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Addition of Me_3SiCN to trifluoromethyl derivates of *N*-(pyridylmethylidene) anilines catalyzed by Lewis acids

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A series of novel Shiff bases (1a–h) was synthesized by condensation of pyridinecarboxaldehydes (1–4) with 3- and 4-trifluoromethylanilines (5, 6) in the presence of molecular sieves (4 Å). It was found that $AlCl_3$ and $AlBr_3$ catalyzed the addition of Me_3SiCN to the C═N bond of the imines obtained, whereas the other Lewis acids studied (YCl_3, $LaCl_3$, ZnI_2) were not active. The reactivity of the imines in the title reaction, on the whole, correlated with their basicity. Besides the addition giving the expected α-amino nitriles (2a,b,d–f,h), an unusual reaction leading to unsaturated nitriles (3a–h) was observed. The structures of saturated and unsaturated products 2d and 3c were determined by X-ray diffraction. Copyright © 2001 John Wiley & Sons, Ltd.

Keywords: trimethylsilylcyanation; Lewis acid catalysis; pyridine Shiff bases; α-amino nitriles

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INTRODUCTION

Catalytic cyanation of imines, the 'Strecker reaction', has been studied intensively in recent years (for reviews on this subject, see Ref. 1–4). In our previous work it was found that $AlCl_3$ acts as an effective catalyst for the addition of Me_3SiCN to heterocyclic aldehydes.[5] Later, we demonstrated that $AlCl_3$, and especially $AlBr_3$, catalyzed the trimethylsilylcyanation of furan and thiophene aldimines to afford the corresponding α-amino nitriles.[6] Aromatic amino nitriles were found to be suitable for good antihypertensive activity[7] and also as psychotomimetic agents.[8] In the present paper we are reporting the results of the investigation on the interaction of Me_3SiCN with a series of pyridine-based aldimines (**1a**–**h**), previously synthesized by the condensation of pyridinecarboxaldehydes (**1**–**4**) with 3- and 4-trifluoromethylanilines (**5**, **6**). The heterocyclic derivatives containing a CF_3 group were used in this work as substrates, as these promise biological activity in the products.[9,10]

EXPERIMENTAL

General procedure

In a typical procedure for the trimethylsilylcyanation of imines, in a 5 cm^3 Pierce reaction vial, 1.0 equivalent of imine **1a–h** in dichloromethane (2 ml) reacted with 1.2 equivalents of trimethylsilyl cyanide (CAUTION: toxic!) in the presence of catalytic amounts of $AlBr_3$ (5 or 20 mol%) and 4 Å molecular sieves (0.5 g) at ambient temperature under an argon atmosphere. The reaction progress was monitored by thin-layer chromatography (TLC) on Merck aluminum sheets silica gel 60 F_{254} (for the eluents see Table 6). When the reaction was completed, saturated aqueous $NaHCO_3$ was added and the product was extracted with diethyl ether. After the organic layer was dried over $MgSO_4$ and evaporated, the products were isolated by column chromatography on Merck silica gel 60 (230–400 mesh) using various eluents (Table 6) or by recrystallization from hexane/ethyl acetate (50/50).

Imines **1a**–**h** were synthesized by the reactions of the corresponding pyridine aldehydes (**1**–**4**) with

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Table 1 Characteristics of the pyridylaldimines obtained

Imine	R	Pyridine isomer	CF_3 position	Isolated yield (%)	M.p./B.p. (°C)	Color
1a	H	α	3-	88	45–46	Yellow
1b	H	β	3-	68	38–39	Yellow
					123–125/0.1 mm	
1c	H	γ	3-	72	118–120/0.1 mm	Yellow
1d	CH_3	α	3-	67	125–127/0.1 mm	Yellow
1e	H	α	4-	80	62–63	White
1f	H	β	4-	64	46–47	White
1g	H	γ	4-	78	51–52	White
1h	CH_3	α	4-	60	76–78	White

Table 2 Elemental analysis of solid pyridylaldimines

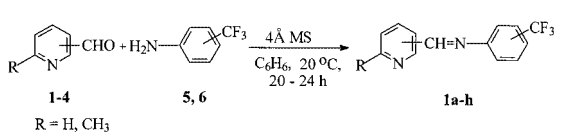
Imine	Mol. formula	Found/calculated (%)		
		C	H	N
1a	$C_{13}H_9N_2F_3$	62.02/62.40	3.53/3.63	11.04/11.19
1b	$C_{13}H_9N_2F_3$	62.33/62.40	3.56/3.63	11.25/11.19
1e	$C_{13}H_9N_2F_3$	61.85/62.40	3.79/3.63	11.07/11.19
1f	$C_{13}H_9N_2F_3$	62.23/62.40	3.63/3.63	11.12/11.19
1g	$C_{13}H_9N_2F_3$	62.39/62.40	3.67/3.63	11.19/11.19
1h	$C_{14}H_{11}N_2F_3$	63.59/63.64	4.22/4.20	10.59/10.60

3- or 4-trifluoromethylaniline (**5**, **6**). A starting aldehyde (5 mmol) was mixed with a starting amine (5 mmol) in dry benzene (20 ml) at ambient temperature in the presence of 4 Å molecular sieves (2.0 g). After some time (20–24 h) the molecular sieves were removed by filtration, the reaction mixture was concentrated, and the imine was isolated by recrystallization from hexane or by vacuum distillation.

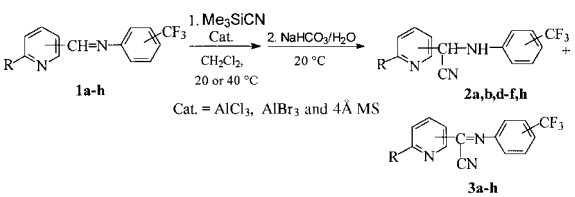
Materials and methods

The solvents were dried—dichloromethane over P_2O_5 and benzene over CaH_2—and distilled prior to use. Trimethylsilyl cyanide (Aldrich) was used without further purification. $AlCl_3$, $AlBr_3$, YCl_3, $LaCl_3$, ZnI_2 and the chemicals for the synthesis of the imines were obtained from commercial sources (Fluka, Aldrich). Molecular sieves 4 Å (VEB Laborchemie Apolda) and silica gel for column chromatography (Kieselgel 60, 0.063–0.200 mm, Merck) were used in the work. TLC was performed on Merck aluminium sheets silica gel 60 F_{254} with various eluents.

