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Reactions of aromatic methyl ketimines with halonitriles as a new route to pyrimidines with two polyhaloalkyl groups

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Abstract—*N*-Isopropyl-(1-phenylethylidene)amine reacts with trichloroacetonitrile to give 1-azabutadiene derivative, which undergoes a double addition reaction with a variety of halonitriles affording fluoro- and chloro-containing pyrimidines. Pyrimidines with two polyhaloalkyl groups were obtained by the reaction of methyl ketimines with an excess of trichloroacetonitrile, trifluoroacetonitrile and 2,2,3,3-tetrafluoropropionitrile.

1. Introduction

The insertion of halogens into the α-position of aldehydes, ketones, esters, imines and nitriles activates molecules of these compounds with respect to nucleophilic reagents. It has previously been shown that the condensation of methyl ketones with fluoro- and chloro-containing ketones, esters and imidoyl chlorides (iodides) in the presence of bases affords β-hydroxyketones,[1] β-diketones[2,3] and β-aminovinyl ketones,[4,5] respectively. The latter were also obtained from the reaction of methyl ketones with halogenated nitriles.[6,7] Methyl ketimines react with fluorinated ketones and acyl fluorides without a catalyst at room temperature to form β-hydroxyimines[8,9] and β-aminovinyl ketones,[10] but their reactions with fluorinated esters and imidoyl chlorides proceed in the presence of diisopropylamide lithium to give β-aminovinyl ketones[4,11] and β-diimines,[4] which were exclusively isolated in the vinylogous amidine form (β-aminovinyl imines). Non-fluorinated diimines were obtained by reaction of Schiff bases with aromatic and aliphatic nitriles in the presence of $AlCl_3$,[12] from α-C-lithiated Schiff bases and saturated nitriles,[13] and when the 1-aryl-4,6-disubstituted pyrimidin-2(1*H*)-ones were treated with an alkoxide, both photochemically and thermally.[14] To the best of our knowledge, there are no reports on the reaction of methyl ketimines with nitriles activated by halogens.

2. Results and discussion

As part of our continuing study on the reactivity of halonitriles,[15–19] we now report our results on the condensation of these compounds with methyl ketimines **1a**,**b** prepared from acetophenone, 2-acetothienone and isopropylamine under $TiCl_4$ catalysis.[20] It seemed possible for us that CCl_3CN with its highly activated cyano group might react with ketimines **1a**,**b** to give diimines **2** under mild conditions. Actually, we found that *N*-isopropyl-(1-phenylethylidene)amine **1a** existing as an equilibrium mixture of the *Z*- and *E*-isomers with the latter predominating (ca. 90%)[21] reacts with trichloroacetonitrile in a molar ratio of 1:1 without a catalyst at room temperature within 4 days and leads to diimine **2**, existing in the vinylogous amidine form. This crystalline compound was obtained in high yield (74%) and may be stored at room temperature for months without deterioration. Hydrolysis of compound **2** to the corresponding β-aminovinyl ketone **3** can be easily performed in excellent yield by the action of H_2SO_4 in aqueous THF at room temperature.

It was shown previously[22,23] that Schiff bases derived from β-diketones and aliphatic amines are present in solution to an extent ≥95% as the keto-enamine by observing coupling between the intramolecularly hydrogen-bonded proton and the α-proton of the amine fragment. There is no apparent solvent effect upon the equilibrium. In the ^{1}H NMR spectrum of **3**, the methyne signal of the isopropyl group appears as a doublet of septets at δ 3.70 ($J_{NH,CH}$=9.7 Hz, $J_{CH,CH3}$=6.3 Hz). That the value of the coupling constant $J_{NH,CH}$ of all the 3-aryl-3-isopropylaminoprop-2-en-1-ones is in the range 9.6–9.7 Hz[24,25] suggests that they all exist in the keto-enamine form to the same extent. In contrast, β-aminovinyl imine **2** exists in equilibrium between tautomers **2A** and **2B** depending on the solvent as evidenced

