LATVIJAS ORGANISKĀS SINTĒZES INSTITŪTS

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HETEROCIKLISKO ALDIMĪNU HIDROSILILĒŠANAS UN TRIMETILSILILCIANĒŠANAS REAKCIJAS

Promocijas darbs ķīmijas nozarē, organiskās ķīmijas apakšnozarē

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KOPSAVILKUMS

Heterociklisko aldimīnu hidrosililēšanas un trimetilsililcianēšanas reakcijas. Autore-Ļ. Golomba. Zinātniskie vadītāji-Dr. habil. chem., profesors E. Lukevics, Dr. habil. chem., I. Jovele. Promocijas darbs: 62 lappuses, 3 attēli, 19 tabulas, 15 shēmas, 93 literatūras avoti, 1 pielikums. Latviešu valodā.

HETEROCIKLISKIE ALDIMĪNI , ŠIFA BĀZES, PĀREJAS METĀLU KOMPLEKSI, HIDROSILILĒŠANA, KATALĪZE, HETEROCIKLISKIE AMĪNI, TRIMETILSILILCIANĒŠANA, LUISA SKĀBES, α-AMINONITRILI, ASIMETRISKĀ SINTĒZE, PROPENILIDĒNANILĪNI, TRIFLUORMETILANILĪNU SILILATVASINĀJUMI, NEIROTROPĀ AKTIVITĀTE, CITOTOKSICITĀTE.

Darba trešajā un ceturtajā nodaļās apskatītas katalītiskas silānu $HSiEt_3$, $HSiMe_2Ph$, H_2SiPh_2 pievienošanās reakcijas furāna, tiofēna, piridīna trifluormetilfenilgrupas saturošiem aldimīniem VIII grupas pārejas metālu un zelta Au kompleksu klātbūtnē. Piektajā, sestajā, astotajā nodaļās apkopoti rezultāti, kas iegūti pētot Me_3SiCN katalītiskās pievienošanās reakcijas jaunām furāna, tiofēna, piridīna Šifa bāzēm dažādu Luisa skābju klātbūtnē. Septītajā nodaļā doti Me_3SiCN diastereoselektīvas pievienošanās hirāliem O-, S-, N-aldimīniem izpētes rezultāti. Devītajā nodaļā apkopoti 5-*t*-butil-2-furilmetilidēn-anilīnu trifluormetil-atvasinājumu un to sililanalogu bioloģisko īpašību pētījumu rezultāti.

ABSTRACT

Hydrosilylation and trimethylsilylcyanation of heterocyclic aldimines. Author L. Golomba. Supervisors Dr. habil. chem., professor E. Lukevics, Dr. habil. chem. I. Iovel. Dissertation: 62 pages, 3 figures, 19 tables, 15 schemes, 93 literature references, 1 supplement. In Latvian.

HETEROCYCLIC ALDIMINES, SHIFF BASES, TRANSITION METAL COMPLEXES, HYDROSILYLATION, CATALYSIS, HETEROCYCLIC AMINES, TRIMETHYLSILYLCYANATION, LEWIS ACIDS, α-AMINONITRILES, ASYMMETRIC SYNTHESIS, PROPENYLIDENE-ANILINES, SILYLDERIVATIVES OF TRIFLUOROMETHYLANILINES, NEUROTROPIC ACTIVITY, CYTOTOXICITY.

In the third and fourth chapters of the present work catalytic addition of $HSiEt_3$, $HSiMe_2Ph$, H_2SiPh_2 to furan, thiophene, pyridine trifluoromethylphenyl group containing aldimines in the presence of Group VIII transition metal and gold Au complexes is reviewed. In the fifth, sixth, eighth chapters the catalytic addition of Me_3SiCN to novel furan, thiophene, pyridine Schiff's bases in the presence of various Lewis acids is described. In the seventh chapter of the work diastereoselective addition of Me_3SiCN to chiral O-, S-, N-heterocyclic aldimines is reviewd. The ninth chapter is devoted to the biological properties of the trifluoromethyl derivatives of 5-*tert*--butyl-2-furylmethylidene-anilines and their silyl analogs.

Saturs.

1. Ieskats literatūrā.

Hidrosililēšana ir viena no svarīgākajām reakcijām silīcijorganiskajā ķīmijā, tādēļ jau vairāk kā pusgadsimtu šī reakcija tik intensīvi pētīta. Pēc vairāk nekā piecdesmit gadu ilga laika perioda interese par šo reakciju nav mazinājusies, bet pēdējos gados pat palielinājusies. Rūpnieciskajā ražošanā hidrosililēšanas reakcijai ir praktiska nozīme silīcijorganisko savienojumu-saistvielu, līmju, polimēru iegūšanā. Pētnieciskajās laboratorijās hidrosililēšana ir ļoti ērta un efektīva metode silīcijorganisko savienojumu sintēzei, lai veiktu pētījumus silīcijorganisko savienojumu ķīmijā, kā arī lai iegūtu silīcijsaturošus polimērus kā jaunus materiālus. Dažādu funkcionālu grupu hidrosililēšana, izmantojot par katalizātoriem pārejas metālu kompleksus vai radikāļu iniciātorus, ir vieglākais ceļš dažādu silīcijorganisko reaģentu un sintētisko produktu iegūšanai, kā arī tā ir unikāla metode saites ogleklis-heteroatoms selektīvai reducēšanai. Jaunas reakcijas, kuras ir līdzīgas hidrosililēšanai, tiek pētītas un attīstītas. Pie tām var pieskaitīt sililkarbonilēšanas, sililformilēšanas, sililkarbociklizēšanas reakcijas. Hidrosilānu pievienošanās saitei C=N ir mazāk pētīta nekā saitei C=O aldehīdos, ketonos un to atvasinājumos [1,2]. Literatūrā ir aprakstītas alifātisko un aromātisko t.i. neheterociklisko azometīnu hidrosililēšanas reakcijas. Šajās reakcijās veidojas piesātināti N-sililatvasinājumi, kurus hidrolizējot iegūst attiecīgos amīnus. Daudzu katalizātoru klātbūtnē šie procesi notiek neselektīvi, kā arī vienlaicīgi norit hidrēšana, hidrogenolīze, kondensācija. Pozitīvi rezultāti iegūti, galvenokārt izmantojot astotās grupas pārejas metālu Rh, Pd, kā arī Au kompleksus [3-5]. Pd katalizātori ir efektīvāki lietojot monohidrosilānus, bet Rh katalizātori aktīvāki dihidrosilānu pievienošanās reakcijās [6]. Pēdējos gados, sākot ar Kagana [7,8] un Brunnera [9-11] darbiem, intensīvi tiek pētīta imīnu un oksīmu asimetriska hidrosililēšana [12-21]. Mūsu uzmanību piesaistīja heterociklisko aldimīnu hidrosililēšanas reakcijas.

Ļoti svarīga C-C saites veidošanā ir trimetilsililcianēšanas reakcija jeb Štrekera sintēze [22--24]. Līdz šim literatūrā aprakstīta trimetilsililcianīda pievienošana imīniem, kas iegūti no aromātiskiem un alifātiskiem aldehīdiem, izņemot vienu heterociklisko 3-piridīnaldehīdu [25].

Imīnu asimetriskai cianēšanai ir liela nozīme optiski aktīvu slāpekli saturošu savienojumu iegūšanā [22-24,26,27]. Pirmā asimetriskā Štrekera sintēze literatūrā aprakstīta 1963. gadā (Harada) [28]. Metodes pamatā ir hirālas Šifa bāzes iegūšana aldehīda kondensācijā ar optiski aktīvu amīnu, visplašāk lietotie amīni ir benzilamīni [25,29-35]. Trimetilsililcianīda izmantošana kopā ar Luisa skābi ir plašāk lietota metode nekā NaCN/AcOH(kat.) pielietošana [36-43]. Diastereoselektīva Me_3SiCN pievienošana Šifa bāzēm noved pie jauna hirāla centra veidošanās α-aminonitrilos [44-

-46]. Darbā kā hirāli substrāti izmantoti furāna, tiofēna, piridīna t.i. heterocikliskie aldimīni, kas iegūti no (R)- un (S)-feniletilamīna. Stereoselektivitātes pakāpe atkarīga gan no aldimīna dabas, gan no katalītiskās sistēmas, tādēļ darbā sintezēta sērija heterociklisko optiski aktīvu Šifa bāzu, lai izpētītu trimetilsililcianēšanas reakcijas.

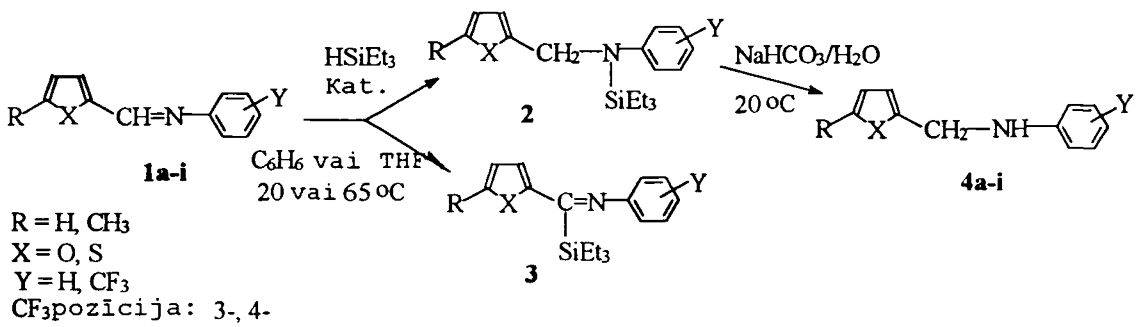
Gan hidrosililēšanas, gan trimetilsililcianēšanas reakcijās kā substrāti izmantoti heterocikliskie-CF_3-fenil grupas saturoši aldimīni, jo šie savienojumi un to reakciju produkti: amīni un nitrili ir potenciāli bioloģiski aktīvi savienojumi [47-51].

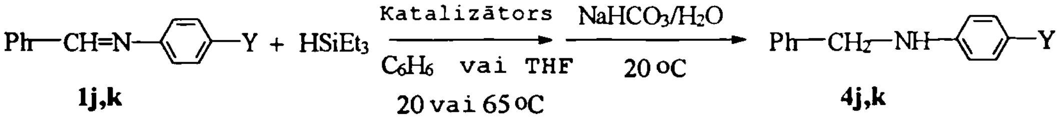
2. Darba mērķi.

1. Izpētīt jaunu furāna, tiofēna, piridīna CF_3 -fenil grupas saturošu Šifa bāzu hidrosililēšanu ar $HSiEt_3$, $HSiMe_2Ph$, H_2SiPh_2. Atrast aktīvākos katalizātorus. Noteikt hidrosilānu pievienošanās likumsakarības dubultsaitei C=N (hetero)aromātiskos azometīnos.
2. Sintezēt hidrosililēšanas produktus: O-, S-, N-heterocikliskos amīnus.
3. Izpētīt trimetilsililcianīda Me_3SiCN katalītisku pievienošanos jaunām furāna, tiofēna, piridīna Šifa bāzēm. Atrast aktīvākos katalizātorus. Noteikt substrātu stuktūras ietekmi uz to reaģētspēju un reakcijas virzienu.
4. Sintezēt trimetilsililcianēšanas reakciju produktus: O-, S-, N-heterocikliskos α-aminonitrilus.
5. Noteikt sintezēto nitrilu pretvēža aktivitāti.
6. Izpētīt jaunu optiski aktīvu furāna, tiofēna, piridīna Šifa bāzu trimetilsililcianēšanas reakcijas. Sintezēt attiecīgos diastereomērus: α-aminonitrilus.
7. Izpētīt saišu sistēmas N=C–C=C trimetilsililcianēšanas reakcijas propenilidēnamīnos.
8. Sintezēt jaunus N-(5-*t*-butil-2-furilmetilidēn)-trifluormetilanilīnus un to sililanalogus, noteikt sintezēto savienojumu bioloģisko aktivitāti.

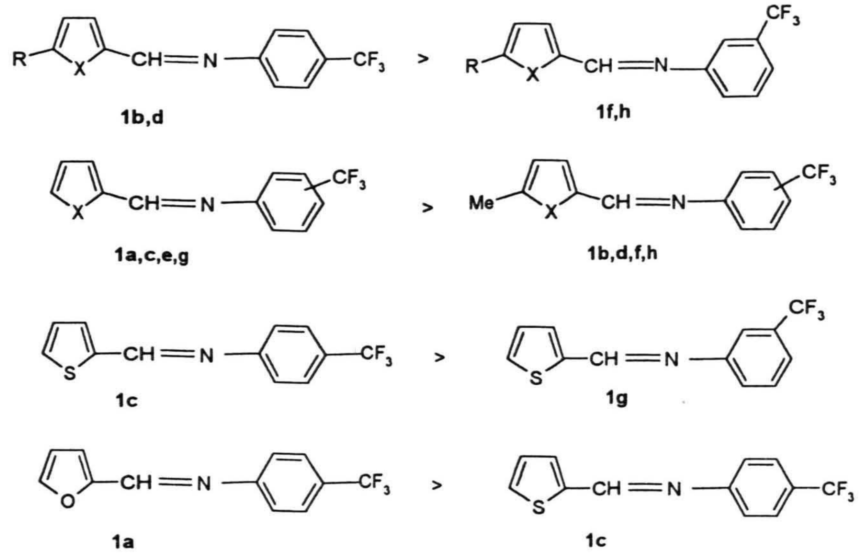
3. N-(hetarilmetilidēn)-3-trifluormetilanilīnu un N-(hetarilmetilidēn)-4-trifluormetilanilīnu, kuros hetaril grupas ir 2-furil, 5-metil-2-furil, 2-tienil, 5-metil-2tienil, hidrosililēšana ar Et_3SiH VIII grupas pārejas metālu Rh, Pd, Pt, Ir, Ru, kā arī Au kompleksu klātbūtnē.

Darbā izpētītas iepriekš sintezēto heterociklisko trifluormetilfenilgrupas saturošu Šifa bāzu **1a-i** [52] un benzilidēnanilīnu **1j,k** [53-55] hidrosililēšanas reakcijas, izmantojot lētāko alkilsilānu Et_3SiH, tādēļ šai reakcijai ir arī praktiska nozīme.

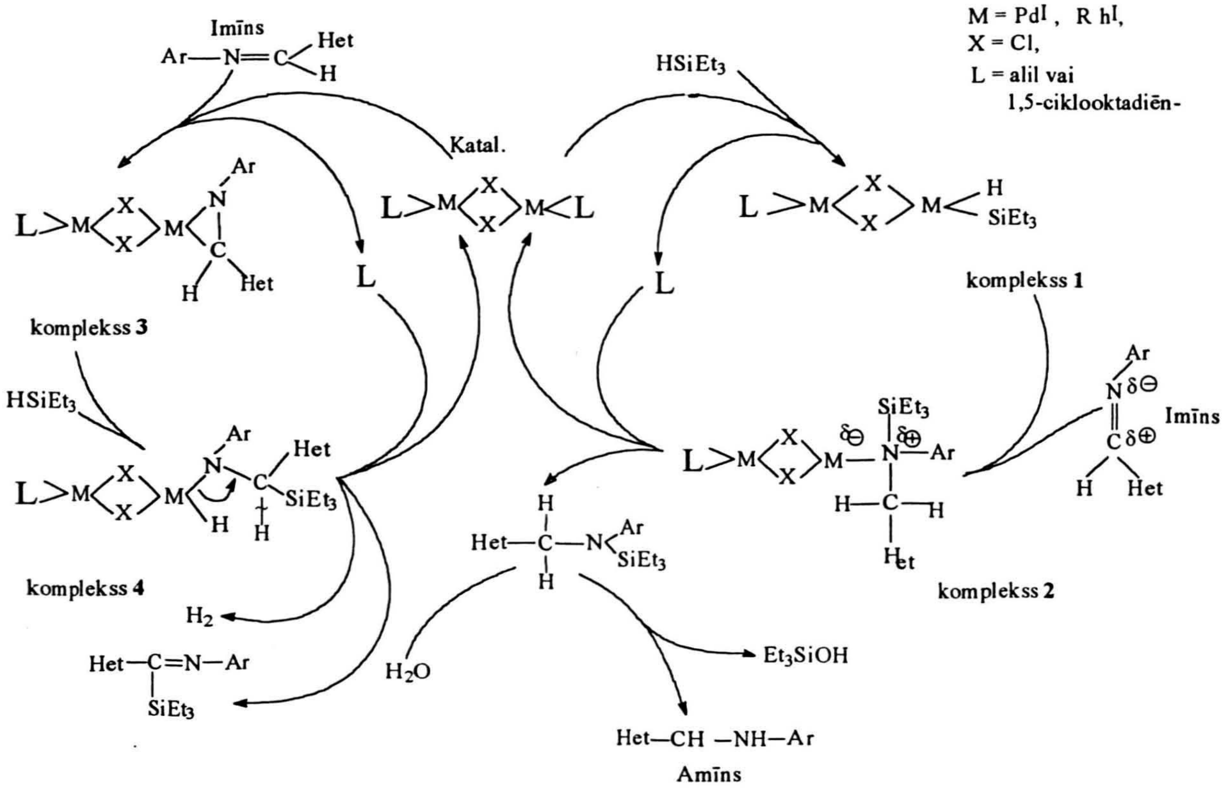




Tika pārbaudīti VIII grupas pārejas metālu kompleksi: $(Ph_3P)_2IrCl(CO)$, $(Ph_3P)_4Pt$, $H_2PtCl_6{\cdot}6H_2O$, $[Rh(COD)acac]$, $[Rh(COD)Cl]_2$, $RhCl_3{\cdot}4H_2O$, $(Ph_3P)_4Pd$, $[Pd(CH_2CHCH_2)Cl]_2$, $(Ph_3P)_2PdCl_2$, $(Ph_3P)_3RuCl_2$ un $AuCl_3$, $HAuCl_4$, kā arī metālu katalizātori 5% Pd/C un 5% Ru/Al_2O_3. No visiem Ir^I, Pd^0, Pd^I, Pd^{II},Pt^0, Pt^{IV}, Rh^I, Rh^{III}, Ru^0, Ru^{II}, Au^{III} kompleksiem reakciju katalizēja tikai Rh^I, Pd^I,Au^{III} kompleksi: $[Rh(COD)Cl]_2$, $[Pd(CH_2CHCH_2)Cl]_2$, $HAuCl_4{\cdot}3H_2O$. Pie tam Pd^I kompleksa aktivitāte izrādījās visaugstākā. Izmantojot bis{[μ-hlor(ciklooktadiēn-1,5)]rodiju}-$[Rh(COD)Cl]_2$, bis{[μ-hloralil]palādiju}-$[Pd(CH_2CHCH_2)Cl]_2$ un tetrahlorzeltskābes trihidrātu-$HAuCl_4{\cdot}3H_2O$ tika sintezēta rinda amīnu **4a-k**, to iznākums pēc attīrīšanas uz hromatogrāfiskām kolonnām bija 70–75% attiecībā pret izreaģējušo imīnu. Reakciju apstākļi un iegūto produktu **4a-k** raksturlielumi apkopoti tabulā 3.1. $[Rh(COD)Cl]_2$ aktivitāte izrādījās augstāka tetrahidrofurānā nekā benzolā. Pd katalizātora klātbūtnē reakcijas ātrums arī atkarīgs no šķīdinātāja dabas. Imīnus **1a-i** pēc to reaģētspējas var sakārtot rindā:



Visi furāna azometīni **1a,b,e,f** aktīvāki par tiofēna imīniem **1c,d,g,h,i**. Metilgrupas esamība heterociklā palēnina reakcijas ātrumu, bet trifluormetilgrupa 4-vietā imīna molekulas azodaļā paātrina reakcijas norisi. Benzilidēnanilīnu **1j,k** aktivitāte ir zemāka par furāna analogu aktivitāti, bet augstāka par tiofēna atvasinājumu aktivitāti. Pirmējie hidrosililēšanas produkti t.i. N-sililētie produkti **2e,f** izdalīti no reakciju maisījumiem N-(2-furilmetilidēn)-3-trifluormetilanilīna **1e** un N-(5-metil-2-furilmetilidēn)-3-trifluormetilanilīna **1f** hidrosililēšanas reakcijās. Pārējiem N-sililētiem savienojumiem **2a,c,g** reģistrēti to masspektri. Šajās reakcijās tika konstatēta arī C-sililēto nepiesātināto savienojumu **3** klātbūtne, tie tika identificēti ar GŠH-MS metodes palīdzību. Šāda veida savienojumi rodas katalītiskās dehidrokondensācijas rezultātā, kas notiek paralēli hidrosililēšanas reakcijai [4]. Reakcijas mehānismu var attēlot shēmā:


M = PdI , RhI,
X = Cl,
L = alil vai
1,5-ciklooktadiēn-
Imīns
Ar—N=C<Het H
HSiEt₃
Katal.
komplekss 1
komplekss 2
komplekss 3
komplekss 4
L
HSiEt₃
Imīns
H₂
Het—C(SiEt₃)=N—Ar
H₂O
Het—CH₂—N(Ar)SiEt₃
Et₃SiOH
Het—CH —NH—Ar
Amīns

Tabula 3.1.

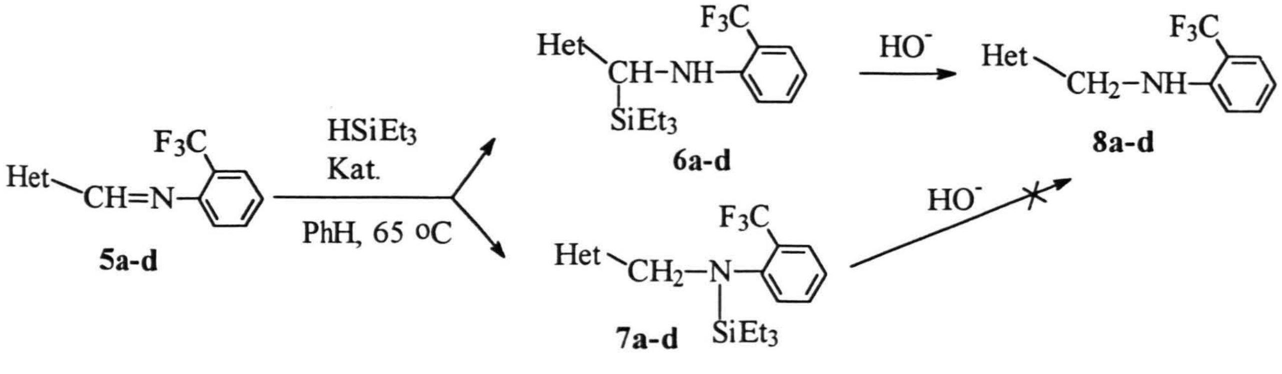
Hidrosililēšanas reakciju un produktu **2a,c,e-g, 4a-k** raksturlielumi.

№	Imīns				Katalizātors (mol %)	Šķīdinātājs	Temp. °C	Laiks st.	Konversija % GŠH	Produkts (iznākums, % (GŠH))	
		X	R	CF_3-pozīcija						pirms hidrolīzes	pēc hidrolīzes
1	**1a**	O	H	4	$H_2PtCl_6{\cdot}6H_2O$ (2)	THF	20	21	21		**4a** (15)
2	**1a**	O	H	4	$[(C_6H_5)_3P]_4Pt$ (2)	THF	20	21	15		**4a** (12)
3	**1a**	O	H	4	$RhCl_3{\cdot}4H_2O$ (2)	THF	20	32,5	reakcija neiet		
4	**1a**	O	H	4	[Rh(COD)acac] (2)	THF	20	17.5			
							65	5.5	reakcija neiet		
5	**1a**	O	H	4	$[Rh(COD)Cl]_2$ (2)	THF	20	21	56	**2a** (54)	**4a** (49)
6	**1b**	O	CH_3	4	$[Rh(COD)Cl]_2$ (2)	THF	20	20			
							65	5	**100**		**4b** (85)
7	**1c**	S	H	4	$[(C_6H_5)_3P]_2IrCl(CO)$ (2)	THF	65	10.5	reakcija neiet		
8	**1c**	S	H	4	$[(C_6H_5)_3P]_4Pd$ (2)	THF	65	10.5	reakcija neiet		
9	**1c**	S	H	4	[Rh(COD)acac] (2)	THF	65	10.5	reakcija neiet		
10	**1c**	S	H	4	$[Rh(COD)Cl]_2$ (2)	THF	65	10.5	58		**4c** (50)
11	**1c**	S	H	4	$[Pd(CH_2CHCH_2)Cl]_2$ (2)	THF	20	5	48		**4c** (44)
12	**1c**	S	H	4	$[Pd(CH_2CHCH_2)Cl]_2$ (2)	C_6H_6	65	3	80	**2c** (76)	**4c** (73)
13	**1d**	S	CH_3	4	$[Rh(COD)Cl]_2$ (2)	C_6H_6	65	18			
					(3)			4	56		**4d** (48)
14	**1e**	O	H	3	$[Rh(COD)Cl]_2$ (2)	C_6H_6	65	10			
					(3)			2	90		**4e** (81)
15	**1e**	O	H	3	$[Rh(COD)Cl]_2$ (2)	C_6H_6	65	19	97	**2e** (88)	**4e** (85)
16	**1f**	O	CH_3	3	$[Rh(COD)Cl]_2$ (3)	C_6H_6	65	19	91	**2f** (70), **3f** (17)	**4f** (68)
17	**1f**	O	CH_3	3	$[Rh(COD)Cl]_2$ (2)	C_6H_6	65	17	88	**2f** (86)	**4f** (70)

18	**1f**	O	CH_3	3	$[Rh(COD)Cl]_2$ (3)	THF	65	7	90	**2f** (69), **3f** (19)	**4f** (65)
19	**1g**	S	H	3	$[Rh(COD)Cl]_2$ (3)	C_6H_6	65	36	**25**	**2g** (22)	
20	**1g**	S	H	3	$[Pd(CH_2CHCH_2)Cl]_2$ (2)	C_6H_6	20	25			
							65	4	**48**	**2g** (46)	**4g** (42)
21	**1g**	S	H	3	$[(C_6H_5)_3P]_4Pd$ (2)	C_6H_6	20	25			
							65	4	reakcija neiet		
22	**1h**	S	CH_3	3	$[Rh(COD)Cl]_2$ (3)	C_6H_6	65	41	22		**4h** (18)
23	**1i**	S	H	-	$[(C_6H_5)_3P]_4Pd$ (2)	C_6H_6	20	26	reakcija neiet		
24	**1i**	S	H	-	$[Rh(COD)Cl]_2$ (2)	C_6H_6	65	30	**38**	**2i** (35)	
25	**1i**	S	H	-	$[Pd(CH_2CHCH_2)Cl]_2$ (2)	C_6H_6	20	26	**96**	**2i** (50), **3i** (38)	**4i** (48)
26	**1i**	S	H	-	$[Pd(CH_2CHCH_2)Cl]_2$ (2)	C_6H_6	65	14	**96**	**2i** (52), **3i** (39)	**4i** (50)
27	**1j**	Ph		4	$[Rh(COD)Cl]_2$ (2)	THF	65	5	**54**		**4j** (50)
28	**1j**	Ph		**4**	$[Pd(CH_2CHCH_2)Cl]_2$ (2)	THF	20	22	88		**4j** (80)
29	**1k**	Ph		-	$[Rh(COD)Cl]_2$ (2)	THF	65	14.5	39		**4k** (37)
30	**1k**	Ph		-	$[Pd(CH_2CHCH_2)Cl]_2$ (2)	C_6H_6	65	14.5	84		**4k** (76)
31	**1k**	Ph		-	$[Pd(CH_2CHCH_2)Cl]_2$ (2)	THF	65	14.5	87		**4k** (78)
32	**1e**	O	H	3	$AuCl_3$ (3)	PhH	65	19	**7**		**4e**(5)
33	**1e**	O	H	3	$HAuCl_4{\cdot}3H_2O$ (3)	PhH	65	19	**12**		**4e** (8)
34	**1e**	O	H	3	$HAuCl_4{\cdot}3H_2O$ (3)	THF	65	6.5	**98**		**4e**(88)
35	**1a**	O	H	4	$AuCl_3$ (3)	THF	65	3	**93**	-	**4a** (78)
36	**1a**	O	H	4	$HAuCl_4{\cdot}3H_2O$ (3)	THF	65	3	**98**	-	**4a** (88)
37	**1f**	O	CH_3	3	$HAuCl_4{\cdot}3H_2O$ (3)	THF	65	5	100	-	**4f** (95)
38	**1b**	O	CH_3	4	$HAuCl_4{\cdot}3H_2O$ (3)	THF	65	5	60	-	**4b** (57)
39	**1g**	S	H	3	$HAuCl_4{\cdot}3H_2O$ (3)	THF	65	23.5	60	-	**4g** (47)
40	**1c**	S	H	4	$HAuCl_4{\cdot}3H_2O$ (3)	THF	65	19	53	-	**4c**(47)
41	**1h**	S	CH_3	3	$HAuCl_4{\cdot}3H_2O$ (3)	THF	65	22.5	68	-	**4h**(63)
42	**1d**	S	CH_3	4	$HAuCl_4{\cdot}3H_2O$ (3)	THF	65	45	**56**	-	**4d** (46)
43	**1i**	S	H	-	$HAuCl_4{\cdot}3H_2O$ (3)	THF	65	45	**58**	-	**4i** (57)
44	**1j**	Ph		4	$HAuCl_4{\cdot}3H_2O$ (3)	THF	65	18	**60**	-	**4j** (26)
45	**1k**	Ph		-	$HAuCl_4{\cdot}3H_2O$ (3)	THF	65	45	100	-	**4k** (89)

4. N-(hetarilmetilidēn)-2-trifluormetilanilīnu, kuros hetaril grupas ir 2-furil, 5-metil-2-furil, 2-tienil, 5-metil-2-tienil, 2-, 3-, 4-piridil, un N-(6-metil-2-piridilmetilidēn)-2-aminopiridīna hidrosililēšana ar Et_3SiH, $HSiMe_2Ph$, H_2SiPh_2 VIII grupas pārejas metālu Pd, Rh kompleksu klātbūtnē.

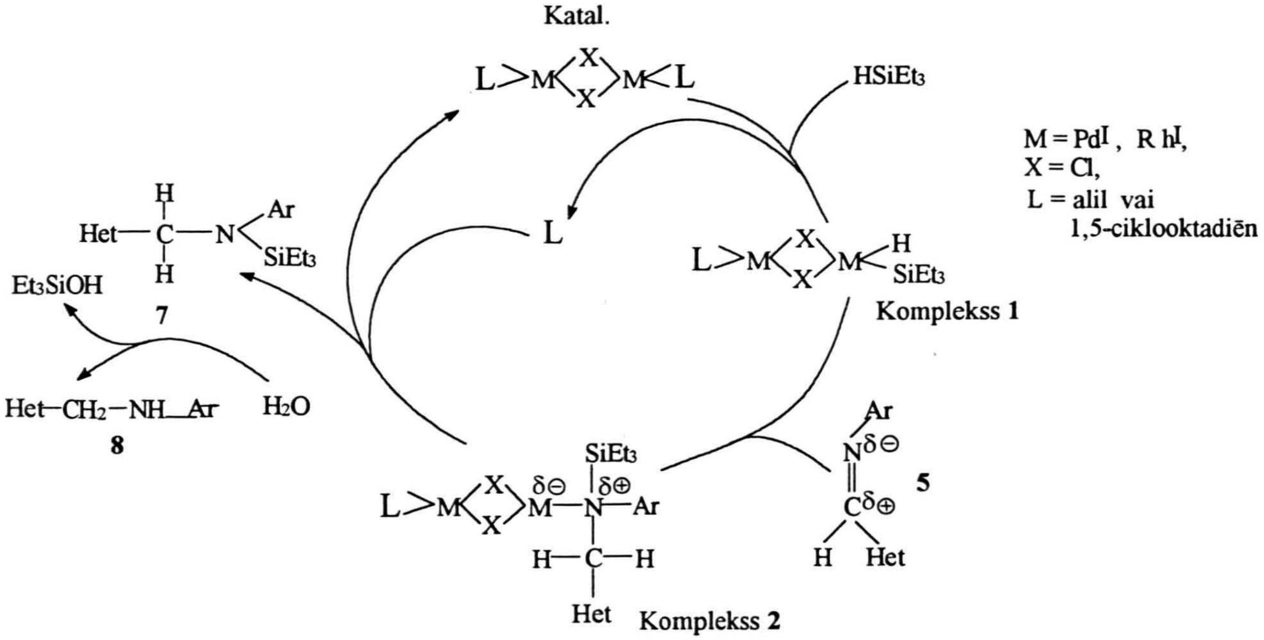
Iepriekš sintezēto N-(hetarilmetilidēn)-2-trifluormetilanilīnu **5a-d** un 2-, 3-, 4-piridilmetilidēn-2-trifluormetilanilīnu **5e,f,g** [56] hidrosililēšanas reakciju gadījumā ar Et_3SiH aktīvākie katalizātori izrādījās vienvērtīgā rodija Rh^I un palādija Pd^I dimērie kompleksi: $[Rh(COD)Cl]_2$ un $[Pd(CH_2CHCH_2)Cl]_2$ analoģiski kā mūsu iepriekšējā darbā [57]. Šo katalizātoru klātbūtnē izpētītas sekojošas reakcijas: N-(hetarilmetilidēn)-2-trifluormetilanilīnu **5a-g** hidrosililēšanas reakcijas ar Et_3SiH, kuros hetaril grupas ir 2-furil, 5-metil-2-furil, 2-tienil, 5-metil-2-tienil, 2-, 3-, 4-piridil, kā arī N-(6-metil-2-piridilmetilidēn)-2-aminopiridīna **5h** hidrosililēšana ar $HSiEt_3$, $HSiMe_2Ph$, H_2SiPh_2. Abu furāna imīnu **5a,b** gadījumā aktīvāks izrādījās $[Rh(COD)Cl]_2$, bet tiofēna imīnu **5c,d** gadījumā aktīvāks $[Pd(CH_2CHCH_2)Cl]_2$. Acīmredzot, tiofēna substrāti dezaktivē Rh kompleksu. Pēc O- un S-heterociklisko imīnu hidrosililēšanas reakciju veikšanas, reakciju maisījumi analizēti ar ^1H KMR metodi. Uzņemtie spektri (pirms hidrolīzes) satur signālus, kas liecina par divu veidu sililēto produktu **6a-c** un **7a-c** veidošanos.



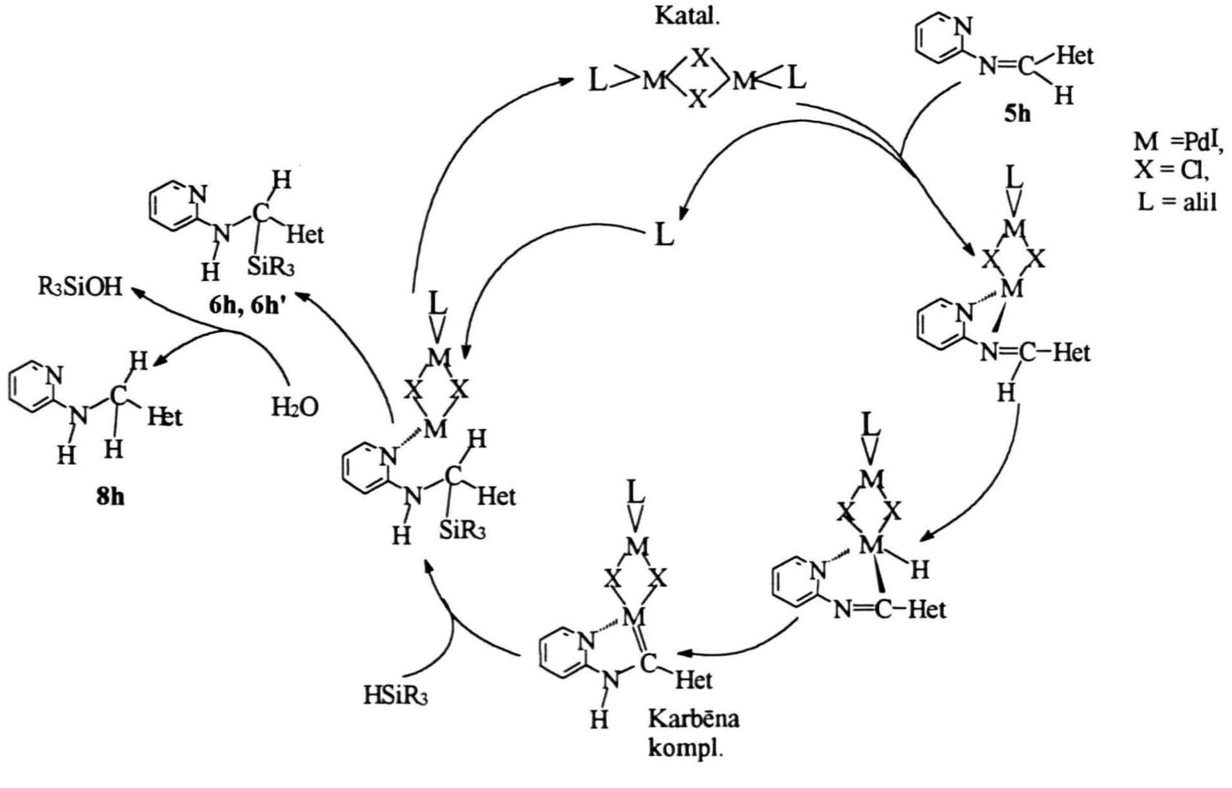
Het: **5a** = 2-furil, **5b** = 5-metil-2-furil, **5c** = 2-tienil, **5d** = 5-metil-2-tienil

Grupas Et_3SiCH-NH esamību raksturo grupas CH-NH divi protonu dubleti, bet grupas CH_2-$NSiEt_3$ esamību pierāda grupas CH_2 protonu singlets. Iepriekšējos darbos [1,2,6,57,58] parādīts, ka saites C=N hidrosililēšanas produkti ir N-sililētie produkti, kuri viegli hidrolizējas. Šajā gadījumā pārsvarā rodas C-sililētie produkti **6a-d** (80-85% no kopējā daudzuma). Pēc hidrolīzes šie produkti pilnībā pārvēršas attiecīgos amīnos **8a-d**, bet N-sililētie produkti **7a-d** nehidrolizējas pat pēc divkāršas un trīskāršas hidrolīzes procedūras veikšanas. Pateicoties N-sililēto produktu **7a-d** stabilitātei, tie izdalīti ar kolonnu hromatogrāfijas metodes palīdzību. Hidrosililēšanas produktu **6a-c,g,h,h'**, **7a-d,g**, **8a-d,g,h** raksturlielumi apkopoti tabulā 4.1.

N-sililēto produktu **7a-d** veidošanās mehānisms:



C-sililēto produktu veidošanās mehānisms:



Tabula 4.1.

Hidrosililēšanas reakciju un produktu **6a-c,g,h,h’**, **7a-d,g**, **8a-d,g,h** raksturlielumi.

Imīns	Silāns	Katalizātors	Temp., °C/ Laiks, st.	Imīna konversija, % (GŠH)	Produkts		^{1}H KMR (CDCl$_3$), ķīmiskā nobīde, δ, m.d., *J*, Hz					
					pirms hidrolīzes*	pēc hidrolīzes^{2}*	CH$_3$ (3H, s)	SiCH–NH (struktūra **6**) CH (d)	NH (d)	CH$_2$–NSi (struktūra 7) CH$_2$ (2H, s)	CH$_2$–NH (struktūra **8**) CH$_2$ (d)	NH (ps)
5a	HSiEt$_3$	[Rh(COD)Cl]$_2$	65/15	85	**6a**		-	3.95	4.53	4.33	4.18	4.67
					7a	**7a**^{4}*	-	*J* = 8.0	*J* = 8.0		*J* = 6.0	
						8a^{4}*	-					
5a	HSiEt$_3$	[Pd(alil)Cl]$_2$	65/31	10	-							
5b	HSiEt$_3$	[Rh(COD)Cl]$_2$	65/11	88	**6b**		2.26	3.95	4.33	4.32	4.16	4.64
					7b	**7b**^{4}*	2.27	*J* = 7.5	*J* = 7.5		*J* = 6.0	
						8b^{4}*	2.29					
5b	HSiEt$_3$	[Pd(alil)Cl]$_2$	65/23	16	-							
5c	HSiEt$_3$	[Rh(COD)Cl]$_2$	65/25	~ 0	-							
5c	HSiEt$_3$	[Pd(alil)Cl]$_2$	65/25	80	**6c**		-	4.20	4.7	4.60	4.55	4.7
					7c	**7c**^{5}*	-	*J* = 6.0	p s		*J* = 5.4	
						8c^{5}*	-					
5d	HSiEt$_3$	[Rh(COD)Cl]$_2$	65/30	~ 0	-							
5d	HSiEt$_3$	[Pd(alil)Cl]$_2$	65/30	82		**7d**^{5}*	2.40	-		4.49	4.47	4.7
					- ^{3}*	**8d**^{5}*	2.44				*J* = 5.4	
5e	HSiEt$_3$	[Rh(COD)Cl]$_2$	65/20	~ 0	-							
5e	HSiEt$_3$	[Pd(alil)Cl]$_2$	65/21	~ 0	-							
5f	HSiEt$_3$	[Rh(COD)Cl]$_2$	65/16	~ 0	-							

5f	$HSiEt_3$	$[Pd(alil)Cl]_2$	65/21	~ 5	-							
5g	$HSiEt_3$	$[Rh(COD)Cl]_2$	65/20	72		**7g**[6*]	-	-		4.89	4.42	5.0
5g	$HSiEt_3$	$[Pd(alil)Cl]_2$	65/21	~ 100	-[3*]	**8g**[6*]	-				$J = 6.0$	
5h	$HSiMe_2Ph$	$[Rh(COD)Cl]_2$	65/18	~ 0	-							
5h	$HSiMe_2Ph$	$[Pd(alil)Cl]_2$	65/12	80		**6h**[6*]	2.42	5.43	5.56	-	4.58	5.6
					-[3*]	**8h**[6*]	2.55	$J = 6.4$	$J = 6.4$		$J = 5.2$	
5h	H_2SiPh_2	$[Rh(COD)Cl]_2$	20/50, 65/9	~ 0	-							
5h	H_2SiPh_2	$[Pd(alil)Cl]_2$	20/50	77		**6h'**[6*]	2.44	5.47	5.55	-	4.58	5.6
					-[3*]	**8h**[6*]	2.55	$J = 6.0$	$J = 6.0$		$J = 5.2$	

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* Pēc ^{1}H KMR datiem produktu maisījumi.

[2*] Produkti izdalīti ar kolonnu hromatogrāfijas metodes palīdzību.