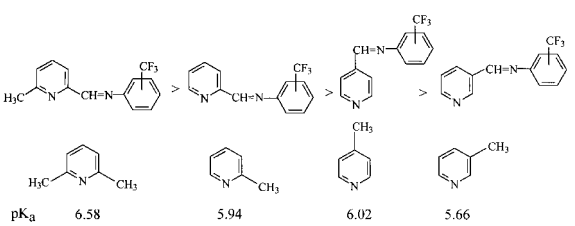
^{1}H NMR spectra were registered on Bruker WH-90/DS (90 MHz) and Varian Mercury (200 MHz) spectrometers using $CDCl_3$ as a solvent and Me_4Si



Scheme 1 Synthesis of imines.



Scheme 2 Trimethylsilylcyanation of imines.



Scheme 3 Order the reactivity of imines.

Table 3 ^{1}H NMR data for the pyridylaldimines

	Chemical shift (ppm), *J* (Hz)			
			Ring protons	
Imine	CH_3, s	CH=N, s	Pyridine	Aromatic
1a	–	8.59	7.38, ddd, *J* = 7.0, 4.5, 1.1, PyH-5 7.83, m, *J* = 7.0, 1.6, PyH-4 8.19, dt, *J* = 7.0, 1.1, PyH-3 8.72, m, *J* = 4.5, 1.6, 1.1, PyH-6	7.3–7.6, m, ArH_4
1b	–	8.46	7.2–7.8, m, 5H, PyH-5, ArH_4, 8.25, dt, *J* = 7.0, 1.5, PyH-4 8.69, dd, *J* = 4.3, 1.5, PyH-6 9.00, d, *J* = 1.5, 1.6, PyH-2	
1c	–		7.76, dd, *J* = 4.3, 0.7, PyH-3,5 8.78, dd, *J* = 4.3, 0.7, PyH-2,6	7.2–7.6, m, ArH_4
1d	2.63	8.57	7.26, d, *J* = 6.8, PyH-5 7.71, t, *J* = 6.8, PyH-4 8.00, d, *J* = 6.8, PyH-3	7.3–7.6, m, ArH_4
1e	–	8.57	7.39, ddd, *J* = 8.0, 5.0, 1.0, PyH-5 7.83, m, *J* = 8.0, 7.6, 1.8, PyH-4 8.19, m, *J* = 7.6, PyH-3 8.73, m, *J* = 5.0, PyH-6	7.31, d, *J* = 8.2, ArH-3,5 7.66, d, *J* = 8.2, ArH-2,6
1f	–	8.48	7.45, dd, *J* = 8.1, 4.8, PyH-5 8.31, m, *J* = 8.1, 2.0, 1.6, PyH-4 8.74, dd, *J* = 4.8, 1.6, PyH-6 9.03, d, *J* = 2.0, PyH-2	7.26, d, *J* = 8.5, ArH-3,5 7.66, d, *J* = 8.5, ArH-2,6
1g	–	8.42	7.78, dd, *J* = 6.0, 2.0, PyH-3,5 8.78, dd, *J* = 6.0, 2.0, PyH-2,6	7.27, d, *J* = 8.8, ArH-3,5 7.69, d, *J* = 8.8, ArH-2,6
1h	2.64	8.55	7.27, d, *J* = 8.0, PyH-5 7.72, m, *J* = 8.0, 7.6, PyH-4 8.00, d, *J* = 7.6, PyH-3	7.31, d, *J* = 8.2, ArH-3,5 7.65, d, *J* = 8.2, ArH-2,6

as an internal standard. The mass spectra were obtained on MS-50 (70 eV) (electron impact) and HP 6890 GC/MS instruments. Elemental analysis was performed on a Carlo Erba EA-1108 apparatus. Melting points were determined with a Kofler instrument.

X-ray crystallographic study

Monocrystals of compounds **2d** and **3c** were grown from ethyl acetate/hexane (50/50). The intensity data for **2d** were collected on a MACH-3 diffractometer with graphite-monochromated Cu Kα radiation. For compound **3c**, the intensity data were collected on a Syntex $P2_1$ automatic four-circle computer-controlled single-crystal diffractometer (Mo Kα radiation with graphite monochromator) using the $\theta/2\theta$ scan technique. The data for **2d** and **3c** were collected at room temperature and corrected for Lorentz and polarization factors; for **2d** a correction was also made for absorption. Both structures were solved by direct methods and refined by full-matrix least squares. Structure **2d** was solved by use of SHELXS-97[11] and refined against F^2 using SHELXL-97[12] programs. Calculations for **3c** were carried out with the AREN complex of programs[13] for crystallographic computations. By calculations all the H-atoms were placed in ideal positions and refined with the rigid model and fixed isotropic displacement parameters.