Keywords: methyl ketimines; trichloroacetonitrile; trifluoroacetonitrile; 2,2,3,3-tetrafluoro-propionitrile; CCl_3-containing β-aminovinyl imine and ketone; pyrimidines with two polyhaloalkyl groups.
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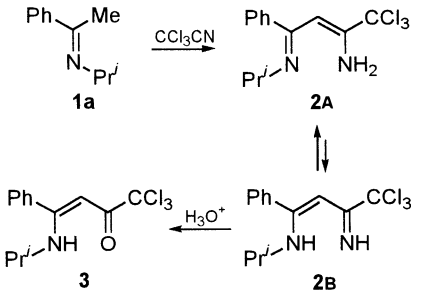
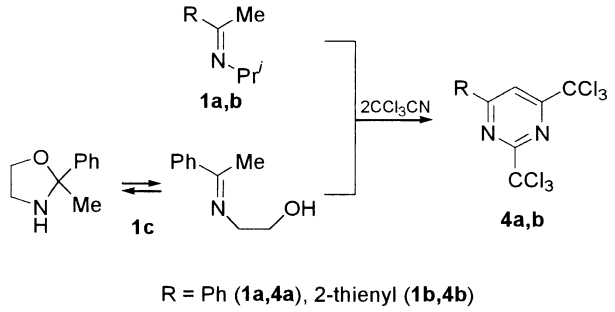


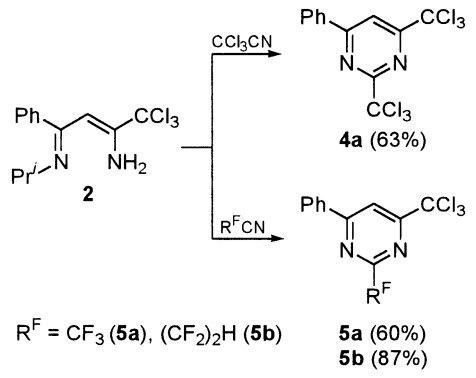
Scheme 1.



Scheme 3.

by its ^{1}H NMR spectra (Scheme 1). In $CDCl_3$ or CD_3CN solution a septet with J=6.3 Hz at δ 3.58 ppm was observed due to the CH proton of the isopropyl group suggesting that **2** exists in the imino-enamine form **2A**. In DMSO-d_6 solution the methyne hydrogen of **2** appears as a doublet of septets at δ 3.50 ppm due to the additional coupling with the NH of the enaminic form **2B**. The coupling constant between these protons was 3.1 Hz indicating an approximately 7:3 mixture of the tautomers **2A** and **2B**, respectively, because the observed coupling is a weighted average of the contributions from **2A** and **2B**. It should be noted that fluorinated *N*,*N*′-disubstituted β-aminovinyl imines exist as single tautomers with the imine fragment nearest to R^F group.[4]

Compound **2** is an aza-analogue of the β-alkoxyvinyl-β-aryl trichloromethyl ketones, which are readily available building blocks for the regiospecific construction of pyrazoles,[26] isoxazoles,[27] pyrimidines[28] and benzodiazepines,[29] bearing a trichloromethyl substituent. On the other hand, β-aminovinyl imine **2** may be considered as 1-azabutadiene derivative. It is well known that non-halogenated 1-azabutadiene derivatives are useful precursors for the synthesis of various five- and six-membered heterocycles. Thus, these compounds react with saturated nitriles and acetylenedicarboxylic acid ester to give rise to convenient synthetic methods for the preparation of pyrimidines[30] and pyridines,[31] respectively. From these results it seems likely that 1-azabutadiene **2** might be a suitable precursor for heterocycles containing the CCl_3 group in the ring. With this in mind we have investigated the reaction of **2** with CCl_3CN and R^FCN. The latter is potentially able to generate fluorinated pyrimidines which are of great interest because of their herbicidal, fungicidal, antibiotic, antiviral or antineoplastic properties (see Ref. 32 and references therein).

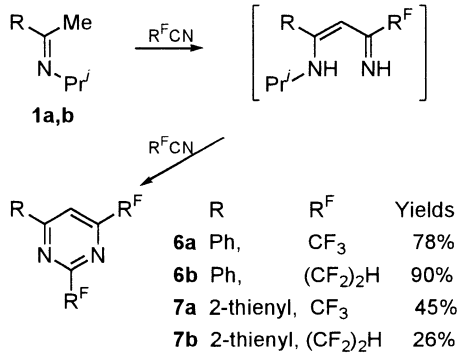


Scheme 2.

When 1-azabutadiene **2** was treated with CCl_3CN at 80°C for 6 h, pyrimidine **4a** with two CCl_3 groups was obtained in 63% yield after usual workup (Scheme 2). Although this heterocycle could be generated by a hetero-Diels–Alder reaction, it is more likely to suppose a double addition reaction or an addition followed by an electrocyclic ring closure.[33] Under such conditions spontaneous elimination of isopropylamine converted the primary intermediate into the aromatic product. The reactions of diimine **2** with CF_3CN at room temperature and $H(CF_2)_2CN$ at 65°C in a sealed tube afforded pyrimidine derivatives **5a**,**b** in good yields. To our knowledge, this is the first synthesis of pyrymidines containing both the CCl_3 and R^F groups in the ring.

