = 268.2 Hz, $^3J_{F(1B),F(2A)}$ = 15.3 Hz, $^3J_{F(1A),H}$ = 8.8 Hz, $^3J_{F(1B),F(2B)}$ = 8.2 Hz); 50.46 (dd, 1 F, $HCF_2C\underline{F}_2$, J_{1AB} = 268.2 Hz, $^3J_{F(2A),F(1B)}$ = 15.3 Hz). The ^{13}C NMR spectrum is given in Table 1.

3-Difluoroacetyl-2-hydroxy-4-phenyl-4*H*-pyrido[1,2-*a*]pyrimidine (3a). The yield was 47%, m.p. 246—248 °C. Found (%): C, 63.42; H, 3.84; F, 12.43; N, 9.13. $C_{16}H_{12}F_2N_2O_2$. Calculated (%): C, 63.58; H, 4.00; F, 12.56; N, 9.25. IR, ν/cm^{-1}: 3090 (C—H); 2690 (OH); 1660 (C=O); 1580, 1540, 1500 (C=C, C=N); 1100—1090 (C—F). ^{1}H NMR (DMSO-d$_6$), δ: 6.90 (s, 1 H, H(4)); 7.04 (t, 1 H, HCF_2, $^2J_{H,F}$ = 55.6 Hz); 7.09—7.37 (m, 7 H, H(7), H(9), Ph); 8.12 (t, 1 H, H(8), $^3J_{H(8),H(9)}$ = $^3J_{H(8),H(7)}$ = 7.3 Hz); 8.71 (dd, 1 H, H(6), $^3J_{H(6),H(7)}$ = 5.6 Hz, $^4J_{H(6),H(8)}$ = 1.5 Hz); 10.92 (br.s, 1 H, OH). ^{19}F NMR (DMSO-d$_6$), δ: 37.79 (d, HCF_2, $^2J_{F,H}$ = 55.6 Hz).

2-Hydroxy-4-phenyl-3-trifluoroacetyl-4*H*-pyrido[1,2-*a*]pyrimidine (3b). The yield was 25%, m.p. 235—238 °C. Found (%): C, 60.09; H, 3.48; F, 17.96; N, 8.68. $C_{16}H_{11}F_3N_2O_2$. Calculated (%): C, 60.00; H, 3.46; F, 17.80; N, 8.75. IR, ν/cm^{-1}: 3448, 3340, 2700 (OH); 3098 (C—H); 1677 (C=O); 1645, 1595, 1550 (C=C, C=N); 1202—1098 (C—F). ^{1}H NMR (DMSO-d$_6$), δ: 6.93 (s, 1 H, H(4)); 7.11 (m, 2 H, Ph); 7.27—7.37 (m, 5 H, H(7), H(9), Ph); 8.18 (ddd, 1 H, H(8), $^3J_{H(8),H(9)}$ = 8.7 Hz, $^3J_{H(8),H(7)}$ = 7.3 Hz, $^4J_{H(8),H(6)}$ = 1.4 Hz); 8.80 (br.d, 1 H, H(6), $^3J_{H(6),H(7)}$ = 6.5 Hz); 10.93 (s, 1 H, OH). ^{19}F NMR (DMSO-d$_6$), δ: 92.45 (s, CF_3).

2-Hydroxy-4-(4-methoxyphenyl)-3-trifluoroacetyl-4*H*-pyrido[1,2-*a*]pyrimidine (3c). The yield was 48%, m.p. 210—211 °C. Found (%): C, 58.17; H, 3.56; F, 16.48; N, 7.94. $C_{17}H_{13}F_3N_2O_3$. Calculated (%): C, 58.29; H, 3.74; F, 16.27; N, 8.00. IR, ν/cm^{-1}: 3087 (C—H); 3443, 2685 (OH); 1675 (C=O); 1645, 1596, 1552 (C=C, C=N); 1138—1200 (C—F). ^{1}H NMR (DMSO-d$_6$), δ: 3.70 (s, 3 H, OMe); 6.83 (s, 1 H, H(4)); 6.88, 7.10 (both d, 2 H each, C_6H_4, $^3J_{H,H}$ = 8.7 Hz); 7.29 (dd, 1 H, H(9), $^3J_{H(9),H(8)}$ = 8.8 Hz, $^4J_{H(9),H(7)}$ = 1.0 Hz); 7.33 (ddd, 1 H, H(7), $^3J_{H(7),H(6)}$ = 6.0 Hz, $^3J_{H(7),H(8)}$ = 7.0 Hz, $^4J_{H(7),H(9)}$ = 1.0 Hz); 8.14 (ddd, 1 H, H(8), $^3J_{H(8),H(9)}$ = 8.8 Hz, $^3J_{H(8),H(7)}$ = 7.0 Hz, $^4J_{H(8),H(6)}$ = 1.1 Hz); 8.82 (dd, 1 H, H(6), $^3J_{H(6),H(7)}$ = 6.0 Hz, $^4J_{H(6),H(8)}$ = 1.1 Hz); 10.90 (s, 1 H, OH). ^{19}F NMR (DMSO-d$_6$), δ: 92.42 (s, CF_3).

