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Regioselective Addition of Trimethylsilyl Cyanide to β-Alkoxyvinyl Alkyl Ketones

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Abstract—The 1,2- and 1.4-addition reactions of trimethylsilyl cyanide to alkyl vinyl ketones were studied. Regioselectivity of this reaction depends on the structure of alkyl vinyl ketones, the reaction temperature and the nature of catalyst. The presence of alkoxy group in β-position of α,β-enone is the important condition for realization of 1,4-addition. Ambient temperature (25°C) or base catalyst (NEt_3) directed the reaction predominantly into 1,2-addition; higher temperature, electrophilic catalyst (I_2) and bulky alkyl substituents near the carbonyl group directed the reaction in 1,4-addition route. Hydrolysis of 1,4-adducts yields saturated fluorine-containing ketones containing CN- and ethoxy groups at the β-position. © 2000 Published by Elsevier Science Ltd.

Introduction

Introduction of fluorine atoms or fluorinated groups in organic molecules is well known to provoke significant and useful changes in their chemical and physical properties. These peculiarities of fluorine stimulate increasing activity in developing of new effective methods to prepare fluorine-containing compounds.[1] While direct perfluoroalkylation is the most attractive and powerful tool to construct desired compounds, perfluoro-containing synthons are often used as more accessible and convenient starting compounds.[2] Recently[3] we showed that trimethylsilyl cyanide (TMSCN) reacts with easily accessible *E*-4-ethoxy-1,1,1-trifluorobut-3-en-2-one[4] **1a** to give both 1,2- and 1,4-adducts, which are of interest as polyfunctional trifluoromethyl-containing building block. The use of low temperature or basic catalysts was demonstrated to direct the reaction predominantly by 1,2-addition route, and highs temperatures and acid catalysts direct the reaction to 1,4-addition.[3]

The addition of TMSCN to carbonyl compounds has been known for 25 years in organic synthesis in preparation of very useful compounds—silylated cyanohydrines.[5] Nevertheless the first attempts to realize conjugated addition of TMSCN to α,β-unsaturated carbonyl compounds led exclusively to formation of 1,2-addition products.[6] These results created previous statements, that TMSCN did not participate in conjugated addition.[7] Utimoto with coworkers[8] has first obtained 1,4-addition product of TMSCN to cyclohexenone in the presence of Lewis acids such as Et_3Al, ZnI_2 and $AlCl_3$. Recently Onaka et al.[9] reported that 1,4-adducts of TMSCN with some enones are formed in the presence of strong solid Lewis acids—Fe^{3+} and Sn^{4+} ion-exchanged montmorillonite, whereas 1,2-adducts are obtained in the presence of solid bases, such as CaO and MgO. On the other hand, there are only disparate and often contradictory communications about regioselectivity of TMSCN addition to α,β-unsaturated ketones with alkoxy group in β-position. For example, two different β-alkoxyvinyl alkyl ketones of cyclic structure reacted with TMSCN in the Lewis acid presence as 1,2-addition with ZnI_2 catalyst[10] and as 1,4-addition with $BF_3{\cdot}Et_2O$.[11] We found that the regioselectivity of TMSCN addition reaction to enone **1a** has high sensitivity to reaction conditions that allows synthesis of various fluorine-containing products.[3]

In this communication we describe the synthesis of new fluorinated synthons and the study of regioselectivity of the TMSCN addition to fluorine-containing and non-fluorine-containing α,β-unsaturated ketones (Scheme 1).

Results and Discussion

We investigated the temperature influence on regioselectivity of TMSCN addition reaction with enones **1a**–**h** (Table 1) in the absence of solvent at 20 and 145°C, as were previously shown by us,[3] in optimal conditions for preparation of 1,2-**3a** and 1,4-adducts **4a**, respectively. Difluoromethyl enone **1b** reacts with TMSCN at 20°C to give only 1,2-adduct **3b**. Increasing the number of fluorine atoms in the alkyl group bonded to the carbonyl (enones **1a**–**d**) increases the fraction of 1,4-adducts **4a**–**d** in the reaction

Keywords: addition reactions; regioselectivity; trimethylsilyl cyanide; enones; catalysis.