Next we examined reactions of the methyl ketimines **1a**–**c** with an excess of trichloroacetonitrile. On treatment with CCl_3CN at 80°C for 3 days, ketimine **1a** gave pyrimidine **4a** as a sole identifiable product, no diimine **2** was detected. In contrast to the case of ketimine **1a**, interaction of *N*-isopropyl-[1-(2-thienyl)ethylidene]amine **1b** with trichloroacetonitrile is accompanied by resinification, and we were able to isolate pyrimidine **4b** only in poor yield. At the same time, ketimine **1c** prepared from acetophenone and 2-aminoethanol (in $CDCl_3$ solution this compound exists as an equilibrium mixture of the ring and open-chain forms[34]) reacts easily with CCl_3CN at room temperature for 2 days to give pyrimidine **4a** irrespective of the reagents ratio (Scheme 3). The maximum yield of **4a** (78%) was obtained from **1c** when an excess (4.5 equiv.) of CCl_3CN was used. This reaction is the most convenient route to pyrimidine **4a**, which owing to the labile trichloromethyl substituents might be employed in the synthesis of pyrimidines with other functional groups. Previously, 5-cyano-2,4-bis(trichloromethyl)-6-phenylpyrimidine[35] and 6-amino-5-cyano-2,4-bis(trichloromethyl)pyrimidine[36] were obtained by a two-step sequence from trichloroacetonitrile and benzoylacetonitrile and malononitrile, respectively.

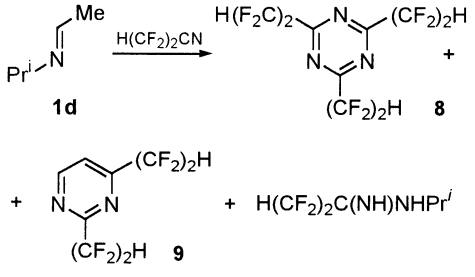
The reactions of trifluoroacetonitrile and 2,2,3,3-tetrafluoropropionitrile with methyl ketimines **1a**,**b** were also investigated. In this case, the fluorinated analogues of diimine **2** were not formed when ketimines **1a**,**b** were treated with R^FCN in a sealed tube. Instead, pyrimidines **6a**,**b** and **7a**,**b** with two polyfluoroalkyl groups were obtained in 78,90% and 45,26% yields, respectively (Scheme 4). The fact that no 1:1 adducts were observed in these reactions under various conditions and relations of the reactants suggests a



Scheme 4.

higher reactivity of the fluorinated nitriles in comparison to chlorinated one. It should be noted that in the case of $H(CF_2)_2CN$ the formation of 2,4,6-tris(1,1,2,2-tetrafluoroethyl)-1,3,5-triazine **8** as a product of trimerization of the nitrile was observed. Thus, when imine **1b** was heated with an excess of $H(CF_2)_2CN$ in a sealed tube at 80°C for 6 h a mixture of pyrimidine **7b** and triazine **8** was formed after recrystallization from ethanol in exactly 3:1 molar ratio, respectively. The results obtained from various experiments pointed to the following trends: higher temperatures and an increase of the reaction time promoted triazine formation. Previously, 2,4-bis(perfluorooctyl)pyrimidine and 2,4,6-tris(perfluorooctyl)pyrimidine were prepared by using chloro-substituted pyrimidines as substrates in copper-mediated cross-coupling reactions with perfluorooctyl iodide;[37] 4,6-bis(trifluoromethyl)-2-methoxypyrimidine-5-carbaldehyde was obtained from 3-anilinomethylene-1,1,1,5,5,5-hexafluoroacetylacetone and *O*-methylisourea.[38]

To extend the scope of the synthesis of fluoro- and chloro-containing pyrimidines, the reaction of ethylideneisopropylamine **1d**[39] with halonitriles was studied. This reaction showed considerably different behaviour from those observed for aromatic ketimines **1a–c**. For instance, CCl_3CN did not react with **1d** under the conditions used for **1a–c** and $H(CF_2)_2CN$ in a sealed tube both at 80°C and room temperature gave a complex mixture of at least three products from which only the crystalline previously unknown triazine **8** was isolated in an analytically pure state. The ^1H NMR spectrum of the mother liquor purified by distillation is best interpreted in terms of the presence of *N*-isopropyl-2,2,3,3-tetrafluoropropioamidine in an addition to the expected 2,4-bis(1,1,2,2-tetrafluoroethyl)pyrimidine **9** (Scheme 5). The structures of all the products (except pyrimidine **9**) were determined by their elemental analyses and spectral data.



Scheme 5.