Table 4 GC–MS data for the pyridylaldimines

Imine	*m/z* (I_{rel}, %)
1a	251 (11, $[M+H]^+$), 250 (77, M^+), 249 (100, $[M-H]^+$), 231 (20, $[M-F]^+$), 223 (66, $[M-CN]^+$), 203 (20, $[M-CN-F-H]^+$), 181 (14, $[M-CF_3]^+$), 172 (13, $[M-Py]^+$), 154 (45), 145 (78, $[C_6H_4CF_3]^+$), 125 (24), 105 (22, $[M-C_6H_4CF_3]^+$), 95 (25), 79 (41, $[PyH]^+$), 78 (24, Py^+), 75 (27), 69 (11, $[CF_3]^+$), 63 (14), 52 (22), 51 (20), 39 (8), 38 (5)
1b	251 (14, $[M+H]^+$), 250 (100, M^+), 249 (92, $[M-H]^+$), 231 (11, $[M-F]^+$), 181 (5, $[M-CF_3]^+$), 172 (16, $[M-Py]^+$), 152 (2), 145 (59, $[C_6H_4CF_3]^+$), 125 (12), 105 (5, $[M-C_6H_4CF_3]^+$), 95 (14), 79 (12, $[PyH]^+$), 78 (7, Py^+), 75 (14), 69 (6, $[CF_3]^+$), 63 (12), 51 (15), 39 (5), 38 (6)
1c	251 (15, $[M+H]^+$), 250 (100, M^+), 249 (59, $[M-H]^+$), 231 (10, $[M-F]^+$), 181 (3, $[M-CF_3]^+$), 172 (44, $[M-Py]^+$), 145 (87, $[C_6H_4CF_3]^+$), 125 (11), 105 (6, $[M-C_6H_4CF_3]^+$), 95 (16), 79 (38, $[PyH]^+$), 78 (6, Py^+), 75 (14), 69 (6, $[CF_3]^+$), 63 (9), 51 (14), 39 (5), 38 (4)
1d	265 (12, $[M+H]^+$), 264 (71, M^+), 263 (20, $[M-H]^+$), 245 (11, $[M-F]^+$), 237 (40, $[M-HCN]^+$), 236 (100, $[M-HCN-H]^+$), 216 (6), 195 (7, $[M-CF_3]^+$), 172 (7, $[M-MeC_5H_3N]^+$), 167 (8), 145 (60, $[C_6H_4CF_3]^+$), 125 (10), 119 (40, $[M-C_6H_4CF_3]^+$), 95 (18), 93 (29, $[MeC_5H_3NH]^+$), 92 (21, $[MeC_5H_3N]^+$), 75 (18), 69 (7, $[CF_3]^+$), 65 (24), 51 (13), 39 (22)
1e	250 (75, M^+), 249 (100, $[M-H]^+$), 231 (16, $[M-F]^+$), 223 (61, $[M-HCN]^+$), 222 (15, $[M-HCN-H]^+$), 203 (24, $[M-F-HCN-H]^+$), 181 (10, $[M-CF_3]^+$), 172 (15, $[M-Py]^+$), 154 (36), 145 (77, $[C_6H_4CF_3]^+$), 125 (16), 105 (27, $[M-C_6H_4CF_3]^+$), 95 (23), 79 (62, $[PyH]^+$), 78 (27, Py^+), 75 (22), 69 (10, $[CF_3]^+$), 63 (9), 52 (22), 51 (20), 50 (16), 39 (8)
1f	251 (14, $[M+H]^+$), 250 (100, M^+), 249 (95, $[M-H]^+$), 231 (11, $[M-F]^+$), 181 (5, $[M-CF_3]^+$), 172 (17, $[M-Py]^+$), 145 (64, $[C_6H_4CF_3]^+$), 125 (11), 105 (6, $[M-C_6H_4CF_3]^+$), 95 (15), 79 (28, $[PyH]^+$), 78 (8, Py^+), 75 (13), 69 (5, $[CF_3]^+$), 63 (10), 52 (9), 51 (14), 50 (10), 38 (5)
1g	251 (15, $[M+H]^+$), 250 (100, M^+), 249 (59, $[M-H]^+$), 231 (12, $[M-F]^+$), 181 (5, $[M-CF_3]^+$), 172 (41, $[M-Py]^+$), 145 (82, $[C_6H_4CF_3]^+$), 125 (12), 105 (6, $[M-C_6H_4CF_3]^+$), 95 (15), 79 (31, $[PyH]^+$), 78 (5, Py^+), 75 (12), 69 (5, $[CF_3]^+$), 63 (8), 52 (10), 51 (18), 50 (10), 38 (5)
1h	265 (13, $[M+H]^+$), 264 (83, M^+), 263 (30, $[M-H]^+$), 245 (13, $[M-F]^+$), 237 (47, $[M-HCN]^+$), 236 (100, $[M-HCN-H]^+$), 217 (5, $[M-F-HCN-H]^+$), 195 (6, $[M-CF_3]^+$), 172 (9, $[M-MeC_5H_3N]^+$), 145 (55, $[C_6H_4CF_3]^+$), 125 (11), 119 (38, $[M-C_6H_4CF_3]^+$), 95 (15), 93 (69, $[MeC_5H_3NH]^+$), 92 (21, $[MeC_5H_3N]^+$), 75 (14), 69 (8, $[CF_3]^+$), 67 (25), 66 (24), 51 (10), 50 (9), 39 (18)

Table 5 Trimethylsilylcyanation of N-(pyridylmethylidene)amines

Starting imine	Catalyst (amount (mol%))	Temp. (°C)	Reaction time (h)	Product (isolated yield (%))	
				α-Amino nitrile	Unsaturated nitrile
1a	$AlCl_3$ (20)	40	32	**2a** (32)	**3a** (30)
	$AlBr_3$ (20) + 4Å MS	20	2	**2a** (45)	**3a** (20)
1b	$AlCl_3$ (20)	40	45	**2b** (30)	**3b** (18)
	$AlBr_3$ (20) + 4Å MS	20	7	**2b** (50)	**3b** (15)
1c	$AlCl_3$ (20)	40	38	–	**3c** (62)
	$AlBr_3$ (20) + 4Å MS	20	2.5	–	**3c** (58)
1d	$AlCl_3$ (20)	40	28	**2d** (35)	**3d** (30)
	$AlBr_3$ (20) + 4Å MS	20	1.5	**2d** (52)	**3d** (16)
1e	$AlBr_3$ (5) + 4Å MS	20	2	**2e** (63)	**3e**
1f	$AlBr_3$ (5) + 4Å MS	20	5	**2f** (60)	**3f**
1g	$AlBr_3$ (5) + 4Å MS	20	3	–	**3g** (60)
1h	$AlBr_3$ (5) + 4Å MS	20	1.5	**2h** (65)	**3h**

Table 6 Characteristics of the products isolated

Compound	Column chromatography eluent	M.p. (°C)	Mol. formula	Found/calculated (%) C	H	N
2a	C_6H_6:MeOH = 10:1	Oil	$C_{14}H_{10}N_3F_3$			
3a	C_6H_6:MeOH = 10:1	Oil	$C_{14}H_8N_3F_3$			
2b	$CHCl_3$:MeOH = 9:1	Oil	$C_{14}H_{10}N_3F_3$			
3b	$CHCl_3$:MeOH = 9:1	Oil	$C_{14}H_8N_3F_3$			
3c	–	92–93	$C_{14}H_8N_3F_3$	60.50/61.09	2.91/2.93	14.99/15.27
2d	–	113–114	$C_{15}H_{12}N_3F_3$	61.29/61.85	4.05/4.15	14.09/14.43
3d	C_6H_6:MeOH = 10:1	75–80	$C_{15}H_{10}N_3F_3$	62.03/62.29	3.51/3.48	14.19/14.53
2e	C_6H_6:MeOH = 10:1 then CH_2Cl_2:MeOH = 10:1	Oil	$C_{14}H_{10}N_3F_3$			
2f	CH_2Cl_2:MeOH = 10:1	97–98	$C_{14}H_{10}N_3F_3$	60.61/60.65	3.48/3.64	15.21/15.16
3g	$CHCl_3$:MeOH = 9:1	121–122	$C_{14}H_8N_3F_3$	60.85/61.09	2.90/2.93	15.08/15.27
2h	CH_2Cl_2:MeOH = 20:1	163–164	$C_{15}H_{12}N_3F_3$	61.40/61.85	4.08/4.15	14.15/14.43