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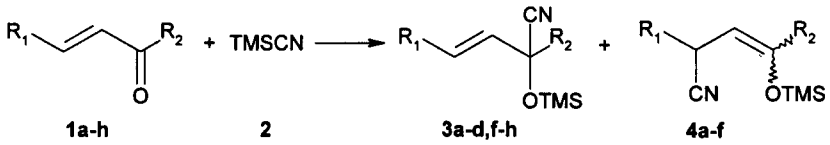


1a-h 2 3a-d,f-h 4a-f

	1,3,4							
	a	**b**	**c**	**d**	**e**	**f**	**g**	**h**
R_1	EtO	EtO	EtO	EtO	EtO	EtO	MeO	H
R_2	CF_3	CHF_2	C_2F_5	C_3F_7	$CH(CF_3)_2$	CCl_3	Me	Me

Scheme 1.

mixture from 0 (for **4b**) to 17% (**4d**). An increasing in the proportion of 1,4-adduct is induced by an increase in the size of the polyfluoroalkyl group near the carbonyl, that makes 1,2-addition difficult, and by some growth of the positive charge on the β-vinyl carbon atom,[12] that facilitates 1,4-addition. The presence of the bulky hexafluoroisopropyl group in enone **1e** results in complete absence of 1,2-adduct **3e** in the reaction products and in significant deceleration of the reaction rate (from 1–3 days to 1 month at 86% conversion). Furthermore, the adduct **4e** is isolated as a mixture of two *Z*- and *E*-isomers in 9:91 ratio, whereas enones **1a**–**d** give single *Z*-isomeric 1,4-adducts **4a**–**d**. The addition of TMSCN to trichloromethyl enone **1f** proceeds very slowly at 20°C (21% conversion in 1 month) and yields only 1,2-adduct **3f**. Such a low reaction rate can be explained by the presence of the bulky trichloromethyl group near the carbonyl centre (analogously enone **1e**), and 1,2-regioselectivity by electronic effects[12] (analogously to enone **1b**).

Methyl enone **1g** reacts also with TMSCN very slowly (22% conversion for 1 month) to yield a mixture of unidentified products, in which we could not detect adducts **3g** and **4g** by ^{1}H NMR spectroscopy. In that time, vinyl methyl ketone **1h**, which lacks the alkoxy group in β-position, decreasing the electrophilicity of C=O carbon atom, gives 1,2-adduct **3h** in high yield after five days only.

The double bond of the 1,2-products **3** retains the *E*-configuration: $^3J_{HH}$=12.5–13 Hz (Table 2). The configuration of 1,4-adducts **4** depends on the structure of fluoroalkyl group. Previously[3] we described *Z*-configuration for adduct **4a** on the basis of ^{13}C NMR spectra data. The analysis of ^{1}H NMR spectra of adducts **4a**–**d**,**f**, which are formed as single isomer, demonstrated that J_{H1H2} constants have values very close to 8.4–8.8 Hz (Table 2). The isomers of adduct **4e** have the value of J_{H1H2} in 8.5 and 7.6 Hz. This finding allows by us to assign *Z*-configuration for the isomers of 1,4-adducts **4a**–**e** with J_{H1H2}=8.4–8.8 Hz, and *E*-configuration for the isomer of adduct **4e** with J_{H1H2}=7.6 Hz.

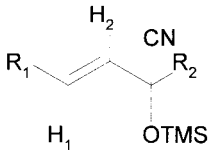
Increase of the reaction temperature from 20 to 145°C results in increase of both the reaction rate and 1,4-adduct portion in reaction products (Table 1). For a number of fluoro-containing enones **1a**–**d** increasing of fluorine atoms in acyl residue leads to an increase of 1,4-adduct share from 45 (for **1b**) to 100% (for **1d**), and the reaction time is decreased from 5.5 (for **1b**) to 2.5 h (for **1e**). At 145°C enones **1a**–**d**,**f** yield only *Z*-**4a**–**d**,**f** (as at 20°C), whereas enone **1e** gives 1,4-adduct **4e** as a mixture of *Z*/*E*-isomers in 33:67 ratio. Also trichloromethyl enone **1f** yields merely 1,4-adduct. The reaction of methyl enone **1g** with TMSCN at 145°C is accompanied by significant darkening of the reaction mixture and we did not detected signals of both 1,2- and 1,4-adducts in the ^{1}H NMR spectrum of the one but two doublets of *trans*-vinyl protons at

Table 1. Temperature influence on regioselectivity of the reaction between **1** and **2** (0.6 g (6.06 mM) **2** was added to 0.8 g (4.76 mM) **1** at corresponding temperature in sealed micro vial with GLC monitoring of the reaction mixture, product ratios were analyzed by ^{19}F and ^{1}H NMR spectroscopy)

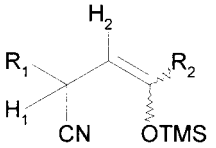
Entry	**1**	20°C				145°C			
		Time, day	Yield **3**+**4** (conv.)[a], %	Ratio		Time, h	Yield **3**+**4** (%)	Ratio	
				3	***Z*-4**			**3**	***Z*-4**
1	**a**	1	>99	95	5	3.8	85	18	82
2	**b**	3	>99	100	0	5.5	54	55	45
3	**c**	1	>99	90	10	3.5	84	3	97
4	**d**	1	>99	83	17	2.5	86	0	100
5	**e**	30	93(86)	0	100[b]	1.5	90	0	100[c]
6	**f**	30	>99(21)	100	0	4.5	72	0	100
7	**g**	30	0(22)	–	–	6.5	24[d]	0	100[d]
8	**h**	5	90	100	0	1.2	47	100	0

[a] If the conversion is 100%, it is not shown.
[b] Ratio *Z*/*E*=9:91.
[c] Ratio *Z*/*E*=33:67.
[d] 24% **6** is formed.