2-Hydroxy-4-phenyl-3-(2,2,3,3-tetrafluoropropionyl)-4*H*-pyrido[1,2-*a*]pyrimidine (3d). The yield was 56%, m.p. 245—247 °C. Found (%): C, 57.79; H, 3.49; F, 21.35; N, 7.96. $C_{17}H_{12}F_4N_2O_2$. Calculated (%): C, 57.96; H, 3.43; F, 21.57; N, 7.95. IR, ν/cm^{-1}: 3340, 2712 (OH); 3080 (C—H); 1655 (C=O); 1593, 1565, 1519 (C=C, C=N); 1129—1100 (C—F). ^{1}H NMR (DMSO-d$_6$), δ: 6.97 (s, 1 H, H(4)); 7.08 (dddd, 1 H, $(CF_2)_2H$, $^2J_{H,F(2A)}$ = 53.5 Hz, $^2J_{H,F(2B)}$ = 55.3 Hz, $^3J_{H,F(1B)}$ = 10.0 Hz, $^3J_{H,F(1A)}$ = 4.3 Hz); 7.09 (m, 2 H, Ph); 7.25—7.39 (m, 5 H, H(7), H(9), Ph); 8.19 (ddd, 1 H, H(8), $^3J_{H(8),H(9)}$ = 8.7 Hz, $^3J_{H(8),H(7)}$ = 7.3 Hz, $^4J_{H(8),H(6)}$ = 1.4 Hz); 8.83 (dd, 1 H, H(6), $^3J_{H(6),H(7)}$ = 6.8 Hz, $^4J_{H(6),H(8)}$ = 1.4 Hz); 10.92 (s, 1 H, OH). ^{19}F NMR (DMSO-d$_6$), δ: 24.78 (m, 2 F, $HC\underline{F}_2CF_2$, AB system, Δ_{2AB} = 2.46, J_{2AB} = 297.3 Hz, $^2J_{F(2A),H}$ = 53.5 Hz, $^2J_{F(2B),H}$ = 55.3 Hz, $^3J_{F(2A),F(1B)}$ = 11.5 Hz, $^3J_{F(2B),F(1A)}$ = 10 Hz); 40.97 (m, 2 F, $HCF_2C\underline{F}_2$, AB system, Δ_{1AB} = 5.89, J_{1AB} = 258.5 Hz, $^3J_{F(1A),F(2B)}$ = $^3J_{F(1B),F(2B)}$ = $^3J_{F(1B),H}$ = 10 Hz, $^3J_{F(1A),F(2A)}$ = $^3J_{F(1A),H}$ = 4.3 Hz). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 352 $[M]^+$ (3); 275 $[M - Ph]^+$ (4); 259 $[M - C_5H_4N - NH]^+$ (100); 223 $[M - CO(CF_2)_2H]^+$ (100); 102 $[CH - Ph]^+$ (10); 78 $[C_5H_4N]^+$ (9). The ^{13}C NMR spectrum is given in Table 1.

2-Hydroxy-4-(4-methoxyphenyl)-3-(2,2,3,3-tetrafluoropropionyl)-4*H*-pyrido[1,2-*a*]pyrimidine (3e). The yield was 52%, m.p. 224—225 °C. Found (%): C, 56.51; H, 3.87; F, 19.72; N, 7.26. $C_{18}H_{14}F_4N_2O_3$. Calculated (%): C, 56.55; H, 3.69; F, 19.88; N, 7.33. IR, ν/cm^{-1}: 3474, 3310, 2689 (OH); 3151, 3096 (C—H); 1660 (C=O); 1593, 1547, 1510 (C=C, C=N); 1121—1100 (C—F). ^{1}H NMR (DMSO-d$_6$), δ: 3.69 (s, 3 H, OMe); 6.87* (s, 1 H, H(4)); 6.87*, 7.09 (both d, 2 H each, C_6H_4, $^3J_{H,H}$ = 8.7 Hz); 7.12 (dddd, 1 H, $(CF_2)_2H$, $^2J_{H,F(2A)}$ = 53.4 Hz, $^2J_{H,F(2B)}$ = 54.6 Hz, $^3J_{H,F(1B)}$ = 9.4 Hz, $^3J_{H,F(1A)}$ = 2.5 Hz); 7.32 (br.d, 1 H, H(9), $^3J_{H(9),H(8)}$ = 8.6 Hz); 7.33 (br.t, 1 H, H(7), $^3J_{H(7),H(6)}$ = 6.9 Hz); 8.14 (br.t, 1 H, H(8), $^3J_{H(8),H(9)}$ = 8.6 Hz); 8.84 (br.d, 1 H, H(6), $^3J_{H(6),H(7)}$ = 6.9 Hz);