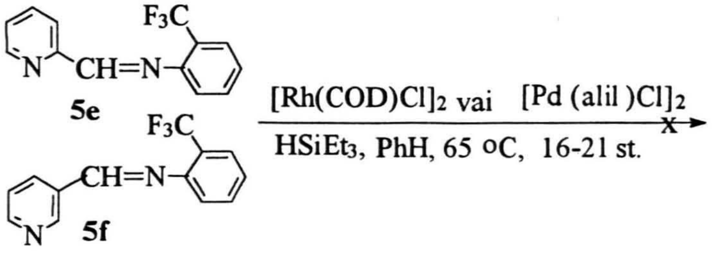
[3*] ^{1}H KMR spektri reakciju maisījumiem nav reģistrēti.

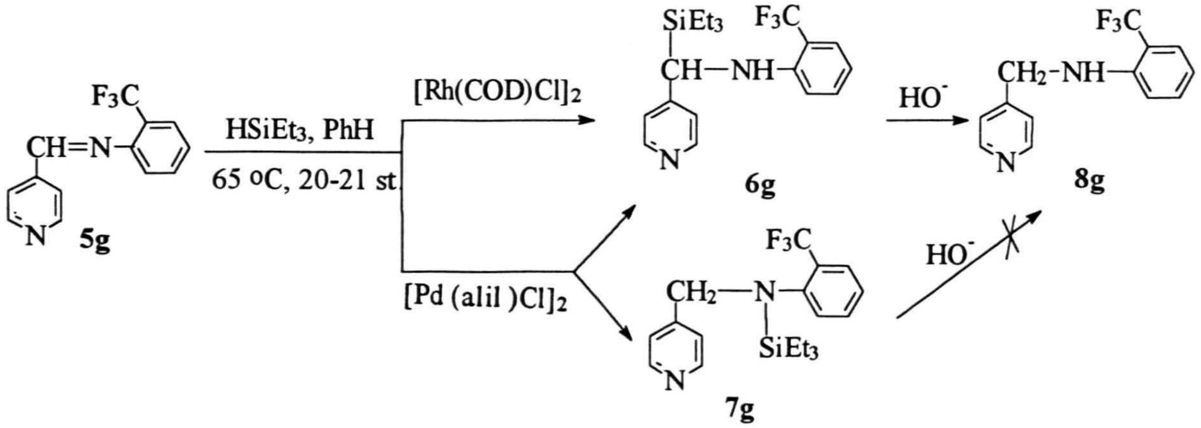
[4*] Eluents: benzols–etilacetāts, 9 : 1.

[5*] Eluents: benzols-etilacetāts, 9.5 : 0.5.

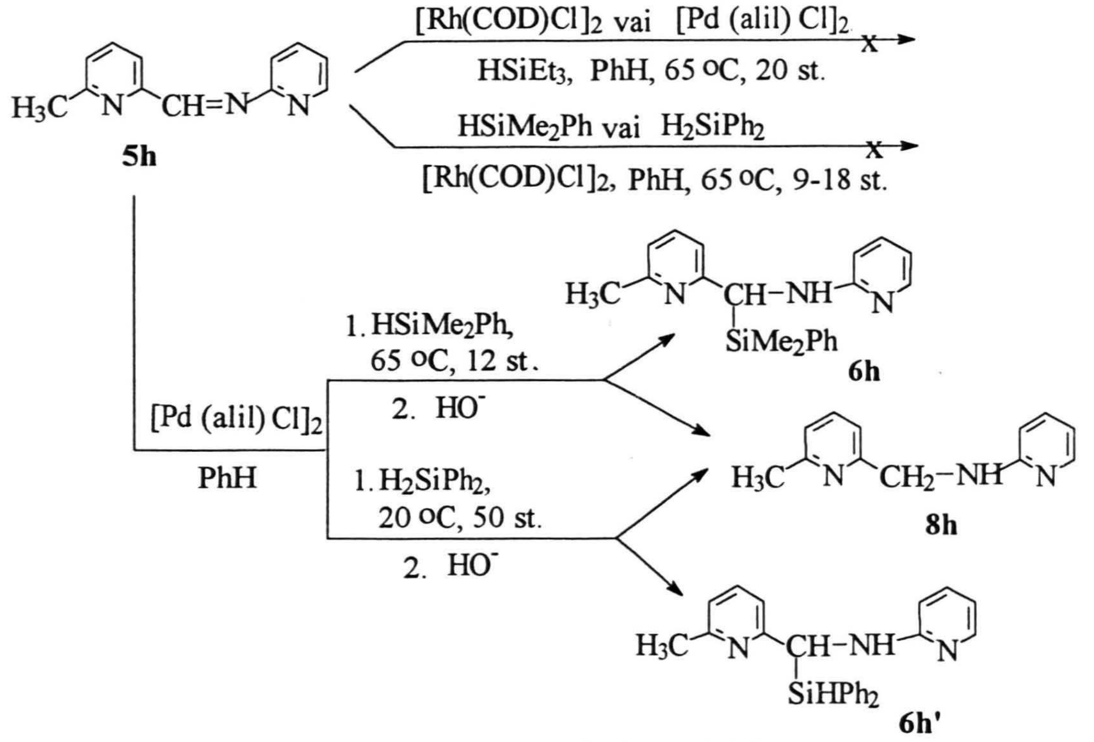
[6*] Eluents: hloroforms–metanols 9 : 1.

2-, 3-Piridilmetilidēn-2-trifluormetilanilīni **5e,f** abu iepriekš minēto katalizātoru klātbūtnē ar Et_3SiH praktiski nereaģēja. Hidrosililējās tikai 4-piridilmetilidēn-2-trifluormetilanilīns **5g**. Rh katalizātora $[Rh(COD)Cl]_2$ klātbūtnē iegūts C-sililētais produkts **6g**, kuru hidrolizējot izdalīts amīns **8g** ar kolonnu hromatogrāfijas metodes palīdzību. Katalizātora $[Pd(CH_2CHCH_2)Cl]_2$ klātbūtnē bez amīna iegūts arī neliels N-sililētā produkta **7g** daudzums.





N-(6-metil-2-piridilmetilidēn)-2-aminopiridīna **5h** gadījumā $[Rh(COD)Cl]_2$ un $[Pd(CH_2CHCH_2)Cl]_2$ kompleksu klātbūtnē reakcijas ar Et_3SiH nenotiek. Ar aktīvākiem silāniem $HSiMe_2Ph$, H_2SiPh_2 [59] hidrosililēšanas reakcijas notiek tikai Pd kompleksa klātbūtnē.



Pēc hidrolīzes netika konstatēti N-sililētie produkti, kas šajā gadījumā viegli hidrolizējas. No reakciju maisījumiem izdalīti amīns **8h** un neliels daudzums C-sililēto produktu **6h,h'**. Visu sintezēto amīnu: N-hetero-2-trifluormetilanilīnu **8a-d,h** iznākums bija 65-70%. N-(hetarilmetil)-aromātisko amīnu **8a-h** un sililatvasinājuma **7g** masspektri apkopoti tabulā 4.2.

Tabula 4.2

N-(hetarilmetil)-aromātisko amīnu **8a-h** un sililatvasinājuma **7g** masspektri.

Savienojums	*m/z* ($I_{rel.}$, %)*
8a	241 (33, M$^+$), 240 (12, [M – H]$^+$), 213 (14, [M – CO]$^+$), 202 (3), 192 (2), 182 (2), 172 (5, [M – C_4H_3O – H_2]$^+$), 165 (1), 154 (4), 145 (6, [$C_6H_4CF_3$]$^+$), 127 (9), 114 (6), 107 (2), 95 (4), 88 (2), 81 (100, [$C_4H_3OCH_2$]$^+$), 75 (7), 69 (4), 63 (4), 53 (39)
8b	255 (15, M$^+$), 216 (2), 202 (3), 196 (3), 185 (1), 172 (2), 154 (2), 145 (4, [$C_6H_4CF_3$]$^+$), 127 (8), 114 (3), 107 (2), 95 (100, [$H_3CC_4H_2OCH_2$]$^+$), 83 (1), 75 (4), 67 (5), 53 (6)
8c	257 (24, M$^+$), 218 (5), 145 (5, [$C_6H_4CF_3$]$^+$), 127 (9), 114 (5), 97 (100, [$C_4H_3SCH_2$]$^+$), 75 (4), 69 (8), 63 (6), 53 (13)
8d	271 (17, M$^+$), 232 (5), 202 (3), 172 (2), 154 (3), 145 (5, [$C_6H_4CF_3$]$^+$), 127 (11), 111 (100, [$H_3CC_4H_2SCH_2$]$^+$), 95 (5), 85 (2), 78 (9), 77 (10), 67 (6), 59 (5), 51 (7)
7g	366 (2, M$^+$), 337 (9, [M – Et]$^+$), 317 (6, [M – Et – HF]$^+$),231 (4, [M – $SiEt_3$ – HF]$^+$), 214 (15), 213 (100, [M – $SiEt_3$ – 2F]$^+$), 193 (19, [M – $SiEt_3$ – 2F – HF]$^+$), 166 (5), 154 (4), 145 (2, [$C_6H_4CF_3$]$^+$), 127 (10, [$C_6H_5CF_2$]$^+$), 109 (14), 95 (11), 92 (7), 77 (31), 65 (8), 59 (9), 52 (20)

8g	253 (15, $[M + H]^+$), 252 (100, M^+), 231 (24, $[M - H - HF]^+$), 174 (25, $[M - Py]^+$), 172 (7), 154 (76, $[M - Py - HF]^+$), 145 (9, $[C_6H_4CF_3]^+$), 127 (68, $[C_6H_5CF_2]^+$), 125 (14), 107 (14, $[PyCH_2NH]^+$), 92 (27, $[PyCH_2]^+$), 80 (24), 79 (19), 78 (12, Py^+), 75 (17), 69 (8), 65 (36), 63 (20), 52 (20), 51 (10), 50 (18)
8h	200 (13, $[M + H]^+$), 199 (100, M^+), 197 (5, $[M - H_2]^+$), 196 (13), 183 (14, $[M - H - Me]^+$), 169 (7), 155 (2), 144 (1), 132 (2), 122 (6), 121 (72, $[M - Py]^+$), 119 (7, $[M - Py - H_2]^+$), 107 (39, $[PyNHCH_2]^+$), 94 (27, $[PyNH_2]^+$), 93 (7), 92 (5), 80 (8), 79 (15), 78 (24, Py^+), 65 (7), 63 (20), 52 (7), 51 (7)

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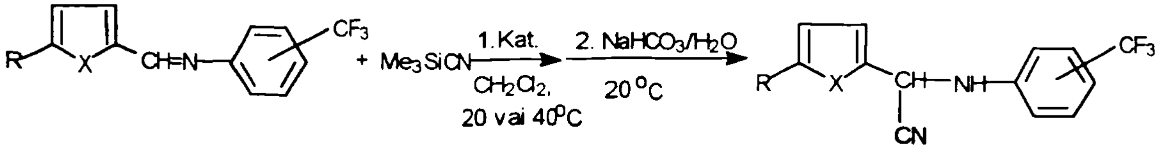
*Doti raksturīgo jonu signāli (relatīvā intensitāte uzrādīta iekavās).
Py-piridil.

5. N-(hetarilmetilidēn)-3-trifluormetilanilīnu un N-(hetarilmetilidēn)-4-trifluormetilanilīnu, kuros hetaril grupas ir 2-furil, 5-metil-2-furil, 2-tienil, 5-metil-2-tienil, 2-, 3-, 4-piridil, katalītiska trimetilsililcianēšana ar Me_3SiCN Luisa skābju klātbūtnē.

Šajā darbā kā katalizātorus esam izmantojuši Luisa skābes: $AlCl_3$, $AlBr_3$. $AlCl_3$ un īpaši $AlBr_3$ darbojas kā efektīvi katalizātori furāna un tiofēna aldimīnu trimetilsililcianēšanā [60,61]. Šīs reakcijas produkti ir α-aminonitrili, kurus var izmantot aminoskābju un citu slāpekli saturošu savienojumu sintēzē [62], to skaitā medicīnas preparātu sintēzē [63]. Aromātiskiem aminonitriliem piemīt antihipertoniska aktivitāte un psihotropa iedarbība [64]. Trimetilsililcianīda izmantošana nātrija cianīda NaCN vai ciānskābes HCN vietā ievērojami vienkāršo cianēšanas procedūru. Tika veiktas trimetilsililcianēšanas reakcijas ar iepriekš sintezētiem aldimīniem **1a-h** un **10a-h**, kas iegūti piridīnkarboksialdehīdu kondensācijas reakcijās ar 3- vai 4-trifluormetilanilīnu, kā arī furāna un tiofēna aldehīdu kondensācijā ar 3- vai 4-trifluormetilanilīnu Luisa skābju klātbūtnē pēc metodikas, kas aprakstīta darbā [52]. Furāna un tiofēna imīnu **1a-h** trimetilsililcianēšanas reakciju rezultātā sintezēti attiecīgie α-aminonitrili **9a-h** ar 38-80% lielu iznākumu.

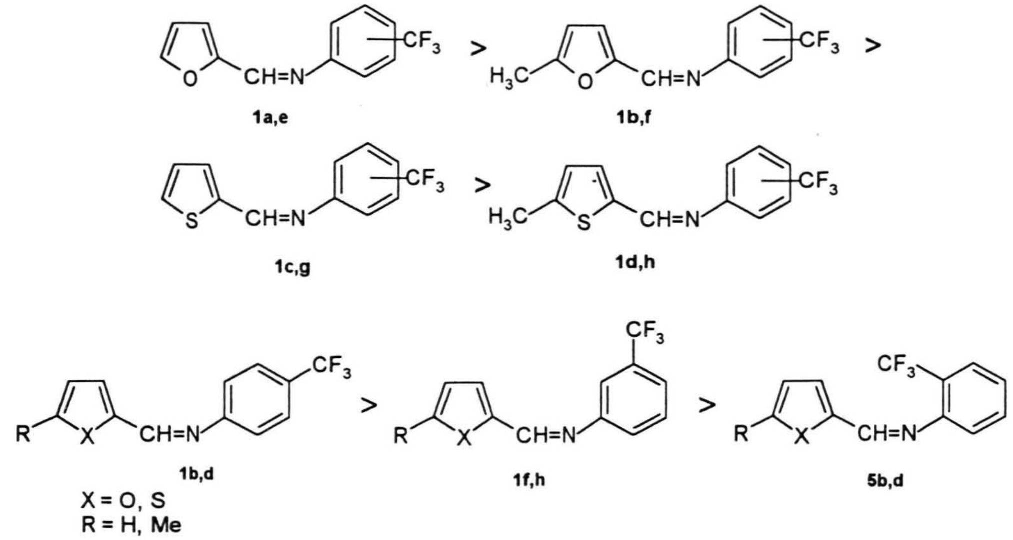
Reakciju apstākļi un produktu **9a-h** iznākumi apkopoti tabulā 5.1., bet α-aminonitrilu **9a-d,g,h** elementanalīzes dati tabulā 5.2. Sintezēto α-aminonitrilu **9a-h** ^1H KMR spektri doti tabulā 5.3, **9a-h** masspektri apkopoti tabulā 5.4.



1a-h **9a-h**

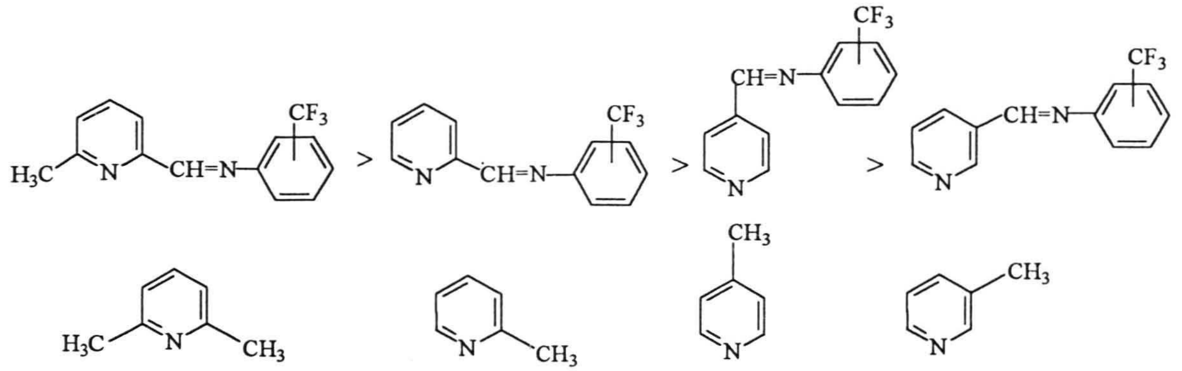
R=H; CH_3
X=O; S
CF_3 pozīcija: 3-, 4-

Tika izpētīts, ka molekulārie sieti 4A paātrina pievienošanās reakcijas ātrumu un palielina produktu iznākumu. Izmantotos katalizātorus var sakārtot aktivitātes rindā: $AlBr_3$ + 4A MS > $AlBr_3$ > $AlCl_3$ > Ti[O(iPr)]$_4$. Furāna Šifa bāzes **1a,b,e,f** Me_3SiCN pievienošanas reakcijās aktīvākas par tiofēna aldimīniem **1c,d,g,h**. Substrātus pēc to aktivitātes var izkārtot rindā:



Tika izstrādāta ļoti vienkārša piridilazometīnu iegūšanas metode, reakcijā izmantojot molekulāros sietus 4A. Molekulārie sieti šajā reakcijā darbojas ne tikai kā dehidratējoši aģenti, bet arī kā reakcijas katalizātori, kas novērš šīs reakcijas blakusproduktu: aminālu veidošanos. Par molekulāro sietu katalītisku darbību liecina 2-piridilazometīnu **10a-h** augstie iznākumi (līdz 96%). Uz molekulāro sietu virsmas veidojas Brensteda un Luisa skābie centri, kas veido σ-kompleksus ar piridīnsaturošiem savienojumiem (ar piridīna gredzena slāpekļa atomu), kas paaugstina protona kustīgumu aminogrupā, veicinot tā eliminēšanu un imīnu veidošanos.

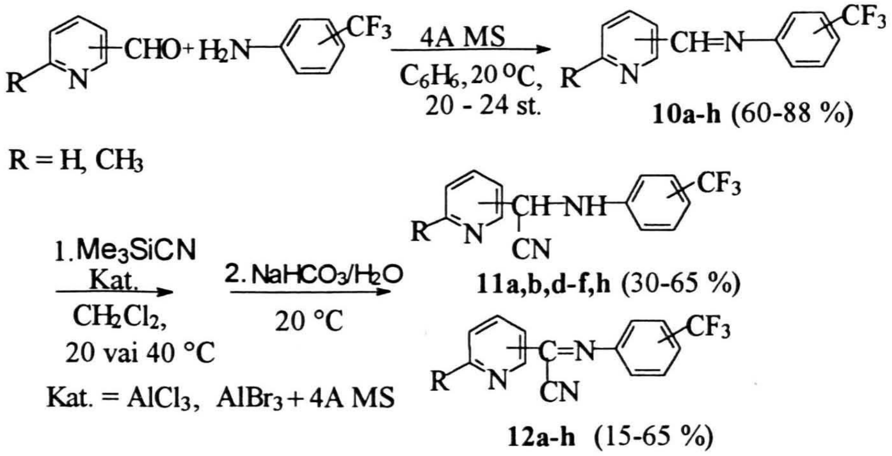
Šī jaunā metode, salīdzinot ar literatūras datiem [52], ļāva izvairīties no reakcijas veikšanas augstā temperatūrā (varīšanas toluolā), kā arī no kondensācijas reakcijas veikšanas bezūdens skābē HCOOH vai no skābā katalizātora $POCl_3$ izmantošanas. Molekulāro sietu kā dehidratējošu aģentu un kā skābo katalizātoru pielietošana izrādījās ļoti produktīva. Piridilazometīnu **10a-h** trimetilsililcianēšanas gadījumā, tāpat kā furāna un tiofēna azometīnu **1a-h** trimetilsililcianēšanā, $AlBr_3$ izrādījās aktīvāks par $AlCl_3$, pie tam 4-trifluormetilatvasinājumi **1a-d** aktīvāki par 3-trifluormetilsavienojumiem **1e-h**. Acīmredzot, šo azometīnu aktivitāte atkarīga no stēriskajiem faktoriem. Lai prognozētu sintezēto azometīnu **10a-h** aktivitāti, izmantojām metilpiridīnu bazicitāti [65], tā kā jauno sintezēto imīnu bazicitāte nav zināma.



pK$_a$ 6.58 5.94 6.02 5.66

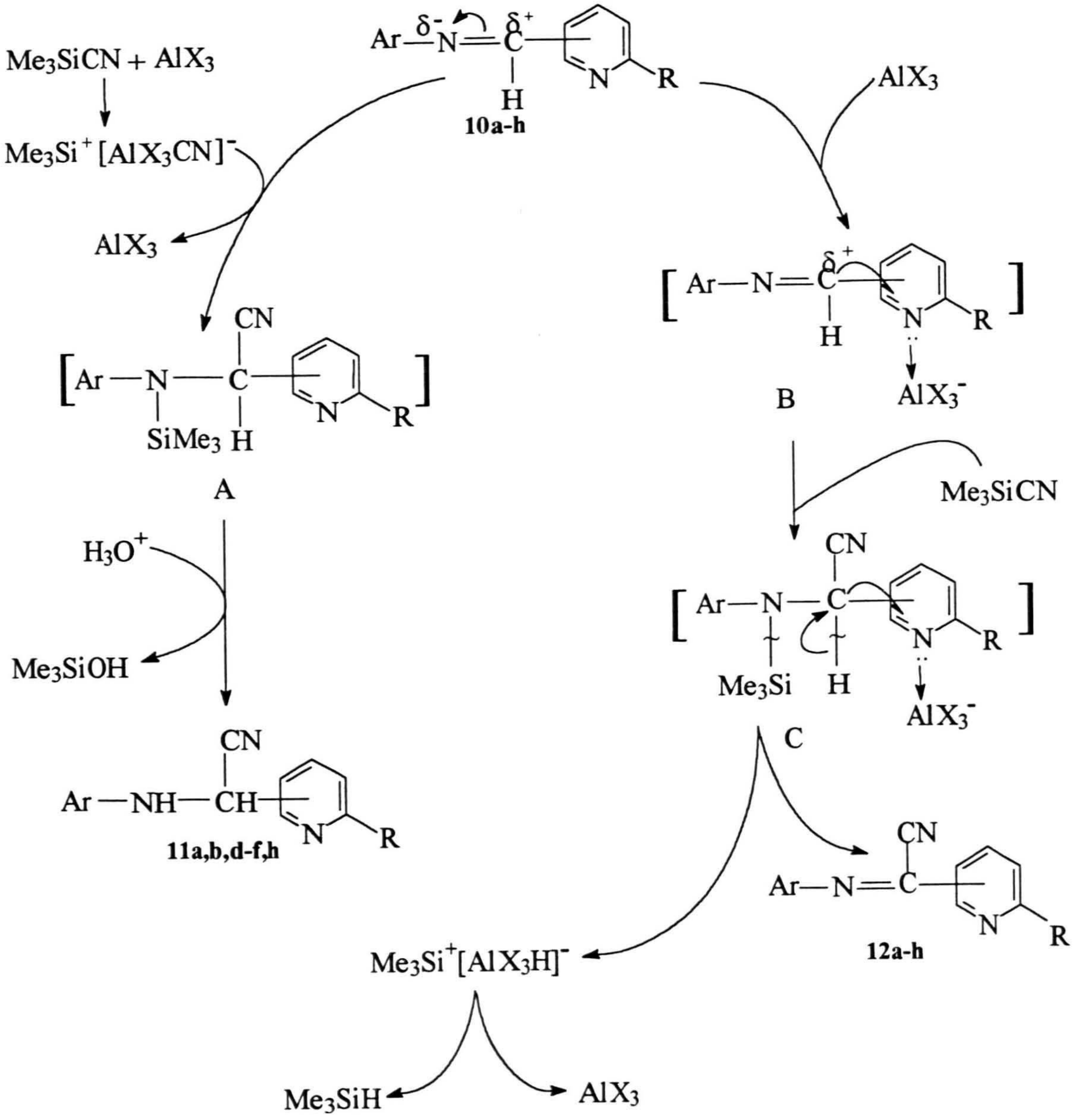
Eksperimentālie rezultāti parādīja, ka imīnu **10a-h** reaģētspēja palielinās, pieaugot attiecīgo metilpiridīnu pKa lielumam. Piridilazometīnu **10a-h** trimetilsililcianēšanas rezultātā iegūti attiecīgie α-aminonitrili **11a,b,d-f,h**, kā arī nepiesātinātie nitrili **12a-h**. Parasti trimetilsililcianēšanas reakcija (furāna un tiofēna atvasinājumu **1a-h** gadījumā) noved pie α-aminonitrilu **9a-h** veidošanās, bet piridilazometīnu **10a-h** gadījumā izšķiroša nozīme ir piridīna gredzena N-atomam, kas piedalās σ-kopleksa veidošanā, kā rezultātā pavājinās C-H saite un notiek trimetilsilāna $HSiMe_3$ eliminēšana, tādejādi ir iespējami arī nepiesātinātie produkti **12a-h**. γ-Piridilimīnu **10c,g** gadījumā tika iegūti un izdalīti tikai nepiesātinātie nitrili **12c,g**. α, β-Piridilimīnu **10a,b,d-f,h** gadījumā nepiesātinātie nitrili veidojās ar zemiem iznākumiem un tika identificēti tikai ar masspektrometrijas metodes palīdzību. N-(piridilmetilidēn)-amīnu **10a-h** trimetilsililcianēšanas reakciju apstākļi un produktu **11a,b,d-f,h**, kā arī **12a-h** iznākumi apkopoti tabulā 5.5. Izdalīto produktu **11a,b,d-f, h** un **12a-d,g** raksturlielumi apkopoti tabulā 5.6. Sintezēto α-aminonitrilu **11a,b,d-f, h** un nepiesātināto nitrilu **12a-d,g** ^{1}H KMR spektri apkopoti tabulā 5.7 α-Aminonitrilu **11a, b, d-f, h** un nepiesātināto nitrilu **12a-h** masspektri apkopoti tabulā 5.8.

Lai izvairītos no iespējamās hidrolīzes, trimetilsililcianēšanas reakcijas tika veiktas molekulāro sietu 4A klātbūtnē, kas darbojas kā dehidratējoši aģenti. Šajos apstākļos iegūti un izdalīti furāna un tiofēna α-aminonitrili **9a-h** ar augstiem iznākumiem līdz 80%. Izpētīts, ka molekulāro sietu klātbūtnē, trimetilsililcianēšanas reakcija noris bez katalizātora klātbūtnes, tādejādi, reakcijā izmantojot katalizātoru kopā ar molekulārajiem sietiem, tiek ievērojami palielināts reakcijas ātrums.



Imīns	R	Piridīna izomērs	CF_3 pozīcija
10a	H	α	3-
10b	H	β	3-
10c	H	γ	3-
10d	CH_3	α	3-
10e	H	α	4-
10f	H	β	4-
10g	H	γ	4-
10h	CH_3	α	4-

Trimetilsilicianēšanas reakciju mehānisms.



Tabula 5.1.

Trimetilsililcianēšanas reakciju apstākļi un produktu **9a-h** iznākumi.

Produkts	X	R	CF_3-pozīcija	Kat. (mol %)	Temp. °C	Laiks st.	Konversija, % [a]	Iznākums, %	T. kuš. °C [b]
9e	O	H	3-	$AlCl_3$ (20)	20	5.5	-	46 [d]	šķidra viskoza viela
				4A MS [c]	20	6.5	27	-	
9f	O	CH_3	3-	$AlCl_3$ (20)	20	21	-	40 [d]	šķidra viskoza viela
				$AlCl_3$ (20)	20	5	50	-	
				$AlBr_3$ (20)	20	0.5	74	-	
				$Ti(OPr^i)_4$ (20)	20	23	68	-	
9g	S	H	3-	$AlCl_3$ (5)	20	49			
					40	5.5	-	26 [d]	-
				$AlBr_3$ (20)	20	1	100	80	69-70
9h	S	CH_3	3-	$AlCl_3$ (5)	20	49			
					40	5.5	30	-	-
				$AlBr_3$ (20)	20	5	38	-	-
				$AlBr_3$(20) + 4A MS	20	26	70	68	84-85
9a	O	H	4-	$AlBr_3$ (20) + 4A MS	20	2	100	47 [d]	143-144
9b	O	CH_3	4-	$AlBr_3$ (20) + 4A MS	20	1	76	40 [d]	95-96
9c	S	H	4-	$AlBr_3$ (20) + 4A MS	20	6.5	70	38 [d]	100-101
9d	S	CH_3	4-	$AlBr_3$(20) + 4A MS	20	4	81	40 [d]	131-132

[a] -noteikta ar ^1H KMR metodi

[b] -noteikta pēc pārkristalizēšanas no etilacetāta/heksāna vai benzola/heksāna

[c] -MS, molekulārie sieti

[d] -produkts izdalīts ar kolonnu hromatogrāfijas metodes palīdzību

Tabula 5.2.

α-Aminonitrilu **9a-d,g,h** elementanalīzes dati.

Produkts	Mol. formula	Mol. masa	iegūts, % / aprēķināts, %			
			C	H	N	S
9g	$C_{13}H_9N_2SF_3$	282.29	54.60/55.31	3.21/3.21	9.41/9.92	11.20/11.36
9h	$C_{14}H_{11}N_2SF_3$	296.32	56.72/56.75	3.59/3.74	9.42/9.45	10.85/10.82
9a	$C_{13}H_9N_2OF_3$	266.22	58.64/58.65	3.50/3.41	10.38/10.52	-
9b	$C_{14}H_{11}N_2OF_3$	280.25	60.40/60.00	4.18/3.96	9.86/9.99	-
9c	$C_{13}H_9N_2SF_3$	282.29	55.36/55.31	3.12/3.21	10.07/9.92	11.34/11.36
9d	$C_{14}H_{11}N_2SF_3$	296.32	56.85/56.75	3.71/3.74	9.46/9.45	10.78/10.82

Tabula 5.3.

Sintezēto α-aminonitrilu **9a-h** ^{1}H KMR spektri.

Savienojums	Ķīmiskā nobīde (m.d.), J (Hz)				
	CH$_3$, d, J = 0.9-1	NH, d,	CHCN, d, J = 8 - 9	Gredzenu protoni	
9e	-	4.47	5.46	6.38 (1H, dd, J=4, 3.5; FurH-4) 6.53 (1H, dd, J=4, 1.5; FurH-3) 7.40 (1H, dd, J=3.5, 1.5; FurH-5)	6.71 – 7.33 (4H, m; ArH$_4$)
9f	2.29	4.33	5.41	5.97 (1H, d.k, J=4, 0.9; FurH-4) 6.44 (1H, d, J=4; FurH-3)	6.78 – 7.64 (4H, m; ArH$_4$)
9g	-	4.44	5.63	6.78 – 7.60 (7H, m; ThH$_3$, ArH$_4$)	
9h	2.49	4.31	5.57	6.69 (1H, d.k, J=4, 0.9; ThH-4) 7.13 (1H, d, J=4; ThH-3)	6.82 – 7.51 (4H, m; ArH$_4$)
9a	-	4.49	5.53	6.47 (1H, dd, J=4, 3.8; FurH-4) 6.62 (1H, m, J=4, 1; FurH-3) 7.49 (1H, dd, J=3.8, 1; FurH-5)	6.80 (2H, d, J=8; ArH-3,5) 7.53 (2H, d, J=8; ArH-2,6)
9b	2.31	4.49	5.44	6.00 (1H, d.k, J=4.4, 0.9; FurH-4) 6.47 (1H, d, J=4.4; FurH-3)	6.78 (2H, d, J=8; ArH-3,5) 7.51 (2H, d, J=8; ArH-2,6)
9c	-	4.58	5.64	7.02 (1H, d, J=5, 4.5; ThH-4) 7.24 – 7.40 (2H, m, J=5, 4.5, 2; ThH-3,5)	6.78 (2H, d, J=8; ArH-3,5) 7.49 (2H, d, J=8; ArH-2,6)
9d	2.49	4.42	5.58	6.64 (1H, d.k, J=4, 1; ThH-4) 7.11 (1H, d, J=4; ThH-3)	6.75 (2H, d, J=8; ArH-3,5) 7.47 (2H, d, J=8; ArH-2,6)

Tabula 5.4.

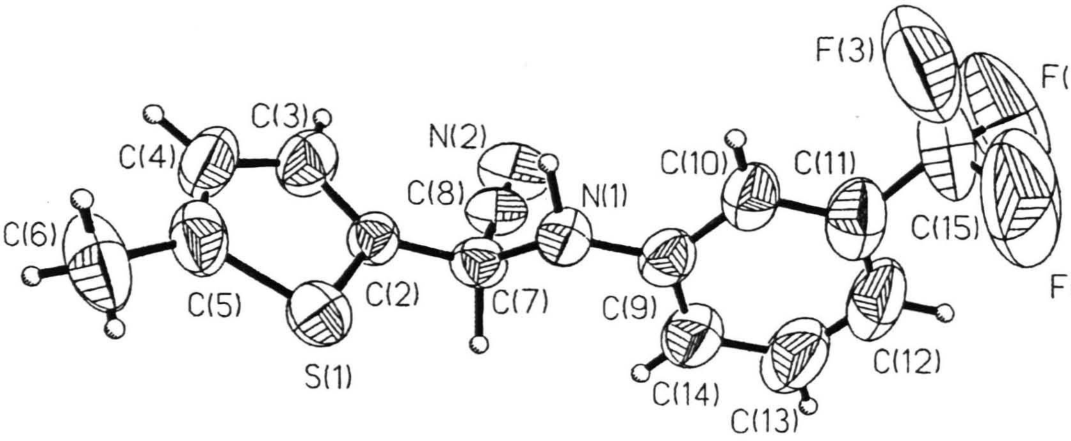
Sintezēto α-aminonitrilu **9a-h** masspektri.

Savienojums	MS, m/z (I_{rel}, %)
9e	266 (8, M^+), 240 (20, $[M - CN]^+$), 239 (100, $[M - HCN]^+$), 238 (52, $[M - HCN - H]^+$), 220 (16, $[M - HCN - F]^+$), 211 (38, $[M - CN - HCO]^+$), 210 (36, $[M - HCN - HCO]^+$), 190 (18), 185 (20), 183 (19), 172 (21, $[M - HCN - \text{Fur}]^+$), 170 (25, $[M - HCN - CF_3]^+$), 145 (68, $[C_6H_4\text{-}CF_3]^+$), 125 (29), 115 (28), 106 (38, $[\text{Fur-CHCN}]^+$), 95 (32), 75 (26), 71 (52), 69 (25, $[CF_3]^+$), 57 (30), 55 (31), 43 (40), 41 (41), 39 (42), 27 (49, $[HCN]^+$)
9f	280 (10, M^+), 254 (20, $[M - CN]^+$), 253 (100, $[M - HCN]^+$), 252 (30, $[M - HCN - H]^+$), 238 (25, $[M - HCN - Me]^+$), 211 (22, $[M - CN - \text{Me-CO}]^+$), 210 (25, $[M - HCN - \text{Me-CO}]^+$), 190 (31), 172 (25), 161 (26), 145 (47, $[C_6H_4\text{-}CF_3]^+$), 120 (51, $[\text{Me-}C_4H_2O\text{-CHCN}]^+$), 95 (18), 69 (12, $[CF_3]^+$), 53 (23), 43 (39, $[H_3CCO]^+$), 39 (17), 27 (30, $[HCN]^+$)
9g	282 (2, M^+), 263 (1, $[M - F]^+$), 255 (100, $[M - HCN]^+$), 145 (68, $[C_6H_4\text{-}CF_3]^+$), 122 (30, $[C_4H_3S\text{-CHCN}]^+$), 112 (28), 111 (31), 95 (44), 84 (46, $[\text{ThH}]^+$), 69 (22, $[CF_3]^+$), 43 (30), 39 (42), 27 (38, $[HCN]^+$)
9h	296 (3, M^+), 294 (2, $[M - 2H]^+$), 277 (1, $[M - F]^+$), 269 (98, $[M - HCN]^+$), 268 (100, $[M - HCN - H]^+$), 250 (18, $[M - HCN - F]^+$), 200 (17, $[M - HCN - CF_3]^+$), 172 (16), 161 (15), 145 (72, $[C_6H_4\text{-}CF_3]^+$), 136 (70, $[\text{Me-}C_4H_2S\text{-CHCN}]^+$), 125 (12), 97 (60, $[\text{Me-}C_4H_2S]^+$), 95 (52), 76 (36), 69 (40, $[CF_3]^+$), 59 (35), 53 (42), 45 (43), 39 (32), 27 (39, $[HCN]^+$)
9a	266 (5, M^+), 240 (16, $[M - CN]^+$), 239 (100, $[M - HCN]^+$), 238 (68, $[M - HCN - H]^+$), 220 (13, $[M - HCN - F]^+$), 211 (33, $[M - CN - HCO]^+$), 210 (38, $[M - HCN - HCO]^+$), 190 (8), 185 (19), 183 (14), 172 (9, $[M - HCN - \text{Fur}]^+$), 170 (12, $[M - HCN - CF_3]^+$), 145 (85, $[C_6H_4\text{-}CF_3]^+$), 125 (18), 115 (17), 106 (62, $[\text{Fur-CHCN}]^+$), 95 (22), 78 (12), 75 (15), 73 (10), 69 (5, $[CF_3]^+$), 57 (15), 55 (16), 51 (21), 43 (18), 41 (19), 39 (33), 27 (48, $[HCN]^+$)
9b	280 (3, M^+), 278 (2, $[M - 2H]^+$), 254 (15, $[M - CN]^+$), 253 (100, $[M - HCN]^+$), 252 (32, $[M - HCN - H]^+$), 239 (8, $[M - HCN - Me]^+$), 234 (12, $[M - HCN - F]^+$), 211 (40, $[M - CN - \text{Me-CO}]^+$), 210 (44, $[M - HCN - \text{Me-CO}]^+$), 190 (5), 183 (15), 172 (6), 145 (60, $[C_6H_4\text{-}CF_3]^+$), 120 (42, $[\text{Me-}C_4H_2O\text{-CHCN}]^+$), 95 (33), 81 (18), 79 (16), 75 (15), 73 (16), 69 (22, $[CF_3]^+$), 53 (25), 43 (52, $[H_3CCO]^+$), 41 (15), 39 (26), 27 (38, $[HCN]^+$)
9c	282 (6, M^+), 280 (1, $[M - 2H]^+$), 279 (1), 263 (1, $[M - F]^+$), 255 (98, $[M - HCN]^+$), 254 (100, $[M - HCN - H]^+$), 236 (15, $[M - HCN - F]^+$), 234 (12), 186 (14), 145 (62, $[C_6H_4\text{-}CF_3]^+$), 122 (58, $[C_4H_3S\text{-CHCN}]^+$), 95 (42), 84 (15, $[\text{ThH}]^+$), 75 (7), 69 (28, $[CF_3]^+$), 45 (33), 39 (38), 27 (41, $[HCN]^+$)
9d	296 (1, M^+), 294 (7, $[M - 2H]^+$), 293 (5), 271 (5), 279 (10), 269 (100, $[M - HCN]^+$), 268 (98, $[M - HCN - H]^+$), 250 (8, $[M - HCN - F]^+$), 200 (12, $[M - HCN - CF_3]^+$), 172 (13), 149 (5), 145 (65, $[C_6H_4\text{-}CF_3]^+$), 136 (28, $[\text{Me-}C_4H_2S\text{-CHCN}]^+$), 125 (12), 97 (49, $[\text{Me-}C_4H_2S]^+$), 94 (41), 69 (31, $[CF_3]^+$), 53 (22), 43 (30), 39 (24), 27 (40, $[HCN]^+$)

Fur = furil, Th = tienil

N-(5-metil-2-tienilciānometil)-3-trifluormetilanilīna **9h** rentgenstruktūranalīze (1.attēls) parādīja, ka iegūts šī savienojuma viens enantiomērs t.i. R-izomērs. Savienojuma **9h** kristāli iegūti lēnā kristalizācijā no etilacetāta/heksāna. Pēc rentgenstruktūranalīzes datiem var secināt, ka savienojumā **9h** pieclocekļu un sešlocekļu cikli ir planāri, bet saišu garumi šajos ciklos pierāda π-elektronu delokalizāciju sistēmā. Molekulas detalizēta analīze veikta pēc literatūrā [66-70] aprakstītām metodēm.

1.attēls.



Tabula 5.5.

N-(piridilmetilidēn)-amīnu **10a-h** trimetilsililcianēšanas reakciju apstākļi un produktu **11a,b,d-f,h, 12a-h** iznākumi.

Imīns	Katalizātors (mol. %)	Temp. °C	Reakcijas laiks, st.	Produkts (iznākums, %)	
				α-Amino nitrils	Nepiesātināts nitrils
10a	$AlCl_3$ (20)	40	32	**11a** (32)	**12a** (30)
	$AlBr_3$ (20) + 4A MS	20	2	**11a** (45)	**12a** (20)
10b	$AlCl_3$ (20)	40	45	**11b** (30)	**12b** (18)
	$AlBr_3$ (20) + 4A MS	20	7	**11b** (50)	**12b** (15)
10c	$AlCl_3$ (20)	40	38	-	**12c** (62)
	$AlBr_3$ (20) + 4A MS	20	2.5	-	**12c** (58)
10d	$AlCl_3$ (20)	40	28	**11d** (35)	**12d** (30)
	$AlBr_3$ (20) + 4A MS	20	1.5	**11d** (52)	**12d** (16)
10e	$AlBr_3$ (5) + 4A MS	20	2	**11e** (63)	**12e**
10f	$AlBr_3$ (5) + 4A MS	20	5	**11f** (60)	**12f**
10g	$AlBr_3$ (5) + 4A MS	20	3	-	**12g** (60)
10h	$AlBr_3$ (5) + 4A MS	20	1.5	**11h** (65)	**12h**

Tabula 5.6.

Izdalīto produktu **11a,b,d-f, h** un **12a-d,g** raksturlielumi.

Savienojums	Eluents kolonnu hromatogrāfijai	Kušanas punkts, °C	Mol. formula	Atrasts, % / Aprēķināts, %		
				C	H	N
11a	C_6H_6:MeOH = 10:1	šķidra viskoza viela	$C_{14}H_{10}N_3F_3$			
12a	- " -	šķidra viskoza viela	$C_{14}H_8N_3F_3$			
11b	$CHCl_3$:MeOH = 9:1	šķidra viskoza viela	$C_{14}H_{10}N_3F_3$			
12b	- " -	šķidra viskoza viela	$C_{14}H_8N_3F_3$			
12c	-	92-93	$C_{14}H_8N_3F_3$	60.50/61.09	2.91/2.93	14.99/15.27
11d	-	113-114	$C_{15}H_{12}N_3F_3$	61.29/61.85	4.05/4.15	14.09/14.43
12d	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
11e	C_6H_6:MeOH =10:1 CH_2Cl_2:MeOH = 10:1	šķidra viskoza viela	$C_{14}H_{10}N_3F_3$			
11f	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
12g	$CHCl_3$:MeOH = 9:1	121-122	$C_{14}H_8N_3F_3$	60.85/61.09	2.90/2.93	15.08/15.27
11h	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

Tabula 5.7.