RESULTS AND DISCUSSION

Synthesis of imines and their conversions

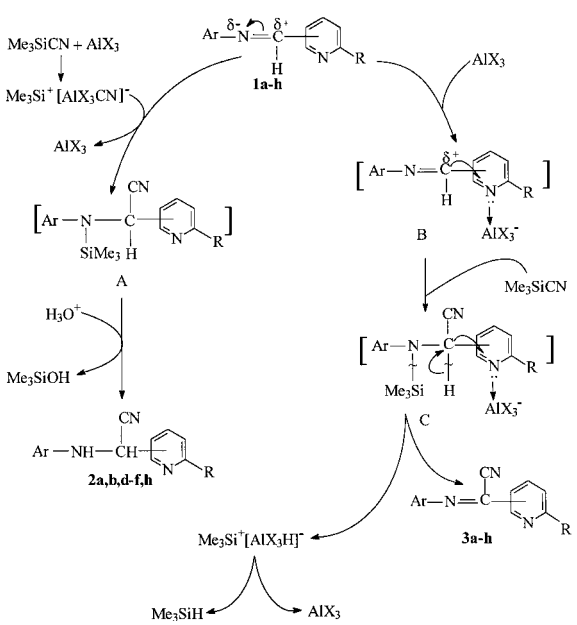
The synthesis and characterization of the pyridylaldimines

We have found that condensation of the pyridinecarboxaldehydes with 3- and 4-CF_3 derivatives of aniline, being very slow under the action of ordinary dehydration agents or by distillation of water azeotropes, can be efficiently realized in the presence of 4 Å molecular sieves at ambient temperature for 20–24 h. The corresponding pyridine azomethynes were isolated in 60–88% yields as oils or crystals and identified by elemental analysis, ^{1}H NMR and mass spectrometry (MS) (Scheme 1, Tables 1–4).

Lewis-acid-catalyzed addition of Me_3SiCN to pyridylaldimines

Recently, we have found that the trimethylsilylcyanation of furan and thiophene aldimines catalyzed by $AlBr_3$ (at 20 °C) and $AlCl_3$ (at 40 °C) leads to the expected α-amino nitriles.[6] Now, we wish to describe the first examples of the reactions of Me_3SiCN with pyridine imines. It was found that $AlCl_3$ and $AlBr_3$ catalyzed the addition of Me_3SiCN to the CH═N bond of all the imines investigated (Table 5); however, the other Lewis acids studied (YCl_3, $LaCl_3$, ZnI_2) were not active in these reactions. $AlBr_3$ was more active than $AlCl_3$. In most cases the reactions were carried out in the presence of 4 Å molecular sieves together with the catalyst to avoid the hydrolysis problems (Scheme 2).

The reactivities of the 4-CF_3 derivatives (**1e–h**) were higher than those of the 3-CF_3 compounds (**1a–d**), perhaps because of the modifications to the electronic and/or steric factors. The reactivity order of the pyridine azomethynes studied was as given in Scheme 3. Since the basic properties of the novel



Scheme 4 Proposed mechanism of the Lewis-acid-catalyzed addition of Me_3SiCN to pyridine imines.

Table 7 ^{1}H NMR data of the α-amino nitriles and unsaturated nitriles synthesized

	Chemical shift (ppm), *J* (Hz)				
				Ring protons	
Compound	CH_3, s	NH	CHCN	Pyridine	Aromatic
2a	–	5.50, d *J* = 6.4	5.47, d	7.4–7.6, 2H, m, *J* = 8.0, 5.0, 1.8, 1.0, PyH-3,5 7.81 1H, td, *J* = 8.0, 1.8, PyH-4 8.66, 1H, m, *J* = 5.0, 1.0, PyH-6	6.9–7.2, 4H, m, ArH_4
3a	–	–	–	7.54, 1H, ddd, *J* = 8.0, 5.0, 1.0, PyH-5 7.89, 1H, td, *J* = 8.0, 1.7, PyH-4 8.28, 1H, dt, *J* = 8.0, 1.0, PyH-3 8.84, 1H, m, *J* = 5.0, 1.0, PyH-6	7.4–7.7, 4H, m, ArH_4
2b	–	5.18, d *J* = 8.0	5.52, d	7.44, 1H, ddd, *J* = 7.9, 4.8, 0.7, PyH-5 7.95, 1H, m, *J* = 7.9, 2.3, 1.7, PyH-4 8.73, 1H, dd, *J* = 4.8, 1.7, PyH-6 8.87, 1H, d, *J* = 2.3, PyH-2	6.7–7.3, 4H, m, ArH_4
3b	–	–	–	7.51, 1H, ddd, *J* = 8.0, 4.9, 0.8, PyH-5 8.42, 1H, m, *J* = 8.0, 2.0, 1.7 PyH-4 8.86, 1H, dd, *J* = 4.9, 1.7, PyH-6 9.37, 1H, d, *J* = 2.0, PyH-2	7.4–7.7, 4H, m, ArH_4
3c	–	–	–	7.95, 2H, dd, *J* = 6.0, 2.0, PyH-3,5 8.87, 2H, dd, *J* = 6.0, 2.0, PyH-2,6	7.3–7.9, 4H, m, ArH_4
2d	2.57	5.60, d *J* = 6.4	5.40, d	7.22, 1 H, dd, *J* = 6.8, 1.8, PyH-5 7.32, 1 H, dd, *J* = 6.8, 1.8, PyH-3 7.68, 1H, t, *J* = 6.8, PyH-4	7.0–7.3, 4H, m, ArH_4
3d	2.68	–	–	7.35, 1 H, d, *J* = 6.8, PyH-5 7.75, 1H, t, *J* = 6.8, PyH-4 8.05, 1H, d, *J* = 6.8, PyH-3	7.3–7.6, 4H, m, ArH_4
2e	–	5.62, d *J* = 7.0	5.42, d	7.27–7.42, 2H, m, *J* = 8, 4, 2, <1, PyH-3,5 7.82, 1 H, td, *J* = 8, 2, PyH-4 8.67, 1H, m, *J* = 4, <1, PyH-6	6.84, 2H, d, *J* = 8.6, ArH-3,5 7.51, 2H, d, *J* = 8.6, ArH-2,6
2f	–	4.98, d *J* = 8.8	5.55, d	7.30, 1H, ddd, *J* = 8.0, 4.8, 0.7, PyH-5 7.93, 1H, dt, *J* = 8.0, 2.4, 2.0, PyH-4 8.64, 1H, dd, *J* = 4.8, 2.0, PyH-6 8.78, 1H, d, *J* = 2.4, PyH-2	6.80, 2H, d, *J* = 9.0, ArH-3,5 7.51, 2H, d, *J* = 9.0, ArH-2,6
3g	–	–	–	7.95, 2H, dd, *J* = 4.6, 2.0, PyH-3,5 8.87, 2H, dd, *J* = 4.6, 2.0, PyH-2,6	7.27, 2H, d, *J* = 8.0, ArH-3,5 7.75, 2H, d, *J* = 8.0, ArH-2,6
2h	2.60	5.71, d *J* = 7.6	5.38, d	7.18, 1 H, d, *J* = 7.4, PyH-5 7.49, 1 H, d, *J* = 7.4, PyH-3 7.64, 1H, t, *J* = 7.4, PyH-4	6.82, 2H, d, *J* = 8.0, ArH-3,5 7.27, 2H, d, *J* = 8.0, ArH-2,6