In conclusion, the reaction of methyl ketimines with chloro- and fluoro-containing nitriles provides a simple and convenient one-pot process from the readily available materials to pyrimidines with two polyhaloalkyl substituents, which are expected to be biologically active. This reaction makes it possible to obtain pyrimidines with either the same or different groups in the ring, which substantially enhances its synthetic significance. 1-Azabutadiene derivative **2** may be considered as a new CCl_3-containing building block for the synthesis of a wide variety of heterocycles with one or two CCl_3 groups in the ring.

3. Experimental

3.1. General

^1H NMR spectra were recorded on a Bruker WM-250 spectrometer operating at 250.13 MHz in $CDCl_3$ solutions with TMS as the internal standard. IR spectra were measured on an IKS-29 instrument as suspensions in vaseline oil. Elementary analyses were performed at the Microanalysis Services of the Institute of Organic Synthesis, Ural Branch, Russian Academy of Sciences. Melting points are uncorrected. The starting methyl imines **1a–d** were prepared by direct condensation of the appropriate carbonyl compound and amine according to described procedure.[20,34,39,40] All the reactions with participation of CF_3CN and $H(CF_2)_2CN$ were carried out in a heavy walled glass tube of approximately 15 ml capacity, previously constricted for sealing.

3.1.1. 3-Isopropylimino-3-phenyl-1-trichloromethylpropenylamine (2). A mixture of the ketimine **1a** (5.0 g, 31.0 mmol) and trichloroacetonitrile (4.5 g, 31.2 mmol) was kept at room temperature for 4 days in the dark. Then the reaction mixture was diluted with 10 ml of 70% ethanol and the crystalline material was isolated by filtration, washed with aqueous ethanol and crystallized from ethanol to give the *title compound* **2** (7.0 g, 74%) as a colourless needles, mp 81°C; (Found: C, 51.25; H, 4.90; N, 9.12. $C_{13}H_{15}Cl_3N_2$ requires C, 51.09; H, 4.95; N, 9.17%); ν_{max} 3330 (NH_2), 1620, 1605, 1570 (C=N, C=C) cm^{-1}; δ_H ($CDCl_3$) 9.51 (2H, br s, NH_2), 7.41 (5H, s, Ph), 5.21 (1H, s, CH=), 3.58 (1H, sept, J=6.3 Hz, CH), 1.16 (6H, d, J=6.3 Hz, 2Me); δ_H (CD_3CN) 9.46 (2H, br s, NH_2), 7.34–7.49 (5H, m, Ph), 5.14 (1H, s, CH=), 3.57 (1H, sept, J=6.3 Hz, CH), 1.11 (6H, d, J=6.3 Hz, 2Me); δ_H (DMSO-d_6) 9.43 (2H, br s, NH_2), 7.44–7.50 (3H, m, arom.), 7.34–7.36 (2H, m, arom.), 5.12 (1H, s, CH=), 3.50 (1H, d sept, $J_{CH,NH}$=3.1 Hz, $J_{CH,CH3}$=6.3 Hz, CH), 1.09 (6H, d, J=6.3 Hz, 2Me).

3.1.2. 1,1,1-Trichloro-4-isopropylamino-4-phenylbut-3-en-2-one (3). To a solution of diimine **2** (0.1 g, 0.33 mmol), THF (0.5 ml) and H_2O (0.5 ml) was added 3 drops of conc. H_2SO_4. The mixture was stirred for 20 min at room temperature and then was diluted with 10 ml H_2O. The solid product obtained on standing was collected by filtration, washed with water and dried to give the *title compound* **3** (0.09 g, 90%) as a colourless needles, mp 95–96°C. After recrystallization from ethanol, the melting point did not change. (Found: C, 50.73; H, 4.74; N, 4.57. $C_{13}H_{14}Cl_3NO$

requires C, 50.92; H, 4.60; N, 4.57%); ν_{max} 1615, 1590, 1575 (C=O, C=C) cm^{-1}; δ_H 10.64 (1H, br s, NH), 7.45–7.49 (3H, m, arom.), 7.35–7.40 (2H, m, arom.), 5.67 (1H, s, CH=), 3.70 (1H, d sept, $J_{CH,NH}$=9.7 Hz, $J_{CH,CH3}$=6.3 Hz, CH), 1.22 (6H, d, J=6.3 Hz, 2Me).