Table 2. ^{1}H and ^{19}F NMR spectra of **3** and **4** (chemical shifts δ, ppm, coupling constants J, Hz)

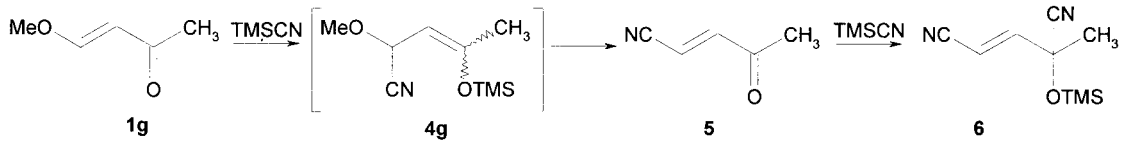


3a-d,f-h



4a-f

Entry	**3** or **4**	**3**					**4**				
		^{1}H NMR				^{19}F NMR	^{1}H NMR				^{19}F NMR
		H_1	H_2	TMS, s	Other		H_1	H_2	TMS, s	Other	
1	**a**	6.98 (d, 12.5)	4.83 (d, 12.5)	0.26	1.32 (t, 7.1, 3H), 3.85 (q, 7.1, 2H)	−82.0 (s)	5.57 (d, 8.4)	4.86 (d, 8.4)	0.29	1.27 (t, 7.0, 3H), 3.55 (dq, 8.7, 7.0, 1H), 3.81 (dq, 8.7, 7.0, 1H)	−72.66 (s)
2	**b**	6.90 (d, 12.5)	4.78 (d, 12.5)	0.24	1.31 (t, 7.2, 3H), 3.83 (q, 7.2, 2H), 5.56 (t, 56.1, 1H)	−130.77 (dd, 272.1, 56.1, 1F), −125.98 (dd, 272.1, 56.1, 1F)	5.29 (d, 8.5)	4.90 (d, 8.5)	0.27	1.28 (t, 7.1, 3H), 3.55 (dq, 8.7, 7.1, 1H), 3.80 (dq, 8.7, 7.1, 1H), 5.87 (t, 54.1, 1H)	−120.88 (d, 54.1)
3	**c**	7.00 (d, 13.0)	4.87 (d, 13.0)	0.28	1.36 (t, 7.0, 3H), 3.88 (q, 7.0, 2H)	−126.38 (d, 267.9, 1F), −118.79 (d, 267.9, 1F), −78.57 (s, 3F)	5.62 (d, 8.7)	4.88 (d, 8.7)	0.30	1.28 (t, 7.0, 3H), 3.55 (dq, 8.7, 7.0, 1H), 3.80 (dq, 8.7, 7.0, 1H)	−120.62 (s, 2F), −83.49 (s, 3F)
4	**d**	7.00 (d, 12.6)	4.88 (d, 12.6)	0.27	1.36 (t, 7.0, 3H), 3.87 (q, 7.0, 2H)	−124.55 (dd, 291.6, 10.6, 1F), −122.51 (dd, 291.6, 11.0, 1F), −122.07 (d.br.m, 275.9, 1F), −116.06 (d.'pent', 275.9, 11.0, 1F), −81.40 (t, 9.1, 3F)	5.6 (d, 8.5)	4.89 (dt, 8.5, 1.4)	0.30	1.28 (t, 7.0, 3H), 3.55 (dq, 8.8, 7.0, 1H), 3.80 (dq, 8.8, 7.0, 1H)	−126.99 (s, 2F), −117.95 (q, 9.8, 2F), −81.17 (t, 9.8, 3F)
5	*Z*-**e**	–	–	–	–	–	5.22 (d, 8.5)	4.90 (d, 8.5)	0.28	1.26 (t, 7.0, 3H), 3.56 (dq, 8.6, 7.0, 1H), 3.76 (dq, 8.6, 7.0, 1H), 4.03 (hept, 7.6, 1H)	−65.40 (m)
6	*E*-**e**	–	–	–	–	–	5.09 (d, 7.6)	4.70 (d, 7.6)	0.28	1.27 (t, 7.0, 3H), 3.58 (dq, 8.7, 7.0, 1H), 3.79 (dq, 8.7, 7.0, 1H), 4.14 (hept, 7.6, 1H)	−64.80 (qd, 8.9, 7.6, 3F), −64.25 (qd, 8.9, 7.6, 3F)
7	**f**	7.00 (d, 12.6)	5.04 (d, 12.6)	0.30	1.35 (t, 7.0, 3H), 3.87 (q, 7.0, 2H)	–	5.92 (d, 8.8)	4.79 (d, 8.8)	0.37	1.28 (t, 7.0, 3H), 3.55 (dq, 8.7, 7.0, 1H), 3.81 (dq, 8.7, 7.0, 1H)	–
8	**g**	6.81 (d, 12.6)	4.79 (d, 12.6)	0.22	1.65 (s, 3H), 3.55 (s, 3H)	–	–	–	–	–	–
9	**h**	5.54 (dd, 16.9, 1.2, 1H)	5.86 (dd, 16.9, 9.4, 1H)	0.22	1.63 (s, 3H), 5.26 (dd, 9.4, 1.2, 1H)	–	–	–	–	–	–