imines **1a–h** are not known, we used the basicity of methylpyridines[14] for a comparison. The result permits us to suppose that the reactivity of imines generally correlates with their basicity.

After the reactions were completed and hydrolysis undertaken, TLC analysis, ^{1}H NMR and gas chromatography (GC)–MS spectra indicated that complex mixtures of the products were obtained. The isolation of the products was realized by column chromatography or by recrystallization from hexane/ethyl acetate mixtures. Besides the corresponding α-amino nitriles of structure **2** (Scheme 2), the formation of the unexpected unsaturated nitriles **3a–h** was found. This unusual

Table 8 MS spectra data of the α-amino nitriles and unsaturated nitriles obtained

Compound	*m/z* (I_{rel}, %)
2a	277 (33, M^+), 276 (11, $[M - H]^+$), 274 (13), 258 (10, $[M - F]^+$), 251 (14, $[M - CN]^+$), 250 (73, $[M - HCN]^+$), 249 (100, $[M - HCN - H]^+$), 231 (16, $[M - HCN - F]^+$), 223 (64), 203 (27), 181 (9), 172 (14, $[M - HCN - Py]^+$), 154 (41), 145 (90, $[C_6H_4CF_3]^+$), 132 (4, $[M - C_6H_4CF_3]^+$), 125 (20), 105 (31), 95 (28), 79 (69, $[PyH]^+$), 78 (33, $[Py]^+$), 75 (26), 69 (12, $[CF_3]^+$), 63 (13), 52 (30), 51 (32)
3a	276 (5, $[M + H]^+$), 275 (46, M^+), 274 (100, $[M - H]^+$), 256 (9, $[M - F]^+$), 249 (8, $[M - CN]^+$), 223 (26), 206 (11, $[M - CF_3]^+$), 203 (15), 154 (25), 145 (30, $[C_6H_4CF_3]^+$), 125 (10), 105 (5), 95 (13), 78 (18, Py^+), 75 (12), 69 (5, $[CF_3]^+$), 51 (14)
2b	277 (15, M^+), 251 (12, $[M - CN]^+$), 250 (100, $[M - HCN]^+$), 249 (88, $[M - HCN - H]^+$), 231 (10, $[M - HCN - F]^+$), 172 (16, $[M - HCN - Py]^+$), 160 (8), 145 (56, $[C_6H_4CF_3]^+$), 125 (11), 117 (20, $[PyCHCN]^+$), 95 (15), 79 (9, $[PyH]^+$), 76 (9), 75 (9), 63 (12), 51 (16), 50 (9)
3b	276 (16, $[M + H]^+$), 275 (100, M^+), 274 (59, $[M - H]^+$), 256 (14, $[M - F]^+$), 250 (17), 249 (39, $[M - CN]^+$), 248 (18), 206 (34, $[M - CF_3]^+$), 197 (4, $[M - Py]^+$), 180 (6), 172 (9), 145 (55, $[C_6H_4CF_3]^+$), 130 (11, $[M - C_6H_4CF_3]^+$), 125 (15), 104 (8), 95 (16), 78 (5, Py^+), 75 (13), 69 (8, $[CF_3]^+$), 63 (10), 51 (11), 50 (9)
3c	276 (17, $[M + H]^+$), 275 (100, M^+), 274 (31, $[M - H]^+$), 256 (10, $[M - F]^+$), 249 (35, $[M - CN]^+$), 206 (10, $[M - CF_3]^+$), 197 (13), 172 (11), 145 (93, $[C_6H_4CF_3]^+$), 130 (13, $[M - C_6H_4CF_3]^+$), 125 (10), 104 (10), 95 (12), 78 (9, Py^+), 75 (17), 69 (9, $[CF_3]^+$), 63 (8), 51 (20), 50 (12)
2d	292 (8, $[M + H]^+$), 291 (48, M^+), 290 (13, $[M - H]^+$), 272 (11, $[M - F]^+$), 265 (20, $[M - CN]^+$), 264 (72, $[M - HCN]^+$), 263 (24), 245 (13, $[M - HCN - F]^+$), 237 (42), 236 (100), 222 (5, $[M - CF_3]^+$), 217 (7), 199 (6, $[M - MeC_5H_3N]^+$), 172 (8, $[M - HCN - MeC_5H_3N]^+$), 146 (17, $[M - C_6H_4CF_3]^+$), 145 (66, $[C_6H_4CF_3]^+$), 132 (10), 125 (15), 119 (47, $[M - HCN - C_6H_4CF_3]^+$), 104 (6), 95 (20), 93 (80, $[MeC_5H_4N]^+$), 92 (26, $[MeC_5H_3N]^+$), 78 (13), 77 (12), 75 (18), 69 (11, $[CF_3]^+$), 66 (24), 65 (29), 63 (15), 51 (13), 50 (10), 39 (26)
3d	290 (13, $[M + H]^+$), 289 (65, M^+), 288 (32, $[M - H]^+$), 270 (12, $[M - F]^+$), 263 (13, $[M - CN]^+$), 237 (65), 236 (100), 220 (7, $[M - CF_3]^+$), 217 (12), 167 (13), 145 (44, $[C_6H_4CF_3]^+$), 125 (14), 119 (10, $[M - C_6H_4CF_3]^+$), 95 (21), 92 (20, $[MeC_5H_3N]^+$), 75 (15), 69 (11, $[CF_3]^+$), 65 (27), 51 (10), 50 (12), 39 (16)
2e	277 (54, M^+), 276 (19, $[M - H]^+$), 258 (9, $[M - F]^+$), 251 (11, $[M - CN]^+$), 250 (50, $[M - HCN]^+$), 249 (100, $[M - HCN - H]^+$), 231 (14, $[M - HCN - F]^+$), 223 (34), 222 (10), 208 (4, $[M - CF_3]^+$), 199 (14, $[M - Py]^+$), 181 (10), 172 (11, $[M - HCN - Py]^+$), 154 (27), 145 (65, $[C_6H_4CF_3]^+$), 133 (2, $[M - C_6H_4CF_3]^+$), 125 (18), 117 (7, $[PyCHCN]^+$), 107 (7), 105 (24), 95 (20), 79 (68, $[PyH]^+$), 78 (28, Py^+), 75 (19), 69 (10, $[CF_3]^+$), 63 (15), 52 (25), 51 (26)
3e	275 (37, M^+), 274 (100, $[M - H]^+$), 256 (10, $[M - F]^+$), 223 (13), 206 (15, $[M - CF_3]^+$), 197 (2, $[M - Py]^+$), 154 (20), 145 (25, $[C_6H_4CF_3]^+$), 125 (9), 105 (5), 95 (11), 78 (16, Py^+), 75 (11), 69 (5, $[CF_3]^+$), 51 (14)
2f	277 (35, M^+), 258 (5, $[M - F]^+$), 251 (16, $[M - CN]^+$), 250 (100, $[M - HCN]^+$), 249 (95, $[M - HCN - H]^+$), 231 (13, $[M - HCN - F]^+$), 223 (3), 208 (4, $[M - CF_3]^+$), 199 (4, $[M - Py]^+$), 181 (6), 172 (18, $[M - HCN - Py]^+$), 160 (8), 145 (68, $[C_6H_4CF_3]^+$), 140 (7), 133 (2), 125 (15), 117 (59, $[PyCHCN]^+$), 105 (7), 95 (17), 90 (11), 79 (9, $[PyH]^+$), 75 (15), 69 (7, $[CF_3]^+$), 63 (21), 51 (16), 50 (11)
3f	276 (16, $[M + H]^+$), 275 (100, M^+), 274 (59, $[M - H]^+$), 256 (14, $[M - F]^+$), 249 (39, $[M - CN]^+$), 248 (18, $[M - CN - H]^+$), 206 (34, $[M - CF_3]^+$), 197 (5), 180 (6), 172 (9), 154 (3), 145 (55, $[C_6H_4CF_3]^+$), 130 (11), 125 (15), 104 (8), 95 (16), 78 (7, Py^+), 75 (13), 69 (8, $[CF_3]^+$), 63 (10), 51 (11), 50 (11)
3g	276 (15, $[M + H]^+$), 275 (100, M^+), 274 (43, $[M - H]^+$), 256 (13, $[M - F]^+$), 249 (30, $[M - CN]^+$), 206 (26, $[M - CF_3]^+$), 197 (8), 172 (10), 145 (61, $[C_6H_4CF_3]^+$), 130 (8, $[M - C_6H_4CF_3]^+$), 125 (12), 104 (5), 95 (14), 78 (2, Py^+), 75 (10), 69 (5, $[CF_3]^+$), 63 (5), 51 (13), 50 (12)