3.1.3. 2,4-Bis(trichloromethyl)-6-phenylpyrimidine (4a). *Method A*. A mixture of the ketimine **1a** (0.5 g, 3.1 mmol) and trichloroacetonitrile (1.35 g, 9.3 mmol) was heated at 80°C for 3 days. The cooled mixture was diluted with 4 ml of 70% ethanol and left overnight at room temperature. The solid product obtained on standing was collected by filtration and crystallized from ethanol to give the *title compound* **4a** (0.5 g, 41%) as a colourless needles, mp 102–103°C; (Found: C, 36.95; H, 1.58; N, 7.24. $C_{12}H_6Cl_6N_2$ requires C, 36.87; H, 1.55; N, 7.17%); ν_{max} 1575 (C=N), 1535 (C=C) cm^{-1}; δ_H 8.33 (1H, s, H^5), 8.25–8.27 (2H, m, arom.), 7.56–7.64 (3H, m, arom.).

Method B. A mixture of 2-methyl-2-phenyloxazolidine **1c** (0.5 g, 3.1 mmol) and trichloroacetonitrile (2.0 g, 13.9 mmol) was kept for 2 days at room temperature. After the reaction mixture was diluted with 2 ml of 50% acetic acid, 3 ml of ethanol and 1 drop of conc. HCl was added for crystallization. The solid product was removed by filtration and crystallized from ethanol to give the *title compound* **4a** (0.94 g, 78%).

Method C. A mixture of diimine **2** (1.0 g, 3.3 mmol) and trichloroacetonitrile (1.0 g, 6.9 mmol) was heated at 80°C for 6 h. The cooled mixture was stirred with 5 ml of 70% ethanol and the solid product was collected by filtration and crystallized from ethanol to give the *title compound* **4a** (0.8 g, 63%).

3.1.4. 2,4-Bis(trichloromethyl)-6-(2-thienyl)pyrimidine (4b). A mixture of the ketimine **1b** (0.5 g, 3.0 mmol) and trichloroacetonitrile (1.3 g, 9.0 mmol) was heated at 80°C for 3 h. The cooled mixture was diluted with 10 ml of 70% ethanol and left overnight at room temperature. The dark solid obtained on standing was collected by filtration, washed with 5 ml of 70% ethanol and dissolved in 10 ml of boiling hexane. After filtration and evaporation of the solvent the residue was recrystallized twice from ethanol to give the *title compound* **4b** (0.1 g, 8%) as a colourless needles, mp 105–106°C. (Found: C, 30.18; H, 1.06; N, 7.17. $C_{10}H_4Cl_6N_2S$ requires C, 30.26; H, 1.02; N, 7.06%); ν_{max} 3110 (=C–H), 1570 (C=N), 1520 (C=C) cm^{-1}; δ_H 8.10 (1H, s, H^5), 8.01 (1H, dd, $J_{H5',H4'}$=3.8 Hz, $J_{H5',H3'}$=1.1 Hz, $H^{5'}$), 7.67 (1H, dd, $J_{H3',H4'}$=5.0 Hz, $J_{H3',H5'}$=1.1 Hz, $H^{3'}$), 7.24 (1H, dd, $J_{H4',H3'}$=5.0 Hz, $J_{H4',H5'}$=3.8 Hz, $H^{4'}$).

3.1.5. 4-Trichloromethyl-2-trifluoromethyl-6-phenylpyrimidine (5a). A mixture of the diimine **2** (0.3 g, 1.0 mmol) and trifluoroacetonitrile obtained from trifluoroacetamide (1.5 g, 13.3 mmol) and P_2O_5 (3.0 g) and condensed at −95°C was kept at room temperature for one day in a sealed tube. Then the reaction mixture was diluted with 3 ml of 50% ethanol and the crystalline material was recrystallized from 70% ethanol to give the *title compound* **5a** (0.2 g, 60%) as a colourless needles, mp 128°C; (Found: C, 42.23; H, 1.81; N, 8.21. $C_{12}H_6Cl_3F_3N_2$ requires C, 42.20; H, 1.77; N, 8.20%); ν_{max} 1580 (C=N), 1540 (C=C) cm^{-1}; δ_H 8.47 (1H, s, H^5), 8.22–8.24 (2H, m, arom.), 7.56–7.63 (3H, m, arom.).

3.1.6. 4-Trichloromethyl-2-(1,1,2,2-tetrafluoroethyl)-6-phenylpyrimidine (5b). A mixture of the diimine **2** (0.3 g, 1.0 mmol) and 2,2,3,3-tetrafluoropropionitrile obtained from 2,2,3,3-tetrafluoropropioamide (1.5 g, 10.3 mmol) and P_2O_5 (3.0 g) and condensed at −40°C was kept at 65°C for 16 h in a sealed tube. Then the reaction mixture was diluted with 3 ml of 70% ethanol and the crystalline material was recrystallized from hexane to give the *title compound* **5b** (0.32 g, 87%) as a colourless needles, mp 93°C; (Found: C, 41.76; H, 1.83; N, 7.42. $C_{13}H_7Cl_3F_4N_2$ requires C, 41.80; H, 1.89; N, 7.50%); ν_{max} 1570 (C=N), 1545 (C=C) cm^{-1}; δ_H 8.44 (1H, s, H^5), 8.20–8.23 (2H, m, arom.), 7.56–7.64 (3H, m, arom.), 6.59 (1H, tt, $^2J_{H,F}$=52.9 Hz, $^3J_{H,F}$=5.3 Hz, CF_2CF_2H).