Sintezēto α-aminonitrilu **11a,b,d-f, h** un nepiesātināto nitrilu **12a-d,g**.
^{1}H KMR spektri.

Savie-nojums	Ķīmiskā nobīde(m.d.), *J* (Hz)				
	CH_3, s	NH	CHCN	Gredzenu protoni	
				Piridīna gredzens	Aromātiskais gredzens
11a	-	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
12a	-	-	-	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
11b	-	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
12b	-	-	-	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
12c	-	-	-	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
11d	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
12d	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
11e	-	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
11f	-	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
12g	-	-	-	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
11h	2.60	5.71, d	5.38, d	7.18, 1 H, d, *J*=7.4, PyH-5	6.82, 2H, d, *J*=8.0,

J=7.6	7.49, 1 H, d, J=7.4, PyH-3 7.64, 1H, t, J=7.4, PyH-4	ArH-3,5 7.27, 2H, d, J=8.0, ArH-2,6

Tabula 5.8.

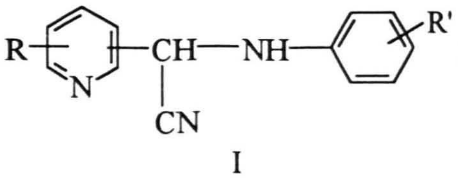
α-Aminonitrilu **11a, b, d-f, h** un nepiesātināto nitrilu **12a-h** masspektri.

Savienojums	MS, m/z (I_{rel}, %)
11a	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
12a	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)
11b	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)
12b	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)
12c	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)
11d	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)
12d	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)
11e	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)
12e	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)
11f	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

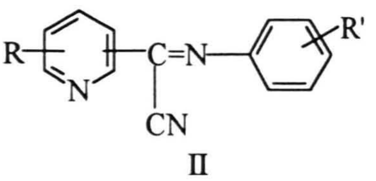
	(6), 172 (18, $[M - HCN - Py]^+$), 160 (8), 145 (68, $[C_6H_4CF_3]^+$), 140 (7), 133 (2), 125 (15), 117 (59, $[PyCHCN]^+$), 105 (7), 95 (17), 90 (11), 79 (9, $[PyH]^+$), 75 (15), 69 (7, $[CF_3]^+$), 63 (21), 51 (16), 50 (11)
12f	276 (16, $[M + H]^+$), 275 (100, M^+), 274 (59, $[M - H]^+$), 256 (14, $[M - F]^+$), 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)
12g	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)
11h	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)
12h	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)

Py-piridil.

Diviem nitriliem **11d** un **12c** veikta rentgenstruktūranalīze (2. un 3. attēls): N-(6-metil-2--piridil-ciānometil)-3-trifluormetilanilīnam **11d** (2. attēls) un N-(4-piridilciānometilidēn)-3--trifluormetilanilīnam **12c** (3. attēls), kuru struktūras var attēlot ar vispārīgām formulām I un II. Ar rentgenstruktūranalīzi pierādīts, ka struktūrai **11d** ir R-konfigurācija, asimetriskais atoms C(7). Molekulāro struktūru **12c** var raksturot ar trīs planāriem fragmentiem (A,B,C). Fragments A ir piridīna gredzens, fragments B ir dubultsaite C(7)=N(2) un ciānogrupa, fragments C-fenilgredzens kopā ar atomu C(15). Diedrālie leņķi ir 7.4(3)° un 63.2(3)° starp A un B; B un C attiecīgi. Molekulu struktūra analizēta ar literatūrā [69,70] aprakstītām metodēm.



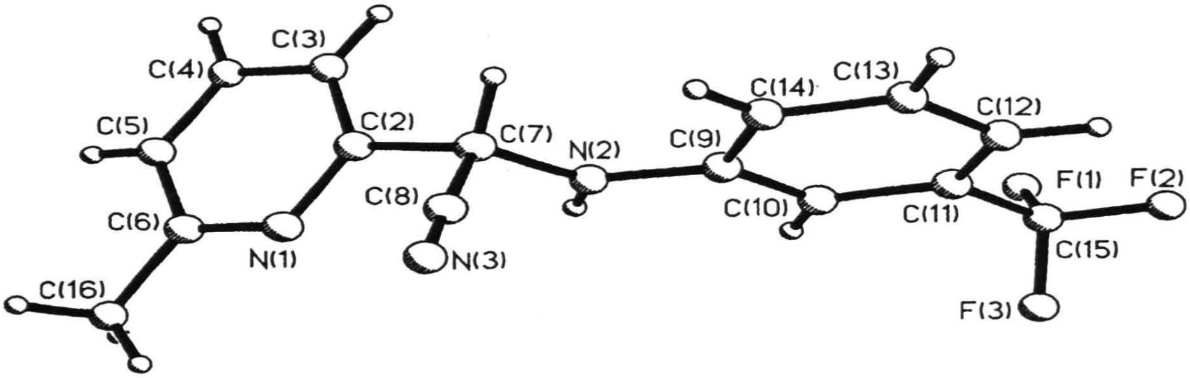
I



II

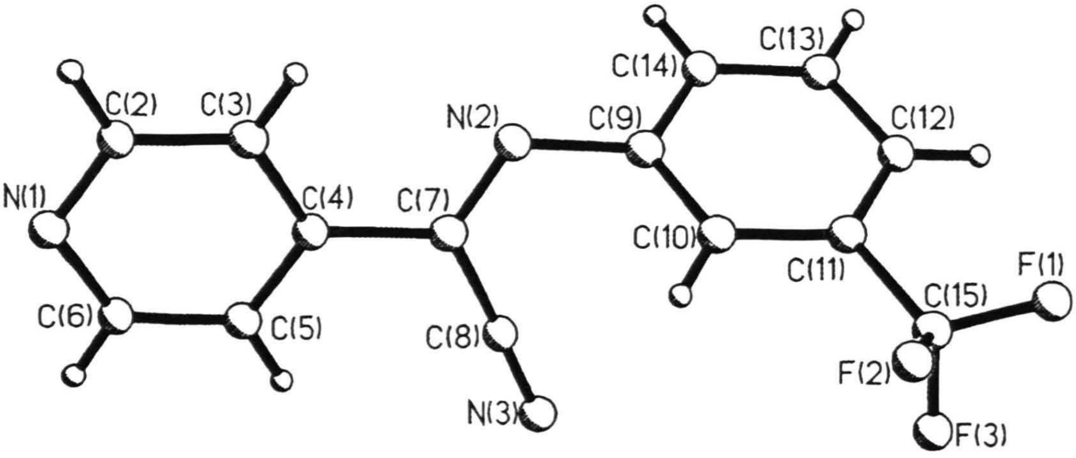
α -Aminonitrila **11d** molekulārā struktūra:

2. attēls.



Nepiesātinātā nitrila **12c** molekulārā struktūra:

3. attēls



Sintezēto nitrilu **12a,c** citotoksiskās aktivitātes pētījumi *in vitro* parādīja, ka šie savienojumi uzrāda augstu citotoksisko efektu. Citotoksicitāte jeb vielu koncentrācija, kas noved pie 50% vēža šūnu bojā ejas, tika noteikta pēc standarta metodoloģijas [71] uz šūnu līnijām: HT-1080 (cilvēka plaušu fibrosarkoma), MG-22A (peļu hepatoma), B16 (peļu melanoma), Neuro 2A (peļu neiroblastoma). Augstu citotoksicitāti sintezētie nitrili **12a** un **12c** uzrādīja uz cilvēka plaušu fibrosarkomas, peļu hepatomas un peļu melanomas abos testos CV un MTT. Minētie nitrili uzrādīja augstāku citotoksicitāti par zināmo pretvēža preparātu Ftorafūru (Phthorafurum), kas ir viens no efektīvākajiem pretvēža ķīmijterapijas līdzekļiem. Citotoksiskās aktivitātes lielumi apkopoti tabulā 5.9.

Tabula 5.9.

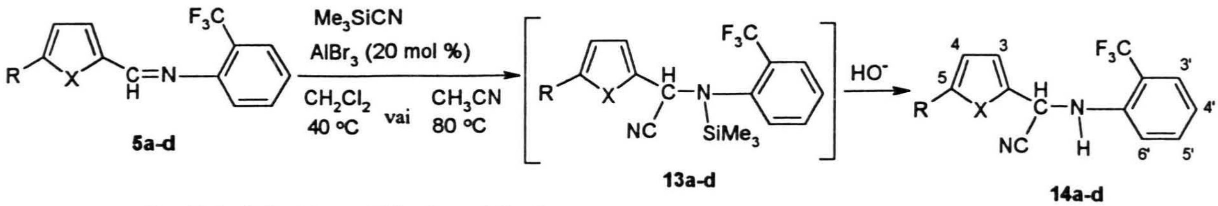
	Citotoksiskā aktivitāte^a.							
Šūnu līnija:	HT-1080		MG-22A		B16		Neuro 2A	
Tests:	CV	MTT	CV	MTT	CV	MTT	CV	MTT
Savienojums								
12a	7.5	10	10	10	6.5	45	30	35
12c	15	17	10	10	5	5.5	7.5	8
Ftorafūrs	20	10	45	30	10	15	5	7

^{a} Koncentrācija (µg/ml), kas noved pie 50 % vēža šūnu bojā ejas efekta.

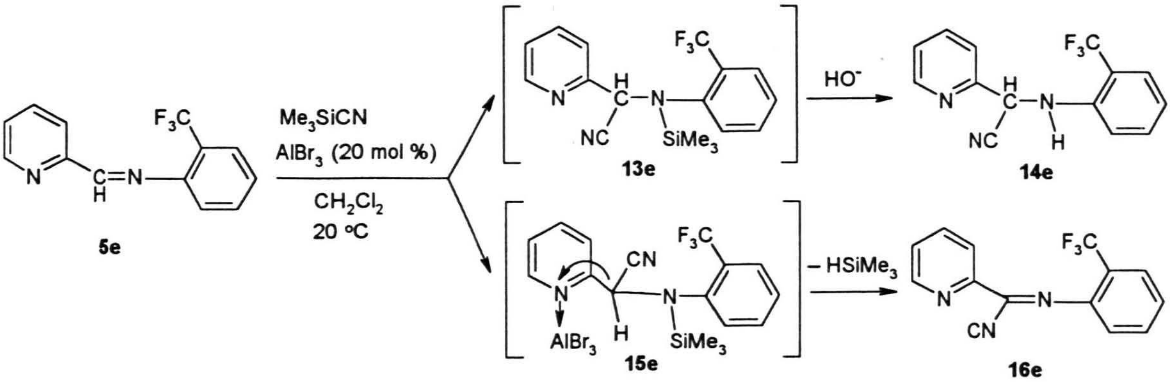
6. N-(hetarilmetilidēn)-2-trifluormetilanilīnu, kuros hetaril grupas ir 2-furil, 5-metil-2-furil, 2-tienil, 5-metil-2-tienil, 2-, 3-, 4-piridil, katalītiska trimetilsililcianēšana ar Me_3SiCN Luisa skābju klātbūtnē.

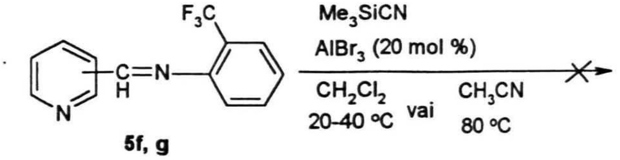
Pētot 2-trifluormetilanilīna aldimīnu hidrosililēšanas reakcijas [72], tika konstatēts, ka CF_3 grupai aromātiskā gredzena orto-stāvoklī ir liela ietekme uz reakciju norisi, tādēļ tika izpētītas arī iepriekš sintezētu N-(hetarilmetilidēn)-2-trifluormetilanilīnu **5a-g** [73] trimetilsililcianēšanas reakcijas. Aktīvākais katalizātors no visām pielietotām Luisa skābēm ($AlCl_3$, $AlBr_3$, $LaCl_3$, ZnI_2) trimetilsililcianīda pievienošanā dubultsaitei CH=N [61,74] arī šajā gadījumā izrādījās $AlBr_3$. Lai novērstu izejvielu t.i. imīnu hidrolītisku sadalīšanos, tika izmantoti molekulārie sieti 4A kā dehidratējoši aģenti. Atšķirībā no 3- un 4-trifluormetilaizvietotiem analogiem **1a-h**, furāna un tiofēna imīni **5a-d** ar CF_3 grupu aromātiskā gredzena orto-stāvoklī izrādījās mazāk reaģētspējīgi. Reakcijas istabas temperatūrā praktiski negāja. Produkti radās tikai ilgstoši sildot (24-51h) metilēnhlorīdā 40^{0}C temperatūrā. Zemās reaģētspējas iemesls ir stēriski apjomīgās 2-CF_3 grupas klātbūtne kaimiņos reaģējošai dubultsaitei CH=N. Pēc furāna un tiofēna substrātu **5a-d** trimetilsililcianēšanas un hidrolīzes veikšanas iegūti produkti-attiecīgie amīni t.i.

N-(hetarilciānometil)-2-trifluormetilanilīni **14a-d** ar iznākumu (40-80%) pēc attīrīšanas ar kolonnu hromatogrāfijas metodes palīdzību.



a, c R = H, b, d R = Me; a, b X = O, c, d X = S





5 f, g β- un γ-izomēri

Abu furāna substrātu **5a,b** reaģētspēja augstāka par tiofēna imīnu **5c,d** reaģētspēju. Ievadot Me grupu heterociklā, pazeminās gan furāna, gan tiofēna azometīnu aktivitāte. Šie rezultāti ir līdzīgi tiem, kas iegūti 3- un 4-CF_3 aizvietoto izomēru analogu gadījumā. Tika mēģināts paaugstināt tiofēna substrātu **5c,d** konversiju un attiecīgo produktu iznākumu, veicot trimetilsililcianēšanas reakcijas augstākā temperatūrā 80^{0}C, karsējot benzolā vai acetonitrilā. Benzolā konversija sasniedza tikai 10% sliktās katalizātora šķīdības dēļ, bet, ilgstoši karsējot acetonitrilā, reakcijas iznākums palielinājās tikai nedaudz, ko varētu izskaidrot ar katalizātora $AlBr_3$ un acetonitrila daļēju koordināciju.

Pētot piridīnaldimīnu **5e-g** ar CF_3 grupu aromātiskā gredzena orto-stāvoklī trimetilsililcianēšanas reakcijas, izrādījās, ka β- un γ-izomēru **5f,g** reaģētspēja ir ļoti zema, un iegūt produktus gan pie 40^{0}C metilēnhlorīdā, gan pie 80^{0}C acetonitrilā neizdevās.

Tikai α-azometīns **5e** reaģēja ar trimetilsililcianīdu jau istabas temperatūrā, pie tam tika iegūti divi produkti-sagaidāmais produkts α-aminonitrils: N-(2-piridilciānometil)-2-trifluormetilanilīns **14e** un nepiesātinātais nitrils: N-(piridilciānometilidēn)-2-trifluormetilanilīns **16e**.

Nepiesātināto produktu rašanās ir neraksturīga furāna un tiofēna substrātu **5a-d** trimetilsililcianēšanas reakcijām. Piridilimīna **5e** gadījumā nepiesātinātā produkta rašanos var izskaidrot ar koordinācijas struktūras **15e** izveidošanos. Koordinatīvā saite savienojumā **15e** starp piridīna gredzena donora slāpekļa atomu un $AlBr_3$ noved pie saišu C-H un C-Si pavājināšanās un attiecīgās nepiesātinātās struktūras **16e** veidošanās. Imīnu **5a-d** trimetilsililcianēšanas reakciju raksturlielumi un produktu **14a-e, 16e** iznākumi apkopoti tabulā 6.1., bet sintezēto nitrilu **14a-e, 16e** masspektri tabulā 6.2. Nitrilu **14a-e, 16e** ^1H KMR spektri apkopoti tabulā 6.3

Tabula 6.1.

Imīnu **5a-d** trimetilsililcianēšanas reakciju raksturlielumi un produktu **14a-e, 16e** iznākumi.

Aldimīns	Šķīdinātājs	Temp., °C / Laiks, st.	Konversija, %	Eluents	Produkts	Iznākums, %
5a	CH_2Cl_2	40/24	95	PhH–EtOAc 9.5 : 0.2	**14a**	80
5b	CH_2Cl_2	40/24	85	PhH–EtOAc 9.5 : 0.2	**14b**	55
5c	CH_2Cl_2	40/27	80	PhH–EtOAc 9.5 : 0.2	**14c**	50
5d	CH_2Cl_2	40/51	63	PhH–EtOAc 9.5 : 0.2	**14d**	40
5d	PhH	80/26	10	-	-	
5d	MeCN	80/50	70	PhH–EtOAc 9.5 : 0.2	**14d**	45
5e	CH_2Cl_2	20/13	90	CH_2Cl_2–MeOH 9.5 : 0.2	**14e** **16e**	40 30
5f	CH_2Cl_2	40/10	10	-	-	
5f	MeCN	80/45	15	-	-	
5g	CH_2Cl_2	20/8	~ 0	-	-	
5g	MeCN	80/54	18	CH_2Cl_2–MeOH 9 : 1	-	

Tabula 6.2.

Sintezēto nitrilu **14a-e**, **16e** masspektri.

Savienojums	m/z ($I_{rel.}$, %)*
14a	266 (20, M^+), 246 (10, $[M - HF]^+$), 240 (8, $[M - CN]^+$), 239 (22, $[M - HCN]^+$), 220 (7, $[M - HCN - F]^+$), 210 (5, $[M - HCN - HCO]^+$), 199 (5, $[M - Fur]^+$), 191 (4), 172 (4, $[M - HCN - Fur]^+$), 170 (5, $[M - HCN - CF_3]^+$), 152 (7), 145 (17, $[C_6H_4CF_3]^+$), 125 (9), 114 (9), 106 (100, $[FurCHCN]^+$), 95 (8), 78 (15), 75 (9), 69 (2, $[CF_3]^+$), 63 (8), 51 (24)
14b	280 (12, M^+), 254 (7, $[M - CN]^+$), 253 (35, $[M - HCN]^+$), 252 (13, $[M - HCN - H]^+$), 236 (2), 234 (2, $[M - CN - F]^+$), 218 (5, $[M - HCN - HF - Me]^+$), 210 (25, $[M - HCN - MeCO]^+$), 191 (5), 172 (5), 161 (14), 152 (5), 145 (23, $[C_6H_4CF_3]^+$), 125 (8), 121 (9), 120 (100, $[MeC_4H_2OCHCN]^+$), 95 (10), 75 (8), 69 (5, $[CF_3]^+$), 65 (14), 53 (13), 51 (15), 50 (10)
14c	282 (22, M^+), 255 (37, $[M - HCN]^+$), 254 (45, $[M - HCN - H]^+$), 236 (4), 234 (4, $[M - CN - F]^+$), 152 (6), 145 (25, $[C_6H_4CF_3]^+$), 122 (100, $[C_4H_3SCHCN]^+$), 114 (5), 105 (5), 95 (17), 91 (5), 84 (2, $[ThH]^+$), 77 (11), 69 (12, $[CF_3]^+$), 63 (7), 58 (7), 51 (7)
14d	296 (6, M^+), 269 (14, $[M - HCN]^+$), 268 (18, $[M - HCN - H]^+$), 161 (10), 145 (11, $[C_6H_4\text{-}CF_3]^+$), 137 (12), 136 (100, $[MeC_4H_2SCHCN]^+$), 125 (5), 109 (14), 95 (7), 83 (3), 69 (8, $[CF_3]^+$), 65 (6), 59 (5), 51 (7)
14e	277 (73, M^+), 256 (22, $[M - F - 2H]^+$), 231 (27, $[M - HCN - F]^+$), 208 (60, , $[M - CF_3]^+$), 204 (12), 181 (100, $[M - HCN - CF_3]^+$), 179 (23), 154 (27), 152 (57), 132 (38, $[M - C_6H_4CF_3]^+$), 127 (13), 126 (28), 125 (17), 119 (20), 118 (48, $[PyCH_2CN]^+$) 107 (32), 105 (56), 102 (22), 95 (26), 80 (33), 79 (90, $[PyH]^+$), 78 (95, $[Py]^+$), 77 (25), 75 (21), 69 (28, $[CF_3]^+$), 64 (30), 63 (49), 62 (37), 52 (54), 51 (54), 50 (9), 39 (35), 38 (29)
16e	274 (5, $[M - H]^+$), 256 (4, $[M - F]^+$), 207 (16), 206 (100, $[M - CF_3]^+$), 181 (1), 154 (4), 145 (14, $[C_6H_4CF_3]^+$), 125 (7), 104 (2), 95 (9), 78 (10, Py^+), 75 (9), 69 (5, $[CF_3]^+$), 51 (14)

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*Doti raksturīgo jonu signāli (relatīvā intensitāte uzrādīta iekavās).
Fur = furil, Th = tienil, Py = piridil.

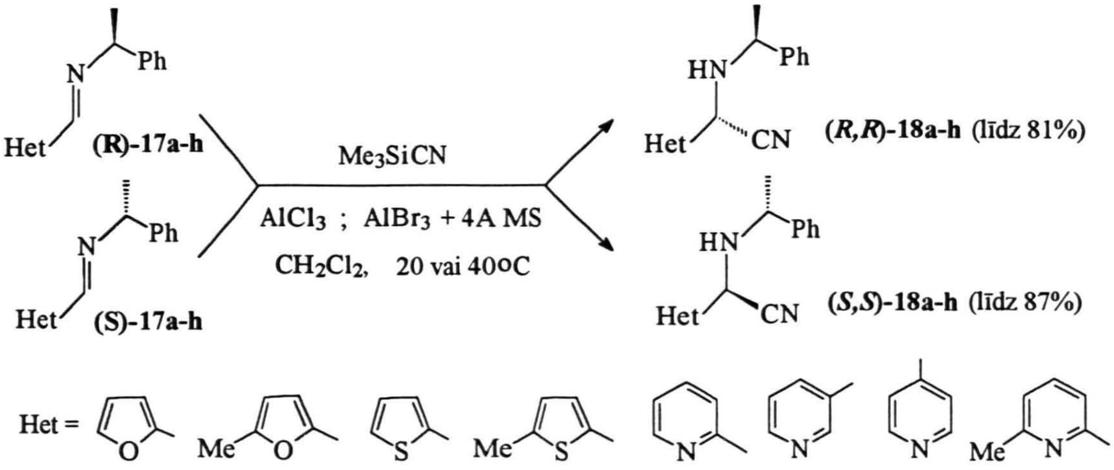
Tabula 6.3.

Nitrilu **14a-e, 16e** ^{1}H KMR spektri.

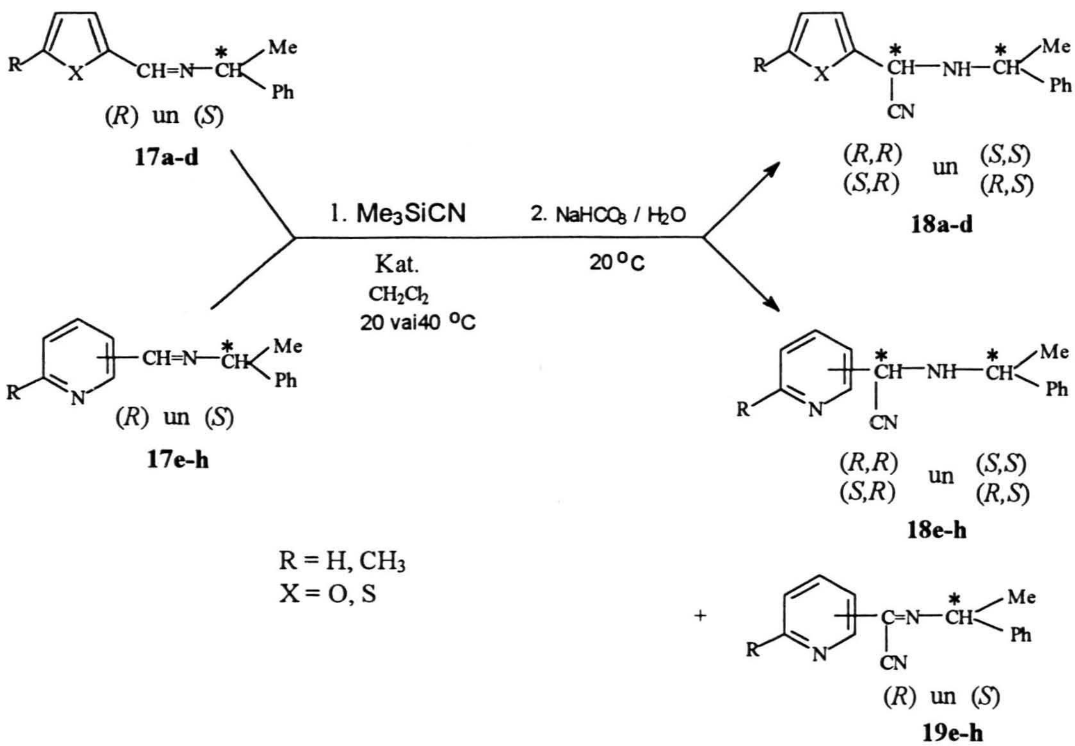
Savienojums	Ķīmiskā nobīde ($CDCl_3$), δ, m.d.; J, Hz			
	CH_3, s	NH, d	CHCN, d	Gredzena protoni
14a	-	4.82 J = 7.8	5.55	6.45 (1H, dd , J = 1.8, 2.8, H-4), 6.61 (1H, dd, J = 2.8, H-3), 6.97 (2H, m, H-3', H-5'), 7.4–7.6 (3H, m, H-5, H-4', H6')
14b	2.32	4.78 J = 7.6	5.47	6.01 (1H, dd, J = 2.8, 0.6, H-4), 6.47 (1H, dd, J = 2.8, H-3), 6.96 (2H, m, H-3', H-5'), 7.50 (2H, m, H-4', H6')
14c	-	4.80 J = 8.4	5.69	6.9–7.0 (2H, m, H-3', H-5'), 7.07 (1H, dd, J = 5.0, 3.6, H-4), 7.3–7.4 (2H, m, H-3, H-5), 7.5–7.6 (2H, m, H-4', H-6')
14d	2.49	4.75 J = 7.8	5.60	6.70 (1H, d, J = 3.2, H-4), 6.9–7.1 (2H, m, J = 7.4, H-3', H-5'), 7.16 (1H, d, J = 3.2, H-3), 7.4–7.7 (2H, m, J = 7.4, H-4', H-6')
14e	-	6.02 J = 5.4	5.13	6.42 (1H, m, J = 8.2, H-3), 7.1 (2H, m, J = 8.4, H-3', H-5'), 7.40 (1H, m, J = 8.2, 4.4, H-5), 7.5 (2H, m, J = 8.4, H-4', H-6'), 7.60 (1H, d.t, J = 8.2, 1.4, H-4), 8.70 (1H, m, J = 4.4, H-6)
16e	-	-	-	7.21 (1H, d, J = 8.6, H-3'), 7.43 (1H, t, J = 8.6, H-5'), 7.53 (1H, m, J = 8.0, 5.2, 1.0, H-5), 7.67 (1H, t, J = 8.6, H-4'), 7.78 (1H, d, J = 8.6, H-6'), 7.91 (1H, d.t, J = 8.0, 2.0, H-4), 8.29 (1H, d.t, J = 8.0, 1.0, H-3), 8.83 (1H, m, J = 5.2, H-6)

7. Dažu heterociklisko imīnu asimetriska trimetilsililcianēšana ar Me_3SiCN Luisa skābju klātbūtnē.

Imīnu asimetriskai cianēšanai ir liela nozīme optiski aktīvu slāpekli saturošu savienojumu iegūšanā [22-24,26,27]. Iepriekšējos darbos [60,61,74] aprakstīta trimetilsililcianīda pievienošanās (hetero)aromātiskiem aldehīdiem un ahirāliem heterocikliskiem imīniem. Imīnu, kas iegūti no hirāliem amīniem, cianēšana aprakstīta literatūrā [75]. Diastereoselektīva Me_3SiCN pievienošana Šifa bāzēm noved pie jauna hirāla centra veidošanās α-aminonitrilos. Darbā kā hirāli substrāti izmantoti furāna, tiofēna, piridīna aldimīni, kas iegūti no (R)- un (S)-1-feniletilamīna [76]. Stereoselektivitātes pakāpe atkarīga gan no aldimīna dabas, gan no katalītiskās sistēmas. Darbā sintezēta sērija heterociklisko optiski aktīvu Šifa bāzu **(R)-17a-h** un **(S)-17a-h**, kas tālāk izmantotas trimetilsililcianēšanas reakcijā.



Optiski aktīvi hirāli imīni (R)- un (S)- tika izmantoti Štrekera sintēzē, kā katalizātoru lietojot $AlCl_3$ vai $AlBr_3$ (5-20 mol%) istabas temperatūrā vai 40^0C metilēnhlorīdā. Substrātu konversija sasniedza 78-100%. Daži no iegūtiem produktiem izrādījās termiski nestabili gāzes hromatogrāfijas analīzes apstākļos. Pēc reakciju maisījumu hidrolīzes ar $NaHCO_3$ un attīrīšanas uz hromatogrāfiskām kolonnām iegūti attiecīgie α-aminonitrili **18a-h** ar augstiem iznākumiem līdz 91%. No visiem piridīnimīniem iegūti arī nepiesātinātie nitrili **19e-h** (iznākumi līdz 33%).



Kā jau iepriekš minēts [61,74], šo produktu veidošanās ir iespējama pateicoties koordinācijas σ-kompleksam, kas rodas starp katalizātoru AlX_3 un imīna piridīna gredzena slāpekļa atomu. Visos gadījumos iegūti α-aminonitrilu **18a-h** diastereomēru maisījumi ar vienu dominējošo diastereomēru. α-Aminonitrili, kas iegūti no (S)-imīniem izrādījās optiski negatīvi(-), bet no (R)--izomēriem iegūti(+)-produkti. Kad imīna konfigurācija attiecībā pret slāpekļa atomu bija R, iegūtie produkti (R,R)-α-aminonitrili dominēja pār (S,R)-izomēriem, bet (S,S)-pievienošanās produkti veidojās galvenokārt no (S)-izomēriem. Visi α-aminonitrili **18a-h** iegūti ar viduvēju diastereotīrību līdz 81% (R,R)-izomēriem un līdz 87% (S,S)-izomēriem. β-Piridīnimīna **18f** trimetilsililcianēšanas gadījumā iegūta diastereoizomēru attiecība 80:20, kas atbilst literatūrā aprakstītajai sintēzei ar analoģisku β-piridilimīnu (sintēzi veic bez katalizātora 6 dienas) [25] ar diastereoizomēru attiecību 79:21, tas liecina par mūsu eksperimentu augsto precizitātes pakāpi. Me_3SiCN pievienošanās apstākļi furāna, tiofēna un piridīna imīniem, kā arī iegūto produktu iznākumi apkopoti tabulā 7.1. Asimetriskās trimetilsililcianēšanas produktu **18a-h** (R,R); (SR) un (S,S); (R,S), kā arī **19e-h** (R) un (S) ^1H KMR spektri apkopoti tabulā 7.2. Savienojumu **18a-h** raksturlielumi un spektri atbilst literatūras [77-79] datiem.

Tabula 7.1.

Me_3SiCN pievienošanās apstākļi furāna, tiofēna un piridīna imīniem **17a-h**, kā arī iegūto produktu **18a-h** un **19e-h** raksturlielumi.

Nr.	Imīns	Kat. (mol %)	Temp °C	Laiks st.	Konversija %[a]	Eluents kolonnu hromatogrāfijai.	Produkts[b,c]	Iznākums, %	da[a,d]	$[\alpha]_{546}$, grādi. (c benzolā)
1	(*R*)-**17a**	$AlCl_3$ (5)	20	25	n.n.[e]	C_6H_6: EtOAc= 9:1	**18a**(*R*)	43	78:22	+88.9 (0.84)
2	(*S*)-**17a**	$AlCl_3$ (5)	20	20	n.n.	C_6H_6: EtOAc= 9:1	**18a**(*S*)	38	67:33	−80.6 (0.5)
3	(*R*)-**17b**	$AlBr_3$(20)	20	1	~100	-	**18b**(*R*)	82	74:26	+105.5 (0.7)
4	(*S*)-**17b**	$AlBr_3$(20)	20	1	~100	-	**18b**(*S*)	80	74:26	−103.2 (0.7)
5	(*R*)-**17c**	$AlBr_3$(10) +MS 4A	20	6.5	80	Hex: EtOAc= 5:1	**18c**(*R*)	75	79:21	+119.4 (2.1)
6	(S)-**17c**	$AlBr_3$(10) +MS 4A	20	6.5	78	Hex: EtOAc= 5:1	**18c**(*S*)	72	78:22	−103.2 (1.8)
7	(*R*)-**17d**	$AlBr_3$(20)	20	1	80	Hex: EtOAc= 5:1	**18d**(*R*)	58	77:23	+69.1 (1.3)
8	(*S*)-**17d**	$AlBr_3$(20)	20	1	87	Hex: EtOAc= 5:1	**18d**(*S*)	62	75:25	−69.1 (1.3)
9	(*R*)-**17e**	$AlCl_3$(20)	40	19	75	-	**18e**(*R*)	n.n.	71:29	
10	(*R*)-**17e**	$AlBr_3$(10) +MS 4A	40	2	87	$CHCl_3$: MeOH= 9.5:0.5	**18e**(*R*)	40	78:22	+55.8 (1.2)
						---''---	(*R*)-**19e**	33	-	+43.8 (0.8)
11	(*S*)-**17e**	$AlCl_3$(20)	40	19	n.n.	$CHCl_3$: MeOH= 9:1	**18e**(*S*)	61	74:26	−45.5 (1.2)
						---''---	(*S*)-**19e**	10	-	
12	(*S*)-**17e**	$AlBr_3$(10)	20	41	40	-	**18e**(*S*)	-	71:29	
13	(*S*)-**17e**	$AlBr_3$(10) +MS 4A	40	8.5	96	$CHCl_3$: MeOH= 9.5:0.5	**18e**(*S*)	73	79:21	−47.3 (1.3)
						---''---	(*S*)-**19e**	18	-	−42.8 (0.5)
14	(*R*)-**17f**	$AlBr_3$(10) +MS 4A	40	21	95	CH_2Cl_2: MeOH= 10:1	**18f**(*R*)	70	75:25	+93.4 (1.8)
						---''---	(*R*)-**19f**	15	-	

15	(*S*)-**17f**	$AlBr_3$(10) +MS 4A	40	22.5	82	CH_2Cl_2: MeOH= 10:1	**18f**(*S*)	75	80:20	−89.7 (2.5)
16	(*R*)-**17g**	$AlBr_3$(10) +MS 4A	20	8.5	97	CH_2Cl_2: MeOH= 10:1	**18g**(*R*)	60	81:19	+72.4 (1.8)
						—''—	(*R*)-**19g**	25	-	+38.3 (0.8)
17	(*S*)-**17g**	$AlBr_3$(10) +MS 4A	20	6	91	CH_2Cl_2: MeOH= 10:1	**18g**(*S*)	64	87:13	−82.3 (1.2)
						—''—	(*S*)-**19g**	12	-	
18	(*R*)-**17h**	$AlBr_3$(10) +MS 4A	20	2	98	CH_2Cl_2: MeOH= 20:1	(*R*)**18h**	70	80:20	+85.1 (1.4)
						—''—	(*R*)-**19h**	20	-	+77.7 (0.6)
19	(*S*)-**17h**	$AlBr_3$(10) +MS 4A	20	2.5	~100	-	**18h**(*S*)	85	76:24	−92.6 (3.7)

[a] Noteikts ar ^{1}H KMR.

[b] CH(Me)Ph grupas konfigurācija ir dota.

[c] Visi savienojumi ir šķidras viskozas vielas, izņemot **18d**(*S*): cieta viela, kušanas temp. 48-49°C.

[d] da = diastereoizomēru attiecība.

[e] n.n. = nav noteikts.

Tabula 7.2.

Asimetriskās trimetilsililcianēšanas produktu **18a-h** (R,R); (SR) un (S,S); (R,S), kā arī **19e-h** (R) un (S) ^{1}H KMR spektri.

Savienojums[a]	Ķīmiskā nobīde ($CDCl_3$), δ, m.d.; *J*, Hz					
	$C\underline{H}_3CH$ d	$C\underline{H}_3$ s	NH	CHCN	$C\underline{H}Me$ k	Gredzena protoni
18a(*R*) mažora	1.43, *J*=6.4	-	2.0, ps	4.43, ps	4.19, *J*=6.4	6.3-6.4, m, FurH-3,4; 7.2-7.4, m, FurH-5, Ph
18a(*S*) minora	1.37, *J*=6.4	-	-''-	4.68, ps	3.92, *J*=6.4	---''---
18b(*R*) mažora	1.43, *J*=6.4	2.28	1.9, ps	4.35, ps	4.18, *J*=6.4	5.92, m, *J*=2.2, FurH-4; 6.25, m, *J*=2.2, FurH-3; 7.2-7.4, m, Ph
18b(*S*) minora	1.37, *J*=6.4	-''-	-''-	4.61, ps	3.93, *J*=6.4	5.92, m, *J*=2.2, FurH-4; 6.20, m, *J*=2.2, FurH-3; 7.2-7.4, m, Ph
18c(*R*) mažora	1.37, *J*=7.0	-	1.95, d, *J*=12.0	4.49, d, *J*=12.0	4.15, *J*=7.0	6.8-7.5, m, ThH-3,4, Ph; 7.64, m, ThH-5
18c(*S*) minora	1.35, *J*=7.0	-	-''-	-''-	3.99, *J*=7.0	—''—

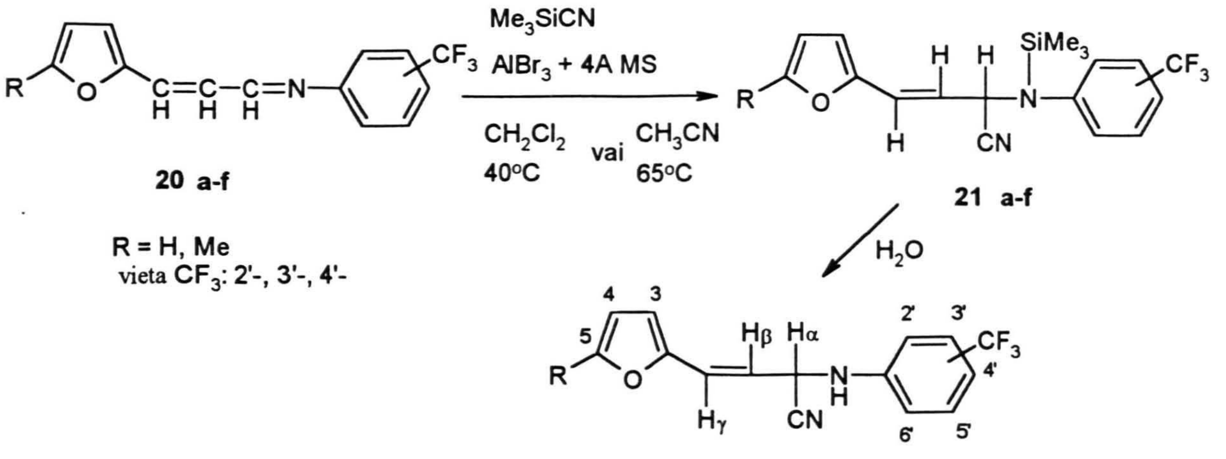
18d(*R*) mažora	1.35, *J*=6.6	2.42	1.95, d, *J*=11.6	4.45, d, *J*=11.6	4.16, *J*=6.6	6.57, d, *J*=3.4, ThH-4; 6.94, d, *J*=3.4, ThH-3; 7.2-7.4, m, Ph
18d(*S*) minora	1.33, *J*=6.6	-''-	1.9, pd	4.46, d, *J*=11.6	4.00, *J*=6.6	---''---
18e(*R*) mažora	1.45, *J*=6.6	-	2.5, p s	4.44, s	4.27, *J*=6.6	7.2-7.4, m, PyH-3,5, Ph; 7.70, td, *J*=6.0, 1.2, PyH-4; 8.61, m, *J*=4.6, PyH-6
18e(*S*) minora	1.41, *J*=6.6	-	-''-	4.76, s	3.98, *J*=6.6	---''---
(*R*)-**19e** (*S*)-**19e**	1.64, *J*=6.4	-	-	-	5.25, *J*=6.4	7.3-7.5, m, PyH-5, Ph; 7.73, td, *J*=7.0, 1.6, PyH-4; 8.12, d, *J*=7.0, PyH-3; 8.69, m, *J*=4.8 PyH-6
18f(*R*) mažora	1.44, *J*=6.6	-	2.0, ps	4.43, s	4.24, *J*=6.6	7.2-7.5, m, PyH-5, Ph; 7.83, dt, *J*=8.0, 2.2, PyH-4; 8.60, dd, *J*=5.0, 1.6, PyH-6; 8.73, d, *J*=2.4
18f(S) minora	1.43, *J*=6.6	-	-''-	4.78, s	3.99, *J*=6.6	---''---
(*R*)-**19f**	1.58, *J*=6.6	-	-	-	5.20, *J*=6.6	7.2-7.5, m, PyH-5, Ph; 8.17, dt, *J*=7.8, 2.2, PyH-4; 8.75, dd, *J*=5.0, 1.6, PyH-6; 8.87, d, *J*=2.2
18g(*R*) mažora	1.47, *J*=7.0	-	2.1, ps	4.41, s	4.24, *J*=7.0	7.3-7.6, m, Ph, PyH-3,5; 8.62, dd, *J*=6.0, 2.0, PyH-2,6
18g(S) minora	1.44, *J*=7.0	-	-''-	4.78, s	4.02, *J*=7.0	---''---
(*R*)-**19g** (S)-**19g**	1.67, *J*=7.2	-	-	-	5.22, *J*=7.2	7.2-7.6, m, Ph; 7.84, dd, *J*=6.0, 2.0, PyH-3,5; 8.78, dd, *J*=6.0, 2.0, PyH-2,6
18h(*R*) mažora	1.47, *J*=6.6	2.56	2.3, ps	4.37, s	4.27, *J*=6.6	7.09, d, *J*=7.6, PyH-5; 7.15, d, *J*=7.6, PyH-3; 7.2-7.5, m, Ph; 7.59, t, *J*=7.6, PyH-4
18h(*R*) minora	1.41, *J*=6.4	2.55	-''-	4.70, s	3.98, *J*=6.4	---''---
(*R*)-**19h**	1.64, *J*=6.4	2.62	-	-	5.25, *J*=6.4	7.23, d, *J*=6.5, PyH-5; 7.3-7.5, m, Ph; 7.63, t, *J*=6.5, PyH-4; 7.93, d, *J*=6.5, PyH-3

---

[a] CH(Me)Ph grupas konfigurācija ir dota

8. Trimetilsililcianīda Me_3SiCN pievienošanās reakcijas N-[3-(hetaril)-2-propenilidēn]-trifluoranilīniem, kuros hetaril grupas ir 2-furil, 5-metil-2-furil.