* The signals overlap.

10.89 (br.s, 1 H, OH). ^{19}F NMR (DMSO-d_6), δ: 23.50 (m, 2 F, $HC\underline{F}_2CF_2$, AB system, Δ_B = 2.26, J_{AB} = 297.8 Hz, $^2J_{F(2A),H}$ = 53.4 Hz, $^2J_{F(2B),H}$ = 54.6 Hz, $^3J_{F(2A),F(1B)}$ = 14.2 Hz, $J_{F(2B),F(1A)}$ = 12.8 Hz); 38.03 (ddd, 1 F, $HCF_2C\underline{F}_2$, $^2J_{F,F}$ = 258.7 Hz, $J_{F(1B),F(2A)}$ = 14.2 Hz, $^3J_{F(1B),H}$ = 9.4 Hz); 43.88 (dd, 1 F, $HCF_2C\underline{F}_2$, $J_{F,F}$ = 258.7 Hz, $J_{F(1A),F(2B)}$ = 12.8 Hz). MS (EI, 70 eV), *m*/*z* (I_{rel} (%)): 382 $[M]^+$ (1); 354 $[M - H_2CN]^+$ (2); 253 $[M - CO(CF_2)_2H]^+$ (100); 289 $[M - C_5H_4N - NH]^+$ (100); 132 $[CH - C_6H_4 - OMe]^+$ (15); 89 $[H(CF_2)_2]^+$ (7); 78 $[C_5H_4N]^+$ (39).

(*E*)-*N*-(Pyridin-2-yl)cinnamamide (4a). Compound **3d** (0.01 mol) was refluxed in ethanol (10 mL) for 2 h. The reaction mixture was concentrated and diethyl ether (10 mL) was added. The precipitate that formed was filtered off and recrystallized from hexane to give compound **4a** (1.86 g, 83%), m.p. 127—128 °C. Found (%): C, 74.62; H, 5.25; N, 12.30. $C_{14}H_{12}N_2O$. Calculated (%): C, 74.99; H, 5.39; N, 12.49. IR, ν/cm^{-1}: 3324, 1578 (NH); 3102 (C—H); 1694 (C=O, amide); 1647, 1634 (C=C, C=N). ^{1}H NMR (DMSO-d_6), δ: 7.07 (d, 1 H, H(2), $^3J_{H(2),H(3)}$ = 15.8 Hz); 7.13 (ddd, 1 H, H(5′), $^3J_{H(5'),H(4')}$ = 7.3 Hz, $^3J_{H(5'),H(6')}$ = 4.9 Hz, $^4J_{H(5'),H(3')}$ = 1.0 Hz); 7.44 (m, 3 H, Ph); 7.62 (m, 2 H, Ph); 7.65 (d, 1 H, H(3), $^3J_{H(3),H(2)}$ = 15.8 Hz); 7.82 (ddd, 1 H, H(4′), $^3J_{H(4'),H(3')}$ = 8.4 Hz, $^3J_{H(4'),H(5')}$ = 7.3 Hz, $^4J_{H(4'),H(6')}$ = 1.9 Hz); 8.25 (br.d, 1 H, H(3′), $^3J_{H(3'),H(4')}$ = 8.4 Hz); 8.35 (ddd, 1 H, H(6′), $^3J_{H(6'),H(5')}$ = 4.9 Hz, $^4J_{H(6'),H(4')}$ = 1.9 Hz, $^5J_{H(6'),H(3')}$ = 1.0 Hz); 10.70 (s, 1 H, NH).