3.1.7. 2,4-Bis(trifluoromethyl)-6-phenylpyrimidine (6a). A mixture of the ketimine **1a** (0.5 g, 3.1 mmol) and trifluoroacetonitrile obtained from trifluoroacetamide (3.0 g, 26.5 mmol) and P_2O_5 (6.0 g) was kept at room temperature for one day in a sealed tube. Then the reaction mixture was diluted with 5 ml of 70% ethanol and the crystalline material was isolated by filtration and washed with ethanol to give the *title compound* **6a** (0.71 g, 78%) as a colourless needles, mp 101–102°C; (Found: C, 49.42; H, 2.04; N, 9.64. $C_{12}H_6F_6N_2$ requires C, 49.33; H, 2.07; N, 9.59%); ν_{max} 1600 (C=N), 1560 (C=C) cm^{-1}; δ_H 8.20–8.24 (2H, m, arom.), 8.16 (1H, s, H^5), 7.54–7.66 (3H, m, arom.).

3.1.8. 2,4-Bis(1,1,2,2-tetrafluoroethyl)-6-phenylpyrimidine (6b). A mixture of the ketimine **1a** (1.0 g, 6.2 mmol) and 2,2,3,3-tetrafluoropropionitrile obtained from 2,2,3,3-tetrafluoropropioamide (6.0 g, 41.4 mmol) and P_2O_5 (10.0 g) was kept at 65°C for 12 h in a sealed tube. Then the reaction mixture was diluted with 10 ml of 70% ethanol and the crystalline material was isolated by filtration and crystallized from hexane to give the *title compound* **6b** (2.0 g, 90%) as a colourless needles, mp 76°C; (Found: C, 47.44; H, 2.27; N, 7.84. $C_{14}H_8F_8N_2$ requires C, 47.21; H, 2.26; N, 7.86%); ν_{max} 1600 (C=N), 1550 (C=C) cm^{-1}; δ_H 8.20–8.23 (2H, m, arom.), 8.20 (1H, s, H^5), 7.54–7.67 (3H, m, arom.), 6.51 (1H, tt, $^2J_{H,F}$=52.9 Hz, $^3J_{H,F}$=5.1 Hz, C^2–CF_2CF_2H), 6.40 (1H, tt, $^2J_{H,F}$=52.9 Hz, $^3J_{H,F}$=5.1 Hz, C^4–CF_2CF_2H).

3.1.9. 2,4-Bis(trifluoromethyl)-6-(2-thienyl)pyrimidine (7a). A mixture of the ketimine **1b** (0.5 g, 3.0 mmol) and trifluoroacetonitrile obtained from trifluoroacetamide (3.0 g, 26.5 mmol) and P_2O_5 (5.0 g) was kept at room temperature for one day in a sealed tube. Then the reaction mixture was diluted with 3 ml of 70% ethanol and the crystalline material was isolated by filtration and washed with ethanol to give the *title compound* **7a** (0.4 g, 45%) as a colourless needles, mp 131°C; [Found: C, 40.25; H, 1.23; N, 9.46. $C_{10}H_4F_6N_2S$ requires C, 40.28; H, 1.35; N, 9.39%]; ν_{max} 3110 (=C–H), 1600 (C=N), 1540 (C=C) cm^{-1}; δ_H 7.99 (1H, dd, $H^{5'}$, $J_{H5',H4'}$=3.9 Hz, $J_{H5',H3'}$=1.2 Hz), 7.92 (1H, s, H^5), 7.71 (1H, dd, $J_{H3',H4'}$= 4.9 Hz, $J_{H3',H5'}$=1.2 Hz, $H^{3'}$), 7.24 (1H, dd, $J_{H4',H3'}$=4.9 Hz, $J_{H4',H5'}$=3.9 Hz, $H^{4'}$).