Literatūrā par trimetilsililcianīda iedarbību ar propenilidēnamīniem datu nav. Furilakroleīna, tā atvasinājumu un analogu, kuri satur konjugēto saišu sistēmu O=C-C=C, hidrosililēšanas reakcijās veidojas 1,2- un 1,4-pievienošanās produkti [80]. Pēc analoģijas ar šiem pētījumiem trimetilsililcianēšanas procesi saišu sistēmā N=C-C=C varētu būt līdzīgi. Izpētītas iepriekš sintezētu N-[3-(hetaril)-2-propenilidēn]-2-trifluormetilanilīnu **20a,d**, N-[3-(hetaril)-2-propenilidēn]-3-trifluormetilanilīnu **20b,c**, N-[3-(hetaril)-2-propenilidēn]-4-trifluormetilanilīnu **20c,f** [73,81,82] trimetilsililcianēšanas reakcijas katalizātora $AlBr_3$ klātbūtnē.



20 a-f

R = H, Me
vieta CF_3: 2'-, 3'-, 4'-

21 a-f

22 a-f

Kā jau iepriekš konstatēts [61,74,83], $AlBr_3$ kopā ar molekulārajiem sietiem 4A uzrādīja vislielāko aktivitāti. Salīdzinot substrātu aktivitāti, izrādījās, ka 4-CF_3-fenil grupas saturoši imīni **20c,f** ir reaģētspējīgāki par 2-CF_3 un 3-CF_3 grupas benzola gredzenā aizvietotiem azometīniem **20a,b,d,e**. Metilgrupa, kas atrodas furāna gredzenā neietekmē reakciju norises ātrumu, jo tā atrodas tālu no reaģējošās saites. Pēc trimetilsililcianēšanas reakciju hidrolīzes un maisījumu sadalīšanas ar kolonnu hromatogrāfijas metodes palīdzību visos gadījumos izdalīti 1,2-pievienošanās produkti t.i. attiecīgie α-aminonitrili: N-[3-(hetaril)-1-ciāno-2-propenil]-trifluormetilanilīni **22a-f** ar iznākumu 57-85%. Savienojuma **22f** struktūra pierādīta ar rentgenstruktūranalīzi, izmantojot literatūrā [84-87] aprakstītās metodes. Reakciju produktu **22a-f** raksturlielumi apkopoti tabulā 8.1.

Tabula 8.1

Reakciju produktu **22a-f** raksturlielumi.

Produkts	R	Pozīcija CF_3	Temp °C/ Laiks, st. (šķīdinātājs)	Brutto formula (molmasa)	Iegūts % Aprēķināts, %			T. kuš., °C	Iznākums %
					C	H	N		
22a	H	2'-	40/25, 65/6 (MeCN)	$C_{15}H_{11}N_2OF_3$ (292.26)	-	-	-	šķidra viskoza viela	71
22b	H	3'-	40/6 (CH_2Cl_2)	$C_{15}H_{11}N_2OF_3$ (292.26)	61.70 61.65	3.89 3.79	9.05 9.58	87-88	72
22c	H	4'-	40/4 (CH_2Cl_2)	$C_{15}H_{11}N_2OF_3$ (292.26)	61.50 61.65	3.74 3.79	9.36 9.58	136-137	85
22d	Me	2'-	40/15 (CH_2Cl_2)	$C_{16}H_{13}N_2OF_3$ (306.29)	-	-	-	šķidra viskoza viela	57
22e	Me	3'-	65/5 (MeCN)	$C_{16}H_{13}N_2OF_3$ (306.29)	-	-	-	šķidra viskoza viela	70
22f	Me	4'-	40/3 (CH_2Cl_2)	$C_{16}H_{13}N_2OF_3$ (306.29)	62.47 62.74	4.34 4.28	8.90 9.15	115-116	75

Izveidojušos starpproduktu trimetilsililcianēto azometīnu **21a-f** saites N-Si hidrolīze notiek maigos apstākļos, iedarbojoties ar mitru acetonu istabas temperatūrā. Tādejādi var secināt, ka Me_3SiCN pievienošanās minētajiem azometīniem notiek selektīvi, pievienojoties trimetilsililcianīdam dubultsaitei C=N un neskarot saiti C=C. Reakciju produktu: α-aminonitrilu **22a-f** GŠH-MS spektrus reģistrēt neizdevās, jo šie savienojumi analīzes apstākļos ir termiski nestabili t.i. α-aminonitrila molekula zaudē HCN un veidojas izejviela. Sintezēto savienojumu **22a-f** ^{1}H KMR spektri apkopoti tabulā 8.2.

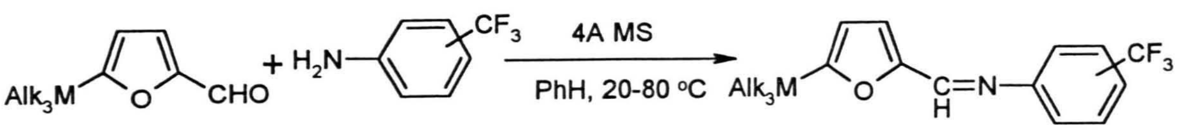
Tabula 8.2.

Sintezēto savienojumu **22a-f** ^1H KMR spektri

Savienojums	Ķīmiskā nobīde ($CDCl_3$), δ, m.d.; *J*, Hz					
	CH_3, s	NH, d	CHN, dd	CH_β, dd	CH_γ, d	Protoni
22a	-	4.51, *J* = 7.8	5.08, *J* = 5.4, 7.8	6.19, *J* = 5.4, 15.7	6.91, *J* = 15.7	6.42 (2H, s, H-3, H-4), 6.9–7.0 (2H, m, H-5', H-6'), 7.40 (1H, s,H-5), 7.5–7.6 (2H, m, H-3', H-4')
22b	-	4.53, *J* = 8.6	5.05, *J* = 5.4, 8.6	6.17, *J* = 5.4, 15.6	6.83, *J* = 15.6	6.40 (2H, s, H-3, H-4), 6.9–7.0 (2H, m, H-2', H-6'), 7.12 (1H, d, *J* = 8.0, H-5'), 7.35 (1H, s, H-5), 7.39 (1H, m, H-2')
22c	-	4.20, *J* = 8.4	5.09, *J* = 5.3, 8.4	6.20, *J* = 5.3, 15.8	6.86, *J* = 15.8	6.42 (2H, s, H-3, H-4), 6.81 (2H, d, *J* = 8.4, H-2', H-6'), 7.41 (1H, s, H-5), 7.51 (2H, d, *J* = 8.4, H-3', H-5')
22d	2.32	4.50, *J* = 7.2	5.06, *J* = 5.2, 7.2	6.12, *J* = 5.2, 15.8	6.80, *J* = 15.8	6.02 (1H, d, *J* = 3.0, H-4), 6.31 (1H, d, *J* = 3.0, H-3), 6.9–7.0 (2H, m, H-5', H-6'), 7.5–7.6 (2H, m, H-3', H-4')
22e	2.32	4.07, *J* = 8.2	5.05, *J* = 4.8, 8.2	6.10, *J* = 4.8, 15.4	6.77, *J* = 15.4	6.01 (1H, d, *J* = 3.1, H-4), 6.30 (1H, d, *J* = 3.1, H-3), 6.9–7.0 (2H, m, H-2', H-6'), 7.12 (1H, d, *J* = 7.4, H-5'), 7.35 (1H, m, H-2')
22f	2.31	4.20, *J* = 8.8	5.04, *J* = 5.4, 8.8	6.09, *J* = 5.4, 15.6	6.80, *J* = 15.6	6.01 (1H, d, *J* = 3.4, H-4), 6.29 (1H, d, *J* = 3.4, H-3), 6.75 (2H, d, *J* = 8.4, H-2', H-6'), 7.54 (2H, d, *J* = 8.4, H-3', H-5')

9. Dažu 5-*t*-butil-2-furilmetilidēnanilīnu trifluormetilatvasinājumu un to sililēto analogu sintēze un bioloģiskā aktivitāte.

Heterocikliskie azometīni, kas satur sililgrupas un CF_3-grupas ir potenciāli bioloģiski aktīvi savienojumi [47-49,50,51], tādēļ tika sintezēta rinda Šifa bāzu **25a-i**, kas satur minētās grupas, pēc mūsu izstrādātas metodikas [82,88,89], kondensējot 5-*t*-butilfurfurolu **23a** un tā trimetilsilil- un trietilsilil- analogus **23b,c** ar 2-, 3-, 4-trifluormetilanilīniem **24a-c** molekulāro sietu 4A klātbūtnē. Iegūti produkti: aldimīni **25a-i** ar 38-100% lielu iznākumu. Visas savienojumu struktūras pierādītas ar ^1H KMR un masspektriem.



23a-c **24a-c** **25a-i**

23a, 25a-c M = C, Alk = Me
23b, 25d-f M = Si, Alk = Me
23c, 25g-i M = Si, Alk = Et

	vieta CF_3
24a, 25a, 25d, 25g	2-
24b, 25b, 25e, 25h	3-
24c, 25c, 25f, 25i	4-

Furfurola trimetilsilil- un trietilsilil- atvasinājumi **23b,c** reaģē ar 3- un 4-trifluormetilanilīniem **24b,c** jau istabas temperatūrā, bet ar 2-trifluormetilanilīnu **24a** paaugstinātā temperatūrā (80^{0}C).

t-Butilaizvietots furfurola atvasinājums **23a** ar iepriekš minētiem amīniem **24a-c** arī reaģē tikai paaugstinātā temperatūrā. Minimāla aktivitāte raksturīga *t*-butilaizvietotam aldehīdam **23a** un 2-trifluormetilanilīnam **24a**, jo 2-CF_3 grupa rada stēriskas grūtības šo savienojumu kondensācijā.

Sintezēto savienojumu **25a-i** bioloģiskā aktivitāte tika noteikta ar dažādām metodēm: neirotropā aktivitāte uz balto peļu līnijas ICR [90,91], kā arī citotoksicitāte uz vēža līnijām *in vitro* [71]. Izpētītie aldimīni **25a-i**, izņemot N-(5-trimetilsilil-2-furilmetilidēn)-4-trifluormetilanilīnu **25f** (LD_{50} 365 mg/kg), ir maztoksiski savienojumi, to LD_{50} lielums pārsniedz 1000 mg/kg, tādēļ terapeitiskās iedarbības indekss šo savienojumu rindā varētu būt pietiekami augsts. Pētot dzīvnieku kustību aktivitāti rotējošā stieņa un cilindra testos, noskaidrots, ka izteiktas deprimējošas īpašības piemīt tikai N-(5-*t*-butil-2-furilmetilidēn)-3-trifluormetilanilīnam **25b**. Citiem savienojumiem šī aktivitāte ir zema vai praktiski tās nav. Vairākumam no izpētītiem savienojumiem piemīt analģēziskas īpašības. Neviens no sintezētiem savienojumiem, izņemot toksisko imīnu **25f**, neietekmē trakciju (tests pievilkšanās pie stieņa). Gandrīz visi azometīni samazina peļu dzīves ilgumu hipoksiskās hipoksijas apstākļos-75-99% (salīdzinot ar kontrollielumu-100%). Savienojumi maz ietekmē fenamīna hipertermiju-iegūtie dati tuvi kontrollielumam (100%). *t*-Butilatvasinājumi **25a-c** un N-(5-trietilsilil-2-furilmetilidēn)-2-trifluormetilanilīns **25g** ievērojami samazina etanola narkozes laiku, bet vairākums no savienojumiem palielina heksenāla narkozes laiku.

Antikonvulsīvas īpašības (korazola krampju tests) piemīt gandrīz visiem sintezētiem imīniem, īpaši trietilsililatvasinājumiem **25g-i**. Pētāmie savienojumi **25a-i** atkarībā no to struktūras rada specifisku iedarbību uz fenamīna farmakoloģiskiem efektiem, tā *t*-butilatvasinājumi **25a-c** ievērojami palielina stimulējošo fenamīna aktivitāti-5.39, 3.17 un 8.59 reizes attiecīgi. Sililatvasinājumi **25d-i** vai nu neietekmē fenamīna aktivitāti, vai rada antagonistisku iedarbību. Citotoksiskās aktivitātes pētījumu mērķis-noteikt sintezēto imīnu **25a-i** spēju nomākt vēža šūnu augšanu *in vitro*, kā arī noteikt šo vielu aktivitāti slāpekļa oksīda radikāļu sintēzē šūnā, jo paaugstināta NO· radikāļu koncentrācija noved pie šūnu bojā ejas [92]. Vielu koncentrāciju, kas nodrošina 50% šūnu bojā eju, noteica uz divām šūnu līnijām: HT-1080 (cilvēka plaušu fibrosarkoma) un MG-22A (peļu hepatoma). Tikai viens no savienojumiem N-(5-trimetilsilil-2--furilmetilidēn)-3-trifluormetilanilīns **25e** neuzrādīja citotoksicitāti. Pārējie sililatvasinājumi **25d-i** uzrādīja mērenu citotoksisko efektu, taču vairums no tiem uzrādīja augstu NO ģenerācijas līmeni, it īpaši trietilsililatvasinājumi **25g-i** uz šūnu līnijas HT-1080, bet imīns N-(5-trimetilsilil-2--furilmetilidēn)-2-trifluormetilanilīns **25d** uz šūnu līnijas MG-22A. Vislielākā citotoksiskā aktivitāte piemīt *t*-butilatvasinājumiem **25a-c**, pie tam to iedarbība ir specifiska uz dažādām šūnām dažādos testos. Maksimālo citotoksicitāti-IC_{50} =0,15µg/ml uz šūnu līnijas HT-1080 uzrādīja N-(5-*t*--butil-2-furilmetilidēn)-3-trifluormetilanilīs **25b**, kā arī N-(5-*t*-butil-2-furilmetilidēn)-2--trifluormetilanilīns **25a**-IC_{50}=0,43µg/ml uz šūnu līnijas MG-22A. Abos gadījumos šī citotoksicitāte noteikta, iekrāsojot mitohondriālos enzīmus ar 3-(4,5-dimetiltiazol-2-il)-2,5-difeniltetrazolija bromīdu (MTT), kas liecina par to oksidējošo-reducējošo īpašību intensitātes pieaugumu testējamo vielu klātbūtnē. N-(5-*t*-butil-2-furilmetilidēn)-4-trifluormetilanilīns **25c** uzrādīja ievērojamu citotoksicitāti uz peļu hepatomas šūnu līnijas, iekrāsojot ar MTT(IC_{50}=4µg/ml), kā arī CV testā, iekrāsojot šūnu membrānas ar kristālvioleto (IC_{50}=5µg/ml). Visos testos morfoloģiskās izmaiņas šūnās netika novērotas.

10. Eksperimentālā daļa.

10.1. Pielietotās metodes un aparatūra.

^1H KMR spektri uzņemti uz spektrometriem Varian Mercury (200 MHz) un Bruker WH-90/DS (90 MHz) $CDCl_3$ šķīdumiem, iekšējais standarts TMS. Masspektri uzņemti uz hromato-masspektrometra HP 6890 GC/MS, kas apgādāts ar kapilāra kolonnu HP-5 MS (30.0 m × 250 µkm), ieprogrammētais temperatūras režīms no 70 līdz 260^{0}C (10^{0}C/min). Optiskā griešana noteikta uz instrumenta Polamat A(Carl Zeiss, Jena). Elementanalīze noteikta, izmantojot instrumentu Carlo Erba EA-1108. Kušanas punkti noteikti ar Kofler instrumentu. Sintezēto savienojumu monokristāli iegūti lēnā kristalizācijā no šķīdinātāju maisījuma benzols-heksāns. Difrakcijas ainas uzņemtas 20^{0}C temperatūrā uz automātiska difraktometra Nonius KappaCCD (MoKα starojums). Savienojumu struktūras noteiktas pēc aprēķiniem, kas veikti ar datorprogrammu SHELXS 97, SIR 97 un maXus palīdzību [66-68].

10.2. Hidrosililēšanas reakciju veikšanas kopējā metodika.

Benzols pirms lietošanas pārdestilēts virs CaH_2, tetrahidrofurāns žāvēts pēc zināmas metodikas. Reakcijās izmantoti firmu Fluka un Acros hidrosilāni un pārejas metālu kompleksi, kā arī VEB Laborchemie Apolda molekulārie sieti. Reakcijas reaktoru Pierce (tilpums 5cm^3) izpūš ar argonu, ievieto tajā 2 ml sausa benzola vai THF, 0.01 mmol katalizātora, 0.5 mmol imīna, maisa istabas temperatūrā ≈ 30 min. Pēc tam iegūto šķīdumu atdzesē ar ledu līdz 0^{0}C un ar šprici pievieno 0.6 mmol hidrosilāna. Reakciju veic pie 65^{0}C vai istabas temperatūrā, periodiski noņemot paraugus un analizējot tos ar PSH, GŠH, GŠH-MS. PSH veic uz plāksnītēm Kieselgel 60 F_{254} (Merck). Pēc sililēšanas beigām reakcijas maisījumu filtrē, ietvaicē pazeminātā spiedienā (30^{0}C/15mm) un reģistrē ^{1}H KMR spektrus. Pēc tam veic hidrolīzi, pievienojot 2.5 ml metanola un 0.5 ml 10% $NaHCO_3$ ūdens šķīduma. Šo maisījumu ekstraģē ar ēteri, ekstraktu žāvē virs bezūdens Na_2SO_4, filtrē un ietvaicē. Atlikumu sadala ar šķidruma hromatogrāfijas metodes palīdzību uz kolonnas ar silikagelu (Kieselgel 60, 0.063-0.200, Merck). Furāna un tiofēna atvasinājumu gadījumā lieto eluentu benzols-etilacetāts, bet piridīna atvasinājumu gadījumā: hloroforms-metanols. Visi iegūtie produkti ir šķidras viskozas vielas dzeltenā vai oranžā krāsā. N-(hetarilmetilidēn)-2-trifluormetilanilīnu hidrosililēšanas rekciju produktu ^{1}H KMR spektri un masspektri apkopoti tabulās 4.1. un 4.2.

10.2.1. N-(hetarilmetilidēn)-3-trifluormetilanilīnu un N-(hetarilmetilidēn)-4-trifluormetilanilīnu, kuros hetaril grupas ir 2-furil, 5-metil-2-furil, 2-tienil, 5-metil-2-tienil hidrosililēšanas reakciju produktu ^{1}H KMR un masspektri.

N-(2-furilmetil)-4-trifluormetilanilīns (4a).
MS-GC, *m/z* ($I_{rel.}$, %): 241 (28, M^+), 240 (6, $[M-H]^+$), 222 (4, $[M-F]^+$), 174 (4, $[M-Fur]^+$), 172 (3, $[M-CF_3]^+$), 145 (9, $[C_6H_4CF_3]^+$), 80 (6), 81 (100, $[FurCH_2]^+$), 69 (3, $[CF_3]^+$), 53 (25), 39 (5).
^{1}H KMR (90 MHz, δ (m.d.), *J* (Hz), $CDCl_3$, TMS): 1.5 (ps, 1H, NH), 4.33 (s, 2H, CH_2), 6.24 (m, *J*=4.0, 1H, FurH-3), 6.31 (m, *J*=4.0, 2.0, 1H, FurH-4), 6.67 (d, *J*=9.4, 2H, ArH-3,5), 7.35 (m, 1H, FurH-5), 7.40 (d, *J*=9.4, ArH-2,6).

N-(2-furilmetil)-trietilsilil-4-trifluormetilanilīns (2a).
MS-GC, *m/z* ($I_{rel.}$, %): 355 (14, M^+), 336 (5, $[M-F]^+$), 326 (37, $[M-Et]^+$), 224 (17), 188 (20), 154 (100), 145 (9, $[C_6H_4CF_3]^+$), 125 (29), 115 (5, $[SiEt_3]^+$), 97 (8), 87 (14), 81 (72, $[FurCH_2]^+$), 69 (2, $[CF_3]^+$), 59 (21), 53 (24).

N-(5-metil-2-furilmetil)-4-trifluormetilanilīns (4b).
MS-GC, *m/z* ($I_{rel.}$, %): 255 (17, M^+), 236 (2, $[M-F]^+$), 211 (11), 174 (5), 172 (4), 160 (1, $[M-MeFur]^+$), 145 (9, $[C_6H_4CF_3]^+$), 95 (100, $[MeFurCH_2]^+$), 65 (4), 51 (5), 43 (10), 39 (5).
^{1}H KMR (90 MHz, δ (m.d.), *J* (Hz), $CDCl_3$, TMS): 1.8 (ps, 1H, NH), 2.27 (d, *J*=1.2, 3H, CH_3), 4.28 (s, 2H, CH_2), 5.89 (dd, *J*=3.6, 1.2, 1H, FurH-4), 6.11 (d, *J*=3.6, 1H, FurH-3), 6.55 (d, *J*=9.5, 2H, ArH-3,5), 7.40 (d, *J*=9.5, ArH-2,6).

N-(2-tienilmetil)-4-trifluormetilanilīns (4c).
MS-GC, *m/z* ($I_{rel.}$, %): 257 (16, M^+), 238 (5, $[M-F]^+$), 174 (5, $[M-Th]^+$), 172 (4), 145 (14, $[C_6H_4CF_3]^+$), 97 (100, $[ThCH_2]^+$), 69 (6, $[CF_3]^+$), 53 (7), 45 (8), 39 (5).

^{1}H KMR (90 MHz,δ (m.d.),*J* (Hz), CDCl$_3$, TMS): 1.55 (ps, 1H, NH), 4.55 (s, 2H, CH$_2$), 6.69 (d, *J*=9.0, 2H, ArH-3,5), 6.9–7.1 (m, 2H, ThH-3,4), 7.24 (dd, *J*=4.0, 2.0, 1H, ThH-5), 7.42 (d, *J*=9.0, ArH- 2,6).

N-(2-tienilmetil)-trietilsilil-4-trifluormetilanilīns (2c).

MS-GC, *m/z* (I$_{rel.}$, %): 371 (22, M$^+$), 353 (2, [M – F]$^+$), 342 (35, [M – Et]$^+$), 284 (1, [M – 3Et]$^+$), 256 (3, [(12), 97 (76, [ThCH$_2$]$^+$), 87 (13), 69 (2, [CF$_3$]$^+$), 59 (21), 45 (8).

N-(5-metil-2-tienilmetil)-4-trifluormetilanilīns (4d).

MS-GC, *m/z* (I$_{rel.}$, %): 271 (16, M$^+$), 252 (1, [M – F]$^+$), 211 (11), 174 (5), 145 (17, [C$_6$H$_4$CF$_3$]$^+$), 125 (6), 111 (100, [MeThCH$_2$]$^+$), 95 (7), 77 (12), 69 (10), 59 (7), 45 (9), 39 (6).

^{1}H KMR (200 MHz, δ (m.d.), *J* (Hz), CDCl$_3$, TMS): 2.43 (s, 3H, CH$_3$), 4.45 (s, 2H, CH$_2$), 5.59 (m, *J*=3.4, 1.2, 1H, ThH-4), 6.73 (d, *J*=8.4, 2H, ArH-3,5), 6.78 (d, *J*=3.4, 1H, ThH-3), 7.42 (d, *J*=8.4, ArH-2,6).

N-(2-furilmetil)-3-trifluormetilanilīns (4e).

MS-GC, *m/z* (I$_{rel.}$, %): 242 (6, [M + H]$^+$), 241 (47, M$^+$), 222 (15, [M – F]$^+$), 213 (5), 172 (9, [M – CF$_3$]$^+$), 145 (23, [C$_6$H$_4$CF$_3$]$^+$), 125 (7), 113 (18), 95 (7), 81 (100, [FurCH$_2$]$^+$), 75 (9), 69 (7, [CF$_3$]$^+$), 63 (8), 53 (21), 39 (12).

^{1}H KMR (200 MHz, δ (m.d.), *J* (Hz), CDCl$_3$, TMS): 4.33 (s, 2H, CH$_2$), 6.24 (dd, *J*=3.2, 0.7, 1H, FurH-3), 6.31 (dd, *J*=3.2, 1.9, 1H, FurH-4), 6.8–6.9 (m, 2H, ArH-5,6), 6.9–7.0 (m, 1H, ArH-4), 7.2–7.3 (m, 1H, ArH-2), 7.36 (dd, *J*=0.7, 1.9, 1H, FurH-5).

N-(2-furilmetil)-trietilsilil-3-trifluormetilanilīns (2e).

MS-GC MS-GC, *m/z* (I$_{rel.}$, %): 355 (10, M$^+$), 336 (2, [M – F]$^+$), 326 (35, [M – Et]$^+$), 224 (16), 188 (11), 154 (100), 153 (35), 145 (6, [C$_6$H$_4$CF$_3$]$^+$), 125 (29), 115 (5, [SiEt$_3$]$^+$), 97 (8), 87 (12), 81 (54, [FurCH$_2$]$^+$), 69 (1, [CF$_3$]$^+$), 59 (19), 53 (18).

^{1}H KMR (90 MHz, δ (m.d.), *J* (Hz), CDCl$_3$, TMS): 0.8–1.0 (m, 15H, SiEt$_3$), 4.43 (s, 2H, CH$_2$), 6.02 (dd, *J*=3.0, 1.0, 1H, FurH-3), 6.22 (dd, *J*=3.0, 2.0, 1H, FurH-4), 6.9–7.3 (m, 4H, ArH$_4$), 7.42 (dd, *J*=2.0, 1.0, 1H, FurH-5).

N-(5-metil-2-furilmetil)-3-trifluormetilanilīns (4f).

MS-GC, *m/z* (I$_{rel.}$, %): 255 (14, M$^+$), 236 (3, [M – F]$^+$), 174 (4), 145 (10, [C$_6$H$_4$CF$_3$]$^+$), 95 (100, [MeFurCH$_2$]$^+$), 51 (6), 43 (15).

^{1}H KMR (200 MHz, δ (m.d.), *J* (Hz), CDCl$_3$, TMS): 2.25 (s, 3H, CH$_3$), 4.25 (s, 2H, CH$_2$), 5.88 (dd, *J*=3.2, 1.0, 1H, FurH-4), 6.11 (d, *J*=3.2, 1H, FurH-3), 6.75–6.9 (m, 2H, ArH-5,6), 6.9–7.0 (m, 1H, ArH-4), 7.2–7.3 (m, 1H, ArH-2).

N-(5-metil-2-furilmetil)-trietilsilil-3-trifluormetilanilīns (2f).

MS-GC, *m/z* (I$_{rel.}$, %): 369 (6, M$^+$), 340 (11, [M – Et]$^+$), 246 (4), 216 (4), 188 (5), 167 (15), 154 (29), 139 (8), 95 (100, [MeFurCH$_2$]$^+$), 87 (6), 77 (3), 59 (10), 43 (11).

^{1}H KMR (90 MHz, δ (m.d.), *J* (Hz), CDCl$_3$, TMS): 0.8–1.0 (m, 15H, SiEt$_3$), 2.20 (s, 3H, CH$_3$), 4.40 (s, 2H, CH$_2$), 5.78 (m, 1H, FurH-4), 5.87 (m, 1H, FurH-3), 6.8–7.5 (m, 4H, ArH$_4$).

[(5-metil-2-furil)-trietilsililmetilēn]-3-trifluormetilanilīns (3f).

MS-GC, *m/z* (I$_{rel.}$, %): 367 (6, M$^+$), 352 (1, [M – Me]$^+$), 348 (1, [M – F]$^+$)337 (26), 338 (100, [M – Et]$^+$), 310 (12), 280 (7), 222 (47), 207 (82), 179 (21), 145 (19, [C$_6$H$_4$CF$_3$]$^+$), 128 (8), 109 (5), 95 (20, [MeFurCH$_2$]$^+$), 77 (14), 59 (9), 43 (30).

N-(2-tienilmetil)-3-trifluormetilanilīns (4g).

MS-GC, *m/z* (I$_{rel.}$, %): 257 (33, M$^+$), 238 (5, [M – F]$^+$), 174 (5, [M – Th]$^+$), 145 (15, [C$_6$H$_4$CF$_3$]$^+$), 113 (5), 97 (100, [ThCH$_2$]$^+$), 69 (6, [CF$_3$]$^+$), 53 (8), 45 (10), 39 (6).

^{1}H KMR (90 MHz, δ (m.d.), *J* (Hz), CDCl$_3$, TMS): 4.2 (ps, 1H, NH), 4.53 (s, 2H, CH$_2$), 6.6–7.6 (m, 7H, ThH-3,4,5, ArH$_4$).

N-(2-tienilmetil)-trietilsilil-3-trifluormetilanilīns (2g).

MS-GC, *m/z* (I$_{rel.}$, %): 371 (19, M$^+$), 353 (2, [M – F]$^+$), 342 (33, [M – Et]$^+$), 256 (3, [M – SiEt$_3$]$^+$), 236 (5), 217 (4), 188 (13), 169 (31), 154 (100), 145 (9, [C$_6$H$_4$CF$_3$]$^+$), 141 (30), 127 (6), 113 (11), 97 (63, [ThCH$_2$]$^+$), 87 (9), 77 (5), 59 (17), 45 (6).

N-(5-metil-2-tienilmetil)-3-trifluormetilanilīns (4h).

MS-GC, *m/z* ($I_{rel.}$, %): 271 (20, M^+), 252 (1, $[M - F]^+$), 174 (5), 145 (14, $[C_6H_4CF_3]^+$), 111 (100, $[MeThCH_2]^+$), 95 (5), 77 (8), 69 (5), 45 (6).

^{1}H KMR (200 MHz, δ (m.d.), *J* (Hz), $CDCl_3$, TMS): 2.43 (s, 3H, CH_3), 4.43 (s, 2H, CH_2), 6.59 (m, *J*=3.2, 1.2, 1H, ThH-4), 6.79 (d, *J*=3.2, 1H, ThH-3), 6.8–6.9 (m, 2H, ArH-5,6), 6.9–7.0 (m, 1H, ArH-4), 7.2–7.3 (m, 1H, ArH-2).

N-(2-tienilmetilidēn)-anilīns (1i).

MS-GC, *m/z* ($I_{rel.}$, %): 187 (85, M^+), 186 (100, $[M - H]^+$), 115 (6), 110 (2, $[M - Ph]^+$), 104 (4, $[M - Th]^+$), 95 (4), 97 (100, $[ThCH_2]^+$), 84 (5, $[ThH]^+$), 77 (40, Ph^+), 69 (5), 63 (5), 58 (5), 51 (26), 45 (9), 39 (14).

^{1}H KMR (90 MHz, δ (m.d.), *J* (Hz), $CDCl_3$, TMS): 7.0–7.5 (m, 8H, Th, Ph), 8.51 (s, 1H, CHN).

N-(2-tienilmetil)-anilīns (4i).

MS-GC, *m/z* ($I_{rel.}$, %): 190 (6), 189 (48, M^+), 187 (8), 186 (10), 154 (2), 106 (4), 97 (100, $[ThCH_2]^+$), 77 (18, Ph^+), 65 (10), 51 (15), 45 (14), 39 (16).

^{1}H KMR (90 MHz, δ (m.d.), *J* (Hz), $CDCl_3$, TMS): 4.0 (ps, 1H, NH), 4.51 (s, 2H, CH_2), 6.5–7.3 (m, 6H, Ph, ThH-3), 6.71 (m, *J*=2, ThH-4), 7.18 (m, *J*=2, ThH-5).

N-(2-tienilmetil)-trietilsililanilīns (2i).

MS-GC, *m/z* ($I_{rel.}$, %): 306 (16), 305 (67, M^+), 276 (3, $[M - Et]^+$), 249 (20), 248 (100, $[M - 2Et - H]^+$), 244 (37), 218 (5), 200 (3), 190 (16), 156 (5), 130 (12), 115 (23, $[SiEt_3]^+$), 104 (6), 87 (47), 77 (28, Ph^+), 59 (50), 45 (8), 31 (5).

[N-(2-tienil)-trietilsililmetilēn]-anilīns (3i).

MS-GC, *m/z* ($I_{rel.}$, %): 304 (11), 303 (45, M^+), 273 (20), 274 (92, $[M - Et]^+$), 246 (5), 216 (2, $[M - 3Et]^+$), 170 (14), 169 (100), 149 (9), 142 (10), 141 (80), 121 (19), 120 (49), 113 (23), 97 (68), 87 (24), 77 (23, Ph^+), 59 (46), 53 (13), 45 (14).

^{1}H KMR (90 MHz, δ (m.d.), *J* (Hz), $CDCl_3$, TMS): 0.7–1.0 (m, 15H, $SiEt_3$), 6.4–7.3 (m, 8H, Th, Ph).

N-fenilmetilidēn-4-trifluormetilanilīns (1j).

MS-GC, *m/z* ($I_{rel.}$, %): 250 (12), 249 (75, M^+), 248 (100, $[M - H]^+$), 230 (4, $[M - F]^+$), 180 (7), 172 (8, $[M - Ph]^+$), 145 (38, $[C_6H_4CF_3]^+$), 126 (7), 125 (9), 95 (12), 89 (5), 77 (11, Ph^+), 75 (9), 69 (7, $[CF_3]^+$), 51 (10), 39 (5).

^{1}H KMR (90 MHz, δ (m.d.), *J* (Hz), $CDCl_3$, TMS): 7.22 (d, *J*=8.4, 2H, ArH-3,5), 7.3–7.6 (m, 3H, PhH-2,4,6), 7.62 (d, *J*=8.4, ArH-2,6), 7.90 (m, 2H, PhH-3,5), 8.42 (s, 1H, CHN).

N-fenilmetil-4-trifluormetilanilīns (4j).

MS-GC, *m/z* ($I_{rel.}$, %): 252 (10), 251 (65, M^+), 250 (14, $[M - H]^+$), 232 (13, $[M - F]^+$), 182 (2), 174 (10, $[M - Ph]^+$), 172 (6), 145 (21, $[C_6H_4CF_3]^+$), 125 (4), 113 (5), 92 (7), 91 (100, $[PhCH_2]^+$), 77 (6, Ph^+), 65 (17), 51 (8), 39 (7).

^{1}H KMR (90 MHz, δ (m.d.), *J* (Hz), $CDCl_3$, TMS): 4.33 (s, 3H, CH_2NH), 6.60 (d, *J*=8.6, 2H, ArH-3,5), 7.33 (s, 5H, Ph), 7.38 (d, *J*=8.6, ArH-2,6).

N-fenilmetilidēnanilīns (1k).

MS-GC, *m/z* ($I_{rel.}$, %): 182 (10), 181 (81, M^+), 180 (100, $[M - H]^+$), 152 (7), 104 (10, $[M - Ph]^+$), 89 (7), 78 (10), 77 (56, Ph^+), 63 (10), 51 (37), 50 (14), 39 (9).

^{1}H KMR (90 MHz, δ (m.d.), *J* (Hz), $CDCl_3$, TMS): 7.1–7.7 (m, 8H, PhH-2,4,6, Ph'H_5), 7.93 (m, 2H, PhH-3,5), 8.49 (s, 1H, CHN).

N-fenilmetilanilīns (4k).

MS-GC, *m/z* ($I_{rel.}$, %): 184 (12), 183 (84, M^+), 182 (33, $[M - H]^+$), 154 (4), 152 (2), 106 (20, $[M - Ph]^+$), 104 (14, $[M - Ph - 2H]^+$), 92 (9), 91 ($[PhCH_2]^+$), 89 (5), 77 (37, Ph^+), 65 (38), 63 (11), 51 (25), 50 (9), 39 (22).

^{1}H KMR (90 MHz, δ (m.d.), *J* (Hz), $CDCl_3$, TMS): 3.9 (ps, 1H, NH), 4.27 (s, 2H, CH_2), 6.5–6.8 (m, 3H, PhH-2,4,6), 7.0–7.4 (m, 7H, PhH-3,5, Ph'H_5).

10.3. Trimetilsililcianēšanas reakciju veikšanas kopējā metodika.

Acetonitrilu pēc kvalifikācijas-ļoti tīrs izmanto bez iepriekšējas attīrīšanas, citus šķīdinātājus pirms lietošanas pārdestilē-metilēnhlorīdu virs P_2O_5, benzolu virs CaH_2. Trimetilsililcianīdu Me_3SiCN (Aldrich) izmanto bez papildus attīrīšanas. Darbā tika izmantoti molekulārie sieti 4A (VEB Laborchemie Apolda), $AlBr_3$ (Fluka), silikagels kolonnu hromatogrāfijai (Kieselgel 60, 0.063-0.200, Merck). PSH analīzes veic uz plāksnītēm Kieselgel 60 F_{254} (Merck). Reakcijas reaktoru Pierce (tilpums 5 cm^3) izpūš ar argonu, ievieto tajā 2 ml sausa šķīdinātāja, 0.5 mmol imīna, 0,1 mmol $AlBr_3$, 0.5 g molekulāro sietu. Pēc tam šim maisījumam ar šprici pievieno 0.6 mmol Me_3SiCN. Reakciju veic 20, 40 vai 80^0C, periodiski noņemot paraugus un analizējot tos ar PSH, GŠH-MS. Pēc trimetilsililcianēšanas reakcijas beigām maisījumu filtrē, ietvaicē pazeminātā spiedienā (30^0C/15mm) un reģistrē ^1H KMR spektrus. Tālāk veic hidrolīzi, pievienojot 2.5 ml metanola un 0.5 ml 10% $NaHCO_3$ ūdens šķīduma. Maisījumu ekstraģē ar ēteri, ekstraktu žāvē virs bezūdens $MgSO_4$, pēc tam filtrē, ietvaicē. Atlikumu sadala ar šķidruma hromatogrāfijas metodes palīdzību uz kolonnas ar silikagelu. Furāna un tiofēna atvasinājumu gadījumā izmanto eluentu benzols-etilacetāts, piridīna atvasinājumu gadījumā: metilēnhlorīds-metanols. Iegūtie nitrili ir šķidras viskozas vai cietas vielas dzeltenā vai oranžā krāsā. Trimetilsililcianēšanas reakciju produktu ^1H KMR spektri un masspektri apkopoti tabulās 5.3., 5.4., 5.7., 5.8., 6.2., 6.3., 7.2., 8.2.

10.4. 5-*t*-Butil-2-furilmetilidēnanilīnu trifluormetilatvasinājumu un to sililanalogu sintēzes metodika un bioloģiskās aktivitātes noteikšana.

Benzolu pirms lietošanas destilē virs CaH_2, anilīnus (Acros) izmanto bez papildus attīrīšanas. Kā dehidratējošus aģentus lieto molekulāros sietus 4A (VEB Laborchemie Apolda). Apaļkolbā ar atteces dzesinātāju ievieto 10 ml sausa benzola un 5 mmol aldehīda un amīna, pēc tam 5g izkarsētus pie 360^0C molekulāro sietu. Reakciju veic istabas temperatūrā vai pie 80^0C, karsējot ūdens vannā argona atmosfērā, periodiski noņemot paraugus un analizējot tos ar PSH metodes palīdzību uz plāksnītēm Kieselgel 60 F_{254} sistēmā heksāns-etilacetāts, kā arī ar GŠH-MS metodes palīdzību.

Pēc noteikta laika atkarībā no substrātiem notiek to pilnīga pārvērtība attiecīgos produktos. Pēc reakcijas beigām molekulāros sietus filtrē, mazgā ar benzolu, filtrātu ietvaicē pazeminātā spiedienā (40^0C/15mm) un atdala nenozīmīgos izejvielu daudzumus vakuumā (45-50^0C/0.1mm). Iegūtie produkti ir šķidras viskozas vielas dzeltenā krāsā.

Neirotropās aktivitātes pētījumi veikti Latvijas Organiskās sintēzes institūta Farmaceitiskās farmakoloģijas laboratorijā Dr. L. Zvejnieces un Dr. Pharm. M. Dambrovas vadībā. Citotoksicitāte noteikta Latvijas Organiskās sintēzes institūta Medicīniskās ķīmijas nodaļā, Eksperimentālās ķīmijterapijas grupā prof. I. Kalviņa vadībā. Neirotropo aktivitāti pētīja uz peļu šūnu līnijas ICR. Eksperimentu metodika aprakstīta darbos [90,91]. Citotoksicitāte pētīta uz vēža šūnu kultūras pēc metodikas [71]. Dzīvo šūnu daudzumu noteica ar divām neatkarīgām kolorimetriskām metodēm pēc šūnu membrānu krāsojuma intensitātes ar kristālvioleto un mitohondriālo enzīmu krāsojuma intensitātes ar 3-(4,5-dimetiltiazol-2-il)-2,5-difeniltetrazolija bromīdu. Testējamo vielu specifisko NO-ģenerēšanas spēju attiecībā pret 100% dzīvo šūnu aprēķināja pēc vienādības:

$$TG_{100} = G_{Ex} \cdot 100/C \text{ (nmol} \cdot 10^2 / 200\mu\text{kl)},$$

kur G_{Ex}- NO koncentrācija (nmol) 200μkl kulturālās vides pēc inkubācijas ar 50 μkg/ml testējamās vielas [93], C- dzīvo šūnu procentuālais daudzums pēc inkubācijas ar 50 μkg/ml testējamās vielas.

10.4.1. 5-*t*-Butil-2-furilmetilidēnanilīnu trifluormetilatvasinājumu un to sililanalogu ^{1}H KMR un masspektri.

N-(5-*t-butil-2-furilmetilidēn)-2-trifluormetilanilīns (25a).*
Masspektrs, *m/z* (I_{rel},%): 296 (7, $[M+H]^+$), 295 (37, M^+), 281 (15), 280 (100, $[M-Me]^+$), 172 (36, $[HCNC_6H_4CF_3]^+$), 145 (42, $[C_6H_4CF_3]^+$), 126 (8), 125 (7), 109 (15), 95 (15), 81 (9), 79 (16), 65 (8), 53 (11). ^{1}H KMR spektrs, δ (m. d.), *J* (Hz): 1.33 (9H, s, $3CH_3$), 6.18 (1H, d, *J* = 4.0, H-4), 6.95 (1H, d, *J* = 4.0, H-3), 6.70 (1H, d, *J* = 8.2, H-3'), 7.20 (1H, t, *J* = 8.2, H-5'), 7.51 (1H, t, *J* = 8.2, H-4'), 7.64 (1H, d, *J* = 8.2, H-6'), 8.09 (1H, s, CH=N).