1g 4g 5 6

Scheme 2.

6.62 and 5.81 ppm with $^3J_{HH}$=16.1 Hz and the singlet of a methyl group at 1.69 ppm is observed, which we attributed to the trimethylsilyl ether of cyanohydrin **6**. A mixture of *E*- and *Z*-isomers of compound **6** was isolated by a catalytic variant of the reaction (see later). Formation of the latter can be possibly explained by initial 1,4-addition of TMSCN to methyl enone **1g** and subsequent elimination of TMSOMe from the unstable 1,4-adduct **4g** to give of ketone **5**, which, reacts with excess TMSCN and yields cyanohydrin **6** (Scheme 2). Thus, introduction of halogen atoms in acyl group of enones **1a**–**f** induces not only an increase of the 1,4-adduct content, but also an increase of stability of the latter in the reaction conditions. Vinyl methyl ketone **1h** gives at 145°C 1,2-adduct **3h** exclusively, as at 20°C.

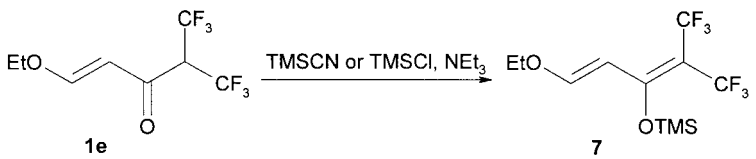
The influence of temperature on the regioselectivity of trimethylsilylcyanation of enones **1a**–**d**,**f** looks as a classic case of a reaction with kinetic (1,2-adducts) and thermodynamic (1,4-adducts) control. However as we have shown earler,[3] all our attempts to carry out an isomerization of **3a** to **4a** under various conditions:**3a** (with or without 2 equiv. of TMSCN) under heating (3 days at 145°C) or in the presence of catalysts (ZnI_2, I_2, $CF_3SO_3SiMe_3$; 1 week at room temperature) were unsuccessful. We observed only slow decomposition of **3a** without formation of any quantity of **4a**, indicating on absence or restriction of the equilibrium between **1a** and **3a** that can be rationalized as an increase of the cyanohydrine stability induced electron-withdrawing trifluoromethyl group or polyhaloalkyl groups for another cases. By these results, 1,2- and 1,4-adducts are kinetic products, on our opinion.

We investigated also the catalytic action of NEt_3 and I_2 on the reaction of enones **1a**–**h** with TMSCN (Table 3). We showed earlier that, these catalysts in 5% mol. concentration were the most effective in the addition reaction of TMSCN to enone **1a** at 20°C without solvent.[3] Fluorine-containing enones **1a**–**d** react very rapidly with TMSCN in the presence of catalytic amounts of NEt_3 in a few minutes. The product composition of the reaction is similar to the composition of the non-catalytic reaction at 20°C—an increase of fluorine atom number results in increasing of 1,4-adduct share from 0 (for **1a**,**b**) to 14% (for **1d**). The interaction of enone **1e** with TMSCN in the presence of NEt_3 does not afford the desired addition products **3e** and/or **4e**. In ^{19}F NMR spectra of the darkened reaction mixture there are two quartets of non-equivalent trifluoromethyl groups at −56.27 and −54.59 ppm with $^4J_{FF}$=9.8 Hz, and in ^{1}H NMR spectra the proton of hexafluoro-*iso*-propyl group is absent, that denotes a participation of the labile