Table 8 Continued

Compound	*m/z* (I_{rel}, %)
2h	292 (7, $[M + H]^+$), 291 (40, M^+), 290 (15, $[M - H]^+$), 272 (7, $[M - F]^+$), 265 (22, $[M - CN]^+$), 264 (81, $[M - HCN]^+$), 263 (14), 245 (14, $[M - HCN - F]^+$), 237 (55), 236 (100), 195 (9), 172 (14, $[M - HCN - MeC_5H_3N]^+$), 167 (9), 146 (10, $[M - C_6H_4CF_3]^+$), 145 (60, $[C_6H_4CF_3]^+$), 132 (10), 125 (13), 119 (45, $[M - HCN - C_6H_4CF_3]^+$), 95 (20), 93 (72, $[MeC_5H_4N]^+$), 92 (25, $[MeC_5H_3N]^+$), 75 (18), 69 (6, $[CF_3]^+$), 66 (25), 65 (23), 51 (15), 50 (12)
3h	290 (14, $[M + H]^+$), 289 (76, M^+), 288 (60, $[M - H]^+$), 270 (15, $[M - F]^+$), 263 (18, $[M - CN]^+$), 238 (11), 237 (79), 236 (100), 220 (9), 167 (10), 145 (37, $[C_6H_4CF_3]^+$), 125 (12), 119 (12, $[M - C_6H_4CF_3]^+$), 95 (16), 92 (18, $[MeC_5H_3N]^+$), 75 (14), 69 (7, $[CF_3]^+$), 65 (25), 63 (9), 51 (7), 50 (7), 39 (14)

reaction direction is especially characteristic for both γ-imines—**1c**,**g** afforded only compounds **3c**,**g**. The products isolated were identified by ^1H NMR and MS spectra, and the solids also by elemental analysis. Compounds **3e**, **3f** and **3h** formed in low yields and were identified by mass spectra only (Tables 6–8).

Usually, the reactions of Me_3SiCN with imines (in particular, furan and thiophene derivatives[6]) lead to α-amino nitriles and not to the unsaturated nitriles. This fact suggests that the N-atom of a pyridine ring plays some role in the formation of products **3a**–**h**. The proposed mechanism of formation for all the products obtained is given in Scheme 4. The α-amino nitriles are formed from pyridine derivatives analogous to the reactions of furan, thiophene and other imines *via* intermediates A. The pathway to unsaturated nitriles proceeds perhaps *via* σ-complexes B and C formed through the N-atom of the pyridine ring. Apparently, such complexes assist the weakening of the C—H bond and probably promote the elimination of $HSiMe_3$.