N-(5-*t-butil-2-furilmetilidēn)-3-trifluormetilanilīns (25b).*
Masspektrs, *m/z* (I_{rel}, %): 296 (5, $[M+H]^+$), 295 (37, M^+), 281 (17), 280 (100, $[M-Me]^+$), 172 (45, $[HCNC_6H_4CF_3]^+$), 145 (47, $[C_6H_4CF_3]^+$), 140 (5), 126 (10), 109 (15), 95 (12), 81 (10), 79 (17), 65 (6), 53 (11). ^{1}H KMR spektrs, δ (m.d.), *J* (Hz): 1.38 (9H, s, $3CH_3$), 6.20 (1H, d, *J* = 4.0, H-4), 6.98 (1H, d, *J* = 4.0, H-3), 7.29 - 7.53 (4H, m, H-2', H-4', H-5', H-6'), 8.18 (1H, s, CH=N).

N-(5-*t-butil-2-furilmetilidēn)-4-trifluormetilanilīns* (25c).
Masspektrs, *m/z* (I_{rel}, %): 296 (4, $[M+H]^+$), 295 (37, M^+), 281 (15), 280 (100, $[M-Me]^+$), 172 (37, $[HCNC_6H_4CF_3]^+$), 145 (40, $[C_6H_4CF_3]^+$), 126 (9), 109 (12), 95 (12), 81 (7), 79 (9), 65 (5), 53 (8). ^{1}H KMR spektrs, δ (m.d.), *J* (Hz): 1.33 (9H, s, $3CH_3$), 6.18 (1H, d, *J* = 4.0, H-4), 6.93 (1H, d, *J* = 4.0, H-3), 7.22 (2H, d, *J* = 8.8, H-3', H-5'), 7.60 (2H, d, *J* = 8.8, H-4', H-6'), 8.09 (1H, s, CH=N).

N-(5-trimetilsilil-2-furilmetilidēn)-2-trifluormetilanilīns (25d).
Masspektrs, *m/z* (I_{rel}, %): 312 (23, $[M+H]^+$), 311 (100, M^+), 296 (6, $[M-Me]^+$), 200 (86), 172 (16, $[HCNC_6H_4CF_3]^+$), 152 (21), 145 (23, $[C_6H_4CF_3]^+$), 126 (13), 125 (10), 107 (5), 95 (5), 81 (6), 77 (30). ^{1}H KMR spektrs, δ (m.d.), *J* (Hz): 0.33 (9H, s, $3CH_3$), 6.78 (1H, d, *J* = 4.0, H-4), 7.02 (1H, d, *J* = 8.0, H-3'), 7.09 (1H, d, *J* = 4.0, H-3), 7.24 (1H, t, *J* = 8.0, H-5'), 7.47 (1H, t, *J* = 8.0, H-4'), 7.66 (1H, d, *J* = 8.0, H-6'), 8.18 (1H, s, CH=N).

N-(5-trimetilsilil-2-furilmetilidēn)-3-trifluormetilanilīns (25e).
Masspektrs, *m/z* (I_{rel}, %): 312 (22, $[M+H]^+$), 311 (100, M^+), 296 (32, $[M-Me]^+$), 268 (5), 252 (5), 230 (5), 218 (14), 202 (52), 172 (12, $[HCNC_6H_4CF_3]^+$), 152 (15), 145 (32, $[C_6H_4CF_3]^+$), 141 (16), 126 (10), 125 (10), 95 (10), 77 (51), 73 (10), 59 (9). ^{1}H KMR spektrs, δ (m.d.), *J* (Hz): 0.33 (9H, s, $3CH_3$), 6.73 (1H, d, *J* = 4.0, H-4), 7.02 (1H, d, *J* = 4.0, H-3), 7.27 - 7.55 (4H, m, H-3', H-4', H-5', H-6') 8.27 (1H, s, CH=N).

N-(5-trimetilsilil-2-furilmetilidēn)-4-trifluormetilanilīns (25f).

Masspektrs, *m/z* (I_{rel}, %): 312 (11, $[M + H]^+$), 311 (53, M^+), 296 (100, $[M - Me]^+$), 200 (86), 178 (4), 145 (19, $[C_6H_4CF_3]^+$), 141 (12), 126 (7), 95 (5), 77 (7), 73 (6), 59 (9). ^{1}H KMR spektrs, δ (m.d.), *J* (Hz): 0.33 (9H, s, $3CH_3$), 6.75 (1H, d, *J* = 4.0, H-4), 7.04 (1H, d, *J* = 4.0, H-3), 7.26 (2H, d, *J* = 8.6, H-3', H-5'), 7.64 (1H, d, *J* = 8.6, H-4', H-6'), 8.29 (1H, s, CH=N).

N-(5-trietilsilil-2-furilmetilidēn)-2-trifluormetilanilīns (25g).

Masspektrs, *m/z* (I_{rel}, %): 354 (5, $[M + H]^+$), 353 (30, M^+), 324 (11, $[M - Et]^+$), 201 (13), 200 (100), 172 (10, $[HCNC_6H_4CF_3]^+$), 152 (10), 145 (10, $[C_6H_4CF_3]^+$), 126 (9), 125 (9), 105 (12), 95 (6), 77 (28), 59 (5). ^{1}H KMR, δ (m.d.), *J* (Hz): 0.84 (6H, k, *J* = 7.2, $3CH_2$), 0.98 (9H, t, *J* = 7.2, $3CH_3$), 6.76 (1H, d, *J* = 3.4, H-4), 7.03 (1H, d, *J* = 7.8, H-3'), 7.09 (1H, d, *J* = 3.4, H-3), 7.24 (1H, t, *J* = 7.8, H-5'), 7.52 (1H, t, *J* = 7.8, H-4'), 7.65 (1H, t, *J* = 7.8, H-6'), 8.23 (1H, s, CH=N).

N-(5-trietilsilil-2-furilmetlidēn)-3-trifluormetilanilīns (25h).

Masspektrs, *m/z* (I_{rel}, %): 354 (22, $[M + H]^+$), 353 (82, M^+), 325 (17), 324 (68, $[M - Et]^+$), 296 (12), 248 (7), 238 (7), 220 (19), 218 (37), 203 (25), 202 (100), 184 (15), 172 (28, $[HCNC_6H_4CF_3]^+$), 152 (27), 145 (59, $[C_6H_4CF_3]^+$), 133 (33), 126 (25), 125 (23), 105 (53), 95 (30), 77 (75), 59 (22).
^{1}H KMR spektrs, δ (m.d.), *J* (Hz): 0.85 (6H, k, *J* = 7.2, $3CH_2$), 1.00 (9H, t, *J* = 7.2, $3CH_3$), 6.80 (1H, d, *J* = 4.0, H-4), 7.09 (1H, d, *J* = 4.0, H-3), 7.31 - 7.58 (4H, m, H-3', H-4', H-5', H-6') 8.28 (1H, s, CH=N).

N-(5-trietilsilil-2-furilmetilidēn)-4-trifluormetilanilīns (25i).

Masspektrs, *m/z* (I_{rel}, %): 353 (23, M^+), 334 (5, $[M - F]^+$), 325 (25), 324 (100, $[M - Et]^+$), 296 (5), 266 (7), 248 (2), 238 (2), 220 (7), 145 (18, $[C_6H_4CF_3]^+$), 133 (3), 126 (7), 95 (5), 77 (4), 59 (6).
^{1}H KMR spektrs, δ (m.d.), *J* (Hz): 0.85 (6H, k, *J* = 7.2, $3CH_2$), 0.99 (9H, t, *J* = 7.2, $3CH_3$), 6.78 (1H, d, *J* = 4.0, H-4), 7.04 (1H, d, *J* = 4.0, H-3), 7.24 (2H, d, *J* = 8.4, H-3', H-5'), 7.62 (1H, d, *J* = 8.4, H-4', H-6'), 8.22 (1H, s, CH=N).

11. Secinājumi.

1. Izpētītas Et_3SiH katalītiskas pievienošanās reakcijas jauniem furāna un tiofēna 3- vai 4-trifluormetilfenilgrupas saturošiem aldimīniem zelta Au kompleksu un VIII grupas pārejas metālu kompleksu klātbūtnē. Divi dimērie kompleksi: $[Pd(CH_2CHCH_2)Cl]_2$ un $[Rh(COD)Cl]_2$, kā arī komplekss $HAuCl_4$ ir aktīvāki šajās reakcijās. Noteikta aldimīnu aktivitātes rinda. Sintezēti 3- vai 4-CF_3-fenil grupas saturošu azometīnu hidrosililēšanas reakciju produkti: heterocikliskie amīni. Šajās reakcijās konstatēti C-sililētie nepiesātinātie produkti, kas rodas katalītiskas dehidrokondensācijas rezultātā.
2. Izpētītas Et_3SiH katalītiskas pievienošanās reakcijas furāna un tiofēna 2-CF_3-fenil grupas saturošiem aldimīniem, kā arī $HSiMe_2Ph$ un H_2SiPh_2 pievienošanās reakcijas piridilazopiridilmetīniem. Divi dimērie kompleksi: $[Pd(CH_2CHCH_2)Cl]_2$ un $[Rh(COD)Cl]_2$ šajās reakcijās izrādījās aktīvāki. Rh katalizātors uzrādīja augstāku aktivitāti furāna imīnu hidrosililēšanas reakcijās, bet Pd katalizātors tiofēna un piridīna imīnu hidrosililēšanas reakcijās. Sintezēti 2-CF_3-fenil grupas saturošu aldimīnu hidrosililēšanas reakciju produkti: attiecīgie amīni. Šajās reakcijās konstatēta divu veidu sililēto produktu veidošanās. Tiek diskutēts abu veidu: N-sililēto un C-sililēto piesātināto produktu veidošanās mehānisms.
3. Izpētītas 2-, 3-, 4-CF_3-fenil grupas saturošu heterociklisko aldimīnu katalītiskas Me_3SiCN pievienošanās reakcijas Luisa skābju klātbūtnē. Šajās reakcijās $AlBr_3$ ir aktīvāks par citām Luisa skābēm. Noteikts, ka $AlBr_3$ kopā ar molekulārajiem sietiem ievērojami paātrina reakciju gaitu un palielina produktu iznākumu. Sintezēti jauni aldimīnu trimetilsililcianēšanas reakciju produkti: α-aminonitrili. Piridīna azometīnu trimetilsililcianēšanas reakcijās konstatēta arī nepiesātināto nitrilu veidošanās, tiek likts priekšā divu veidu produktu: α-aminonitrilu un nepiesātināto nitrilu veidošanās mehānisms. Piesātinātā nitrila N-(6-metil-2-piridilciānometil)-3-trifluormetilanilīna un nepiesātinātā nitrila N-(4-piridilciānometilidēn)-3-trifluormetilanilīna struktūras pierādītas ar rentgenstruktūranalīzi. Sintezēto nepiesātināto nitrilu N-(2-piridilciānometilidēn)-3-trifluormetilanilīna un N-(4-piridilciānometilidēn)-3-trifluormetilanilīna pretvēža aktivitāte ir augstāka par zināmā pretvēža ķīmijterapijas līdzekļa " Ftorafūra" aktivitāti.
4. Izpētītas Me_3SiCN diastereoselektīvas pievienošanās reakcijas optiski aktīviem furāna, tiofēna un piridīna aldimīniem, kas iegūti no (R)- un (S)-1-feniletilamīna Luisa skābju ($AlCl_3$ un $AlBr_3$ kopā ar molekulārajiem sietiem) klātbūtnē. Iegūta sērija attiecīgo diastereomēru α-

aminonitrilu ar labiem iznākumiem (līdz 91%). Piridīna aldimīnu gadījumā bez α-aminonitriliem konstatēti arī nepiesātinātie nitrili.

5. Izpētītas N-[3-(hetaril)-2-propenilidēn]-trifluormetilanilīnu trimetilsililcianēšanas reakcijas Luisa skābes ($AlBr_3$ kopā ar molekulārajiem sietiem) klātbūtnē saišu sistēmā N=C-C=C. Izdalīti 1,2-pievienošanās produkti t.i. attiecīgie α-aminonitrili N-[3-(hetaril)-1-ciāno-2-propenil]-trifluormetilanilīni.
6. Sintezēti jauni aldimīni no 5-*t*-butilfurfurola un tā trimetilsilil- un trietilsililanalogiem kondensācijas reakcijās ar 2-, 3-, 4-trifluormetilanilīniem molekulāro sietu kā dehidratējošu aģentu klātbūtnē. Izpētīta šo savienojumu neirotropā un pretvēža aktivitāte. Fenamīna kustību aktivitātes tests parādīja, ka *t*-butilatvasinājumiem piemīt augsta efektivitāte, kā arī tie samazina etanola narkozes laiku. Dažiem sililatvasinājumiem piemīt ievērojama antikorazola aktivitāte. *t*-Butilatvasinājumiem raksturīga augsta citotoksicitāte uz cilvēka plaušu fibrosarkomas šūnām (3-trifluormetilaizvietotam savienojumam) un uz peļu hepatomas šūnām (2-trifluormetilaizvietotam savienojumam). Vairākums no sintezētiem aldimīniem veicina NO ģenerāciju šūnās.

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Pielikums

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HYDROSILYLATION OF HETEROCYCLIC ALDIMINES CATALYZED BY TRANSITION METAL COMPLEXES*

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The addition of triethylsilane to O- and S- heterocyclic Schiff bases in the presence of Rh, Pd, Pt, and Ir complexes has been studied. A series of the corresponding amines has been synthesized using the most active catalysts, which were the dimeric, monovalent complexes [Rh(1,5-cyclooctadiene)Cl]$_2$ and [Pd(allyl)Cl]$_2$.

Keywords: azomethines, heterocyclic amines, transition metal complexes, hydrosilylation, catalysis.

The addition of hydrosilanes to a C=N double bond has been studied much less than to the C=O bond of aldehydes, ketones, and their derivatives [1, 2]. To our knowledge, there has only been reported in the literature data for the hydrosilylation of aliphatic and aromatic heterocyclic azomethines. In this reaction saturated N-silyl derivatives are formed and these give the corresponding amines upon hydrolysis. In the presence of many catalysts these processes occur unselectively and are accompanied by hydrogenation, hydrogenolysis, and condensations. Basically positive results are obtained when different Rh and Pd complexes [3-5] are used. Palladium catalysts are most effective when used with monohydrosilanes and rhodium catalysts are more active with dihydrosilanes [6].

In recent years, starting with the work of Kagan [7, 8] and Brunner [9-11], the asymmetric hydrosilylation of imines and oximes have been vigorously developed [12-21]. However, this has not broadened the group of substrates investigated.

It is known that heterocyclic amines and, in particular, their fluorinated derivatives are potentially promising precursors of biologically active materials [22-24]. Hence our investigation is directed to the development of novel methods of synthesis of these compounds which have both academic and practical interest. Because the final reaction products are amines, it was of greatest benefit to use the cheapest alkylsilane ($HSiEt_3$) in their preparation.

In this work we have studied the hydrosilylation, using triethylsilane, of the Schiff bases **1a-h**, previously synthesized by us [25] via condensation of furan and thiophene aldehydes with trifluoromethyl anilines. In order to reveal the nature of the processes we additionally prepared some imines (**1i-k**) and studied their reactions. The reactions were carried out in the presence of a wide range of catalysts which included Rh, Pd, Pt, and Ir complexes. The results obtained are shown in Scheme 1 and in Table 1.

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* Dedicated to Academician M. G. Voronkov on his 80th Birthday.

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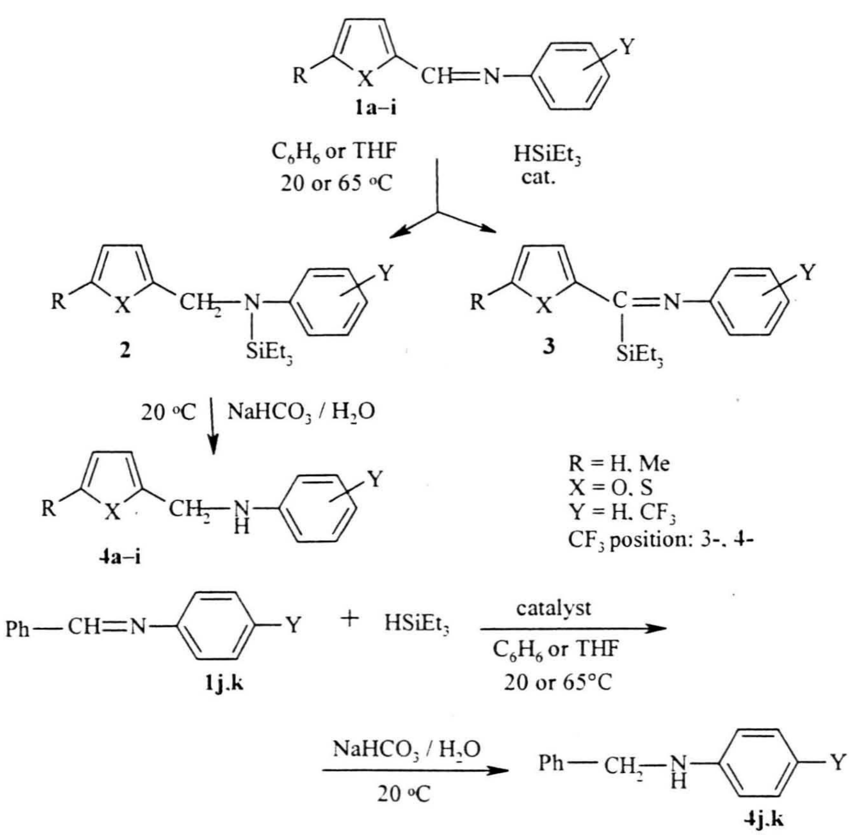
Scheme 1. Synthesis of amines **4a-k** by hydrosilylation of imines **1a-k**



Five different catalysts were tested in the hydrosilylation of the imine **1a**. In the presence of two of these the reaction did not occur (Table 1, experiments 3 and 4). Both platinum catalysts (experiments 1 and 2) were poorly active and only $[Rh(COD)Cl]_2$ catalyzed the process (even at room temperature) and allowed the preparation of the amine **4a** after hydrolysis of the reaction mixture. Amine **4b** was also prepared using this complex (at 65°C). The reaction of $HSiEt_3$ with the imine **1c** was studied in the presence of the five complexes Ir (I), Pd (0), Rh (0), Rh (I), and Pd (I). Only univalent complexes of rhodium and palladium catalyzed the reaction with the activity of the latter significantly higher (see experiments 10 and 12). Amines **4d** and **4e** were prepared by hydrosilylation in the presence of $[Rh(COD)Cl]_2$ in benzene at 65°C. Amine **4f** was synthesized using the same catalyst in benzene or tetrahydrofuran at 65°C. Both of the 3-trifluoromethyl thiophene derivatives (**1g** and **1h**) react slowly with $HSiEt_3$ in the presence of $[Rh(COD)Cl]_2$ (experiments 19, 22). The palladium catalyst $[Pd(CH_2CHCH_2)Cl]_2$ is significantly more active (as in the reaction with **1c**) (compare experiments 19 and 20).

In addition to these heterocyclic trifluoromethyl imine derivatives **1a-h**, azomethines with alternative structures were investigated, i.e. the thiophene without a CF_3 group (**1i**) and non heterocyclics both with and without this group (**1j** and **1k**). As in the other examples (experiments 8 and 21), the $[(C_6H_5)_3]_4Pd$ complex is not active (experiment 23) but $[Pd(CH_2CHCH_2)Cl]_2$ is more active than $[Rh(COD)Cl]_2$ (compare experiments 24 and 25, 27 and 28, 29 and 31). The corresponding amines (**4i-k**) were prepared using both of these catalysts.

When using the $[Rh(COD)Cl]_2$ catalyst the reaction in THF is significantly faster than in benzene (experiments 17 and 18) but the activity of the allyl-palladium complex in both of these solvents is little different (experiments 30 and 31). The corresponding amines were obtained from all of the studied imines in this way by the hydrosilylation method. Their yields after chromatographic column purification were 70-75% based on the reacted imine.

TABLE 1. Parameters for the Hydrosilylation of Imines **1a-k***

Expe-riment	Imine				Catalyst*² (mole %)	Solvent	T, °C	Reaction time, h	Conversion, % (GLC)	Product (yield, % (GLC))	
	Com-pound	X	R	CF_3 position						Before hydrolysis	After hydrolysis
1	2	3	4	5	6	7	8	9	10	11	12
1	**1a**	O	H	4	$H_2PtCl_6\cdot 6H_2O$ (2)	THF	20	21	21		**4a** (15)
2	**1a**	O	H	4	$[(C_6H_5)_3P]_4Pt$ (2)	THF	20	21	15		**4a** (12)
3	**1a**	O	H	4	$RhCl_3\cdot 4H_2O$ (2)	THF	20	32.5		No reaction	
4	**1a**	O	H	4	[Rh(COD)acac] (2)	THF	20	17.5			
							65	5.5		No reaction	
5	**1a**	O	H	4	$[Rh(COD)Cl]_2$ (2)	THF	20	21	56	**2a** (54)	**4a** (49)
6	**1b**	O	CH_3	4	$[Rh(COD)Cl]_2$ (2)	THF	20	20			
							65	5	100		**4b** (85)
7	**1c**	S	H	4	$[(C_6H_5)_3P]_2IrCl(CO)$ (2)	THF	65	10.5		No reaction	
8	**1c**	S	H	4	$[(C_6H_5)_3P]_4Pd$ (2)	THF	65	10.5		No reaction	
9	**1c**	S	H	4	[Rh(COD)acac] (2)	THF	65	10.5		No reaction	
10	**1c**	S	H	4	$[Rh(COD)Cl]_2$ (2)	THF	65	10.5	58		**4c** (50)
11	**1c**	S	H	4	$[Pd(CH_2CHCH_2)Cl]_2$ (2)	THF	20	5	48		**4c** (44)
12	**1c**	S	H	4	$[Pd(CH_2CHCH_2)Cl]_2$ (2)	C_6H_6	65	3	80	**2c** (76)	**4c** (73)
13	**1d**	S	CH_3	4	$[Rh(COD)Cl]_2$ (2)	C_6H_6	65	18			
					(3)			4	56		**4d** (48)
14	**1e**	O	H	3	$[Rh(COD)Cl]_2$ (2)	C_6H_6	65	10			
					(3)			2	90		**4e** (81)

TABLE 1 (continued)

1	2	3	4	5	6	7	8	9	10	11	12
15	**1e**	O	H	3	$[Rh(COD)Cl]_2$ (2)	C_6H_6	65	19	97	**2e** (88)	**4e** (85)
16	**1f**	O	CH_3	3	$[Rh(COD)Cl]_2$ (3)	C_6H_6	65	19	88	**2f** (60), **3f** (17)	**4f** (58)
17	**1f**	O	CH_3	3	$[Rh(COD)Cl]_2$ (2)	C_6H_6	65	17	91	**2f** (86)	**4f** (80)
18	**1f**	O	CH_3	3	$[Rh(COD)Cl]_2$ (3)	THF	65	7	90	**4f** (69), **3f** (19)	**4f** (65)
19	**1g**	S	H	3	$[Rh(COD)Cl]_2$ (3)	C_6H_6	65	36	25	**2g** (22)	
20	**1g**	S	H	3	$[Pd(CH_2CHCH_2)Cl]_2$ (2)	C_6H_6	20	25			
							65	4	48	**2g** (46)	**4g** (42)
21	**1g**	S	H	3	$[(C_6H_5)_3P]_4Pd$ (2)	C_6H_6	20	25 }		No reaction	
							65	4 }			
22	**1h**	S	CH_3	3	$[Rh(COD)Cl]_2$ (3)	C_6H_6	65	41	22		**4h** (18)
23	**1i**	S	H	—	$[(C_6H_5)_3P]_4Pd$ (2)	C_6H_6	20	26		No reaction	
24	**1i**	S	H	—	$[Rh(COD)Cl]_2$ (2)	C_6H_6	65	30	38	**2i** (35)	
25	**1i**	S	H	—	$[Pd(CH_2CHCH_2)Cl]_2$ (2)	C_6H_6	20	26	96	**2i** (50), **3i** (38)	**4i** (48)
26	**1i**	S	H	—	$[Pd(CH_2CHCH_2)Cl]_2$ (2)	C_6H_6	65	14	96	**2i** (52), **3i** (39)	**4i** (50)
27	**1j**	Ph		4	$[Rh(COD)Cl]_2$ (2)	THF	65	5	54		**4j** (50)
28	**1j**	Ph		4	$[Pd(CH_2CHCH_2)Cl]_2$ (2)	THF	20	22	88		**4j** (80)
29	**1k**	Ph		—	$[Rh(COD)Cl]_2$ (2)	THF	65	14.5	39		**4k** (37)
30	**1k**	Ph		—	$[Pd(CH_2CHCH_2)Cl]_2$ (2)	C_6H_6	65	14.5	84		**4k** (76)
31	**1k**	Ph		—	$[Pd(CH_2CHCH_2)Cl]_2$ (2)	THF	65	14.5	87		**4k** (78)

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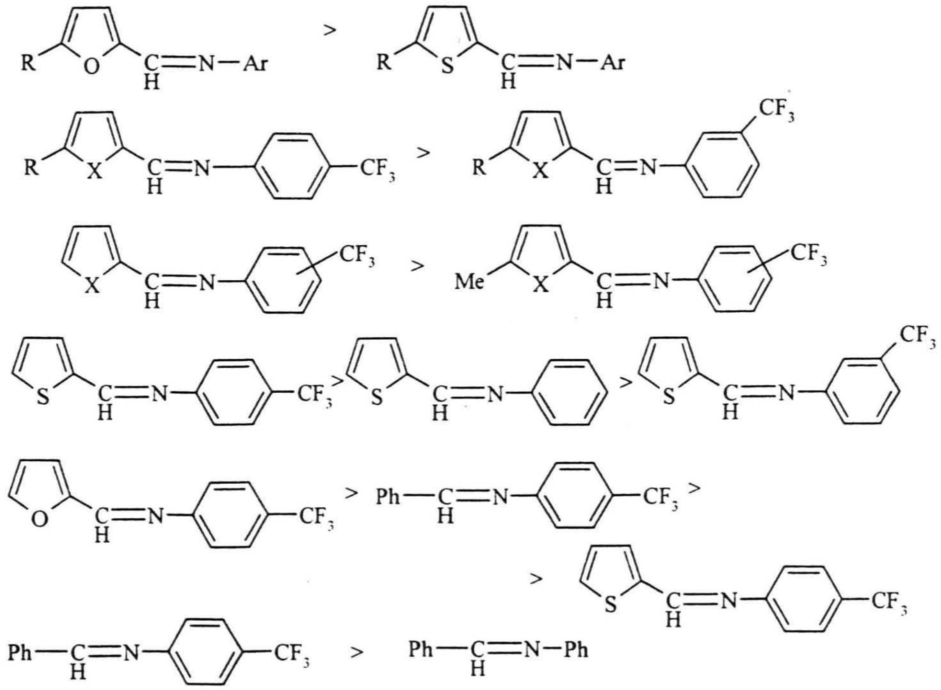
* Compounds **1j-k** are PhCH=N–C_6H_4Y where Y = H, CF_3.

*[2] COD is 1,5-cyclooctadiene; acac is acetylacetonate.

By comparison of the reactivity of the obtained imines (Table 1) it can be concluded that all of the furan azomethines are more active than the thiophene analogs. The presence of a methyl substituent in the heterocycle slows the reaction. A trifluoromethyl group in position 3 of the azo part of the molecule does not assist the reaction but in position 4 increases its rate. The latter is true both for the heteroaromatic and also the aromatic compounds. The activity of the benzylidene amine **1j** is less than the furan but greater than the thiophene analog. This variation is illustrated in Scheme 2.

Scheme 2. Reactivity of the imines towards silylation



The primary products of the reaction of $HSiEt_3$ with the imines are compounds of the structure **2** (Scheme 1). Compounds **2e** and **2f** (the furan derivatives with a 3-CF_3 group) were separated from their reaction mixtures. For the others (**2a**,**c**,**g**,**i**) the mass spectra were recorded for their reaction mixtures. The presence of unsaturated silicon compounds of structure **3** (**3f**,**i**) was also observed and identified by GLC-MS. The formation of the side products may be a result of a catalytic dehydrocondensation as noted in report [4] and occurring in parallel with the hydrosilylation.

We also carried out a comparison of the activity in this reaction of two homogeneous complexes and heterogeneous catalysts which were the metals Pd and Ru coated on different carriers. Reaction of $HSiEt_3$ with imine **1a** was studied in the presence of the following catalysts (2 mole %): $[(C_6H_5)_3P]_2PdCl_2$, $[(C_6H_5)_3P]_3RuCl_2$, and also 5% Pd/C and 5% Ru/Al_2O_3.

The reactions were performed in benzene at 65°C over 42 h. It was found that the Ru/Al_2O_3 complex was inactive in this process. In the presence of the palladium carbon catalyst the conversion was 40% and the yield of **4a** was 35% (GLC). The ruthenium complex was still less effective (32% conversion, 26% yield of amine). The activity of these two catalysts was marked less than for the monovalent rhodium and palladium complexes (Table 1).

TABLE 2. ^{1}H NMR Spectra of the Synthesized Compounds

Compound	δ, (ppm); J (Hz)
4a	1.5 (1H, br. s, NH); 4.33 (2H, s, CH_2); 6.24 (1H, m, J = 4.0, H_{Fur}-3); 6.31 (1H, m, J = 4.0, J = 2.0, H_{Fur}-4); 6.67 (2H, d, J = 9.4, H_{Ar}-3,5); 7.35 (1H, m, H_{Fur}-5); 7.40 (2H, d, J = 9.4, H_{Ar}-2,6)
4b	1.8 (1H, br. s, NH); 2.27 (3H, d, J = 1.2, CH_3); 4.28 (2H, s, CH_2); 5.89 (1H, dd, J = 3.6, J = 1.2, H_{Fur}-4); 6.11 (1H, d, J = 3.6, H_{Fur}-3); 6.55 (2H, d, J = 9.5, H_{Ar}-3,5); 7.40 (2H, d, J = 9.5, H_{Ar}-2,6)
4c	1.55 (1H, br. s, NH); 4.55 (2H, s, CH_2); 6.69 (2H, d, J = 9.0, H_{Ar}-3,5); 6.9-7.1 (2H, m, H_{Th}-3,4); 7.24 (1H, dd, J = 4.0, J = 2.0, H_{Th}-5); 7.42 (2H, d, J = 9.0, H_{Ar}-2,6)
4d	2.43 (3H, s, CH_3); 4.45 (2H, s, CH_2); 5.59 (1H, m, J = 3.4, J = 1.2, H_{Th}-4); 6.73 (2H, d, J = 8.4, H_{Ar}-3,5); 6.78 (1H, d, J = 3.4, H_{Th}-3); 7.42 (2H, d, J = 8.4, H_{Ar}-2,6)
2e	0.8-1.0 (15H, m, $SiEt_3$); 4.43 (2H, s, CH_2); 6.02 (1H, dd, J = 3.0, J = 1.0, H_{Fur}-3); 6.22 (1H, dd, J = 3.0, 2.0, H_{Fur}-4); 6.9-7.3 (4H, m, Ar); 7.42 (1H, dd, J = 2.0, J = 1.0, H_{Fur}-5)
4e	4.33 (2H, s, CH_2); 6.24 (1H, dd, J = 3.2, J = 0.7, H_{Fur}-3); 6.31 (1H, dd, J = 3.2, J = 1.9, H_{Fur}-4); 6.8-6.9 (2H, m, H_{Ar}-5,6); 6.9-7.0 (1H, m, H_{Ar}-4); 7.2-7.3 (1H, m, H_{Ar}-2); 7.36 (1H, dd, J = 0.7, J = 1.9, H_{Fur}-5)
2f	0.8-1.0 (15H, m, $SiEt_3$); 2.20 (3H, s, CH_3); 4.40 (2H, s, CH_2); 5.78 (1H, m, H_{Fur}-4); 5.87 (1H, m, H_{Fur}-3); 6.8-7.5 (4H, m, Ar)
4f	2.25 (3H, s, CH_3); 4.25 (2H, s, CH_2); 5.88 (1H, dd, J = 3.2, J = 1.0, H_{Fur}-4); 6.11 (1H, d, J = 3.2, H_{Fur}-3); 6.75-6.9 (2H, m, H_{Ar}-5,6); 6.9-7.0 (1H, m, H_{Ar}-4); 7.2-7.3 (1H, m, H_{Ar}-2)
4g	4.2 (1H, br. s, NH); 4.53 (2H, s, CH_2); 6.6-7.6 (7H, m, H_{Th}-3,4,5, Ar)
4h	2.43 (3H, s, CH_3); 4.43 (2H, s, CH_2); 6.59 (1H, m, J = 3.2, J = 1.2, H_{Th}-4); 6.79 (1H, d, J = 3.2, H_{Th}-3); 6.8-6.9 (2H, m, H_{Ar}-5,6); 6.9-7.0 (1H, m, H_{Ar}-4); 7.2-7.3 (1H, m, H_{Ar}-2)
1i	7.0-7.5 (8H, m, Th, Ph); 8.51 (1H, s, CHN)
4i	4.0 (1H, br. s, NH); 4.51 (2H, s, CH_2); 6.5-7.3 (6H, m, Ph, H_{Th}-3); 6.71 (1H, m, J = 2, H_{Th}-4); 7.18 (1H, m, J = 2, H_{Th}-5)
1j	7.22 (2H, d, J = 8.4, H_{Ar}-3,5); 7.3-7.6 (3H, m, H_{Ph}-2,4,6); 7.62 (2H, d, J = 8.4, H_{Ar}-2,6); 7.90 (2H, m, H_{Ph}-3,5); 8.42 (1H, s, CHN)
4j	4.33 (3H, s, CH_2NH); 6.60 (2H, d, J = 8.6, H_{Ar}-3,5); 7.33 (5H, s, Ph); 7.38 (2H, d, J = 8.6, H_{Ar}-2,6)
1k	7.1-7.7 (8H, m, H_{Ph}-2,4,6, $Ph'H_5$); 7.93 (2H, m, H_{Ph}-3,5); 8.49 (1H, s, CHN)
4k	3.9 (1H, br. s, NH); 4.27 (2H, s, CH_2); 6.5-6.8 (2H, m, H_{Ph}-2,6); 7.0-7.4 (7H, m, H_{Ph}-3,5, Ph')

TABLE 3. Mass Spectra of the Synthesized Compounds

Compound	m/z (I_{rel}, %)
1	2
2a	355 (14, M^+), 336 (5, $[M - F]^+$), 326 (37, $[M - Et]^+$), 224 (17), 188 (20), 154 (100), 145 (9, $[C_6H_4CF_3]^+$), 125 (29), 115 (5, $[SiEt_3]^+$), 97 (8), 87 (14), 81 (72, $[FurCH_2]^+$), 69 (2, $[CF_3]^+$), 59 (21), 53 (24)
4a	241 (28, M^+), 240 (6, $[M - H]^+$), 222 (4, $[M - F]^+$), 174 (4, $[M - Fur]^+$), 172 (3, $[M - CF_3]^+$), 145 (9, $[C_6H_4CF_3]^+$), 80 (6), 81 (100, $[FurCH_2]^+$), 69 (3, $[CF_3]^+$), 53 (25), 39 (5)
4b	255 (17, M^+), 236 (2, $[M - F]^+$), 211 (11), 174 (5), 172 (4), 160 (1, $[M - MeFur]^+$), 145 (9, $[C_6H_4CF_3]^+$), 95 (100, $[MeFurCH_2]^+$), 65 (4), 51 (5), 43 (10), 39 (5)
2c	371 (22, M^+), 353 (2, $[M - F]^+$), 342 (35, $[M - Et]^+$), 284 (1, $[M - 3Et]^+$), 256 (3, $[M - SiEt_3]^+$), 236 (8), 188 (20), 169 (36), 154 (100), 145 (8, $[C_6H_4CF_3]^+$), 141 (31), 127 (5), 113 (12), 97 (76, $[ThCH_2]^+$), 87 (13), 69 (2, $[CF_3]^+$), 59 (21), 45 (8)
4c	257 (16, M^+), 238 (5, $[M - F]^+$), 174 (5, $[M - Th]^+$), 172 (4), 145 (14, $[C_6H_4CF_3]^+$), 97 (100, $[ThCH_2]^+$), 69 (6, $[CF_3]^+$), 53 (7), 45 (8), 39 (5)
4d	271 (16, M^+), 252 (1, $[M - F]^+$), 211 (11), 174 (5), 145 (17, $[C_6H_4CF_3]^+$), 125 (6), 111 (100, $[MeThCH_2]^+$), 95 (7), 77 (12), 69 (10), 59 (7), 45 (9), 39 (6)
2e	355 (10, M^+), 336 (2, $[M - F]^+$), 326 (35, $[M - Et]^+$), 224 (16), 188 (11), 154 (100), 153 (35), 145 (6, $[C_6H_4CF_3]^+$), 125 (29), 115 (5, $[SiEt_3]^+$), 97 (8), 87 (12), 81 (54, $[FurCH_2]^+$), 69 (1, $[CF_3]^+$), 59 (19), 53 (18)

TABLE 3 (continued)

1	2
4e	242 (6, $[M + H]^+$), 241 (47, M^+), 222 (15, $[M - F]^+$), 213 (5), 172 (9, $[M - CF_3]^+$), 145 (23, $[C_6H_4CF_3]^+$), 125 (7), 113 (18), 95 (7), 81 (100, $[FurCH_2]^+$), 75 (9), 69 (7, $[CF_3]^+$), 63 (8), 53 (21), 39 (12)
2f	369 (6, M^+), 340 (11, $[M - Et]^+$), 246 (4), 216 (4), 188 (5), 167 (15), 154 (29), 139 (8), 95 (100, $[MeFurCH_2]^+$), 87 (6), 77 (3), 59 (10), 43 (11)
3f	367 (6, M^+), 352 (1, $[M - Me]^+$), 348 (1, $[M - F]^+$)337 (26), 338 (100, $[M - Et]^+$), 310 (12), 280 (7), 222 (47), 207 (82), 179 (21), 145 (19, $[C_6H_4CF_3]^+$), 128 (8), 109 (5), 95 (20, $[MeFurCH_2]^+$), 77 (14), 59 (9), 43 (30)
4f	255 (14, M^+), 236 (3, $[M - F]^+$), 174 (4), 145 (10, $[C_6H_4CF_3]^+$), 95 (100, $[MeFurCH_2]^+$), 51 (6), 43 (15)
2g	371 (19, M^+), 353 (2, $[M - F]^+$), 342 (33, $[M - Et]^+$), 256 (3, $[M - SiEt_3]^+$), 236 (5), 217 (4), 188 (13), 169 (31), 154 (100), 145 (9, $[C_6H_4CF_3]^+$), 141 (30), 127 (6), 113 (11), 97 (63, $[ThCH_2]^+$), 87 (9), 77 (5), 59 (17), 45 (6).
4g	257 (33, M^+), 238 (5, $[M - F]^+$), 174 (5, $[M - Th]^+$), 145 (15, $[C_6H_4CF_3]^+$), 113 (5), 97 (100, $[ThCH_2]^+$), 69 (6, $[CF_3]^+$), 53 (8), 45 (10), 39 (6)
4h	271 (20, M^+), 252 (1, $[M - F]^+$), 174 (5), 145 (14, $[C_6H_4CF_3]^+$), 111 (100, $[MeThCH_2]^+$), 95 (5), 77 (8), 69 (5), 45 (6)
1i	187 (85, M^+), 186 (100, $[M - H]^+$), 115 (6), 110 (2, $[M - Ph]^+$), 104 (4, $[M - Th]^+$), 95 (4), 97 (100, $[ThCH_2]^+$), 84 (5, $[ThH]^+$), 77 (40, Ph^+), 69 (5), 63 (5), 58 (5), 51 (26), 45 (9), 39 (14)
2i	306 (16), 305 (67, M^+), 276 (3, $[M - Et]^+$), 249 (20), 248 (100, $[M - 2Et - H]^+$), 244 (37), 218 (5), 200 (3), 190 (16), 156 (5), 130 (12), 115 (23, $[SiEt_3]^+$), 104 (6), 87 (47), 77 (28, Ph^+), 59 (50), 45 (8), 31 (5)
3i	304 (11), 303 (45, M^+), 273 (20), 274 (92, $[M - Et]^+$), 246 (5), 216 (2, $[M - 3Et]^+$), 170 (14), 169 (100), 149 (9), 142 (10), 141 (80), 121 (19), 120 (49), 113 (23), 97 (68), 87 (24), 77 (23, Ph^+), 59 (46), 53 (13), 45 (14)
4i	190 (6), 189 (48, M^+), 187 (8), 186 (10), 154 (2), 106 (4), 97 (100, $[ThCH_2]^+$), 77 (18, Ph^+), 65 (10), 51 (15), 45 (14), 39 (16).
1j	250 (12), 249 (75, M^+), 248 (100, $[M - H]^+$), 230 (4, $[M - F]^+$), 180 (7), 172 (8, $[M - Ph]^+$), 145 (38, $[C_6H_4CF_3]^+$), 126 (7), 125 (9), 95 (12), 89 (5), 77 (11, Ph^+), 75 (9), 69 (7, $[CF_3]^+$), 51 (10), 39 (5).
4j	252 (10), 251 (65, M^+), 250 (14, $[M - H]^+$), 232 (13, $[M - F]^+$), 182 (2), 174 (10, $[M - Ph]^+$), 172 (6), 145 (21, $[C_6H_4CF_3]^+$), 125 (4), 113 (5), 92 (7), 91 (100, $[PhCH_2]^+$), 77 (6, Ph^+), 65 (17), 51 (8), 39 (7)
1k	182 (10), 181 (81, M^+), 180 (100, $[M - H]^+$), 152 (7), 104 (10, $[M - Ph]^+$), 89 (7), 78 (10), 77 (56, Ph^+), 63 (10), 51 (37), 50 (14), 39 (9)
4k	184 (12), 183 (84, M^+), 182 (33, $[M - H]^+$), 154 (4), 152 (2), 106 (20, $[M - Ph]^+$), 104 (14, $[M - Ph - 2H]^+$), 92 (9), 91 ($[PhCH_2]^+$), 89 (5), 77 (37, Ph^+), 65 (38), 63 (11), 51 (25), 50 (9), 39 (22)

EXPERIMENTAL

^{1}H NMR spectra were recorded on Varian Mercury (200 MHz) and Bruker WH-90/DS instruments using $CDCl_3$ solvent and TMS internal standard. Mass spectra were obtained on an HP 6890 GC/MS chromatographic mass spectrometer fitted with an HP-5 MS capillary column (30.0 m × 250 μm × 0.25 μm) at a program temperature from 70-260°C at 10°C/min. Benzene and tetrahydrofuran were purified and dried using known methods before use. The aldehydes and amines were purified by vacuum distillation or recrystallization, after which their properties agreed with the corresponding literature data. The hydrosilane and transition metal complexes used in this work were obtained from Fluka, Merck, and Acros and the 4A molecular sieves from VEB Laborchemie Apolda. The synthesis of the azomethines **1i-k** was carried out as described in [25]. Their parameters agreed with those the data reported in [26-28].