Table 3. Influence of a catalyst on regioselectivity of the reaction between **1** and **2** (0.3 mM of corresponding catalyst was added to 0.6 g (6.06 mM) of **2** under stirring at RT, and then 0.8 g (4.76 mM) of **1** was added with GLC monitoring of the reaction mixture, products ratio were analyzed by ^{19}F and ^{1}H NMR spectroscopy)

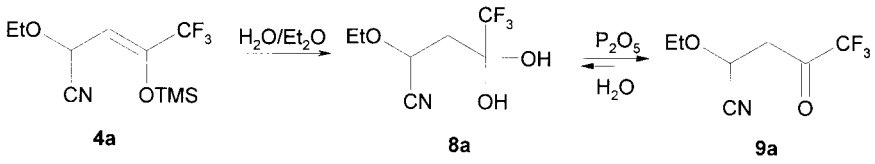
Entry	**1**	NEt_3				I_2			
		Time (min)	Yield **3**+**4** (conv.)[a], %	Ratio		Time (min)	Yield **3**+**4** (%)	Ratio	
				3	*Z*-**4**			**3**	*Z*-**4**
1	**a**	<1	95	100	0	<1	>97	0	100
2	**b**	<2	91	100	0	<2	95	3	97
3	**c**	3	95	93	7	<1	97	0	100
4	**d**	6	93	86	14	<1	95	0	100
5	**e**	<1	(100)[b]	–	–	<2	92	0	100[c]
6	**f**	<2	97	100	0	<2	94	0	100
7	**g**	3 day	26(28)	100	0	3	70[d]	0	100[d]
8	**h**	–[e]	–	–	–	<2	>99	100	0

[a] If the conversion is 100%, it is not shown.
[b] The yield of diene **7** is 28%.
[c] Ratio *Z*/*E*=24:76.
[d] The mixture: 50% **5** and 20% **6**.
[e] The reaction of TMSCN with **8h** with NEt_3 catalysis was not carried out considering the evidence of 1,2-adduct **3h** formation.



1e 7

Scheme 3.



Scheme 4.

α-proton in polyfluoroalkyl group of enone **1e** in the formation of unexpected diene **7** (Scheme 3). Our assumption about the formation of diene **7** in the reaction of enone **1e** with TMSCN in the presence of NEt_3 is endorsed by the synthesis of diene **7** in 79% yield by the reaction of enone **1e** with 2 equiv. TMSCl and 1.5 equiv. NEt_3. The addition of TMSCN to enones **1f** and **1g**, both in the presence and in the absence of NEt_3, gives exclusively 1,2-adducts **3f** and **3g**, but in the last case the reaction rate and the yield of adduct **3g** were low. In this case we could not isolate 1,2-adduct **3g** in a pure state, and its formation was estimated only by ^1H NMR spectroscopy.

Using I_2 as a catalyst for the TMSCN addition with enones **1a**–**g** directs the reaction to the 1,4-route preferentially. Only 3% of 1,2-adduct **3b** is formed in the case of enone **1b**, whereas other halogenated enones **1a**,**c**–**f** yield exclusively 1,4-adducts **3a**,**c**–**f**. In the case with enone **1g** in the reaction mixture we did not observe also 1,2-adduct **3g**, but ketone **5**[13] (50%) and cyanohydrine **6** (20%) were detected, which are formed from 1,4-adduct **4g**, which is unstable under the reaction conditions (overall yield for 1,4-addition was 70%) (Scheme 2). Increase of TMSCN quantity to 2.5 equiv. in iodine catalyzed addition reaction to enone **1g** results in complete transformation of ketone **5** into cyanohydrine **6**, and the mixture of *E*- and *Z*-isomers (ratio *E*/*Z*=77:23) of the latter was obtained after vacuum distillation of complex reaction mixture. Vinyl methyl ketone **1h** gives 1,2-adduct **3h** exclusively, that demonstrates an importance of the alkoxy group presence in β-position of α,β-unsaturated ketones to pass the TMSCN addition reaction by 1,4-route.

A number of synthesized 1,2- and 1,4-adducts of TMSCN to enones **1a**–**h** were obtained in pure state in high yields, that certainly will allow application of the products as accessible and useful synthons. These compounds can be stored for a long time at room temperature without destruction. 1,2-Adducts are stable to water action in the absence of acids, whereas the trimethylsilyl group in 1,4-adducts is hydrolyzed slowly by atmospheric moisture. For example, hydrate **8a** is obtained from the adduct **4a** (Scheme 4).