X-ray crystallographic study

The structure of the two compounds *N*-(6-methyl-2-pyridylcyanomethyl) - 3 - trifluoromethyl-aniline (**2d**) and *N*-(4-pyridylcyanomethylidene)-3-trifluoromethylaniline (**3c**) was investigated by X-ray analysis. From a preliminary search, it was

Table 9 Crystal data and structure refinement for **2d** and **3c**

	2d	**3c**
Empirical formula	$C_{15}H_{12}F_3N_3$	$C_{14}H_8F_3N_3$
Formula weight	291.28	275.23
Crystal system	Monoclinic	Monoclinic
Color	Colorless	Colorless
Space group	*C*2/*c*	$P2_1/c$
Crystal size (mm^3)	0.50 × 0.40 × 0.30	0.30 × 0.25 × 0.10
a (Å)	21.076(1)	11.671(6)
b (Å)	8.8328(5)	7.594(5)
c (Å)	16.0128(7)	14.535(4)
β (°)	109.225(4)	91.08(3)
V ($Å^3$)	2814.6(2)	1288.0(11)
Z	8	4
D_{calc} (Mg m^{-3})	1.375(1)	1.419(1)
Wavelength λ (Å)	1.541 84	0.710 73
$2\theta_{max}$ (°)	145	45
Number of independent reflections	1333	1647
Number of reflections with $I > 2\sigma(I)$	1276	1088
Number of parameters	191	182
R	0.0871	0.0948
Goodness-of-fit	1.071	1.164

Table 10 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for **2d**. U_{eq} is defined as one-third of the trace of the orthogonalized U_{ij} tensor

	x	*y*	*z*	U_{eq}
N(1)	561(2)	237(4)	8549(3)	52(1)
C(2)	−8(2)	253(5)	8750(3)	51(1)
C(3)	−316(3)	−1045(6)	8911(4)	65(1)
C(4)	−13(4)	−2430(6)	8870(4)	75(2)
C(5)	569(3)	−2447(6)	8680(4)	72(2)
C(6)	850(3)	−1102(6)	8516(3)	63(1)
C(7)	−320(3)	1806(5)	8770(3)	56(1)
C(8)	219(3)	2973(7)	9123(4)	66(2)
N(3)	607(3)	3883(6)	9394(4)	90(2)
N(2)	−775(2)	2180(5)	7926(3)	72(1)
C(9)	−1246(3)	3339(6)	7778(3)	57(1)
C(14)	−1325(3)	4199(6)	8470(4)	62(1)
C(13)	−1828(3)	5264(7)	8290(4)	74(2)
C(12)	−2242(3)	5551(7)	7449(5)	75(2)
C(11)	−2169(2)	4683(6)	6766(4)	61(1)
C(10)	−1672(3)	3593(5)	6922(4)	59(1)
C(15)	−2616(3)	4942(8)	5861(5)	80(2)
C(16)	1482(4)	−1096(8)	8300(5)	89(2)
F(1)	−2946(4)	3784(7)	5472(4)	225(4)
F(2)	−3056(3)	5975(10)	5741(4)	210(4)
F(3)	−2307(3)	5354(11)	5318(4)	207(4)

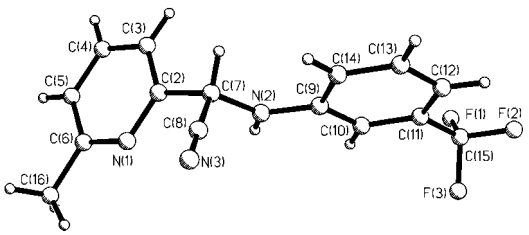
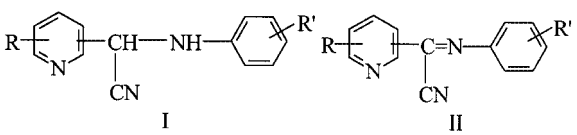


Figure 1 Molecular structure of compound **2d**.

determined that the structures of general formulas I and II are absent in the Cambridge Crystallographic Data Bank.



The molecular structures and crystallographic data obtained for compounds **2d** and **3c** are given in Figs 1 and 2 and Table 9. The atomic coordinates and thermal parameters for non-hydrogen atoms of **2d** and **3c** and some characteristics for these com-

Table 11 Bond lengths and angles for compound **2d**

Distance (Å)		Angle (°)	
N(1)—C(2)	1.342(6)	C(2)—N(1)—C(6)	118.3(4)
N(1)—C(6)	1.338(6)	N(1)—C(2)—C(3)	123.1(5)
C(2)—C(3)	1.383(7)	N(1)—C(2)—C(7)	116.1(4)
C(2)—C(7)	1.525(6)	C(3)—C(2)—C(7)	120.7(5)
C(3)—C(4)	1.391(8)	C(2)—C(3)—C(4)	118.1(6)
C(4)—C(5)	1.359(9)	C(5)—C(4)—C(3)	118.8(5)
C(5)—C(6)	1.391(8)	C(4)—C(5)—C(6)	120.3(5)
C(6)—C(16)	1.483(8)	N(1)—C(6)—C(5)	121.3(5)
C(7)—N(2)	1.415(6)	N(1)—C(6)—C(16)	117.5(6)
C(7)—C(8)	1.499(8)	C(5)—C(6)—C(16)	121.2(5)
C(8)—N(3)	1.127(7)	N(2)—C(7)—C(8)	113.0(4)
N(2)—C(9)	1.390(6)	N(2)—C(7)—C(2)	110.6(4)
C(9)—C(10)	1.388(7)	C(8)—C(7)—C(2)	110.4(4)
C(9)—C(14)	1.398(7)	N(3)—C(8)—C(7)	177.5(6)
C(14)—C(13)	1.374(8)	C(9)—N(2)—C(7)	123.8(4)
C(13)—C(12)	1.366(9)	C(10)—C(9)—N(2)	118.7(5)
C(12)—C(11)	1.385(8)	N(2)—C(9)—C(14)	122.0(5)
C(11)—C(10)	1.384(7)	C(10)—C(11)—C(15)	119.3(5)
C(11)—C(15)	1.463(8)	C(12)—C(11)—C(15)	119.6(5)
C(15)—F(1)	1.278(8)	F(1)—C(15)—F(2)	104.4(7)
C(15)—F(2)	1.270(8)	F(1)—C(15)—F(3)	102.2(8)
C(15)—F(3)	1.297(9)	F(2)—C(15)—F(3)	101.5(7)
		F(1)—C(15)—C(11)	115.3(6)
		F(2)—C(15)—C(11)	117.5(6)
		F(3)—C(15)—C(11)	113.9(6)