(*E*)-*N*-(Pyridin-2-yl)-3-(4-methoxyphenyl)prop-2-enamide (4b) was obtained analogously from compound **3e** (0.01 mol). The yield of compound **4b** was 1.74 g (80%), m.p. 120—122 °C. Found (%): C, 70.79; H, 5.66; N, 10.99. $C_{12}H_{13}N_2O_2$. Calculated (%): C, 70.85; H, 5.55; N, 11.02. IR, ν/cm^{-1}: 3244 (NH); 3042 (C—H); 1693 (C=O, amide); 1629, 1605 (C=C, C=N). ^{1}H NMR (DMSO-d_6), δ: 3.81 (s, 3 H, OMe); 6.91 (d, 1 H, H(2), $^3J_{H(2),H(3)}$ = 15.6 Hz); 7.02 (d, 2 H, C_6H_4, $^3J_{H,H}$ = 8.9 Hz); 7.11 (ddd, 1 H, H(5′), $J_{H(5'),H(4')}$ = 7.2 Hz, $J_{H(5'),H(6')}$ = 4.9 Hz, $J_{H(5'),H(3')}$ = 1.1 Hz); 7.57 (d, 2 H, C_6H_4, $^3J_{H,H}$ = 8.9 Hz); 7.59 (d, 1 H, H(3), $^3J_{H(3),H(2)}$ = 15.6 Hz); 7.80 (ddd, 1 H, H(4′), $^3J_{H(4'),H(3')}$ = 8.5 Hz, $^3J_{H(4'),H(5')}$ = 7.2 Hz, $^4J_{H(4'),H(6')}$ = 1.9 Hz); 8.24 (ddd, 1 H, H(3′), $^3J_{H(3'),H(4')}$ = 8.5 Hz, $J_{H(3'),H(5')}$ = 1.1 Hz, $J_{H(3'),H(6')}$ = 0.9 Hz); 8.34 (ddd, 1 H, H(6′), $J_{H(6'),H(5')}$ = 4.9 Hz, $J_{H(6'),H(4')}$ = 1.9 Hz, $J_{H(6'),H(3')}$ = 0.9 Hz); 10.59 (s, 1 H, NH). MS (EI, 70 eV), *m*/*z* (I_{rel} (%)): 254 $[M]^+$ (29); 226 $[M - H_2CN]^+$ (14); 161 $[M - C_5H_4NNH]^+$ (100); 133 $[C_6H_4 - OMe - CH=CH]^+$ (28); 77 $[Ph]^+$ (9). The ^{13}C NMR spectrum is given in Table 1.

Synthesis of copper(II) complexes 5a,b and 6 (general procedure). A solution of compound **2** or **3** (0.01 mol) in acetone (5 mL) was mixed with copper(II) acetate dihydrate (0.005 mol) in water (5 mL). The resulting oil was subjected to extraction with chloroform. The solvent was removed and the solid residue was reprecipitated from acetone with water and dried *in vacuo*.

Bis{4-phenyl-3-(2,2,3,3-tetrafluoropropionyl)-4*H*-pyrido[1,2-*a*]pyrimidin-2-olato}copper(II) (5a). The yield was 90%, m.p. 224—226 °C. Found (%): C, 53.19; H, 3.05; F, 19.75; N, 7.17. $C_{34}H_{22}CuF_8N_4O_4$. Calculated (%): C, 53.30; H, 2.98; F, 19.84; N, 7.31. IR, ν/cm^{-1}: 1660 (C=O); 1594, 1563 (C=C, C=N); 1097—1166 (C—F).

Bis{4-(4-methoxyphenyl)-3-(2,2,3,3-tetrafluoropropionyl)-4*H*-pyrido[1,2-*a*]pyrimidin-2-olato}copper(II) (5b). The yield was 85%, m.p. 210—212 °C. Found (%): C, 52.45; H, 3.30; F, 18.20; N, 6.75. $C_{36}H_{28}CuF_8N_4O_6$. Calculated (%): C, 52.21; H, 3.41; F, 18.34; N, 6.77. IR, ν/cm^{-1}: 1636 (C=O); 1593, 1563 (C=C, C=N); 1180—1109 (C—F).

Bis(3-ethoxycarbonyl-4-phenyl-2-trifluoromethyl-4*H*-pyrido[1,2-*a*]pyrimidine)diacetatocopper(II) (6). The yield was 93%, m.p. 146—148 °C. Found (%): C, 54.25; H, 4.25; F, 13.21; N, 6.09. $C_{40}H_{36}CuF_6N_4O_8$. Calculated (%): C, 54.70; H, 4.13; F, 12.98; N, 6.38. IR, ν/cm^{-1}: 1714 (C=O); 1583, 1530 (C=C, C=N); 1179—1058 (C—F).

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