General Method for the Synthesis of Amines 4a-k. A reaction tube (Pierce, volume 5 ml) was purged with argon and dry benzene or tetrahydrofuran (2 ml), catalyst (0.01 or 0.015 mmol), and the starting amine (0.5 mmol) were added to it. It was then stirred at room temperature for 30 min, the solution was cooled in ice to

0°C, and triethylsilane (96 µl, 0.6 mmol) was added by syringe. The reaction was carried out at room temperature or at 65°C, periodically removing a sample and analysing by TLC, GLC, or GLC-MS. At the end of the silylation (the reaction time is shown in Table 1) the reaction mixture was evaporated at reduced pressure (30°C, 15 mm) and hydrolyzed by the addition of methanol (2.5 ml) and aqueous $NaHCO_3$ solution (10%, 0.5 ml). The mixture was extracted with ether, the extract dried with anhydrous Na_2SO_4, filtered, and evaporated. The residue was then separated using liquid chromatography on a silica gel column (Kieselgel 60, 0.063-0.200 mesh, Merck) using benzene-ethyl acetate eluent (18:1 or 20:1). All of the products obtained are yellow or orange, oily materials. Their ^1H NMR and mass spectra are given in Tables 2 and 3.

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CATALYTIC HYDROSILYLATION OF FURAN, THIOPHENE, AND PYRIDINE ALDIMINES

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The addition of hydrosilanes ($HSiEt_3$, $HSiMe_2Ph$, H_2SiPh_2) to the CH=N bond of heterocyclic azomethines has been studied in the presence of monovalent complexes of rhodium and palladium. The effect on the reaction of the CF_3 group of the aldimines, which were obtained from O-, S-, and N-heteroaromatic aldehydes and 2-trifluoromethylaniline, has been clarified, as were other regularities of the processes being studied. A series of corresponding furans, thiophenes, and pyridine amines has been synthesized.

Keywords: heterocyclic Schiff's bases, transition metal complexes, hydrosilylation, catalysis.

We have recently synthesized a series of new heterocyclic amines by the condensation of furan, thiophene, and pyridine aldehydes with 2-trifluoromethylaniline, and also with aminopyridines [1,2]. As a continuation of the previous investigation of the reaction of triethylsilane with various imines [3], the hydrosilylation of a series of new aldimines has been studied in the present work. According to the data of [3] the dimeric complexes of monovalent rhodium and palladium are the most active catalysts for these processes among the numerous organometallic compounds used. In view of these results the following compounds were used as catalysts in the present investigation: bis{[μ-chloro(cycloocta-1,5-diene)]rhodium} or $[Rh(COD)Cl]_2$ and bis{[μ-chloroallyl]palladium} or $[Pd(allyl)Cl]_2$. The interaction of triethylsilane in the presence of these complexes has been studied with N-(hetarylmethylidene)-2-trifluoromethylanilines **1a-g** (where hetaryl = 2-furyl, 5-methyl-2-furyl, 2-thienyl, 5-methyl-2-thienyl, 2-, 3-, 4-pyridyl) and N-(6-methyl-2-pyridylmethylidene)-2-aminopyridine (**1h**), and also the last imine with two other hydrosilanes $HSiMe_2Ph$ and H_2SiPh_2. The reaction was carried out in benzene on heating (65°C) or at room temperature (with H_2SiPh_2) at a molar substrate–silane ratio of 1:1.2 and a catalyst concentration of 2 mol %.

The investigations showed that in reactions of both furan imines **1a,b** with triethylsilane the rhodium catalyst was significantly more active than the palladium. However the latter catalyzes the hydrosilylation of the thiophene aldimines **1c,d** though the rhodium did not display activity in these processes (Table 1). Seemingly the thiophene substrates deactivate the rhodium complex.

After carrying out the hydrosilylation of the O- and S-heterocyclic imines the reaction mixtures were investigated by ^1H NMR. The spectra of the products (before hydrolysis) contained two sets of signals, which indicates the formation of two types of silyl products, structures **2** and **3** (Scheme 1), containing the grouping $Et_3SiCH–NH$ and $CH_2–NSiEt_3$, characterized by two doublets of protons for the CH–NH group and a singlet for CH_2 respectively (Table 1). In previous work cited in reviews [4-7] (and also in [3]) it was shown that the hydrosilylation of a CH=N double bond leads mainly to the formation of products silylated at nitrogen, which are readily hydrolyzed.

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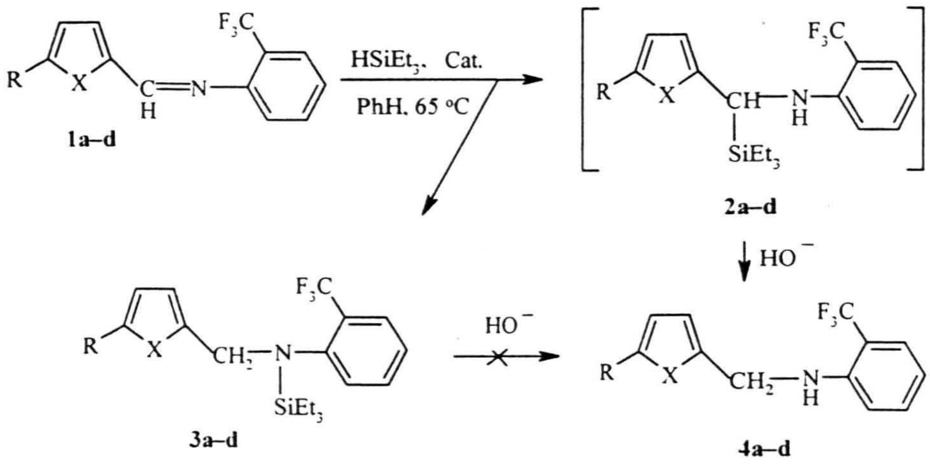
In difference to these data it was shown when investigating the hydrosilylation of imines **1a-d** that the silylated structures **2a-d** predominated in the products (80-85% of total quantity). After hydrolysis these compounds disappeared, being converted into the corresponding amines **4a-d**. Silyl products of structure **3a-d** are not hydrolyzed (even after repeating the hydrolysis procedure 2 or 3 times), and due to their stability (unlike structures **2a-d**) may be isolated using column chromatography on silica gel (Kieselgel 60). It is possible that the presence of the CF_3 group in position 2 of the aromatic ring by displaying electronic and steric factors largely directs hydrosilylation of the CH=N towards the formation of a C–Si rather than a N–Si bond. Moreover the latter bond is difficult to hydrolyze, also probably due to the effect of the neighboring CF_3 group.

Scheme 1



1-4 a, c R = H, **b, d** R = Me; **a, b** X = O, **c, d** X = S; **a, b** Cat = $(Rh(COD)Cl)_2$, **c, d** Cat = $(Pd(allyl)Cl)_2$

Investigations of the interaction of triethylsilane with pyridine aldimines **1a-g** showed that substrates **1e** and **1f** did not react in practice in the presence of both catalysts $[Rh(COD)Cl]_2$ and $[Pd(allyl)Cl]_2$, only the 4-derivative **1g** was hydrosilylated (conversion was 72 and 100% respectively). After carrying out the hydrolysis the main product **4g** was isolated by column chromatography from the reaction mixture. In addition a small quantity of silyl product **3g** was also obtained (on catalysis with the palladium complex). The molecule of **3g** contains a CH_2–NSi grouping characterized by the presence in the ^{1}H NMR spectrum of a singlet at 4.89 ppm (integrating as two protons). The structure of **3g** is analogous to the structures **3a-d** isolated on silylating the furan and thiophene aldimines. The data obtained enable the assumption that, as in the hydrosilylation of O- and S-heteroaromatic azomethines **1a-d**, the process of adding hydrosilane to the N-heterocyclic imine **1g** occurs with the formation mainly of the intermediate structure **2g** which, as in the previous cases, may be caused by the effect of the 2-CF_3 group (Scheme 2).

The investigations showed that imine **1h** does not react with triethylsilane on using either the Rh or the Pd complexes. Reaction of this aldimine with two other more reactive [8] silanes ($HSiMe_2Ph$, H_2SiPh_2) is catalyzed only by the palladium complex $[Pd(allyl)Cl]_2$. In the products after hydrolysis, in difference to the silylation of all the imines obtained from 2-trifluoromethylaniline, no products of structure **3** containing a grouping with a N–Si bond were detected. Probably this is readily hydrolyzed in this case. On the other hand the corresponding compounds **2h** and **2h'** were isolated in small quantity from the reaction mixture after hydrolysis only on hydrosilylating imine **1h**. These have in their structure the SiCH–NH group characterized in the ^{1}H NMR spectra by two doublets integrating as 1H each (Scheme 3, Table 1).

TABLE 1. Characteristics of the Hydrosilylation Reactions and Their Products

Initial imine	Silane	Catalyst	Temp. °C/Time, h	Conversion of imine, % (GLC)	Product		^{1}H NMR (CDCl$_3$), chemical shift, δ, ppm, *J* (Hz)					
					before hydrolysis*	after hydrolysis*[2]	CH$_3$ (3H, s)	SiCH–NH (structure **2**)		CH$_2$–NSi (structure **3**) (2H, s)	CH$_2$–NH (structure **4**)	
								CH (d)	NH (d)		CH$_2$ (d)	NH (br. s)
1	2	3	4	5	6	7	8	9	10	11	12	13
1a	HSiEt$_3$	[Rh(COD)Cl]$_2$	65/15	85	**2a**		—	3.95 *J* = 8.0	4.53 *J* = 8.0			
					3a	**3a**	—			4.33		
						4a	—				4.18 *J* = 6.0	4.67
	HSiEt$_3$	[Pd(allyl)Cl]$_2$	65/31	10	—							
1b	HSiEt$_3$	[Rh(COD)Cl]$_2$	65/11	88	**2b**		2.26	3.95 *J* = 7.5	4.33 *J* = 7.5			
					3b	**3b**	2.27			4.32		
						4b	2.29				4.16 *J* = 6.0	4.64
	HSiEt$_3$	[Pd(allyl)Cl]$_2$	65/23	16	—							
1c	HSiEt$_3$	[Rh(COD)Cl]$_2$	65/25	~0	—							
	HSiEt$_3$	[Pd(allyl)Cl]$_2$	65/25	80	**2c**		—	4.20 *J* = 6.0	4.7 br. s			
					3c	**3c**	—			4.60		
						4c	—				4.55 *J* = 5.4	4.7
1d	HSiEt$_3$	[Rh(COD)Cl]$_2$	65/30	~0	—							
	HSiEt$_3$	[Pd(allyl)Cl]$_2$	65/30	82		**3d**	2.40	—	—	4.49		
					—*[3]	**4d**	2.44				4.47 *J* = 5.4	4.7

TABLE 1 (continued)

1	2	3	4	5	6	7	8	9	10	11	12	13
1e	$HSiEt_3$	$[Rh(COD)Cl]_2$	65/20	~0	—							
	$HSiEt_3$	$[Pd(allyl)Cl]_2$	65/21	~0	—							
1f	$HSiEt_3$	$[Rh(COD)Cl]_2$	65/16	~0	—							
	$HSiEt_3$	$[Pd(allyl)Cl]_2$	65/21	~5	—							
1g	$HSiEt_3$	$[Rh(COD)Cl]_2$	65/20	72		**3g**	—	—	—	4.89		
	$HSiEt_3$	$[Pd(allyl)Cl]_2$	65/21	~100	—*[3]	**4g**					4.42 $J = 6.0$	5.0
1h	$HSiMe_2Ph$	$[Rh(COD)Cl]_2$	65/18	~0	—							
	$HSiMe_2Ph$	$[Pd(allyl)Cl]_2$	65/12	80		**2h**	2.42	5.43 $J = 6.4$	5.56 $J = 6.4$	—		
					—*[3]	**4h**	2.55				4.58 $J = 5.2$	5.6
	H_2SiPh_2	$[Rh(COD)Cl]_2$	20/50, 65/9	~0	—							
	H_2SiPh_2	$[Pd(allyl)Cl]_2$	20/50	77		**2h'**	2.44	5.47 $J = 6.0$	5.55 $J = 6.0$	—		
					—*[3]	**4h**	2.55				4.58 $J = 5.2$	5.6

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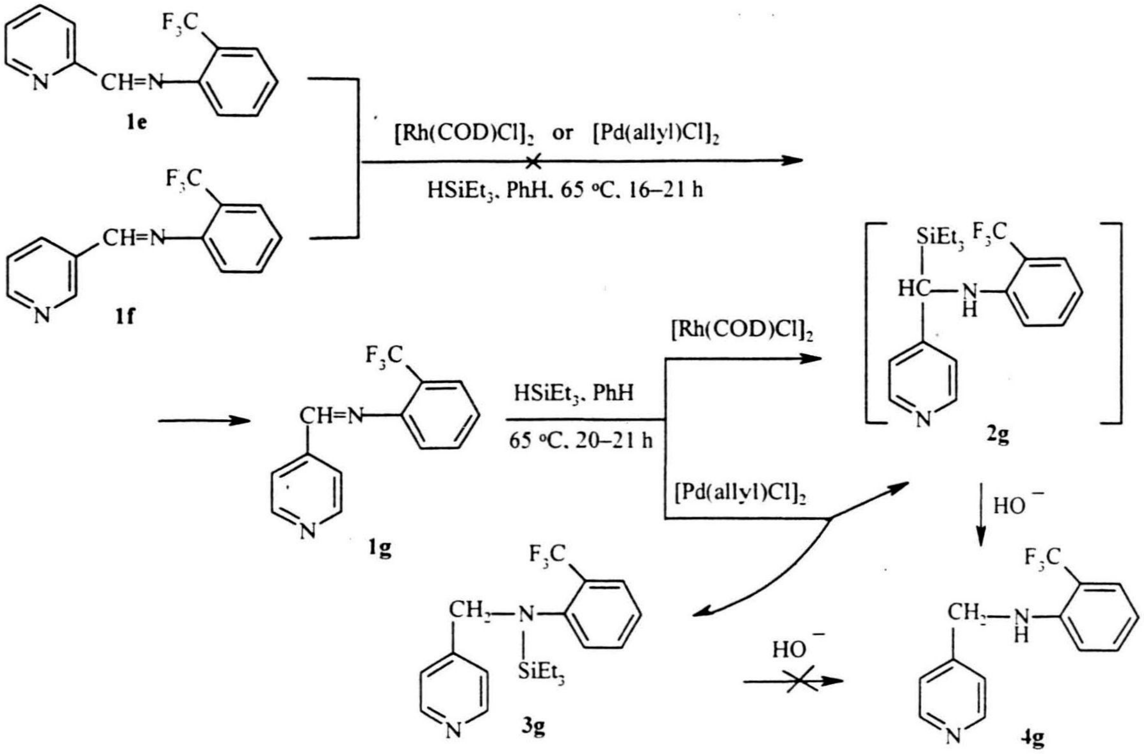
* Mixture of products according to ^1H NMR spectra.

*[2] Products were isolated by column chromatography. Eluent: benzene–ethyl acetate, 9:1 (**3a,b** and **4a,b**), benzene–ethyl acetate, 9.5:0.5 (**3c,d** and **4c,d**), chloroform–methanol, 9:1 (**3g**, **4g**, **2h**, **2h'**, **4h**).

*[3] The ^1H NMR spectra of mixtures of products were not recorded.

Scheme 2



Scheme 3

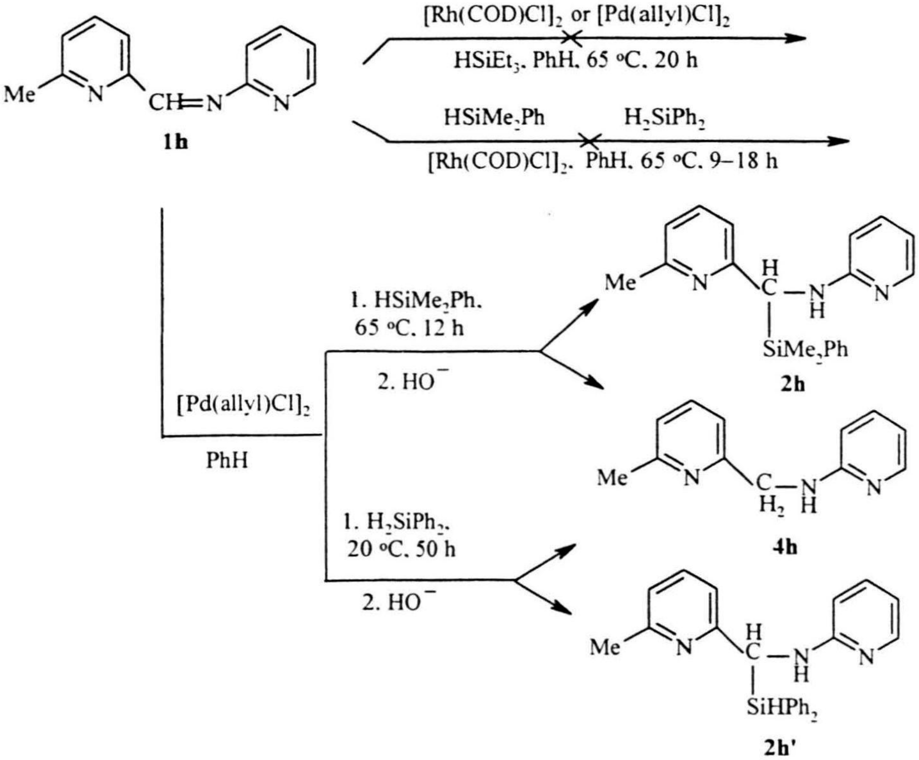


TABLE 2. Mass Spectra of the Synthesized N-(Hetarylmethyl)aromatic Amines **4a-h** and the Silyl Derivative **3g**

Compound	m/z (I_{rel}, %)*
4a	241 (33, M^{+}), 240 (12, $[M - H]^{+}$), 213 (14, $[M - CO]^{+}$), 202 (3), 192 (2), 182 (2), 172 (5, $[M - C_4H_3O - H_2]^{+}$), 165 (1), 154 (4), 145 (6, $[C_6H_4CF_3]^{+}$), 127 (9), 114 (6), 107 (2), 95 (4), 88 (2), 81 (100, $[C_4H_3OCH_2]^{+}$), 75 (7), 69 (4), 63 (4), 53 (39)
4b	255 (15, M^{+}), 216 (2), 202 (3), 196 (3), 185 (1), 172 (2), 154 (2), 145 (4, $[C_6H_4CF_3]^{+}$), 127 (8), 114 (3), 107 (2), 95 (100, $[H_3CC_4H_2OCH_2]^{+}$), 83 (1), 75 (4), 67 (5), 53 (6)
4c	257 (24, M^{+}), 218 (5), 145 (5, $[C_6H_4CF_3]^{+}$), 127 (9), 114 (5), 97 (100, $[C_4H_3SCH_2]^{+}$), 75 (4), 69 (8), 63 (6), 53 (13)
4d	271 (17, M^{+}), 232 (5), 202 (3), 172 (2), 154 (3), 145 (5, $[C_6H_4CF_3]^{+}$), 127 (11), 111 (100, $[H_3CC_4H_2SCH_2]^{+}$), 95 (5), 85 (2), 78 (9), 77 (10), 67 (6), 59 (5), 51 (7)
3g	366 (2, M^{+}), 337 (9, $[M - Et]^{+}$), 317 (6, $[M - Et - HF]^{+}$), 231 (4, $[M - SiEt_3 - HF]^{+}$), 214 (15), 213 (100, $[M - SiEt_3 - 2F]^{+}$), 193 (19, $[M - SiEt_3 - 2F - HF]^{+}$), 166 (5), 154 (4), 145 (2, $[C_6H_4CF_3]^{+}$), 127 (10, $[C_6H_5CF_2]^{+}$), 109 (14), 95 (11), 92 (7), 77 (31), 65 (8), 59 (9), 52 (20)
4g	253 (15, $[M + H]^{+}$), 252 (100, M^{+}), 231 (24, $[M - H - HF]^{+}$), 174 (25, $[M - Py]^{+}$), 172 (7), 154 (76, $[M - Py - HF]^{+}$), 145 (9, $[C_6H_4CF_3]^{+}$), 127 (68, $[C_6H_4CF_2]^{+}$), 125 (14), 107 (14, $[PyCH_2NH]^{+}$), 92 (27, $[PyCH_2]^{+}$), 80 (24), 79 (19), 78 (12, Py^{+}), 75 (17), 69 (8), 65 (36), 63 (20), 52 (20), 51 (10), 50 (18)
4h	200 (13, $[M + H]^{+}$), 199 (100, M^{+}), 197 (5, $[M - H_2]^{+}$), 196 (13), 183 (14, $[M - H - Me]^{+}$), 169 (7), 155 (2), 144 (1), 132 (2), 122 (6), 121 (72, $[M - Py]^{+}$), 119 (7, $[M - Py - H_2]^{+}$), 107 (39, $[PyNHCH_2]^{+}$), 94 (27, $[PyNH_2]^{+}$), 93 (7), 92 (5), 80 (8), 79 (15), 78 (24, Py^{+}), 65 (7), 63 (20), 52 (7), 51 (7)

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* Signals of characteristic ions are indicated.

In the ^{1}H NMR spectra of all the silylated compounds obtained by reaction of imines with triethylsilane the $SiEt_3$ grouping is displayed as two groups of signals for the CH_2 (6H, q) and CH_3 (9H, t) protons in the range δ 0.5-1.6 ppm. The chemical shift of the signal of the $SiMe_2$ group protons in the spectrum of silylated derivative **2h** is 1.25 ppm (6H, s). The spectra in the region of the proton signals of the heterocyclic rings and aromatic azo portion of the molecules of the synthesized products were close to those reported previously [1-3].

The following amines have been synthesized in this work: N-(2-furylmethyl)-2-trifluoromethylaniline (**4a**), N-(5-methyl-2-furylmethyl)-2-trifluoromethylaniline (**4b**), N-(2-thienylmethyl)-2-trifluoromethylaniline (**4c**), N-(5-methyl-2-thienylmethyl)-2-trifluoromethylaniline (**4d**), N-(4-pyridylmethyl)-2-trifluoromethylaniline (**4g**), and N-(6-methyl-2-pyridylmethyl)-2-aminopyridine (**4h**). The yield of these amines (on using the best catalyst) was 65-70%. Only the pyridine derivative **3g**, N-(4-pyridylmethyl)-N-triethylsilyl-2-trifluoromethylaniline, proved to be thermally stable of all the heterocyclic silyl-containing compounds mentioned. Its mass spectrum was recorded (Table 2).

EXPERIMENTAL

The ^{1}H NMR spectra were investigated on Varian Mercury (200 MHz) and Bruker WH-90/DS (90 MHz) spectrometers for solutions in $CDCl_3$, internal standard was TMS. The mass spectra were obtained on an HP 6890 GC/MS chromato-mass spectrometer fitted with an HP-5 MS (30.0 m × 250 μm × 0.25 μm) capillary column, with temperature programing from 70 to 260°C (10°C/min). The benzene was distilled over CaH_2 before use. The hydrosilanes and transition metal complexes used in the work were obtained from Fluka and Acros.

General Procedure for Hydrosilylation. A Pierce 5 cm^3 capacity reaction tube was purged with argon, then dry benzene (2 ml), catalyst (0.01 mmol), and the starting imine (0.5 mmol) were placed in it, after which the contents were mixed for 30 min at room temperature. The solution was cooled with ice to 0°C and hydrosilane (0.6 mmol) was added with a syringe. Reaction was carried out at 65°C or at room temperature, periodically removing a sample and analyzing it by TLC, GLC, and GLC-MS. At the end of the silylation (the process duration is shown in Table 1) the reaction mixture was evaporated at reduced pressure (30°C/15 mm) and the ^1H NMR spectrum recorded. Hydrolysis was then carried out by adding methanol (2.5 ml) and 10% aqueous $NaHCO_3$ solution (0.5 ml). The mixture was extracted with ether, the extract dried over anhydrous Na_2SO_4, then filtered, and evaporated. The residue was separated by liquid chromatography on a column of silica gel (Kieselgel 60, 0.063-0.200 mesh, Merck). The eluent was benzene–ethyl acetate for the furan and thiophene derivatives and chloroform–methanol for the pyridine derivatives. All the products obtained were yellow oily substances.

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APPLIED ORGANOMETALLIC CHEMISTRY
Appl. Organometal. Chem. **14**, 721–726 (2000)

Trimethylsilylcyanation of heterocyclic imines catalysed by Lewis acids

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The addition of Me_3SiCN to Shiff bases 1a–8a, synthesized by the reaction of furan and thiophene aldehydes with 3- and 4-aminobenzotrifluorides, has been studied in the presence of various Lewis acids. A series of the corresponding trifluoromethyl derivatives of heterocyclic *α*-aminonitriles 1–8 was synthesized in 38–80% isolated yields. It was found that 4A molecular sieves (MS) accelerate the addition and increase the yields of the products. The investigated catalysts are ranked by their activity in the following order: $AlBr_3$ + 4AMS > $AlBr_3$ > $AlCl_3$ > Ti[O(*i*Pr)]$_4$. A single crystal of *N*-(5-methyl-2-thienylcyanomethyl)-3-trifluoromethylaniline was obtained and studied by X-ray diffraction. The results showed that it was the crystal of the (*R*) isomer of this compound. Copyright © 2000 John Wiley & Sons, Ltd.

Keywords: trimethylsilylcyanation; catalysis; Lewis acids; Shiff bases; *α*-aminonitriles

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INTRODUCTION

Catalytic cyanation of imines (the Strecker reaction), has been studied intensively in several directions (for recent reviews on this subject, see Refs. 1–3). The products of these additions (α-aminonitriles) are useful intermediates for the synthesis of amino acids[4] and other nitrogen-containing compounds, including precursors of medicines.[5] The addition of hydrocyanic acid to a carbon–nitrogen double bond forms a new chiral centre in the molecule; therefore a large number of studies[6–10] of the synthesis of diastereomeric α-aminonitriles from optically active Shiff bases and catalytic asymmetric cyanation (e.g. Ref. 11) have been reported. The novel catalysts of the Strecker synthesis have also been investigated.[12] Application of trimethylsilyl cyanide (TMSCN) instead of sodium cyanide and hydrocyanic acid as a cyano-anion source provides promising and safer routes to α-aminonitriles.[13,14] In our previous work,[15] the addition of Me_3SiCN to (hetero)aromatic aldehydes was investigated. In the present work, trimethylsilylcyanation of a series of the heterocyclic aldimines is reported. Heterocyclic derivatives containing trifluoromethyl (CF_3) groups were used as substrates that promise high biological activity in the products.[16,17]

EXPERIMENTAL

General procedure

In a typical procedure for trimethylsilylcyanation of imines, in a 5-ml Pierce reaction vial, 1.0 equiv. of imine **1a–8a** in 2 ml dichloromethane reacted with 1.1 equiv. of trimethylsilyl cyanide (**Caution: Toxic!**) in the presence of catalytic amounts of $AlBr_3$ (20 mol%) and 4A molecular sieves (0.5 g) at ambient temperature under argon. When the reaction was complete (monitored by TLC), saturated aqueous $NaHCO_3$ was added, and the product was extracted with diethyl ether. After the organic layer had been dried over $MgSO_4$ and evaporated, the product was isolated by column chromatography on silica gel.

Materials and methods

Dichloromethane was dried over P_2O_5 and distilled prior to use. Trimethylsilyl cyanide (Aldrich) was used without further purification. $AlCl_3$, $AlBr_3$, Ti[O(*i*Pr)]$_4$ and the chemicals for the synthesis of imines were obtained from commercial sources. Molecular sieves 4A (VEB Laborchemie Apolda)

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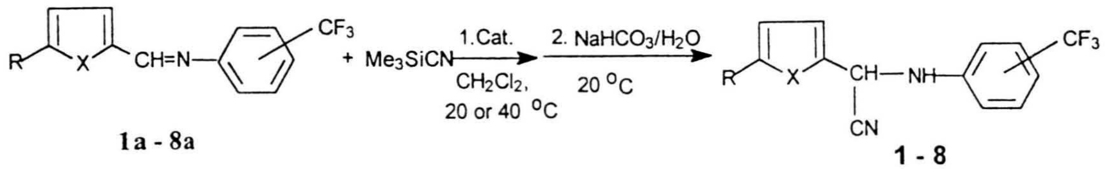
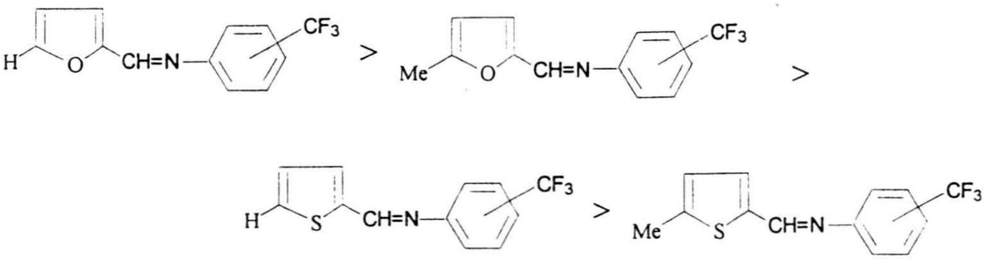


Scheme 1



Scheme 2

and silica gel for column chromatography (Kieselgel 60, 0.063–0.200 mm, Merck) were used.

^{1}H NMR spectra were recorded on Bruker WH-90/DS (90 MHz) and Varian Mercury (200 MHz) spectrometers using $CDCl_3$ as a solvent and Me_4Si as internal standard. Mass spectra were obtained on an MS-50 (70 eV) instrument. Elemental analysis was performed on a Carlo Erba EA-1108 instrument.

X-ray crystallographic study

A four-circle computer-controlled single-crystal

Table 1 The characteristics of the reaction and the products

Product	X	R	CF_3	Catalyst (mol%)	Temp. (°C)	Time (h)	Conversion, (%)[a]	Isolated yield (%)	M.p. (°C)[b]
1	O	H	3-	$AlCl_3$(20)	20	5.5	—	46[d]	Oil
				4A MS[c]	20	6.5	27	—	
2	O	CH_3	3-	$AlCl_3$(20)	20	21	—	40[d]	Oil
				$AlCl_3$(20)	20	5	50	—	
				$AlBr_3$(20)	20	0.5	74	—	
				Ti[O(*i*pr)]$_4$(20)	20	23	68	—	
3	S	H	3-	$AlCl_3$(5)	20	49			
					40	5.5	—	26[d]	—
				$AlBr_3$(20)	20	1	100	80	69–70
4	S	CH_3	3-	$AlCl_3$(5)	20	49			
					40	5.5	30	—	—
				$AlBr_3$(20)	20	5	38	—	—
				$AlBr_3$ (20) + 4A MS	20	26	70	68	84–85
5	O	H	4-	$AlBr_3$(20) + 4A MS	20	2	100	47[d]	143–144
6	O	CH_3	4-	$AlBr_3$(20) + 4A MS	20	1	76	40[d]	95–96
7	S	H	4-	$AlBr_3$(20) + 4A MS	20	6.5	70	38[d]	100–101
8	S	CH_3	4-	$AlBr_3$(20) + 4A MS	20	4	81	40[d]	131–132

[a] Determined by ^{1}H NMR.

[b] After recrystallization from ethyl acetate/hexane or benzene/hexane.

[c] MS, molecular sieves.

[d] The products were isolated by column chromatography.

Table 2 Elemental analysis of the solid α-amino nitriles obtained

			Found (%)/Calculated (%)			
Product	Mol. formula	Mol. mass	C	H	N	S
3	$C_{13}H_9N_2SF_3$	282.29	54.60/55.31	3.21/3.21	9.41/9.92	11.20/11.36
4	$C_{14}H_{11}N_2SF_3$	296.32	56.72/56.75	3.59/3.74	9.42/9.45	10.85/10.82
5	$C_{13}H_9N_2OF_3$	266.22	58.64/58.65	3.50/3.41	10.38/10.52	—
6	$C_{14}H_{11}N_2OF_3$	280.25	60.40/60.00	4.18/3.96	9.86/9.99	—
7	$C_{13}H_9N_2SF_3$	282.29	55.36/55.31	3.12/3.21	10.07/9.92	11.34/11.36
8	$C_{14}H_{11}N_2SF_3$	296.32	56.85/56.75	3.71/3.74	9.46/9.45	10.78/10.82

Table 3 ^1H NMR spectra of the α-aminonitriles synthesized

	Chemical shift (ppm), J (Hz)				
	$J = 0.9–1$	$J = 8–9$			
Compound	CH_3, d	NH, d	CHCN, d	Ring protons	
1	—	4.47	5.46	6.38 (1H, dd, J=4, 3.5; FurH-4)	6.71–7.33 (4H, m; ArH_4)
				6.53 (1H, dd, J=4, 1.5; FurH-3)	
				7.40 (1H, dd, $J = 3.5$, 1.5; FurH-5)	
2	2.29	4.33	5.41	5.97 (1H, dq, $J = 4$, 0.9; FurH-4)	6.78–7.64 (4H, m; ArH_4)
				6.44 (1H, d, $J = 4$; FurH-3)	
3	—	4.44	5.63	6.78–7.60 (7H, m; ThH_3, ArH_4)	
4	2.49	4.31	5.57	6.69 (1H, dq, $J = 4$, 0.9; ThH-4)	6.82–7.51 (4H, m; ArH_4)
				7.13 (1H, d, $J = 4$; ThH-3)	
5	—	4.49	5.53	6.47 (1H, dd, $J = 4$, 3.8; FurH-4)	6.80 (2H, d, $J = 8$; ArH-3,5)
				6.62 (1H, m, $J = 4$, 1; FurH-3)	
				7.49 (1H, dd, $J = 3.8$, 1; FurH-5)	7.53 (2H, d, $J = 8$; ArH-2,6)
6	2.31	4.49	5.44	6.00 (1H, dq, $J = 4.4$, 0.9; FurH-4)	6.78 (2H, d, $J = 8$; ArH-3,5)
				6.47 (1H, d, $J = 4.4$; FurH-3)	7.51 (2H, d, $J = 8$; ArH-2,6)
7	—	4.58	5.64	7.02 (1H, d, $J = 5$, 4.5; ThH-4)	6.78 (2H, d, $J = 8$; ArH-3,5)
				7.24–7.40 (2H, m, $J = 5$, 4.5, 2; ThH-3,5)	7.49 (2H, d, $J = 8$; ArH-2,6)
8	2.49	4.42	5.58	6.64 (1H, dq, $J = 4$, 1; ThH-4)	6.75 (2H, d, $J = 8$; ArH-3,5)
				7.11 (1H, d, $J = 4$; ThH-3)	7.47 (2H, d, $J = 8$; ArH-2,6)

Syntex $P2_1$ diffractometer with graphite-monochromatic Mo-K_α ($\lambda = 0.71069$ Å) radiation was used for intensity data collection. A total of 1336 unique reflection intensities were collected at room temperature using the $\theta/2\theta$-scan technique up to $2\theta_{max} = 50°$; one standard reflection showed no significant decay; Lorentz and polarization corrections were applied to the data.

The crystals of **8** are monoclinic, space group $P2_1$; the lattice parameters are as follows: $a = 5.337(2)$, $b = 9.978(4)$, $c = 13.334(4)$ Å, $\beta = 92.44(3)°$; $V = 709.4(4)$ Å^3, $D_x = 1.378(1)$ g cm^{-3}, $F(000) = 304$, $\mu = 0.252$ mm^{-1}, $Z = 2$.

The crystal structure was solved by the direct method and refined by least squares in block-diagonal approximation with anisotropic temperature factors. The hydrogen atoms were found from differential Fourier synthesis. The final R-factor is 0.0531 for 904 reflections with $I > 2(I)$. All calculations were carried out with the help of the AREN complex of programs.[18]

RESULTS AND DISCUSSION

In this work, the addition of Me_3SiCN to imines **1a–8a** (previously synthesized[19]) was studied in the presence of several Lewis acids (5–20 mol%). The reactions were carried out in dichloromethane at 20 or 40°C. Under these conditions the corresponding novel α-aminonitriles (**1–8**) were obtained in isolated yields up to 80% (Scheme 1). $AlBr_3$ was found to be more active than $AlCl_3$ or

Table 4 Mass spectra of the (α)-aminonitriles synthesized

Compound	MS, m/z (I_{rel}, %)
1	266 (8, M^+), 240 (20, $[M-\mathrm{CN}]^+$), 239 (100, $[M-\mathrm{HCN}]^+$), 238 (52, $[M-\mathrm{HCN}-\mathrm{H}]^+$), 220 (16, $[M-\mathrm{HCN}-\mathrm{F}]^+$), 211 (38, $[M-\mathrm{CN}-\mathrm{HCO}]^+$), 210 (36, $[M-\mathrm{HCN}-\mathrm{HCO}]^+$), 190 (18), 185 (20), 183 (19), 172 (21, $[M-\mathrm{HCN}-\mathrm{Fur}]^+$), 170 (25, $[M-\mathrm{HCN}-\mathrm{CF_3}]^+$), 145 (68, $[\mathrm{C_6H_4}\text{—}\mathrm{CF_3}]^+$), 125 (29), 115 (28), 106 (38, $[\mathrm{Fur}\text{—}\mathrm{CHCN}]^+$), 95 (32), 75 (26), 71 (52), 69 (25, $[\mathrm{CF_3}]^+$), 57 (30), 55 (31), 43 (40), 41 (41), 39 (42), 27 (49, $[\mathrm{HCN}]^+$)
2	280 (10, M^+), 254 (20, $[M-\mathrm{CN}]^+$), 253 (100, $[M-\mathrm{HCN}]^+$), 252 (30, $[M-\mathrm{HCN}-\mathrm{H}]^+$), 238 (25, $[M-\mathrm{HCN}-\mathrm{Me}]^+$), 211 (22, $[M-\mathrm{CN}-\mathrm{Me}\text{—}\mathrm{CO}]^+$), 210 (25, $[M-\mathrm{HCN}-\mathrm{Me}\text{—}\mathrm{CO}]^+$), 190 (31), 172 (25), 161 (26), 145 (47, $[\mathrm{C_6H_4}\text{—}\mathrm{CF_3}]^+$), 120 (51, $[\mathrm{Me}\text{—}\mathrm{C_4H_2O}\text{—}\mathrm{CHCN}]^+$), 95 (18), 69 (12, $[\mathrm{CF_3}]^+$), 53 (23), 43 (39, $[\mathrm{H_3CCO}]^+$), 39 (17), 27 (30, $[\mathrm{HCN}]^+$)
3	282 (2, M^+), 263 (1, $[M-\mathrm{F}]^+$), 255 (100, $[M-\mathrm{HCN}]^+$), 145 (68, $[\mathrm{C_6H_4}\text{—}\mathrm{CF_3}]^+$), 122 (30, $[\mathrm{C_4H_3S}\text{—}\mathrm{CHCN}]^+$), 112 (28), 111 (31), 95 (44), 84 (46, $[\mathrm{ThH}]^+$), 69 (22, $[\mathrm{CF_3}]^+$), 43 (30), 39 (42), 27 (38, $[\mathrm{HCN}]^+$)
4	296 (3, M^+), 294 (2, $[M-2\mathrm{H}]^+$), 277 (1, $[M-\mathrm{F}]^+$), 269 (98, $[M-\mathrm{HCN}]^+$), 268 (100, $[M-\mathrm{HCN}-\mathrm{H}]^+$), 250 (18, $[M-\mathrm{HCN}-\mathrm{F}]^+$), 200 (17, $[M-\mathrm{HCN}-\mathrm{CF_3}]^+$), 172 (16), 161 (15), 145 (72, $[\mathrm{C_6H_4}\text{—}\mathrm{CF_3}]^+$), 136 (70, $[\mathrm{Me}\text{—}\mathrm{C_4H_2S}\text{—}\mathrm{CHCN}]^+$), 125 (12), 97 (60, $[\mathrm{Me}\text{—}\mathrm{C_4H_2}S]^+$), 95 (52), 76 (36), 69 (40, $[\mathrm{CF_3}]^+$), 59 (35), 53 (42), 45 (43), 39 (32), 27 (39, $[\mathrm{HCN}]^+$)
5	266 (5, M^+), 240 (16, $[M-\mathrm{CN}]^+$), 239 (100, $[M-\mathrm{HCN}]^+$), 238 (68, $[\mathrm{M}-\mathrm{HCN}-\mathrm{H}]^+$), 220 (13, $[M-\mathrm{HCN}-\mathrm{F}]^+$), 211 (33, $[M-\mathrm{CN}-\mathrm{HCO}]^+$), 210 (38, $[M-\mathrm{HCN}-\mathrm{HCO}]^+$), 190 (8), 185 (19), 183 (14), 172 (9, $[M-\mathrm{HCN}-\mathrm{Fur}]^+$), 170 (12, $[M-\mathrm{HCN}-\mathrm{CF_3}]^+$), 145 (85, $[\mathrm{C_6H_4}\text{—}\mathrm{CF_3}]^+$), 125 (18), 115 (17), 106 (62, $[\mathrm{Fur}\text{—}\mathrm{CHCN}]^+$), 95 (22), 78 (12), 75 (15), 73 (10), 69 (5, $[\mathrm{CF_3}]^+$), 57 (15), 55 (16), 51 (21), 43 (18), 41 (19), 39 (33), 27 (48, $[\mathrm{HCN}]^+$)
6	280 (3, M^+), 278 (2, $[M-2\mathrm{H}]^+$), 254 (15, $[M-\mathrm{CN}]^+$), 253 (100, $[M-\mathrm{HCN}]^+$), 252 (32, $[M-\mathrm{HCN}-\mathrm{H}]^+$), 239 (8, $[M-\mathrm{HCN}-\mathrm{Me}]^+$), 234 (12, $[M-\mathrm{HCN}-\mathrm{F}]^+$), 211 (40, $[M-\mathrm{CN}-\mathrm{Me}\text{—}\mathrm{CO}]^+$), 210 (44, $[M-\mathrm{HCN}-\mathrm{Me}\text{—}\mathrm{CO}]^+$), 190 (5), 183 (15), 172 (6), 145 (60, $[\mathrm{C_6H_4}\text{—}\mathrm{CF_3}]^+$), 120 (42, $[\mathrm{Me}\text{—}\mathrm{C_4H_2O}\text{—}\mathrm{CHCN}]^+$), 95 (33), 81 (18), 79 (16), 75 (15), 73 (16), 69 (22, $[\mathrm{CF_3}]^+$), 53 (25), 43 (52, $[\mathrm{H_3CCO}]^+$), 41 (15), 39 (26), 27 (38, $[\mathrm{HCN}]^+$)
7	282 (6, M^+), 280 (1, $[M-2\mathrm{H}]^+$), 279 (1), 263 (1, $[M-\mathrm{F}]^+$), 255 (98, $[M-\mathrm{HCN}]^+$), 254 (100, $[M-\mathrm{HCN}-\mathrm{H}]^+$), 236 (15, $[M-\mathrm{HCN}-\mathrm{F}]^+$), 234 (12), 186 (14), 145 (62, $[\mathrm{C_6H_4}\text{—}\mathrm{CF_3}]^+$), 122 (58, $[\mathrm{C_4H_3S}\text{—}\mathrm{CHCN}]^+$), 95 (42), 84 (15, $[\mathrm{ThH}]^+$), 75 (7), 69 (28, $[\mathrm{CF_3}]^+$), 45 (33), 39 (38), 27 (41, $[\mathrm{HCN}]^+$)
8	296 (1, M^+), 294 (7, $[M-2\mathrm{H}]^+$), 293 (5), 271 (5), 279 (10), 269 (100, $[M-\mathrm{HCN}]^+$), 268 (98, $[M-\mathrm{HCN}-\mathrm{H}]^+$), 250 (8, $[M-\mathrm{HCN}-\mathrm{F}]^+$), 200 (12, $[M-\mathrm{HCN}-\mathrm{CF_3}]^+$), 172 (13), 149 (5), 145 (65, $[\mathrm{C_6H_4}-\mathrm{CF_3}]^+$), 136 (28, $[\mathrm{Me}\text{—}\mathrm{C_4H_2S}\text{—}\mathrm{CHCN}]^+$), 125 (12), 97 (49, $[\mathrm{Me}\text{—}\mathrm{C_4H_2S}]^+$), 94 (41), 69 (31, $[\mathrm{CF_3}]^+$), 53 (22), 43 (30), 39 (24), 27 (40, $[\mathrm{HCN}]^+$)

[a] Fur, furyl; Th, thienyl.