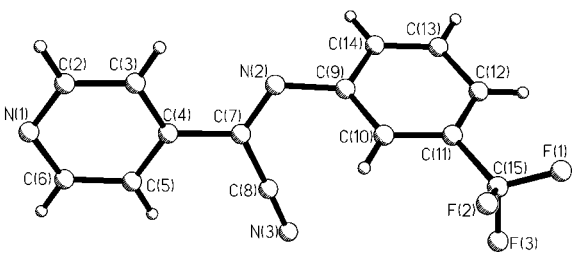


Figure 2 Molecular structure of compound **3c**.

pounds are given in Tables 10–13. In the structure of the crystal of **2d** investigated, the asymmetric C(7) atom had the *R* configuration. This atom, together with the N(2) atom lies in the benzene ring plane (torsion angle C(7)—N(2)—C(9)—C(10) is −179.3(5) °). The torsion angles including the C(8) atom of the cyano group with pyridine and benzene rings were as follows: C(8)—C(7)—C(2)—N(1) = −36.0(6) ° and C(8)—C(7)—N(2)—C(9) = −70.9(7) ° respectively. The molecular structure of **3c** is characterized by three planar fragments (A, B and C). Plane A is the pyridine

Table 12 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for **3c**. U_{eq} is defined as one-third of the trace of the orthogonalized U_{ij} tensor

	x	*y*	*z*	U_{eq}
N(1)	5445(6)	1672(9)	6687(5)	70(2)
C(2)	5553(7)	2707(10)	5956(5)	66(2)
C(3)	4797(6)	2705(9)	5216(5)	59(2)
C(4)	3871(5)	1614(8)	5228(4)	47(2)
C(5)	3735(6)	520(10)	5972(5)	63(2)
C(6)	4539(7)	598(11)	6685(5)	68(2)
C(7)	3050(5)	1574(8)	4426(5)	47(2)
N(2)	3106(5)	2712(7)	3792(4)	56(2)
C(8)	2168(7)	252(11)	4442(5)	69(2)
N(3)	1473(6)	−827(12)	4469(5)	108(3)
C(9)	2342(6)	2582(9)	3008(4)	51(2)
C(10)	2352(6)	1141(9)	2441(5)	54(2)
C(11)	1636(6)	1101(9)	1674(4)	54(2)
C(12)	915(6)	2440(11)	1469(5)	59(2)
C(13)	917(7)	3899(10)	2042(5)	67(2)
C(14)	1610(6)	3983(10)	2798(5)	60(2)
C(15)	1704(7)	−441(10)	1051(5)	63(2)
F(1)	1408(13)	−177(12)	241(5)	235(6)
F(2)	2650(7)	−1072(14)	916(8)	232(6)
F(3)	1144(13)	−1691(11)	1284(7)	291(9)

Table 13 Bond lengths and angles for compound **3c**

Distance (Å)		Angle (°)	
N(1)—C(2)	1.329(10)	C(2)—N(1)—C(6)	116.5(7)
N(1)—C(6)	1.335(10)	N(1)—C(2)—C(3)	123.7(7)
C(2)—C(3)	1.379(10)	C(4)—C(3)—C(2)	119.1(7)
C(3)—C(4)	1.362(10)	C(3)—C(4)—C(5)	118.7(6)
C(4)—C(5)	1.376(10)	C(3)—C(4)—C(7)	120.0(6)
C(4)—C(7)	1.495(9)	C(5)—C(4)—C(7)	121.2(6)
C(5)—C(6)	1.387(11)	C(4)—C(5)—C(6)	118.4(7)
C(7)—N(2)	1.266(8)	N(1)—C(6)—C(5)	123.5(8)
C(7)—C(8)	1.438(11)	N(2)—C(7)—C(8)	122.3(6)
N(2)—C(9)	1.437(8)	N(2)—C(7)—C(4)	120.8(6)
C(8)—N(3)	1.153(10)	C(8)—C(7)—C(4)	116.8(6)
C(9)—C(10)	1.370(10)	C(7)—N(2)—C(9)	119.4(6)
C(9)—C(14)	1.395(10)	N(3)—C(8)—C(7)	178.5(7)
C(10)—C(11)	1.381(9)	C(10)—C(9)—N(2)	121.3(6)
C(11)—C(12)	1.350(10)	C(14)—C(9)—N(2)	119.3(6)
C(11)—C(15)	1.483(10)	C(10)—C(11)—C(15)	118.2(6)
C(12)—C(13)	1.385(10)	F(3)—C(15)—F(2)	103.4(10)
C(13)—C(14)	1.354(10)	F(3)—C(15)—F(1)	104.6(10)
C(15)—F(1)	1.237(10)	F(2)—C(15)—F(1)	98.5(10)
C(15)—F(2)	1.223(10)	F(3)—C(15)—C(11)	114.5(7)
C(15)—F(3)	1.205(10)	F(2)—C(15)—C(11)	117.8(7)
		F(1)—C(15)—C(11)	115.9(7)

ring, plane B is the double bond C(7)=N(2) and cyano group, and plane C is the phenyl ring with atom C(15). The dihedral angles are 7.4(3) ° and 63.2(3) ° between A and B and B and C respectively. Considerable thermal vibrations occur for fluorine atoms (mean value $U_{eq} = 0.214(11)$ Å^2 for **2d** and 0.253(7) Å^2 for **3c**). Therefore, the C—F bond lengths calculated are decreased.[15] The C—F bond lengths could be also decreased due to ionic–covalent resonance.[16] A more detailed analysis of the molecular geometry is difficult owing to the significant standard deviation in atomic coordinates. The intermolecular contacts in the crystals generally correspond to the sums of the van der Waals radii.[16]

The compounds synthesized in this work will be used in further research on their antitumor activity.

Supplementary material

The crystallographic data for the structures reported in this paper were deposited with the Cambridge Crystallographic Centre. The deposition numbers are CCDC 156778 and 156877. Copies of these data can be obtained free of charge from: The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: + 44-1223-336033; e-mail: or www: http://www.ccdc.cam.ac.uk).

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