3.1.10. 2,4-Bis(1,1,2,2-tetrafluoroethyl)-6-(2-thienyl)pyrimidine (7b). A mixture of the ketimine **1b** (0.5 g, 3.0 mmol) and 2,2,3,3-tetrafluoropropionitrile obtained from 2,2,3,3-tetrafluoropropioamide (3.0 g, 20.7 mmol) and 5.0 g P_2O_5 was kept at room temperature for 2 days in a sealed tube. Then the reaction mixture was diluted with 5 ml of 70% ethanol and the crystalline material was isolated by filtration and crystallized from hexane to give the *title compound* **7b** (0.28 g, 26%) as a colourless needles, mp 102–103°C; (Found: C, 39.74; H, 1.51; N, 8.01. $C_{12}H_6F_8N_2S$ requires C, 39.79; H, 1.67; N, 7.73%); ν_{max} 3110 (=C–H), 1600 (C=N), 1575, 1540 (C=C) cm^{-1}; δ_H 7.99 (1H, dd, $J_{H5',H4'}$=3.9 Hz, $J_{H5',H3'}$=1.1 Hz, $H^{5'}$), 7.97 (1H, s, H^5), 7.70 (1H, dd, $J_{H3',H4'}$=5.0 Hz, $J_{H3',H5'}$=1.1 Hz, $H^{3'}$), 7.24 (1H, dd, $J_{H4',H3'}$=5.0 Hz, $J_{H4',H5'}$=3.9 Hz, $H^{4'}$), 6.48 (1H, tt, $^2J_{H,F}$=52.9 Hz, $^3J_{H,F}$=5.2 Hz, C^2–CF_2CF_2H), 6.38 (1H, tt, $^2J_{H,F}$=52.9 Hz, $^3J_{H,F}$=5.2 Hz, C^4–CF_2CF_2H).

3.1.11. 2,4,6-Tris(1,1,2,2-tetrafluoroethyl)-1,3,5-triazine (8). A mixture of the aldimine **1d** (1.2 g, 14.0 mmol) and 2,2,3,3-tetrafluoropropionitrile obtained from 2,2,3,3-tetrafluoropropioamide (10 g, 68.9 mmol) with an excess of P_2O_5 was kept at room temperature for one day and then at 80°C for 2 h in a sealed tube. Then the reaction mixture was distillated under reduce pressure and the crystalline material was isolated by filtration and crystallized from ethanol to give the *title compound* **8** (0.7 g) as a white crystals, mp 93°C; (Found: C, 28.39; H, 0.68; N, 11.08. $C_9H_3F_{12}N_3$ requires C, 28.36; H, 0.79; N, 11.03%); ν_{max} 1560 (C=N) cm^{-1}; δ_H 6.40 (3H, tt, $^2J_{H,F}$=52.5 Hz, $^3J_{H,F}$=4.3 Hz, $3CF_2CF_2H$).

2,4-Bis(1,1,2,2-tetrafluoroethyl)pyrimidine **9** (a colourless oil) was not isolated in a pure state; ν_{max}(liquid film) 3550, 3510, 3450, 3360, 3220, 3120, 1690, 1635, 1605, 1570 cm^{-1}; δ_H 6.35 (1H, tt, $^2J_{H,F}$=52.8 Hz, $^3J_{H,F}$=4.8 Hz, C^4–CF_2CF_2H), 6.44 (1H, tt, $^2J_{H,F}$=52.9 Hz, $^3J_{H,F}$=4.9 Hz, C^2–CF_2CF_2H), 7.88 (1H, d, J=5.1 Hz, H^5), 9.17 (1H, d, J=5.1 Hz, H^6).