$\mathrm{Ti[O(}i\mathrm{Pr)]_4}$ (Table 1). To avoid possible hydrolysis problems during the reactions, we carried out the processes in the presence of a dehydration reagent such as 4A molecular sieves (MS). It was found that the addition proceeded sluggishly in the presence of 4A MS without any catalysts. Under the action of the catalyst and 4A MS together, the reactions proceeded most smoothly. The furan derivatives were more active in the addition of $\mathrm{Me_3SiCN}$ than the thiophene ones. The order of reactivity of the imines studied was according to Scheme 2.

The products were isolated mainly by column chromatography and identified by ^{1}H NMR, MS spectra and elemental analysis (Tables 2–4). All the products were thermally very unstable; therefore the GC and GC-MS analyses could not be used for these compounds.

A single crystal of *N*-(5-methyl-2-thienylcyanomethyl)-3-trifluoromethylaniline (**8**) was obtained

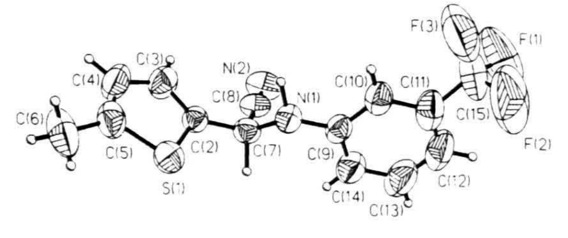


Figure 1 Perspective view of molecule **8** with thermal ellipsoids.

Table 5 Bond lengths and angles for compound **8**

Distance (Å)		Angle (°)	
S(1)–C(5)	1.7077 (0.0076)	C(1)-S(1)-C(5)	92.38 (0.37)
S(1)–C(2)	1.7160 (0.0058)		
C(2)–C(3)	1.3413 (0.0084)	C(3)-C(1)-C(7)	130.19 (0.54)
C(2)–C(7)	1.4793 (0.0071)	C(3)-C(1)-S(1)	110.72 (0.44)
C(2)–S(1)	1.7160 (0.0058)	C(7)-C(1)-S(1)	119.01 (0.40)
C(3)–C(2)	1.3413 (0.0084)	C(1)-C(3)-C(4)	112.51 (0.69)
C(3)–C(4)	1.4118 (0.0104)		
C(4)–C(5)	1.3364 (0.0113)	C(3)-C(4)-C(5)	114.08 (0.64)
C(5)–C(6)	1.5097 (0.0102)	C(4)-C(5)-C(6)	128.68 (0.80)
C(5)–S(1)	1.7077 (0.0076)	C(4)-C(5)-S(1)	110.30 (0.53)
		C(6)-C(5)-S(1)	121.00 (0.76)
C(7)–N(1)	1.4665 (0.0071)	N(1)-C(7)-C(8)	110.78 (0.45)
C(7)–C(8)	1.4807 (0.0097)	C(1)-C(7)-N(1)	110.65 (0.40)
		C(1)-C(7)-C(8)	111.22 (0.47)
C(9)–N(1)	1.4000 (0.0070)	C(7)-N(1)-C(9)	119.98 (0.45)
C(8)–N(2)	1.1511 (0.0072)	C(7)-C(8)-N(1)	175.90 (0.62)
C(9)–C(14)	1.3774 (0.0093)	N(1)-C(9)-C(14)	122.80 (0.60)
C(9)–C(10)	1.4023 (0.0087)	C(10)-C(9)-C(14)	118.88 (0.56)
		C(10)-C(9)-N(1)	118.25 (0.55)
C(10)–C(11)	1.3832 (0.0093)	C(9)-C(10)-C(11)	119.95 (0.68)
C(11)–C(12)	1.3755 (0.0116)	C(10)-C(11)-C(12)	120.64 (0.75)
C(11)–C(15)	1.4806 (0.0135)	C(12)-C(11)-C(15)	119.50 (0.80)
		C(10)-C(11)-C(15)	119.68 (0.92)
C(12)–C(13)	1.3688 (0.0132)	C(11)-C(12)-C(13)	119.70 (0.67)
C(13)–C(14)	1.3945 (0.0101)	C(12)-C(13)-C(14)	120.51 (0.90)
		C(9)-C(14)-C(13)	120.31 (083)
C(15)–F(1)	1.2400 (0.0105)	F(1)-C(15)-F(2)	104.35 (0.86)
		F(1)-C(15)-F(3)	108.91 (1.26)
C(15)–F(2)	1.3544 (0.0135)	F(2)-C(15)-F(3)	99.89 (0.93)
C(15)–F(3)	1.2944 (0.0134)	F(1)-C(15)-C(11)	117.14 (0.94)
		F(2)-C(15)-C(11)	109.23 (1.13)
		F(3)-C(15)-C(11)	115.34 (0.80)

Table 6 Selected torsion angles in molecule **8**

Angle	(°)
C(5)-S(1)-C(2)-C(3)	1.09 (0.50)
C(5)-S(1)-C(2)-C(7)	178.09 (0.45)
C(7)-C(2)-C(3)-C(4)	−177.91 (0.59)
S(1)-C(2)-C(3)-C(4)	−1.36 (0.74)
C(2)-C(3)-C(4)-C(5)	1.00 (0.91)
C(3)-C(4)-C(5)-C(6)	178.21 (0.68)
C(3)-C(4)-C(5)-S(1)	−0.14 (0.80)
C(2)-S(1)-C(5)-C(4)	−0.53 (0.53)
C(2)-S(1)-C(5)-C(6)	−179.04 (0.55)
C(3)-C(2)-C(7)-N(1)	107.39 (0.69)
S(1)-C(2)-C(7)-N(1)	−68.93 (0.57)
C(3)-C(2)-C(7)-C(8)	−16.19 (0.83)
S(1)-C(2)-C(7)-C(8)	167.49 (0.40)
C(8)-C(7)-N(1)-C(9)	−58.69 (0.69)
C(2)-C(7)-N(1)-C(9)	177.47 (0.49)
N(1)-C(7)-C(8)-N(2)	7.23 (8.35)
C(2)-C(7)-C(8)-N(2)	130.74 (8.06)
C(7)-N(1)-C(9)-C(14)	−29.97 (0.86)
C(7)-N(1)-C(9)-C(10)	153.10 (0.54)
C(14)-C(9)-C(10)-C(11)	−0.95 (0.96)
N(1)-C(9)-C(10)-C(11)	176.10 (0.55)
C(9)-C(10)-C(11)-C(12)	0.10 (1.04)
C(9)-C(10)-C(11)-C(15)	175.08 (0.79)
C(10)-C(11)-C(12)-C(13)	0.59 (1.24)
C(15)-C(11)-C(12)-C(13)	−174.40 (1.02)
C(11)-C(12)-C(13)-C(14)	−0.42 (1.50)
N(1)-C(9)-C(14)-C(13)	−175.79 (0.72)
C(10)-C(9)-C(14)-C(13)	1.12 (1.11)
C(12)-C(13)-C(14)-C(9)	−0.44 (1.46)
C(12)-C(11)-C(15)-F(1)	47.44 (1.61)
C(10)-C(11)-C(15)-F(1)	−127.60 (1.13)
C(12)-C(11)-C(15)-F(3)	177.66 (0.96)
C(10)-C(11)-C(15)-F(3)	2.62 (1.50)
C(12)-C(11)-C(15)-F(2)	−70.85 (1.16)
C(10)-C(11)-C(15)-F(2)	114.12 (1.04)

by careful crystallization from ethyl acetate/hexane (1:1) and studied by X-ray diffraction. Figure 1 illustrates the perspective view of molecule **8** with atom labels. Tables 5 and 6 give the bond lengths, valence angles and selected torsion angles. The five- and six-membered rings in structure **8** are planar. The bond lengths in these rings show that there is delocalization of the π-electrons in the system. The bond length N(1)–C(9) 1.400(7) Å indicates conjugation between the six-membered aromatic ring and the lone electron pair on the N(1). However, the nitrogen atom N(1) is not planar, but pyramidal (the sum of the valence angles is 345°). On the whole, the molecule **8** has a normal geometry. The decrease in lengths for the C(11)–C(15) and C–F bonds can be explained[20] by significant thermal vibrations of the F and C(15) atoms (see Fig. 1).

Molecule **8** has a hindered conformation with reference to the C(7)–N(1) bond; the torsion angle C(2)–C(7)–N(1)–C(9) is close to being a flat angle, i.e. both rings have a fully staggered disposition.

There is only one enantiomer (*R*-isomer) in the crystal investigated. An intermolecular hydrogen bond N(1)—H(1)···N(2) was found in the crystal structure. The hydrogen bond length equals 3.207(7) Å; H(1)···N(2) = 2.26 Å, ∠N(1)—H(1)···N(2) = 151°; it is somewhat greater than the mean statistical value (2.98 Å) for the NH···N type of H-bond.[21]

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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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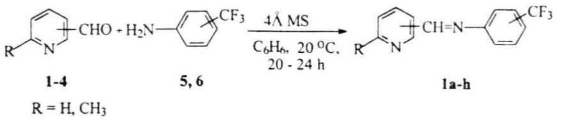
Table 1 Characteristics of the pyridylaldimines obtained

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	38–39 123–125/0.1 mm	Yellow
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

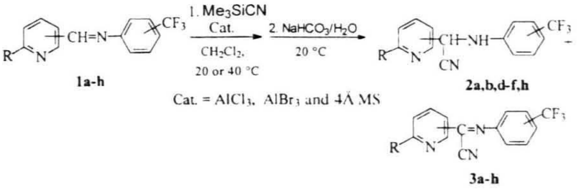
Table 2 Elemental analysis of solid pyridylaldimines

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.



Scheme 1 Synthesis of imines.

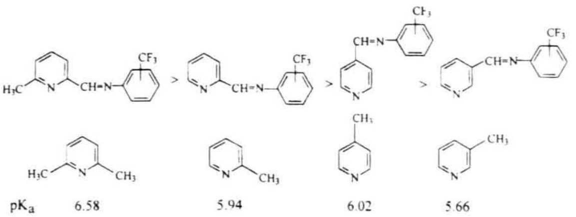


Scheme 2 Trimethylsilylcyanation of imines.

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.

^1H 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 3 Order the reactivity of imines.

Table 3 ^1H 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

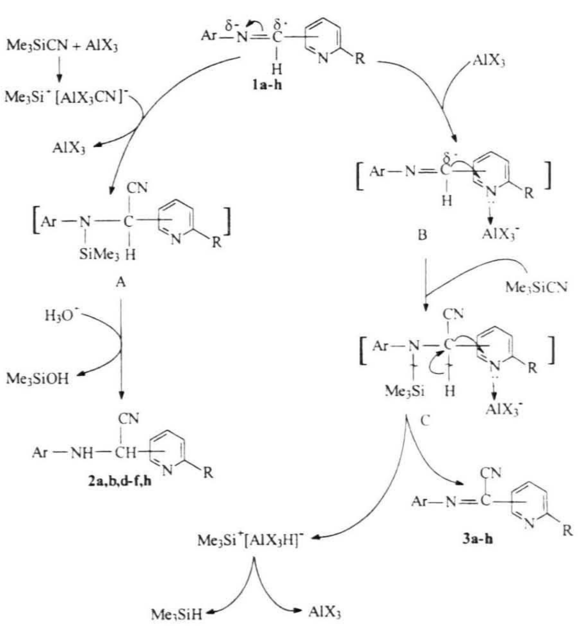
The synthesis and characterization of the pyridylaldimines

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

Table 8 Continued

Compound	m/z (I_{rel}, %)
2h	292 (7, $[\mathrm{M+H}]^+$), 291 (40, M^+), 290 (15, $[\mathrm{M-H}]^+$), 272 (7, $[\mathrm{M-F}]^+$), 265 (22, $[\mathrm{M-CN}]^+$), 264 (81, $[\mathrm{M-HCN}]^+$), 263 (14), 245 (14, $[\mathrm{M-HCN-F}]^+$), 237 (55), 236 (100), 195 (9), 172 (14, $[\mathrm{M-HCN-MeC_5H_3N}]^+$), 167 (9), 146 (10, $[\mathrm{M-C_6H_4CF_3}]^+$), 145 (60, $[\mathrm{C_6H_4CF_3}]^+$), 132 (10), 125 (13), 119 (45, $[\mathrm{M-HCN-C_6H_4CF_3}]^+$), 95 (20), 93 (72, $[\mathrm{MeC_5H_4N}]^+$), 92 (25, $[\mathrm{MeC_5H_3N}]^+$), 75 (18), 69 (6, $[\mathrm{CF_3}]^+$), 66 (25), 65 (23), 51 (15), 50 (12)
3h	290 (14, $[\mathrm{M+H}]^+$), 289 (76, M^+), 288 (60, $[\mathrm{M-H}]^+$), 270 (15, $[\mathrm{M-F}]^+$), 263 (18, $[\mathrm{M-CN}]^+$), 238 (11), 237 (79), 236 (100), 220 (9), 167 (10), 145 (37, $[\mathrm{C_6H_4CF_3}]^+$), 125 (12), 119 (12, $[\mathrm{M-C_6H_4CF_3}]^+$), 95 (16), 92 (18, $[\mathrm{MeC_5H_3N}]^+$), 75 (14), 69 (7, $[\mathrm{CF_3}]^+$), 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 ^{1}H 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 $\mathrm{Me_3SiCN}$ 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 $\mathrm{HSiMe_3}$.

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	$\mathrm{C_{15}H_{12}F_3N_3}$	$\mathrm{C_{14}H_8F_3N_3}$
Formula weight	291.28	275.23
Crystal system	Monoclinic	Monoclinic
Color	Colorless	Colorless
Space group	*C*2/*c*	*P*2$_1$/*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)

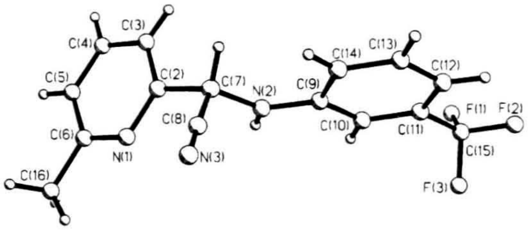
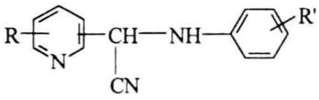
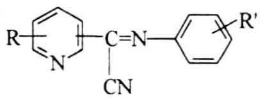


Figure 1 Molecular structure of compound **2d**.

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


I


II

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)

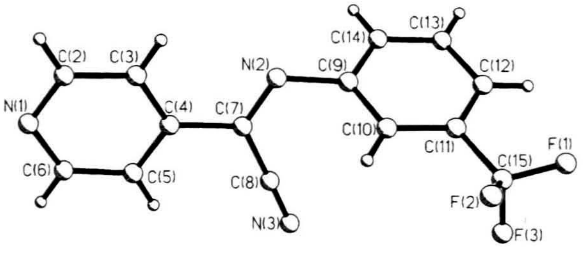


Figure 2 Molecular structure of compound **3c**.

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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Diastereoselective addition of trimethylsilyl cyanide to chiral *O*-, *S*- and *N*-heterocyclic aldimines

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Systematic investigation of asymmetric trimethylsilylcyanation of heterocyclic azomethines has been realized. The addition of trimethylsilyl cyanide to optically active furan, thiophene and pyridine aldimines, derived from (*R*)- and (*S*)-1-phenylethylamine, was studied in the presence of Lewis acids, and a series of the corresponding α-amino nitriles was obtained in fair to good yields (up to 91%). Unsaturated nitriles were also formed from pyridine imines. The sense of asymmetric induction and the degree of diastereoselectivity in the synthesis of α-amino nitriles were determined by means of ^{1}H NMR. The stereochemical outcome is a result of the same sense of asymmetric induction: *Re* face attack to the (*S*)-imines and *Si* face addition to the (*R*)-imines took place. The (*R,R*)- (up to 81%) or (*S,S*)- (up to 87%) α-amino nitriles predominated in the products obtained from the all furan, thiophene and pyridine (*R*)- or (*S*)-imines respectively.

KEYWORDS: asymmetric synthesis; trimethylsilylcyanation; catalysis by Lewis acids; heterocyclic Schiff bases; α-amino nitriles

INTRODUCTION

Asymmetric cyanation of imines (Strecker reaction) provides an important tool for construction of optically active nitrogen-containing molecules (for recent reviews, see Refs 1–5). The cyanation of imines derived from chiral amines is an example of substrate-controlled diastereoselectivity (first-generation asymmetric synthesis[6]). In this diastereoselective reaction, the formation of a new chiral centre is under the control of an existing centre in the same molecule.

The first asymmetric Strecker synthesis was reported in 1963 by Harada.[7] Since that time, the general strategy for the induction of asymmetry in this reaction has been to generate a chiral Schiff base from the condensation of an aldehyde and an optically active primary amine. The diastereoselective addition of a nitrile source introduces a new chiral centre forming stereoenriched α-amino nitriles. One of the most suitable auxiliaries for asymmetric Strecker reactions are benzyl amines (for general examples see Refs 8–15). The use of trimethylsilyl cyanide (Me_3SiCN) in combination with a Lewis acid is preferable over the conventional NaCN/AcOH(cat.) method.[16–23]

The asymmetric synthesis of α-amino nitriles using (*R*)- and (*S*)-1-phenylethylamine as a chiral matrix and a collection of aldehydes has been examined in numerous papers cited above. These studies have shown that the sense and the degree of stereoselectivity are dependent on the nature of both the aldimine and the catalytic system. Nevertheless, the reported data involve addition to imines obtained mainly from aromatic and aliphatic aldehydes. Only one heterocyclic aldehyde (3-pyridinealdehyde) was used recently as a starting substrate in these investigations.[15]

In previous work[24–26] we studied the asymmetric addition of Me_3SiCN to (hetero)aromatic aldehydes and to achiral heterocyclic imines. Herein we report the results of catalytic Me_3SiCN addition to imines prepared specially from the reactions of furan, thiophene and pyridine aldehydes with (*R*)- and (*S*)-1-phenylethylamine. By performing the reaction in both enantiomeric series we are able to compare the results and to obtain the corresponding diastereomeric compounds for further investigation of their biological activity.

EXPERIMENTAL

General

The solvents were dried (dichloromethane over P_2O_5 and benzene over CaH_2) and distilled prior to use. Me_3SiCN

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(Aldrich) was used without further purification. $AlCl_3$, $AlBr_3$ and the chemicals for the synthesis of imines were received from commercial sources (Fluka, Aldrich). 4 Å molecular sieves (VEB Laborchemie Apolda) and silica gel for column chromatography (Kieselgel 60, 0.063–0.200 mm, Merck) were used. Thin-layer chromatography (TLC) was performed on a Merck silica gel 60 F_{254} with various eluents.

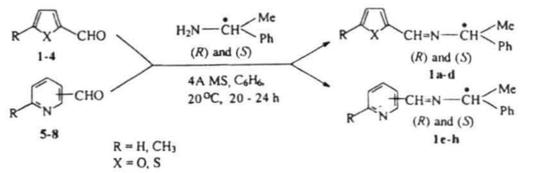
^1H NMR spectra were recorded on Bruker WH-90/DS (90 MHz) and Varian Mercury (200 MHz) spectrometers using $CDCl_3$ as a solvent and HMDSO as internal standard. The mass spectra were obtained on an HP 6890 GC/MS instrument. Optical rotation was determined by means of a Polamat A (Carl Zeiss, Jena) instrument. Elemental analysis was performed using Carlo Erba EA-1108 apparatus. Melting points were determined with a Kofler instrument.

Synthesis of imines (*R*)- and (*S*)-1a–h

Imines **1a–h** were synthesized by the reactions of the corresponding heterocyclic aldehydes (**1–8**) with (*R*)- and (*S*)-1-phenylethylamine. The aldehyde (5 mmol) was mixed with the 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 imine was isolated by recrystallization from hexane or by vacuum distillation.

Trimethylsilylcyanation of chiral heterocyclic aldimines

In a typical procedure, in a 5 cm^3 Pierce reaction vial, 1.0 equivalent of imine in dichloromethane (2 ml) reacted with 1.2 equivalents of Me_3SiCN (CAUTION: toxic!) in the presence of catalytic amounts of $AlBr_3$ (10 mol%) and 4 Å molecular sieves (0.5 g) at 20 or 40 °C under an argon atmosphere. When the reaction was complete [monitored by TLC and gas chromatography-mass spectrometry (GC-MS)], conversion of starting imine was determined by ^1H NMR. Then saturated aqueous $NaHCO_3$ was added, and the organic compounds were extracted with diethyl ether. After the organic layer was dried over $MgSO_4$ and evaporated, the products were isolated by column chromatography on silica gel using various eluents. The ^1H NMR spectra of isolated products were recorded and optical rotation determined.



Scheme 1. Synthesis of imines (*R*)- and (*S*)-**1a–h**.

RESULTS AND DISCUSSION

Synthesis of chiral heterocyclic imines

A series of optically active heterocyclic Schiff bases was synthesized by the reactions of aldehydes **1–8** with (*R*)- and (*S*)-1-phenylethylamine in the presence of 4 Å molecular sieves (Scheme 1, Table 1). The spectral and analytical data for all the imines were in good agreement with their structure (Tables 2–4).

Table 1. Characteristics of aldimines **1a–h**

Imine[a]	R	X	Pyridine isomer	Isolated yield (%)	M.p. (°C)	$[\alpha]_{546}^{20-23}$(deg) (*c* in benzene)	Colour	Lit. [α] (deg)
(*R*)-**1a**	H	O	-	78	oil	−72.2 (7.4)	yellow	$[\alpha]_D^{20}$ − 66.1 (*c* 6.4, benzene)[28]
(*S*)-**1a**	H	O		78	oil	+71.6 (8.0)	yellow	$[\alpha]_D^{25}$ + 76.4 (*c* 1.1, $CHCl_3$)[29]
(*R*)-**1b**	CH_3	O	-	80	oil	−123.4 (8.1)	yellow	
(*S*)-**1b**	CH_3	O		79	oil	+125.3 (7.7)	yellow	
(*R*)-**1c**	H	S	-	83	44–45	−155.3 (7.3)	white	
(*S*)-**1c**	H	S		85	47	+159.6 (3.6)	white	$[\alpha]_{546}^{20}$ + 183.4 (*c* 9.7, acetone)[30]
(*R*)-**1d**	CH_3	S	-	78	40	−229.2 (4.7)	white	
(*S*)-**1d**	CH_3	S		81	39	+225.5 (4.2)	white	
(*R*)-**1e**	H	-	α	79	oil	−55.4 (6.3)	yellow	
(*S*)-**1e**	H	-	α	78	oil	+55.8 (4.4)	yellow	$[\alpha]_D^{25}$ + 37 (*c* 2.24, $CHCl_3$)[29]
(*R*)-**1f**	H	-	β	76	oil	−92.0 (6.7)	white	$[\alpha]_{546}^{20}$ + 55.7 (*c* 51.0, acetone)[30]
(*S*)-**1f**	H	-	β	81	oil	+92.1 (6.6)	white	$[\alpha]_D^{25}$ + 62.1 (*c* 2.1, $CHCl_3$)[29]
(*R*)-**1g**	H	-	γ	80	oil	−66.1 (6.7)	white	
(*S*)-**1g**	H	-	γ	84	oil	+66.2 (8.6)	white	$[\alpha]_D^{25}$ + 27.1 (*c* 1.1, $CHCl_3$)[29]
(*R*)-**1h**	CH_3	-	α	82	28	−20.2 (5.0)	white	
(*S*)-**1h**	CH_3	-	α	89	oil	+21.0 (10.1)	yellow	$[\alpha]_{546}^{20}$ + 29.6 (*c* 10.0, acetone)[30]

[a] Racemic compounds **1a–d** were synthesized previously.[27] The data of the ^1H NMR and MS spectra given for them were identical with the spectra of (*R*)- and (*S*)-isomers.

Table 2. ^{1}H NMR spectra of pyridine aldimines **1e–h**

Imine[a,b]	Chemical shift (ppm), *J* (Hz)					
	*CH_3*CH, d	MeC*H*, q	*CH_3*-ring, s	Ph, m	Protons of pyridine ring	CH–N, s
1e	1.61	4.64	-	7.2-7.5	7.29, ddd, *J* = 7.7, 4.9, 1.4, PyH-5	8.46
	J = 6.9				7.72, m, *J* = 7.7, 1.8, PyH-4	
					8.09, ddd, *J* = 7.7, 1.4, 1.0, PyH-3	
					8.63, m, *J* = 4.9, 1.7, 1.0, PyH-6	
1f	1.57	4.55	-		7.2-7.5, m, 6H, Ph, PyH-5	8.39
	J = 6.6				8.14, dt, *J* = 8.0, 2.0, PyH-4	
					8.61, dd, *J* = 5.2, 2.0, PyH-6	
					8.88, d, *J* = 2.4, PyH-2	
1g	1.58	4.57	-	7.2-7.5	7.60, dd, *J* = 6.0, 2.0, PyH-3,5	8.33
	J = 6.4				8.67, dd, *J* = 6.0, 2.0, PyH-2,6	
1h	1.60	4.62	2.58	7.2-7.4	7.16, d, *J* = 7.7, PyH-5	8.44
	J = 6.8				7.61, t, *J* = 7.7, PyH-4	
					7.92, d, *J* = 7.7, PyH-3	

[a] Identical spectra of the (*R*)-and (*S*)-isomers for all the compounds were found.
[b] Spectra of **1e–h** were comparable with those given in Refs 29, 30 for these imines.

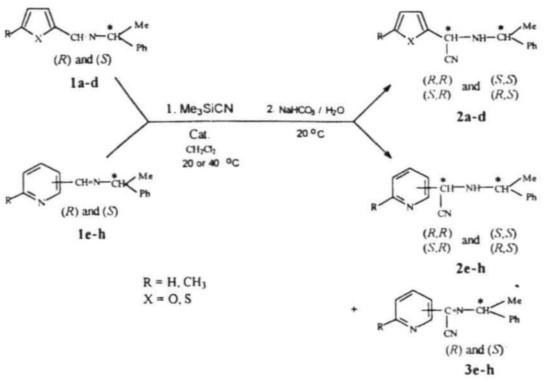
Table 3. Mass spectra of pyridine aldimines **1e–h**

Imine[a,b]	GC-MS, *m/z* (I_{rel}, %)[c]
1e	210 (12, M^+), 209 (9, $[M - H]^+$), 195 (51, $[M - Me]^+$), 181 (6), 168 (7), 133 (10, $[M - Ph]^+$), 118 (2), 105 (100, $[Ph(Me)HC]^+$, $[C_5H_4NCH{=}N]^+$), 92 (18), 79 (22, $[PyH]^+$), 78 (18, Py^+), 77 (35, Ph^+), 65 (12), 51 (21), 39 (13), 28 (22)
1f	210 (18, M^+), 209 (4, $[M - H]^+$), 195 (17, $[M - Me]^+$), 183 (6), 167 (14), 133 (4, $[M - Ph]^+$), 132 (3, $[M - Py]^+$), 115 (3), 106 (23), 105 (100, $[Ph(Me)HC]^+$, $[C_5H_4NCH{=}N]^+$), 103 (10), 91 (16), 79 (28, $[PyH]^+$), 78 (18, Py^+), 77 (34, Ph^+), 63 (16), 51 (33), 39 (11)
1g	210 (15, M^+), 195 (12, $[M - Me]^+$), 183 (12), 167 (10), 131 (5), 106 (18), 105 (100, $[Ph(Me)HC]^+$, $[C_5H_4NCH{=}N]^+$), 103 (9), 91 (5), 91 (4), 79 (27, $[PyH]^+$), 78 (19, Py^+), 77 (31, Ph^+), 63 (13), 51 (37), 39 (10)
1h	224 (29, M^+), 223 (15, $[M - H]^+$), 210 (15), 209 (95, $[M - Me]^+$), 182 (35), 132 (12), 121 (20), 106 (21), 105 (100, $[Ph(Me)HC]^+$), 103 (22), 94 (13), 79 (21), 78 (12), 77 (45, Ph^+), 65 (15), 51 (17), 39 (20)

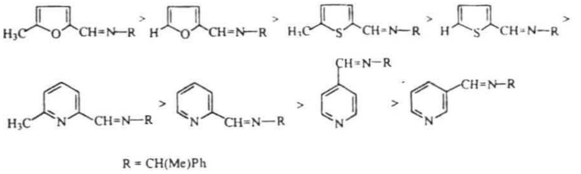
[a] Identical spectra of the (*R*)- and (*S*)-isomers for all the compounds were found.
[b] Spectra of **1e-g** were comparable with those given in Ref. 29 for these imines.
[c] Py = pyridyl.

Table 4. Elemental analysis of the solid aldimines obtained

Imine	Mol. formula	Found/calculated (%)			
		C	H	N	S
(*R*)-**1c**	$C_{13}H_{13}NS$	72.26/72.52	6.00/6.09	6.40/6.50	14.77/14.89
(*S*)-**1c**	$C_{13}H_{13}NS$	72.53/72.52	6.11/6.09	6.47/6.50	14.88/14.89
(*R*)-**1d**	$C_{14}H_{15}NS$	73.22/73.32	6.58/6.59	6.06/6.11	13.89/13.98
(*S*)-**1d**	$C_{14}H_{15}NS$	73.13/73.32	6.52/6.59	6.05/6.11	13.87/13.98
(*R*)-**1h**	$C_{15}H_{16}N_2$	80.33/80.32	7.19/7.19	12.54/12.49	-
(*S*)-**2d**	$C_{15}H_{16}N_2S$	71.02/70.28	6.40/6.29	10.46/10.93	11.93/12.51



Scheme 2. Trimethylsilylcyanation of the optically active heterocyclic imines.



Scheme 3. Reactivity order of heterocyclic imines in the Strecker reaction.

Asymmetric addition of Me_3SiCN to optically active heterocyclic imines

Two chiral imines (*R*)- and (*S*)-**1a–h** prepared were tested in the Strecker synthesis catalysed by Lewis acids: $AlCl_3$ or $AlBr_3$ (5–20 mol%). The addition of Me_3SiCN to imines was carried out in methylene chloride at 20 or 40 °C until imine conversion was mainly 78–100% (monitored by TLC and GC–MS and determined by ^1H NMR). Some of products

Table 5. Characteristics of the trimethylsilylcyanation reactions and the products

Run	Starting imine	Catalyst (mol%)	Temp. (°C)	Time (h)	Conversion (%)^{a,b}	Col. Chrom. eluent	Product^{c,d}	Yield (%)	d.r.^{a,e}	$[\alpha]_{546}^{20-23}$(deg) (*c* in benzene)
1	(*R*)-**1a**	$AlCl_3$ (5)	20	25	n.d.	C_6H_6:EtOAc = 9:1	**2a**(*R*)	43	78:22	+88.9 (0.84)
2	(*S*)-**1a**	$AlCl_3$ (5)	20	20	n.d.	C_6H_6:EtOAc = 9:1	**2a**(*S*)	38	67:33	−80.6 (0.5)
3	(*R*)-**1b**	$AlBr_3$ (20)	20	1	∼100	-	**2b**(*R*)	82	74:26	+105.5 (0.7)
4	(*S*)-**1b**	$AlBr_3$ (20)	20	1	∼100	-	**2b**(*S*)	80	74:26	−103.2 (0.7)
5	(*R*)-**1c**	$AlBr_3$ (10) + MS 4Å	20	6.5	80	Hex:EtOAc = 5:1	**2c**(*R*)	75	79:21	+119.4 (2.1)
6	(*S*)-**1c**	$AlBr_3$ (10) + MS 4Å	20	6.5	78	Hex:EtOAc = 5:1	**2c**(*S*)	72	78:22	−103.2 (1.8)
7	(*R*)-**1d**	$AlBr_3$ (20)	20	1	80	Hex:EtOAc = 5:1	**2d**(*R*)	58	77:23	+69.1 (1.3)
8	(*S*)-**1d**	$AlBr_3$ (20)	20	1	87	Hex:EtOAc = 5:1	**2d**(*S*)	62	75:25	−69.1 (1.3)
9	(*R*)-**1e**	$AlCl_3$ (20)	40	19	75	-	**2e**(*R*)	n.d.	71:29	
10	(*R*)-**1e**	$AlBr_3$ (10) + MS 4Å	40	2	87	$CHCl_3$:MeOH = 9.5:0.5	**2e**(*R*)	40	78:22	+55.8 (1.2)
						$CHCl_3$:MeOH = 9.5:0.5	(*R*)-**3e**	33	-	+43.8 (0.8)
11	(*S*)-**1e**	$AlCl_3$ (20)	40	19	n.d.	$CHCl_3$:MeOH = 9:1	**2e**(*S*)	61	74:26	−45.5 (1.2)
						$CHCl_3$:MeOH = 9:1	(*S*)-**3e**	10	-	
12	(*S*)-**1e**	$AlBr_3$ (10)	20	41	40	-	**2e**(*S*)	-	71:29	
13	(*S*)-**1e**	$AlBr_3$ (10) + MS 4Å	40	8.5	96	$CHCl_3$:MeOH = 9.5:0.5	**2e**(*S*)	73	79:21	−47.3 (1.3)
						$CHCl_3$: MeOH = 9.5:0.5	(*S*)-**3e**	18	-	−42.8 (0.5)
14	(*R*)-**1f**	$AlBr_3$ (10) + MS 4Å	40	21	95	CH_2Cl_2:MeOH = 10:1	**2f**(*R*)	70	75:25	+93.4 (1.8)
						CH_2Cl_2: MeOH = 10:1	(*R*)-**3f**	15	-	
15	(*S*)-**1f**	$AlBr_3$ (10) + MS 4Å	40	22.5	82	CH_2Cl_2:MeOH = 10:1	**2f**(*S*)	75	80:20	−89.7 (2.5)
16	(*R*)-**1g**	$AlBr_3$ (10) + MS 4Å	20	8.5	97	CH_2Cl_2:MeOH = 10:1	**2g**(*R*)	60	81:19	+72.4 (1.8)
						CH_2Cl_2: MeOH = 10:1	(*R*)-**3g**	25	-	+38.3 (0.8)
17	(*S*)-**1g**	$AlBr_3$ (10) + MS 4Å	20	6	91	CH_2Cl_2:MeOH = 10:1	**2g**(*S*)	64	87:13	−82.3 (1.2)
						CH_2Cl_2: MeOH = 10:1	(*S*)-**3g**	12	-	
18	(*R*)-**1h**	$AlBr_3$ (10) + MS 4Å	20	2	98	CH_2Cl_2:MeOH = 20:1	(*R*)-**2h**	70	80:20	+85.1 (1.4)
						CH_2Cl_2: MeOH = 20:1	(*R*)-**3h**	20	-	+77.7 (0.6)
19	(*S*)-**1h**	$AlBr_3$ (10) + MS 4Å	20	2.5	∼100	-	**2h**(*S*)	85	76:24	−92.6 (3.7)

[a] Determined by ^1H NMR.
[b] n.d.: not determined.
[c] Configuration of the newly formed stereocentre is given.
[d] All the compounds were oils except **2d**(*S*): solid, m.p. 48–49 °C.
[e] d.r.: diastereoisomeric ratio.

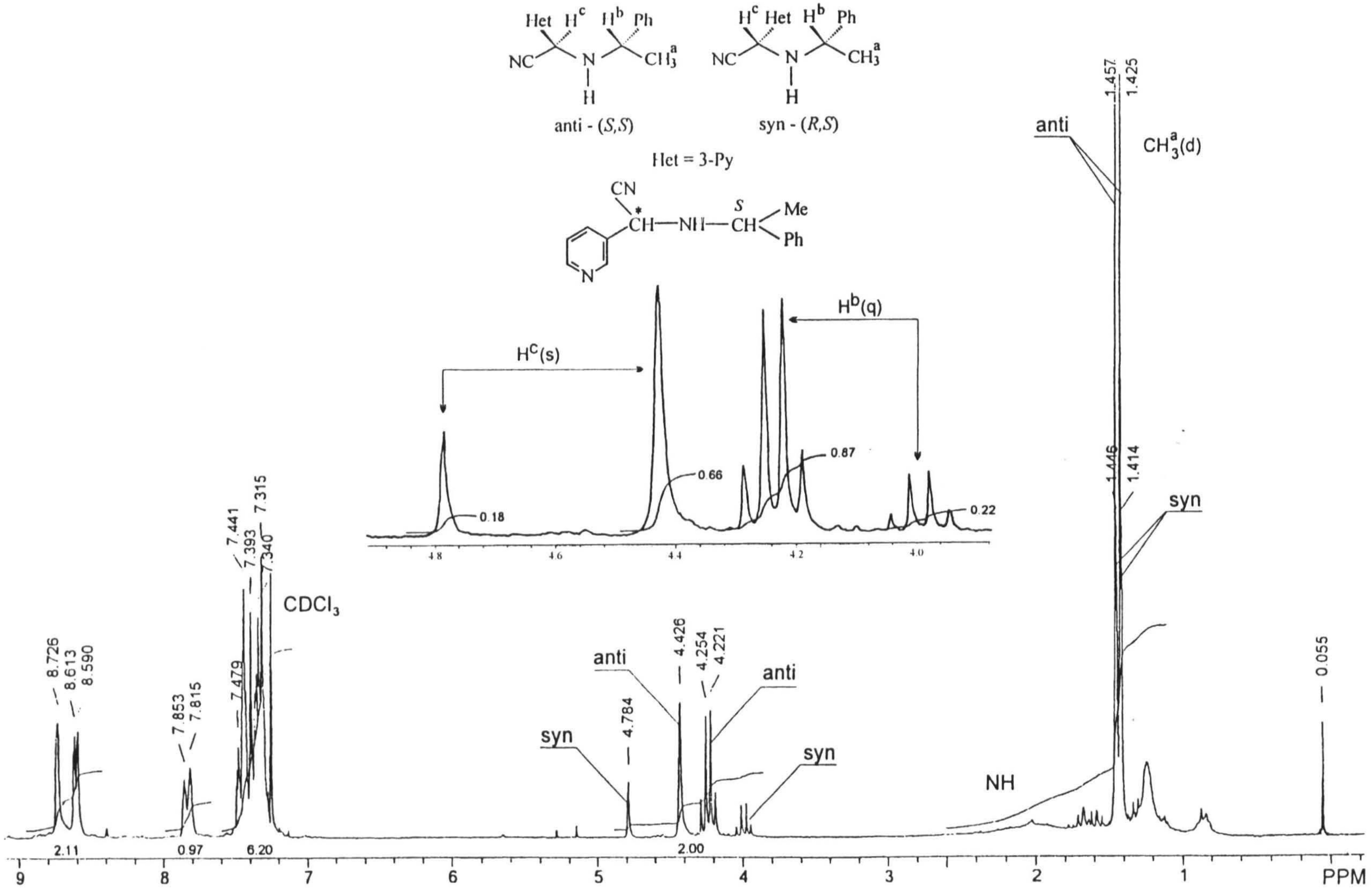


Figure 1. ^1H NMR spectrum of α-amino nitrile **2f** obtained from imine (*S*)-**1f**.