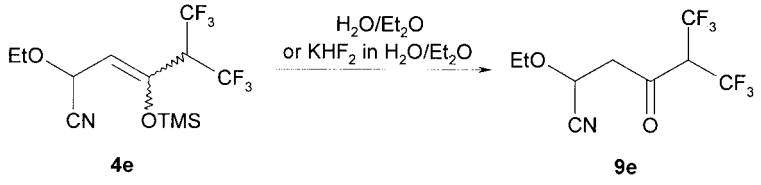
Interaction of the adduct **4a** with a stoichiometric quantity of H_2O in Et_2O results mainly in the formation of hydrate **8a** with partial conversion of **4a**, and with an excess of H_2O in Et_2O we obtained hydrate **8a**, from which ketone **9a** was synthesized by action of P_2O_5. In $CDCl_3$ solution hydrate **8a** exists in an equilibrium with ketone **9a** (ratio **8a**:**9a** is 3:1), whereas in more polar acetone-d_6 we find only signals of hydrate **8a**.

While under the action of excess H_2O in Et_2O on 1,4-adduct **4e**, which is a mixture of *Z* and *E* isomers in 24:76 ratio, only the *Z*-isomer **4e** is hydrolyzed and gives a mixture of ketone **9e** and *E*-isomer **4e** in the same ratio, the *E*-isomer of adduct **4e** is able to hydrolyze by action of more potent desilylation reagents such as aqueous solution of KHF_2 (Scheme 5). Thus, *Z*- and *E*-isomers of **4e** have different stability to hydrolysis, whereas similar reactivity of *Z*-isomeric adducts **4a** and **4e** supports the determination of isomeric geometry for 1,4-adduct **4e**, which has been estimated by ^1H NMR spectra.

In summary, we have studied the reaction and regioselectivity of TMSCN addition to enones **1a**–**h**, which is very sensitive to the ketone structure and the reaction conditions. Thus, one of the basic conditions needed for realization of TMSCN 1,4-addition to acyclic enones is the presence of an alkoxy group in the β-position to the carbonyl group. Increase of steric hindrance near the carbonyl group or increase of electron acceptor character of the acyl residue directs mainly the reaction in a 1,4-direction. Higher temperature and electrophilic catalysts facilitate also TMSCN 1,4-addition, whereas nucleophilic catalysts accelerate both 1,2- and 1,4-addition in nearly equal extent. The high regioselectivity of the TMSCN addition to enones **1a**–**h** and the accessibility of fluorine-containing adducts may be useful in application of these reactive compounds to effective synthesis of bioactive fluorine-containing substances.

Experimental

^1H and ^{19}F NMR spectra were measured at 300 and 282.24 MHz in $CDCl_3$ solution (if not stated elsewhere) using tetramethylsilane (TMS) and $CFCl_3$ as the internal



Scheme 5.

standards, respectively. Column used for GLC analysis: 3.3 m×3 mm i.d. steel column packed with 5% SE-30 on Chromaton N-AW-DMCS. The GLC analysis was performed on Chrom-5 (Prague, Czechoslovakia) with FID and nitrogen as gas-carrier. Enones **1a–f** were prepared via acylation reaction.[12] Enones **1g–h** were purchased from Fluka Chemical Co. and were distilled prior use. TMSCN and TMSCl were purchased from Fluka Chemical Co. Where necessary, solvents and reagents were dried and purified according to recommended procedures.[14] Synthesis of compounds **3a** and **4a** were reported earlier.[3]

General procedure for the preparation of 1,2-adducts 3b–d,f

To a mixture of 50 mg (0.5 mmol) Et_3N and 1.29 g (13 mmol) TMSCN was added 10 mmol of ketone **1a–d,f** under stirring and at 0–5°C. Then the mixture was stirred for 15 min, and the product was isolated by vacuum distillation.

General procedure for the preparation of 1,4-adducts 4b–f and 1,2-adduct 3h

To a mixture of 130 mg (0.5 mmol) I_2 and 1.29 g (13 mmol) TMSCN was added 10 mmol of ketone **1a–f,h** under stirring. The reaction mixture was warmed up to 50–60°C. Then the mixture was stirred for 15 min and the product was isolated by vacuum distillation.

(*E*)-2-Difluoromethyl-4-ethoxy-2-trimethylsilyloxy-3-butenenitrile (3b). 80% Yield; bp 103–105°C/15 mmHg. Anal. Calcd for $C_{10}H_{17}F_2NO_2Si$: C, 48.17; H, 6.87; N, 5.62. Found: C, 48.05; H, 6.99; N, 5.56.

(*E*)-4-Ethoxy-2-pentafluoroethyl-2-trimethylsilyloxy-3-butenenitrile (3c). 74% Yield; bp 93–95°C/18 mmHg; Anal. Calcd for $C_{11}H_{16}F_5NO_2Si$: C, 41.64; H, 5.08; N, 4.41. Found: C, 41.56; H, 5.16; N, 4.49.