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References

1. Sosnovskikh, V. Ya.; Ovsyannikov, I. S.; Aleksandrova, I. A. *Zh. Org. Khim.* **1992**, *28*, 518–526.
2. Reid, J. C.; Calvin, M. *J. Am. Chem. Soc.* **1950**, *72*, 2948–2952.
3. Barkley, L. B.; Levine, R. *J. Am. Chem. Soc.* **1951**, *73*, 4625–4627.
4. Fustero, S.; de la Torre, M. G.; Pina, B.; Fuentes, A. S. *J. Org. Chem.* **1999**, *64*, 5551–5556.
5. Yu, H.-B.; Huang, W.-Y. *J. Fluorine Chem.* **1997**, *84*, 65–67.
6. Sosnovskikh, V. Ya.; Ovsyannikov, I. S. *Zh. Org. Khim.* **1990**, *26*, 2086–2091.
7. Pashkevich, K. I.; Aizikovich, A. Ya. *Dokl. AN SSSR* **1979**, *244*, 618–620.
8. Schlosser, M.; Keller, H. *Liebigs Ann. Chem.* **1995**, 1587–1589.
9. Przyborowski, J. PhD Thesis, University of Bremen, 1999.
10. Przyborowski, J.; Lork, E.; Röschenthaler, G.-V. *J. Fluorine Chem.* **2000**, *104*, 207–213.
11. Keller, H.; Schlosser, M. *Tetrahedron* **1996**, *52*, 4637–4644.
12. Hoberg, H.; Barluenga, J. *Synthesis* **1970**, 142–144.
13. Wittig, G.; Fischer, S.; Tanaka, M. *Liebigs Ann. Chem.* **1973**, 1075–1081.
14. Nishio, T.; Omote, Y. *J. Chem. Soc., Perkin Trans. 1* **1982**, 2149–2152.
15. Sosnovskikh, V. Ya. *Zh. Org. Khim.* **1992**, *28*, 1307–1308.
16. Sosnovskikh, V. Ya.; Ovsyannikov, I. S. *Zh. Org. Khim.* **1993**, *29*, 89–93.
17. Sosnovskikh, V. Ya.; Ovsyannikov, I. S. *Zh. Org. Khim.* **1993**, *29*, 259–264.
18. Sosnovskikh, V. Ya. *Mendeleev Commun.* **1996**, 189–190.
19. Sosnovskikh, V. Ya.; Mel'nikov, M. Yu. *Zh. Org. Khim.* **1998**, *34*, 303–306.
20. Weingarten, H.; Chupp, J. P.; White, W. A. *J. Org. Chem.* **1967**, *32*, 3246–3249.
21. Bjørgo, J.; Boyd, D. R.; Watson, C. G.; Jennings, W. B. *J. Chem. Soc., Perkin Trans. 2* **1974**, 757–762.
22. Dudek, G. O.; Holm, R. H. *J. Am. Chem. Soc.* **1962**, *84*, 2691–2696.
23. Brown, N. M. D.; Nonhebel, D. C. *Tetrahedron* **1968**, *24*, 5655–5664.
24. Cimarelli, C.; Palmieri, G. *Tetrahedron* **2000**, *56*, 475–478.
25. Sosnovskikh, V. Ya.; Usachev, B. I. Unpublished data.
26. Martins, M. A. P.; Freitag, R. A.; da Rosa, A.; Flores, A. F. C.; Zanatta, N.; Bonacorso, H. G. *J. Heterocycl. Chem.* **1999**, *36*, 217–220.
27. Martins, M. A. P.; Flores, A. F. C.; Bastos, G. P.; Sinhorin, A.; Bonacorso, H. G.; Zanatta, N. *Tetrahedron Lett.* **2000**, *41*, 293–297.
28. Madruga, C. C.; Clerici, E.; Martins, M. A. P.; Zanatta, N. *J. Heterocycl. Chem.* **1995**, *32*, 735–738.
29. Bonacorso, H. G.; Bittencourt, S. R. T.; Wastowski, A. D.; Wentz, A. P.; Zanatta, N.; Martins, M. A. P. *J. Heterocycl. Chem.* **1999**, *36*, 45–48.
30. Hoberg, H.; Barluenga, J. *Synthesis* **1970**, 363–365.
31. Barluenga, J.; Fustero, S.; Gotor, V. *Synthesis* **1975**, 191–192.
32. Sevenard, D. V.; Khomutov, O. G.; Koryakova, O. V.; Sattarova, V. V.; Kodess, M. I.; Stelten, J.; Loop, I.; Lork, E.; Pashkevich, K. I.; Röschenthaler, G.-V. *Synthesis* **2000**, 1738–1748.
33. Barluenga, J.; Rubio, V.; Gotor, V. *J. Org. Chem.* **1980**, *45*, 2592–2596.
34. Fülöp, F.; Pihlaja, K.; Neuvonen, K.; Bernáth, G.; Argay, G.; Kálmán, A. *J. Org. Chem.* **1993**, *53*, 1967–1969.
35. Elnagdi, M. H.; Fahmy, S. M.; Hafez, E. A. A.; Elmoghayar, M. R. H.; Amer, S. A. R. *J. Heterocycl. Chem.* **1979**, *16*, 1109–1111.
36. Elnagdi, M. H.; Elfahham, H. A.; Ghozlan, S. A. S.; Elgemeie, G. E. H. *J. Chem. Soc., Perkin Trans. 1* **1982**, 2667–2670.
37. Chen, G. J.; Chen, L. S. *J. Fluorine Chem.* **1995**, *73*, 113–119.
38. Soufyane, M.; van den Broek, S.; Khamliche, L.; Mirand, C. *Heterocycles* **1999**, *51*, 2445–2451.
39. Snyder, H. R.; Matteson, D. S. *J. Am. Chem. Soc.* **1957**, *79*, 2217–2221.
40. Campbell, K. N.; Sommers, A. H.; Campbell, B. K. *J. Am. Chem. Soc.* **1944**, *66*, 82–84.