Table 6. ^{1}H NMR spectra of nitriles **2** and **3**

Compound[a]		Chemical shift (ppm), *J* (Hz)					
		$C\underline{H}_3CH$, d	$C\underline{H}_3$-ring	NH	CHCN	$C\underline{H}Me$, q	Ring protons
2a(*R*)	major	1.43, *J*=6.4	–	2.0, br s	4.43, br s	4.19, *J*=6.4	6.3–6.4, m, FurH-3,4; 7.2–7.4, m, FurH-5, Ph
2a(*S*)	minor	1.37, *J*=6.4	–	2.0, br s	4.68, br s	3.92, *J*=6.4	6.3–6.4, m, FurH-3,4; 7.2–7.4, m, FurH-5, Ph
2b(*R*)	major	1.43, *J*=6.4	2.28	1.9, br s	4.35, br s	4.18, *J*=6.4	5.92, m, *J*=2.2, FurH-4; 6.25, m, *J*=2.2, FurH-3; 7.2–7.4, m, Ph
2b(*S*)	minor	1.37, *J*=6.4	2.28	1.9, br s	4.61, br s	3.93, *J*=6.4	5.92, m, *J*=2.2, FurH-4; 6.20, m, *J*=2.2, FurH-3; 7.2–7.4, m, Ph
2c(*R*)	major	1.37, *J*=7.0	–	1.95, d, *J*=12.0	4.49, d, *J*=12.0	4.15, *J*=7.0	6.8–7.5, m, ThH-3,4, Ph; 7.64, m, ThH-5
2c(*S*)	minor	1.35, *J*=7.0	–	1.95, d, *J*=12.0	4.49, d, *J*=12.0	3.99, *J*=7.0	6.8–7.5, m, ThH-3,4, Ph; 7.64, m, ThH-5
2d(*R*)	major	1.35, *J*=6.6	2.42	1.95, d, *J*=11.6	4.45, d, *J*=11.6	4.16, *J*=6.6	6.57, d, *J*=3.4, ThH-4; 6.94, d, *J*=3.4, ThH-3; 7.2–7.4, m, Ph
2d(*S*)	minor	1.33, *J*=6.6	2.42	1.9, br d	4.46, d, *J*=11.6	4.00, *J*=6.6	6.57, d, *J*=3.4, ThH-4; 6.94, d, *J*=3.4, ThH-3; 7.2–7.4, m, Ph
2e(*R*)	major	1.45, *J*=6.6	–	2.5, br s	4.44, s	4.27, *J*=6.6	7.2–7.4, m, PyH-3,5, Ph; 7.70, td, *J*=6.0, 1.2, PyH-4; 8.61, m, *J*=4.6, PyH-6
2e(*S*)	minor	1.41, *J*=6.6	–	2.5, br s	4.76, s	3.98, *J*=6.6	7.2–7.4, m, PyH-3,5, Ph; 7.70, td, *J*=6.0, 1.2, PyH-4; 8.61, m, *J*=4.6, PyH-6
(*R*)-**3e**		1.64, *J*=6.4	–	–	–	5.25, *J*=6.4	7.3–7.5, m, PyH-5, Ph; 7.73, td, *J*=7.0, 1.6, PyH-4; 8.12, d, *J*=7.0, PyH-3; 8.69, m, *J*=4.8, PyH-6
(*S*)-**3e**							
2f(*R*)	major	1.44, *J*=6.6	–	2.0, br s	4.43, s	4.24, *J*=6.6	7.2–7.5, m, PyH-5, Ph; 7.83, dt, *J*=8.0, 2.2, PyH-4; 8.60, dd, *J*=5.0, 1.6, PyH-6; 8.73, d, *J*=2.4
2f(*S*)	minor	1.43, *J*=6.6	–	2.0, br s	4.78, s	3.99, *J*=6.6	7.2–7.5, m, PyH-5, Ph; 7.83, dt, *J*=8.0, 2.2, PyH-4; 8.60, dd, *J*=5.0, 1.6, PyH-6; 8.73, d, *J*=2.4
(*R*)-**3f**		1.58, *J*=6.6	–	–	–	5.20, *J*=6.6	7.2–7.5, m, PyH-5, Ph; 8.17, dt, *J*=7.8, 2.2, PyH-4; 8.75, dd, *J*=5.0, 1.6, PyH-6; 8.87, d, *J*=2.2
2g(*R*)	major	1.47, *J*=7.0	–	2.1, br s	4.41, s	4.24, *J*=7.0	7.3–7.6, m, Ph, PyH-3,5; 8.62, dd, *J*=6.0, 2.0, PyH-2,6
2g(*S*)	minor	1.44, *J*=7.0	–	2.1, br s	4.78, s	4.02, *J*=7.0	7.3–7.6, m, Ph, PyH-3,5; 8.62, dd, *J*=6.0, 2.0, PyH-2,6
(*R*)-**3g**		1.67, *J*=7.2	–	–	–	5.22, *J*=7.2	7.2–7.6, m, Ph; 7.84, dd, *J*=6.0, 2.0, PyH-3,5; 8.78, dd, *J*=6.0, 2.0, PyH-2,6
(*S*)-**3g**							
2h(*R*)	major	1.47, *J*=6.6	2.56	2.3, br s	4.37, s	4.27, *J*=6.6	7.09, d, *J*=7.6, PyH-5; 7.15, d, *J*=7.6, PyH-3; 7.2–7.5, m, Ph; 7.59, t, *J*=7.6, PyH-4
2h(*R*)	minor	1.41, *J*=6.4	2.55	2.3, br s	4.70, s	3.98, *J*=6.4	7.09, d, *J*=7.6, PyH-5; 7.15, d, *J*=7.6, PyH-3; 7.2–7.5, m, Ph; 7.59, t, *J*=7.6, PyH-4
(*R*)-**3h**		1.64, *J*=6.4	2.62	–	–	5.25, *J*=6.4	7.23, d, *J*=6.5, PyH-5; 7.3–7.5, m, Ph; 7.63, t, *J*=6.5, PyH-4; 7.93, d, *J*=6.5, PyH-3

[a] Configuration of the CH(Me)Ph group is given.

Table 7. Mass spectra of nitriles **2** and **3**

Compound[a,b]	MS, m/z (I_{rel}, %)
2a	211 (15, $[M - Me]^+$), 200 (18), 199 (100, $[M - HCN]^+$), 198 (7), 185 (12), 184 (82, $[M - HCN - Me]^+$), 157 (17), 128 (16), 121 (18, $[M - Ph(Me)HC]^+$), 116 (15), 106 (56), 105 (100, $[Ph(Me)HC]^+$), 104 (25), 103 (32), 91 (10), 79 (47), 78 (30), 77 (73, Ph^+), 65 (12), 63 (10), 53 (15), 52 (32), 51 (55), 50 (17), 39 (50), 38 (12), 27 (65, $[HCN]^+$)
2e	236 (5, $[M - H]^+$), 235 (30, $[M - 2H]^+$), 234 (67, $[M - 3H]^+$), 220 (50, $[M - 2H - Me]^+$), 211 (15, $[M - CN]^+$), 210 (17, $[M - HCN]^+$), 209 (16, $[M - CN - 2H]^+$), 208 (30, $[M - HCN - 2H]^+$), 207 (15), 196 (25, $[M - CN - Me]^+$), 195 (100, $[M - HCN - Me]^+$), 194 (55, $[M - CN - Me - 2H]^+$), 168 (23), 167 (17), 159 (10, [M - Py]), 133 (20), 132 (18, [PyCH(CN)NH]), 131 (21), 130 (16), 121 (28), 120 (95, $[Ph(Me)CHNH]^+$), 118 (28), 117 (55, $[PyCHCN]^+$), 107 (30), 106 (93), 105 (100, $[Ph(Me)CH]^+$), 104 (50), 103 (54), 92 (80), 79 (70, $[PyH]^+$), 78 (68, Py^+), 77 (79, Ph^+), 63 (13), 52 (30), 51 (32), 43 (30), 39 (35), 27 (40, $[HCN]^+$)
3e	235 (24, M^+), 234 (8, $[M - H]^+$), 220 (20, $[M - Me]^+$), 208 (12), 193 (7), 158 (7, [M – Ph]), 157 (7, [M – Py]), 132 (5), 117 (25), 105 (100, $[Ph(Me)CH]^+$), 90 (17), 79 (28, $[PyH]^+$), 78 (21, Py^+), 77 (42, Ph^+), 63 (13), 51 (28), 39 (11)
2f	235 (2, $[M - 2H]^+$), 222 (7, $[M - Me]^+$), 211 (8, $[M - CN]^+$), 210 (30, $[M - HCN]^+$), 209 (16, $[M - CN - 2H]^+$), 183 (15), 168 (14), 167 (13), 117 (8, $[PyCHCN]^+$), 107 (17), 106 (60), 105 (100, $[Ph(Me)CH]^+$), 104 (20), 103 (25), 91 (19), 79 (38, $[PyH]^+$), 78 (48, Py^+), 77 (42, Ph^+), 63 (21), 52 (32), 51 (36), 50 (30), 39 (23), 27 (22, $[HCN]^+$)
3f	235 (19, M^+), 220 (18, $[M - Me]^+$), 192 (8), 166 (6), 157 (7, $[M - Py]^+$), 156 (10), 116 (5), 106 (10), 105 (100, $[Ph(Me)CH]^+$), 103 (15), 89 (9), 79 (15, $[PyH]^+$), 78 (12, Py^+), 77 (26, Ph^+), 63 (7), 51 (20), 39 (6)
2g	236 (2, $[M - H]^+$), 235 (25, $[M - 2H]^+$), 234 (2), 220 (20, $[M - 2H - Me]^+$), 210 (5, $[M - HCN]^+$), 195 (4), 193 (6), 192 (7), 183 (4), 167 (6), 166 (5), 157 (18), 156 (14), 131 (10), 120 (17), 117 (11, $[PyCHCN]^+$), 106 (52), 105 (100, $[Ph(Me)CH]^+$), 104 (20), 103 (22), 89 (15), 79 (40, $[PyH]^+$), 78 (42, Py^+), 77 (42, Ph^+), 63 (17), 53 (23), 52 (40), 51 (25), 39 (15), 27 (12, $[HCN]^+$)
3g	235 (25, M^+), 234 (5, $[M - H]^+$), 220 (18, $[M - Me]^+$), 208 (3), 192 (7), 157 (10, $[M - Py]^+$), 156 (8), 131 (3), 116 (4), 105 (100, $[Ph(Me)CH]^+$), 103 (13), 89 (7), 79 (14, $[PyH]^+$), 78 (15, Py^+), 77 (21, Ph^+), 63 (10), 51 (18), 39 (5)
3h	249 (30, M^+), 248 (95, $[M - H]^+$), 234 (36, $[M - Me]^+$), 223 (15), 222 (58), 221 (27), 209 (8), 131 (14), 119 (15), 106 (7), 105 (100, $[Ph(Me)CH]^+$), 104 (22), 103 (34), 92 (9), 79 (23, $[PyH]^+$), 78 (18, Py^+), 77 (55, Ph^+), 65 (20), 51 (20), 39 (15)

[a] Registration of the mass spectra for some α-amino nitriles was not successful since decomposition of these compounds took place.

[b] Identical spectra of the optical isomers were obtained.

were thermally unstable under GC analysis conditions. After hydrolysis of the reaction mixtures with aqueous $NaHCO_3$, the products were isolated by column chromatography. Besides the corresponding α-amino nitriles **2**, the formation of unexpected unsaturated nitriles **3** from all the pyridine imines was found (Scheme 2, Table 5).

Usually, reactions of Me_3SiCN with imines lead to α-amino nitriles and not to the unsaturated nitriles (in particular, this is so for the furan and thiophene derivatives; see above). This fact suggests that the pyridine N-atom plays some role in the formation of products **3** (yields in our conditions were up to 33% – run 10, Table 5). Comparable results were obtained in previous investigations[25,26] of Me_3SiCN addition to imines (produced from reactions of furan, thiophene and pyridine aldehydes with unchiral amines), and were also accompanied by the formation of the corresponding unsaturated compounds from pyridine imines only. Apparently, the pathway to unsaturated nitriles is achieved *via* formation of the intermediate σ-complex of AlX_3 with imine (through the N-atom of the pyridine ring) leading to an increase in the hydrogen atom mobility in the CH=N group. The proposed scheme of trimethylsilylcyanation of pyridine imines is given in Ref. 26.

It is interesting to compare this with the results of diastereoselective addition of methyllithium to aldimines (including some heterocyclic ones) derived from (*S*)-1-phenylethylamine.[31] Analogous formation of unsaturated byproducts – ketimines in this case – was found by these authors, who proposed a radical mechanism for these reactions. One can notice that the corresponding ketimine has been formed from the 4-pyridine derivative and not in the case from the 2-furyl compound.

$AlBr_3$ was more active than $AlCl_3$ in the Strecker synthesis with the heterocyclic imines studied. It was found that the reactions proceeded most smoothly under the action of a catalyst together with 4 Å molecular sieves. Furan imines were more active in the addition of Me_3SiCN than for thiophene and pyridine imines. The reactivity of methyl derivatives was higher than that of the heterocyclic azomethines themselves. The aldimines studied are arranged with respect to their reactivity according to Scheme 3.

All the products obtained were characterized by ^1H NMR, polarimetry and GC–MS (Tables 5–7). The reactions in all cases afforded mixtures of the α-amino nitrile diastereomers, with one diastereomer predominating, that being shown by the ^1H NMR spectra (Tables 5 and 6). All the spectra were found to have two quartets of benzylic protons and two signals of methine protons. The diastereoisomeric ratios obtained were determined by means of ^1H NMR using the signals of benzyl protons as key signals. A typical ^1H NMR spectrum is shown in Fig. 1 (for the product of Me_3SiCN addition to imine (*S*)-**1f** as an example). The signals of benzyl protons C<u>H</u>(Me)Ph appeared as well-separated quartets: the downfield (major) at δ 4.15–4.27 and the upfield (minor) at δ 3.92–4.02 ppm for all compounds **2** obtained from (*R*)- and from (*S*)-imines. The signals were assigned analogously in recent work[15] on the basis of the study by Ogura and coworkers[14] and taking into consideration the data in Refs 11, 12, 29 as follows: downfield to (*R,R*)- and (*S,S*)-anti-diastereomers and upfield to (*R,S*)- and (*S,R*)-syn-isomers. The signs of optical rotation (Table 5) correlated with ^1H NMR data. The α-amino nitriles obtained from all the (*S*)-imines were laevorotatory, whereas the (*R*)-isomers afforded (+)-products. The addition of Me_3SiCN to all the imines studied followed the same sense of asymmetric induction. When the configuration of the nitrogen auxiliary was *R*, the (*R,R*)-α-amino nitriles predominated over the (*S,R*)-isomer, whereas the (*S,S*)-products of addition formed mainly from (*S*)-imines. Thus, *Re* face attack to the (*S*)-imines and *Si* face addition to the (*R*)-imines occurred in all cases. All α-amino nitriles **2** were obtained with moderate diastereopurity: up to 81% for (*R,R*)- and up to 87% for (*S,S*)-isomers. Almost the same values of diastereoisomeric ratio were obtained in both enantiomeric series. Some differences appeared; these were generally in the isolation step of the products by column chromatography.

The thermodynamic/kinetic possibilities in the asymmetric Strecker synthesis with a number of aldimines based on 1-phenylethylamine (using HCN or NaCN in MeOH without any catalyst) were investigated in Refs 12, 14. Formation of amino nitriles has been found to occur under thermodynamic control. Equilibrium between the diastereomers was established in *ca* 0.5 h[12] or 3 h[14] for derivatives of aromatic and aliphatic aldehydes respectively.

Comparable results were obtained in the present work and in Ref. 15. The diastereoisomeric ratio was 80:20 in the synthesis of **2f** from (*S*)-**1f** (Table 5) and 79:21 (in the reaction without catalyst, 6 days).[15] In our opinion, this fact demonstrates that complete equilibrium between the diastereomers was reached in our experiments.

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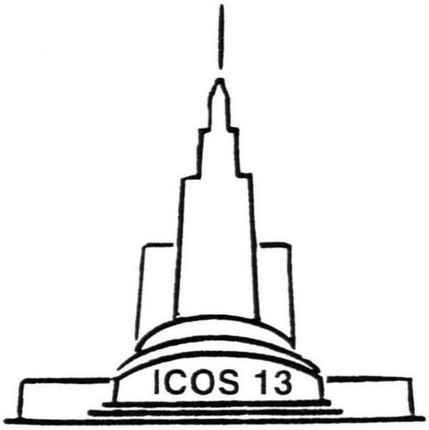

BOOK OF ABSTRACTS

UNDER THE AUSPICES OF
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ADDITION OF Me_3SiCN TO HETEROCYCLIC IMINES CATALYZED BY LEWIS ACIDS

I. Iovel, L. Golomba, S. Belyakov, J. Popelis, S. Grinberga, E. Lukevics
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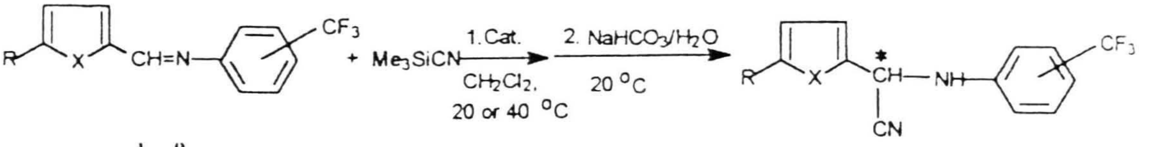
$AlCl_3$ appears to be an efficient catalyst for trimethylsilylcyanation of furan and thiophene aldehydes [1] and some pyridine arylazomethynes [2].

In the current work, the addition of Me_3SiCN to Shiff bases 1 – 8, synthesized previously from the reactions of furan and thiophene aldehydes with 3- and 4-aminobenzotrifluorides, has been studied in the presence of various Lewis acids. A series of the corresponding trifluoromethyl derivatives of heterocyclic α-aminonitriles (1 – 8), potentially biologically active compounds, were obtained in 38 to 80 % isolated yields.

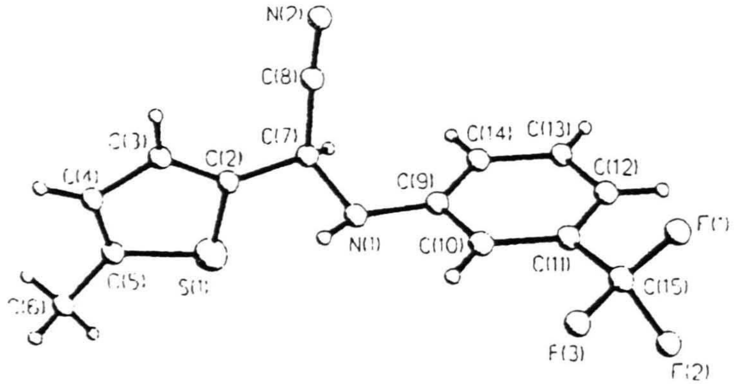


1 - 8 1 - 8

The reactions were carried out in CH_2Cl_2 in the presence of 5 - 20 mol % catalyst at 20 or 40 °C until complete conversions. It was found that 4A molecular sieves (MS) accelerate the addition and increase the yields of the products. The investigated catalysts ranked of their activity in the following order:

$$AlBr_3 + 4A\ MS > AlBr_3 > AlCl_3 > Ti(OPr^i)_4$$

The products were isolated by column chromatography and identified by ^1H NMR, MS spectra and elemental analysis. A single crystal of N-(5-methyl-2-thienylcyanomethyl)-3-trifluoromethylaniline was obtained and studied by X-ray diffraction. The results showed that it was the crystal of (*R*)-isomer of this compound.



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HYDROSILYLATION OF HETEROCYCLIC ALDIMINES CATALYZED BY Au^{III}, Pd^{I} AND Rh^{I} COMPLEXES

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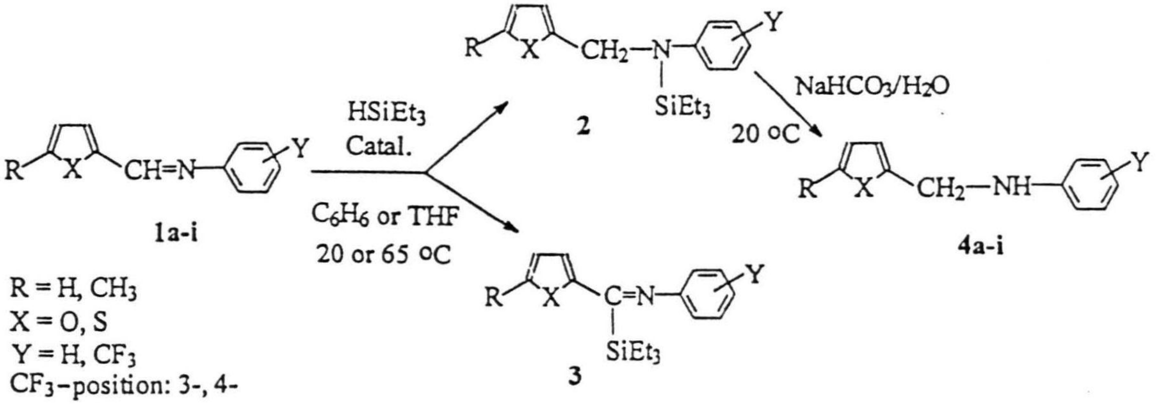
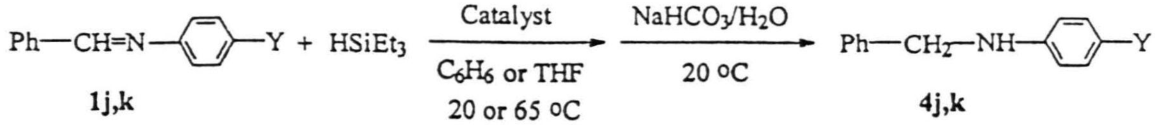
The hydrosilylation of a series of (hetero)aromatic imines was studied in course of our recent investigations of the conversions of heterocyclic substrates [1–3]. Numerous transition metal complexes were used as the catalysts in the addition of $HSiEt_3$ to CH=N bond of furan and thiophene imines and related compounds. Among Au^{III}, Ir^{I}, Pd^{0}, Pd^{I}, Pd^{II}, Pt^{0}, Pt^{IV}, Rh^{I}, Rh^{III}, Ru^{0}, Ru^{II} complexes studied only $AuCl_3$, $HAuCl_4$, $[Pd(allyl)Cl]_2$, $[Rh(COD)Cl]_2$ and $Rh(PPh_3)Cl$ were highly active.



R = H, CH$_3$
X = O, S
Y = H, CF$_3$
CF$_3$-position: 3-, 4-



The influence of the temperature, nature of solvent, structure of substrates and catalysts on these reactions was studied. The mechanism of the hydrosilylation of the imines is proposed. A number of novel target amines were synthesized, isolated by column chromatography and characterized by ^{1}H NMR and MS analysis.

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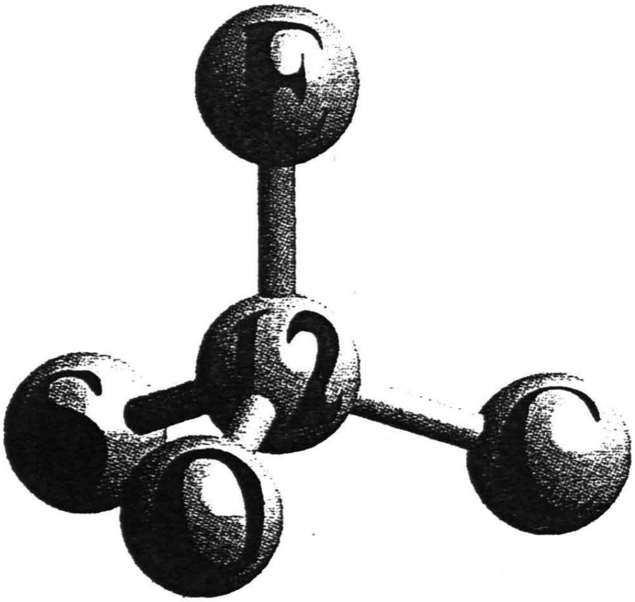

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Catalytic Trimethylsilylcyanation of Novel Pyridylaldimines

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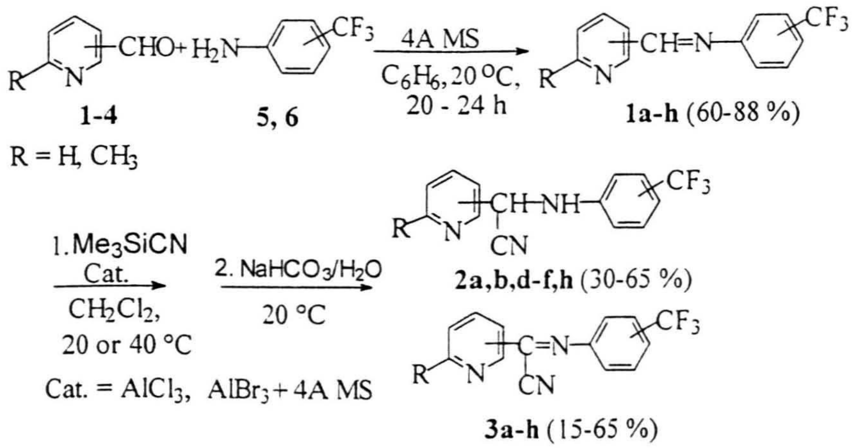
In our previous paper[1] it was demonstrated that $AlCl_3$ catalyzed the trimethylsilylcyanation of furan and thiophene aldimines to afford the corresponding α-amino nitriles. In the present work a series of novel Shiff bases (**1a-h**) was synthesized by condensation of pyridinealdehydes (**1-4**) with 3- and 4-trifluoromethylanilines (**5, 6**) in the presence of molecular sieves 4A (MS) acting as dehydration agent and the solid acid. It has been found that $AlCl_3$ and especially $AlBr_3$ together with MS catalyzed the addition of Me_3SiCN to the C=N bond of the imines obtained, while the other studied Lewis acids (YCl_3, $LaCl_3$, ZnI_2) were inactive. Besides the expected addition giving the α-amino nitriles (**2a,b,d-f,h**) an unusual reaction direction leading to unsaturated nitriles (**3a-h**) was observed. The structures of saturated and unsaturated products **2d** and **3c** were determined by X-ray diffraction. The mechanism of the Lewis acid catalyzed addition of Me_3SiCN to pyridine imines was proposed. Aromatic amino nitriles and heterocyclic derivatives containing a CF_3 group are potential precursors of medicine. That is why some nitriles obtained (**3a, 3c**) were tested for their antitumor activity, and the results were compared with the known anticancer drug FTORAFUR®. Novel nitriles inhibited the growth of tumor cells especially mouse melanoma B16. Their activity was higher than that of Ftorafur in most cases. This fact evidences the perspective for further investigation of these compounds.



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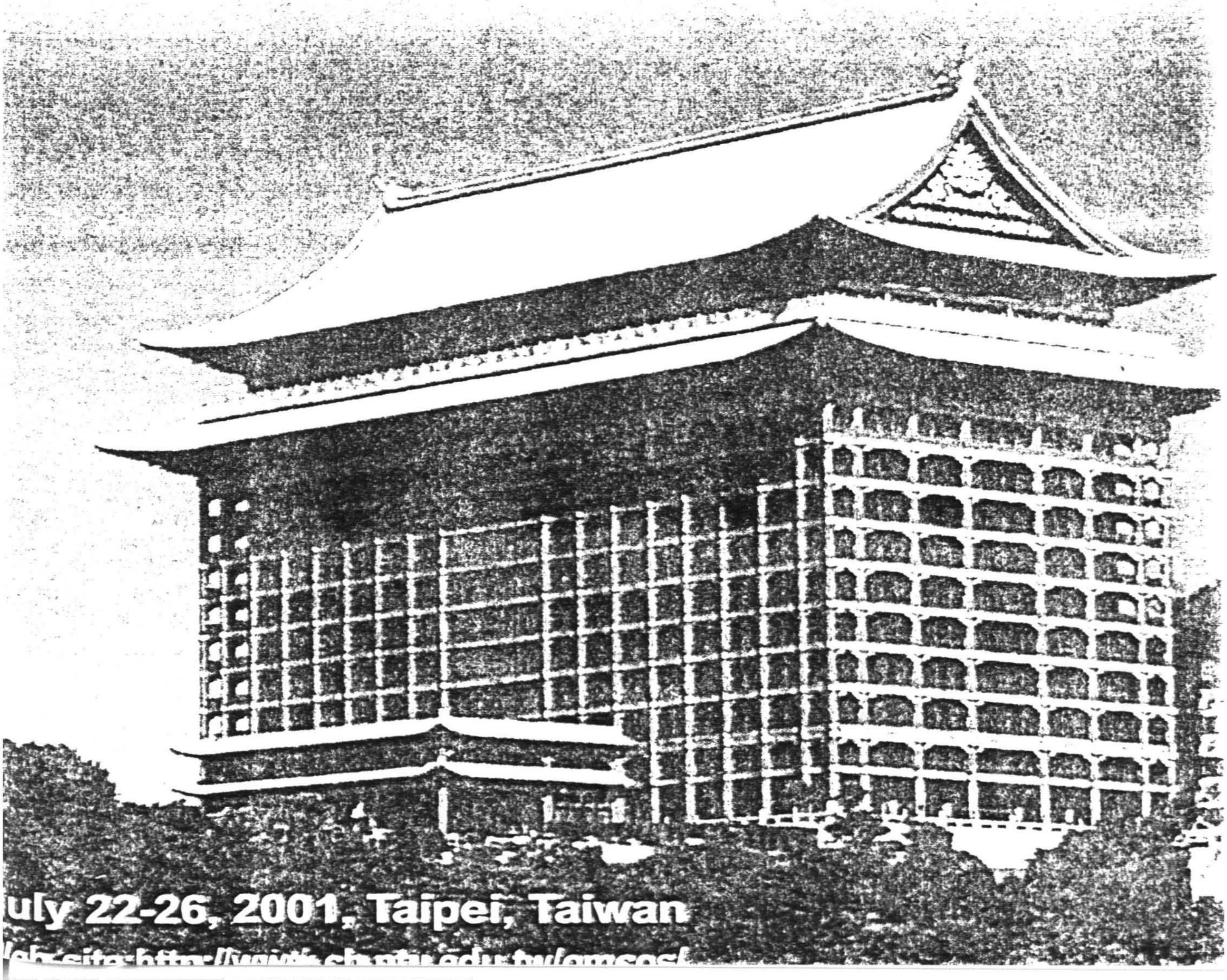

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HYDROSILYLATION OF HETEROCYCLIC IMINES CATALYZED BY TRANSITION METAL COMPLEXES

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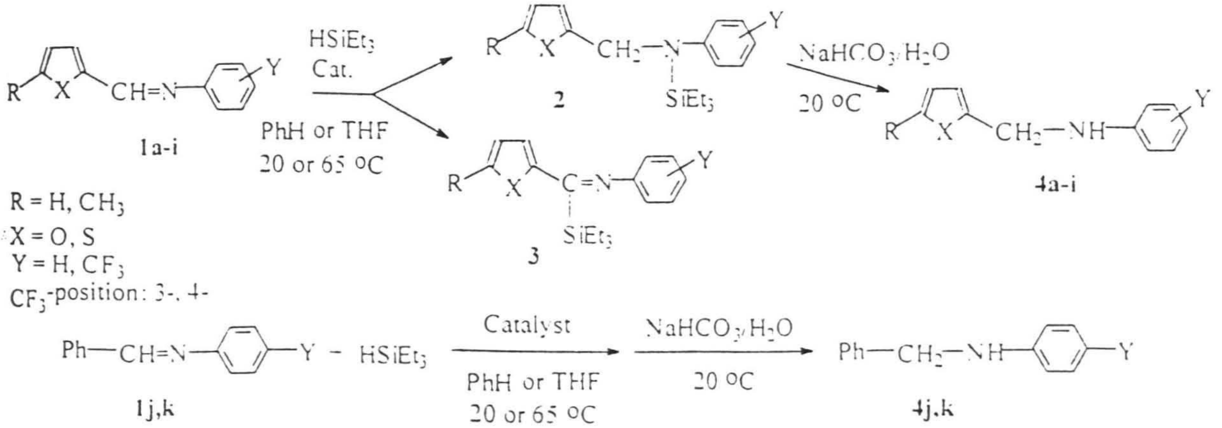
The heterocyclic amines and their fluorine-containing derivatives are the precursors of biologically active compounds and medicines. In the present work the synthesis of a series of such valuable amines was realized by reduction of various Schiff's bases *via* catalytic hydrosilylation under mild conditions. The addition of $HSiEt_3$ to double C=N bond of trifluoromethyl derivatives of furan and thiophene aldimines **1a-h** and related compounds **1i-k** was investigated in the presence of numerous catalysts. The following transition metal complexes were studied: $(Ph_3P)_2IrCl(CO)$, $(Ph_3P)_4Pt$, $H_2PtCl_6{\cdot}6H_2O$, [Rh(COD)acac], $[Rh(COD)Cl]_2$, $RhCl_3{\cdot}4H_2O$, $(Ph_3P)_4Pd$, $[Pd(CH_2CHCH_2)Cl]_2$, $(Ph_3P)_2PdCl_2$, $(Ph_3P)_3RuCl_2$, and also supported metal catalysts 5% Pd/C and 5% Ru/Al_2O_3.



Two dimer complexes of Rh^I and Pd^I were found to be efficient catalysts of the reactions studied: $[Rh(COD)Cl]_2$ and $[Pd(CH_2CHCH_2)Cl]_2$ (more active). The activity of $[Rh(COD)Cl]_2$ was higher in THF than in benzene, while the rate of the reactions catalyzed by $[Pd(CH_2CHCH_2)Cl]_2$ was almost independent from the nature of the solvent.

Some regularities of the structure influence on the reactivity were found. The furan azomethines were more active than the thiophene ones. The 2-CH_3 group in heterocycle rings and 3-CF_3 in azo part of molecules moderate the reactions, on the contrary the 4-CF_3-group accelerates them. The activity of benzylidene anilines was lower than that of furan analoges but higher than for thiophene derivatives.

Compounds **2** were found to be the primary products of hydrosilylation. The unsaturated byproducts **3** formed as the result of dehydrogenative silylation of some imines.

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POSTER July 30 (Mon)

Asymmetric Addition of Me_3SiCN to Chiral Heterocyclic Aldimines

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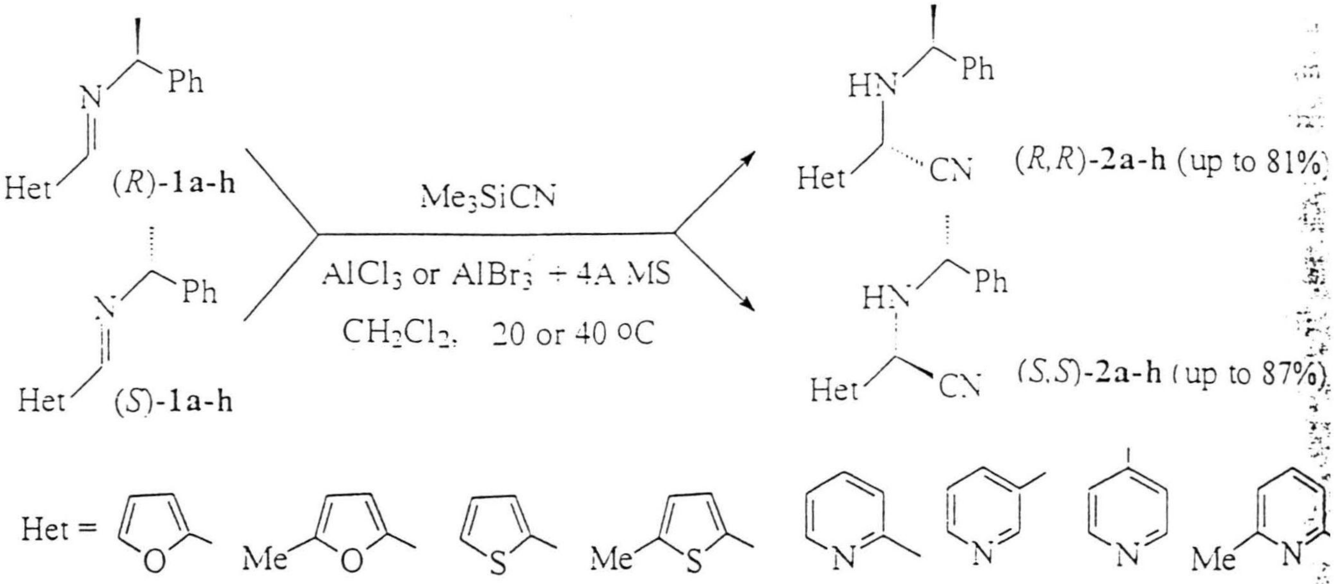
In course of our previous works (1, 2), the diastereoselective addition of trimethylsilyl cyanid optically active furan, thiophene and pyridine aldimines **1** derived from (*R*)- and (*S*)-1-phenylethylamine was investigated in the presence of Lewis acids ($AlCl_3$ or $AlBr_3$ together wit molecular sieves). A series of the corresponding diastereomer α-amino nitriles **2** was obtained fair to good yields (up to 91%). Unprecedently unsaturated nitriles were also formed from pyri imines. The mechanism of the reactions is proposed.



The sense of asymmetric induction and the degree of diastereoselectivity in the synthesis of **2** w determined by ^1H NMR and polarimetry. The reactions in all the cases afforded the mixtures of diastereomers, with one diastereomer predominating. The α-amino nitriles obtained from all the (*S*)-imines were levorotatory while from (*R*)-isomers afforded (+)-products. The diastereoisome ratios of α-amino nitriles obtained were determined by ^1H NMR. The signals of benzyl protons C<u>H</u>(Me)Ph which appeared as well separated quartets were used as the key signals. The downfie (major) at δ 4.15–4.27 signals were assigned to (*R,R*)- and (*S,S*)- anti-diastereomers and the upfi (minor) at δ 3.92–4.02 ppm to (*R,S*)- and (*S,R*)- syn-isomers. When the configuration of the nitrogen auxiliary was *R*, the (*R,R*)-α-amino nitriles predominated over (*S,R*)-isomer while the (*S,S*)-products of addition formed mainly from (*S*)-imines. Thus, the *Si* face addition occurred in cases giving the products in configurations (*R,R*)- (up to 81%) and (S,S)- (up to 87%) from (R)- (S)-imines, respectively.

1) Iovel, I.; Popelis, J.; Fleisher, M.; Lukevics, E. Tetrahedron: Asymmetry 1997, 8, 1279.
2) Iovel, I.; Golomba, L.; Belyakov, S.; Popelis, J.; Grinberga, S.; Lukevics, E. Appl. Organometal. Chem. 1999, 14, 721.

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BOOK OF ABSTRACTS

April 6-10, 2003
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The Netherlands

Catalytic addition of Me_3SiCN to novel heterocyclic aldimines

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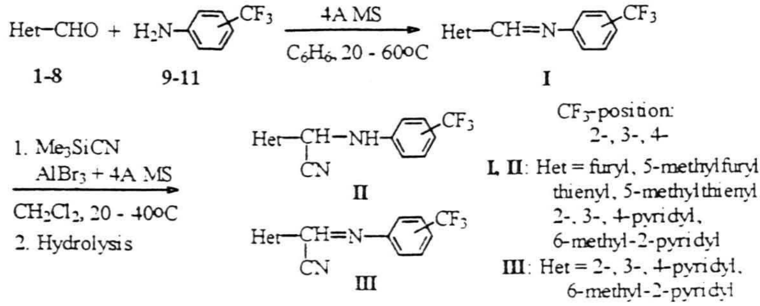
This work pursues our previous researches [1-3] of trimethylsilylcyanation of C=O and C=N double bonds of heterocyclic compounds. A series of novel Shiff bases **I** was synthesized by condensation of furan, thiophene and pyridine aldehydes (**1–8**) with 2-, 3- and 4-trifluoromethylanilines (**9–11**) in the presence of 4A molecular sieves (MS) acting as dehydration agent and the solid acid. The addition of Me_3SiCN to imines **I** has been studied in the presence of various Lewis acids. The most active catalyst among investigated appeared system $AlBr_3$ + 4A MS. A number of the corresponding trifluoromethyl derivatives of heterocyclic α-aminonitriles **II** was obtained. It was found that pyridine imines converted not only to expected compounds **II** but also to unsaturated nitriles **III**. The mechanism of the Lewis acid catalyzed addition of Me_3SiCN to heterocyclic imines will be discussed.



The single crystals of some aldimines and nitriles **I**, **II**, **III** were obtained and their structures were determined by X-ray diffraction.

Some nitriles containing CF_3 group were tested for their anticancer activity, and appeared good inhibitors of the growth of tumor cells in most cases. This fact evidences the perspective for further investigation of these compounds.

[1] I. Iovel, J. Popelis, M. Fleisher, E. Lukevics. *Tetrahedron: Asymmetry* **1997**, *8*, 1279.
[2] I. Iovel, L. Golomba, S. Belyakov, J. Popelis, S. Grinberga, E. Lukevics. *Appl. Organometal. Chem.* **2000**, *14*, 721-726.
[3] I. Iovel, L. Golomba, S. Belyakov, A. Kemme, E. Lukevics. *Appl. Organometal. Chem.* **2001**, *15*, 733.

Book of Abstracts

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Unusual Direction of Hydrosilylation of some Heterocyclic Aldimines Catalyzed by Pd^I and Rh^I Complexes

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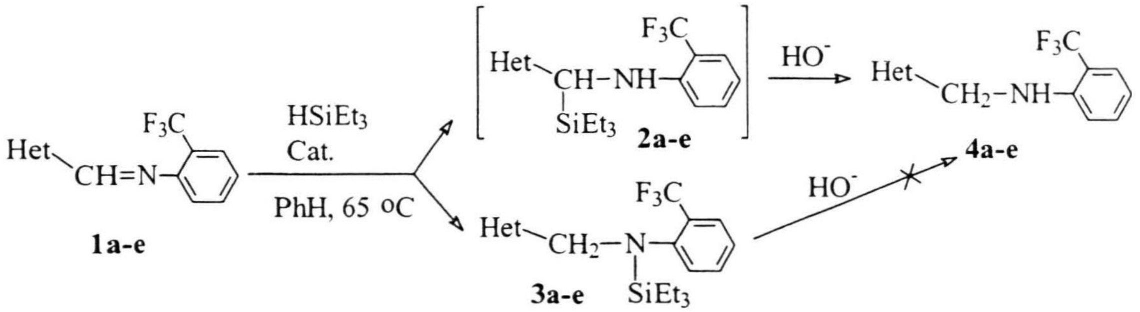
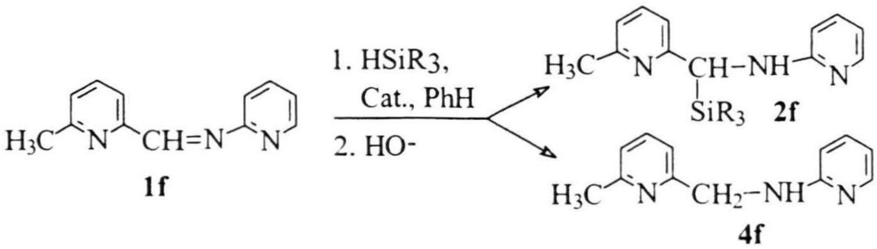
We have investigated the addition of hydrosilanes ($HSiEt_3$, $HSiMe_2Ph$, H_2SiPh_2) to the C=N bond of some furan, thiophene and pyridine azomethines in the presence of dimeric Pd^I and Rh^I complexes, $[Pd(allyl)Cl]_2$ and $[Rh(1,5\text{-cyclooctadiene})Cl]_2$.

Usually the hydrosilylation of imines leads to the saturated N-silyl derivatives which give the corresponding amines upon hydrolysis. In this work we have found for the first time that hydrosilylation of some heterocyclic imines leads to the formation of the products containing C–Si bond.



Het = 2-furyl, 5-methyl-2-furyl, 2-thienyl, 5-methyl-2-thienyl, 4-pyridyl



The proposed mechanism of the C-silylation of imines including the formation of the carbene complexes of the heterocyclic imines with the Pd or Rh catalysts (analogously to the Ref. [1]) will be discussed.

1. Ch. M. Standfest-Hauser, K. Mereiter, R. Schmid, K. Kirchner. *Organometallics* **2002**, *21*, 4891.