(*E*)-4-Ethoxy-2-(1,1,2,2,2,3,3,3-heptafluoropropyl)-2-trimethylsilyloxy-3-butenenitrile (3d). 66% Yield; bp 102–103°C/17 mmHg. Anal. Calcd for $C_{12}H_{16}F_7NO_2Si$: C, 39.24; H, 4.39; N, 3.81. Found: C, 39.33; H, 4.28; N, 3.73.

(*E*)-4-Ethoxy-2-trichloromethyl-2-trimethylsilyloxy-3-butenenitrile (3f). 88% Yield; bp 149–151°C/19 mmHg. Anal. Calcd for $C_{10}H_{16}Cl_3NO_2Si$: C, 37.93; H, 5.09; N, 4.42. Found: C, 37.81; H, 5.21; N, 4.50.

(*E*)-2-Methyl-2-trimethylsilyloxy-3-butenenitrile (3h). 90% Yield; bp 84–85°C/14 mmHg. Anal. Calcd for $C_8H_{15}NOSi$: C, 56.76; H, 8.93; N, 8.27. Found: C, 56.89; H, 8.86; N, 8.19.

(*Z*)-2-Ethoxy-5,5-difluoro-4-trimethylsilyloxy-3-pentenenitrile (4b). 83% Yield; bp 116–118°C/16 mmHg. Anal. Calcd for $C_{10}H_{17}F_2NO_2Si$: C, 48.17; H, 6.87; N, 5.62. Found: C, 48.03; H, 6.81; N, 5.56.

(*Z*)-2-Ethoxy-5,5,6,6,6-pentafluoro-4-trimethylsilyloxy-3-hexenenitrile (4c). 89% Yield; bp 94–96°C/12 mmHg. Anal. Calcd for $C_{11}H_{16}F_5NO_2Si$: C, 41.64; H, 5.08; N, 4.41. Found: C, 41.49; H, 5.17; N, 4.36.

(*Z*)-2-Ethoxy-5,5,6,6,7,7,7-heptafluoro-4-trimethylsilyloxy-3-heptenenitrile (4d). 85% Yield; bp 113–115°C/23 mmHg. Anal. Calcd for $C_{12}H_{16}F_7NO_2Si$: C, 39.24; H, 4.39; N, 3.81. Found: C, 39.12; H, 4.31; N, 3.77.

2-Ethoxy-6,6,6-trifluoro-5-trifluoromethyl-4-trimethylsilyloxy-3-hexenenitrile (mixture of isomers, ratio *Z*/*E*=24:76) (4e). 81% Yield; bp 99–101°C/11 mmHg. Anal. Calcd for $C_{12}H_{17}F_6NO_2Si$: C, 41.26; H, 4.90; N, 4.01. Found: C, 41.34; H, 4.82; N, 3.96.

(*Z*)-5,5,5-Trichloro-2-ethoxy-4-trimethylsilyloxy-3-pentenenitrile (4f). 79% Yield; bp 151–153°C/12 mmHg. Anal. Calcd for $C_{10}H_{16}C_{l3}NO_2Si$: C, 37.93; H, 5.09; N, 4.42. Found: C, 37.99; H, 5.01; N, 4.34.

4-Methyl-4-trimethylsilyloxy-2-pentenedinitrile (6) (mixture of isomers). To a suspension of 5 mg I_2 in 2.50 g (25.3 mmol) of TMSCN was added 1.00 g (10.0 mmol) of enone **1g** under stirring and at 20–30°C. After 30 min the reaction mixture was distilled. The yield of **6** was 1.24 g (64%), ratio *E*/*Z*=77:23, bp 106–108°C/16 mmHg; (*E*)-**6**:^{1}H NMR δ: 0.26 (s, 9H), 1.69 (s, 3H), 5.82 (d, *J*=16.1 Hz, 1H), 6.62 (d, *J*=16.1 Hz, 1H). (*Z*)-**6**:^{1}H NMR δ: 0.33 (s, 9H), 1.76 (s, 3H), 5.55 (d, *J*=11.7 Hz, 1H), 6.37 (d, *J*=11.6 Hz, 1H).

(1*E*)-1-Ethoxy-3-trimethylsilyloxy-5,5,5-trifluoro-4-trifluoromethyl-1,3-pentadiene (7). To a solution of **1e** (0.78 g, 3.12 mmol) and TMSCl (0.68 g, 6.27 mmol) in 6 mL of hexane was added a solution of NEt_3 (0.43 g, 4.26 mmol) in 2 mL hexane under stirring and at 0–5°C. The mixture was stood overnight at 0°C, and the resulting precipitate was filtered off, the filtrate was concentrated, and the residue was distilled under reduced pressure. The yield of **7** was 0.79 g (79%), bp 80–82°C/11 mmHg; ^{1}H NMR δ: 0.28 (s, 9H), 1.36 (t, *J*=7.0 Hz, 3H), 3.93 (q, *J*=7.0 Hz, 2H), 5.78 (d, *J*=12.2 Hz, 1H), 7.10 (d, *J*=12.2 Hz, 1H); ^{19}F NMR δ: −56.27 (q, *J*=9.8 Hz, 3F), −54.59 (q, *J*=9.8 Hz, 3F). Anal. Calcd for $C_{11}H_{16}F_6O_2Si$: C, 40.99; H, 5.00. Found: C, 40.83; H, 5.11.

2-Ethoxy-5,5,5-trifluoro-4,4-dihydroxypentanenitrile (8a). To a solution of **4a** (2.67 g, 10 mmol) in 10 mL of Et_2O was added H_2O (0.36 g, 20 mmol) and the mixture was stirred 30 min at 25°C. Then a solvents were evaporated under vacuum, and the residue was crystallized. The yield of **8a** was 2.12 g (>99%), mp 68–69°C (hexane/Et_2O=1:1); ^{1}H NMR (acetone-d_6) δ: 1.25 (t, *J*=7.0 Hz, 3H), 2.31 (br.dd, *J*=14.5, 7.2 Hz, 1H), 2.41 (br.dd, *J*=14.5, 5.6 Hz, 1H), 3.67 (dq, *J*=9.2, 7.0 Hz, 1H), 3.85 (dq, *J*=9.2, 7.0 Hz, 1H), 4.79 (dd, *J*=7.2, 5.6 Hz, 1H), 6.05 (br.s, 1H), 6.39 (br.s, 1H); ^{19}F NMR (acetone-d_6) δ: −85.51 (br.s). Anal. Calcd for $C_6H_9F_3O_3$: C, 38.72; H, 4.87. Found: C, 38.66; H, 4.98. IR($CHCl_3$) cm^{-1}:3576 $(OH)_{free}$, 3464 $(OH)_{bonded}$.

2-Ethoxy-5,5,5-trifluoro-4-oxopentanenitrile (9a). To a suspension of P_2O_5 (2.20 g, 15.5 mmol) in 20 mL of Et_2O was added hydrate **8a** (1.10 g, 5.2 mmol), and the mixture was stirred 2 h at 25°C. Then the solution was decanted, and the rest was washed 2×5 mL CH_2Cl_2. Organic phases were combined and concentrated under vacuum. A residue was distilled in vacuum. The yield of **9a** was 0.82 g (81%), bp

70–73°C/25 mmHg; ^{1}H NMR δ: 1.23 (t, J=7.0 Hz, 3H), 3.12 (dd, J=18.7, 5.3 Hz, 1H), 3.40 (dd, J=18.7, 7.6 Hz, 1H), 3.57 (dq, J=8.8, 7.0 Hz, 1H), 3.85 (dq, J=8.8, 7.0 Hz,1H), 4.64 (dd, J=7.6, 5.3 Hz, 1H); ^{19}F NMR δ: −79.96 (s). Anal. Calcd for $C_6H_7F_3O_2$: C, 42.87; H, 4.20. Found: C, 42.78; H, 4.26. IR(CCl_4) cm^{-1}: 1777 (C═O).

2-Ethoxy-6,6,6-trifluoro-4-oxo-5-(trifluoromethyl)hexanenitrile (9e). To a solution of **4e** (ratio of isomers *Z*/*E*=24:76) (1.26 g, 3.61 mmol) in 5 mL of Et_2O were added H_2O (1.0 mL, 55.6 mmol) and KHF_2 (0.40 g, 5.1 mmol), and the mixture was stirred 1 h at 25°C. An organic layer was separated and dried $MgSO_4$. A solvent was evaporated, and the residue was distilled in vacuum. The product crystallizes in refrigerator. The yield of **9e** was 0.80 g (80%), bp 84–86°C/16 mmHg; ^{1}H NMR δ: 1.23 (t, J=7.0 Hz, 3H), 3.11 (dd, J=17.8, 4.5 Hz, 1H), 3.32 (dd, J=17.8, 8.3 Hz, 1H), 3.56 (dq, J=8.9, 7.0 Hz, 1H), 3.85 (dq, J=8.9, 7.0 Hz, 1H), 4.14 (sept., J=7.7 Hz, 1H), 4.63 (dd, J=8.3, 4.5 Hz, 1H); ^{19}F NMR δ: −63.60 (dm, J=7.7 Hz). Anal. Calcd for $C_9H_9F_6NO_2$:C, 39.00; H, 3.27; N, 5.05. Found: C, 38.78; H, 3.32; N, 4.94. IR(CCl_4) cm^{-1}: 1754 (C═O).

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