ELSEVIER

Journal of Fluorine Chemistry 72 (1995) 1–7

JOURNAL OF FLUORINE CHEMISTRY

Reactivity of β-(trifluoromethyl) acroleins towards primary alkyl (or aryl) amines: synthesis of (trifluoromethyl)-1-aza-1,3-dienes and secondary (trifluoromethyl) allylamines

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Received 28 October 1993; accepted 18 June 1994

Abstract

Vilsmeier's reaction on trifluoroketones leads to β-chloro-β-(trifluoromethyl)acroleins. The addition of primary alkyl- or aryl-amines to these acroleins leads in all cases to the formation of stable (trifluoromethyl)-1-aza-1,3-dienes which can be transformed quantitatively into secondary (trifluoromethyl) allylamines by reduction with sodium borohydride.

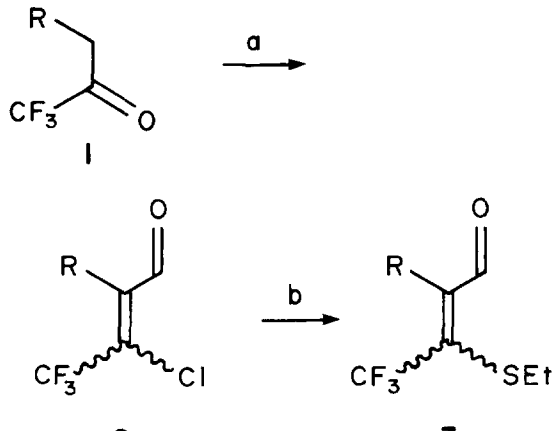
Keywords: β-(Trifluoromethyl)acroleins; (Trifluoromethyl)-1-aza-1,3-dienes; Secondary (trifluoromethyl) allylamines; NMR spectroscopy; IR spectroscopy; Mass spectrometry

1. Introduction

Increasing interest has been paid for several years to the chemistry of organic trifluoromethyl compounds due to their unique physical properties, their specific chemical reactivity and their potential biological activity [1]. The influence of the trifluoromethyl group is often associated with increased lipophilicity. Furthermore, its electronegativity and relatively small size (only two and a half times the volume of a methyl group) are also important factors. The literature reports several syntheses of unfluorinated 1-aza-1,3-dienes [2], and we now report a general synthesis of trifluoromethylated 1-aza-1,3-dienes and their transformation into trifluoromethylated secondary allylamines.

2. Results and discussion

Recently, in a short communication [3], we reported the synthesis of 3-chloro-3-trifluoromethyl-acroleins **2** available from the Vilsmeier reaction on trifluoromethylketones **1** (Scheme 1). Compounds **2** can be converted into 3-ethylthio-3-(trifluoromethyl)acroleins **3** by reaction with ethane thiolate (EtSH/NaH).



Scheme 1. (a) DMF, $POCl_3$ or $COCl_2$; (b) EtSH/NaH, THF.

In all cases, the Vilsmeier reaction gives a mixture of *E*/*Z* geometric isomers. Assignment of the *E*/*Z* configuration can be readily achieved because only one exhibits a coupling constant [$J(^1H–^{19}F)\times 0$] between fluorines and aldehydic protons. It also shows a positive heteronuclear NOE between the fluorine atom and the aldehydic proton. Hence the isomer with $J(^1H–^{19}F)\times 0$ is the *E*-isomer (*J*-range = 1.8–5.5 Hz) and the isomer without a coupling constant, i.e. $J(^1H–^{19}F)=0$, is the

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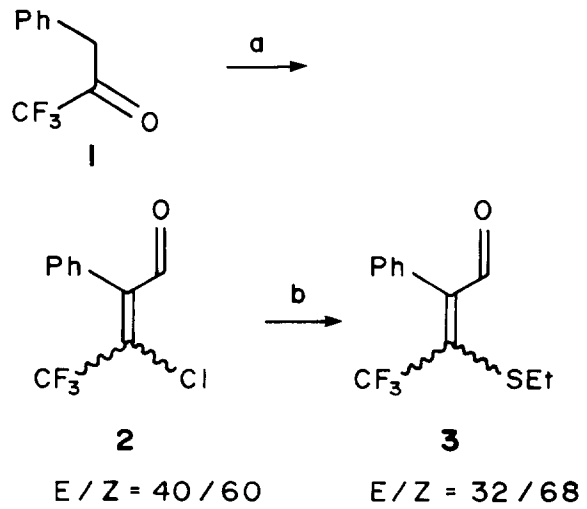
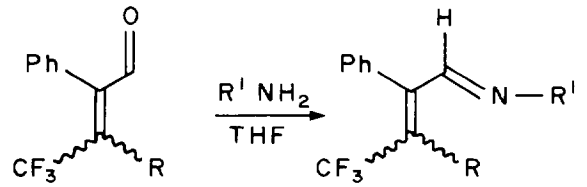
SSDI 0022-1139(94)03166-5



Scheme 2. (a) DMF, $POCl_3$ or $COCl_2$; (b) EtSH/NaH, THF.

Table 1
Addition of primary alkyl (or aryl) amines to trifluoro-acrolein



2 R = Cl
3 R = SEt

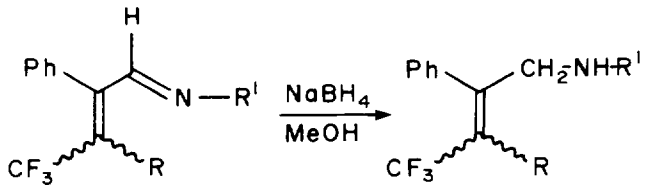
4 R = Cl
5 R = SEt

Entry	R group	R' group	Reaction time (h)	Yield (%)
a	Cl	CH_3	16	63
b	Cl	^{i}Bu	16	95
c	Cl	^{t}Bu	24	87
d	Cl	$(CH_2)_2SH$	15	77
e	Cl	Ph	5	85
f	Cl	*o*-C_6H_4SH	3	88
g	Cl	CH_2Ph	16	85
h	Cl	$N(CH_3)_2$	16	80
i	Cl	NHPh	16	60
j	SEt	CH_3	12	85
k	SEt	propyl	15	85

Z-isomer. On starting from benzyltrifluoromethyl-ketone (**1**), the Vilsmeier reaction gives a mixture of the *E*/*Z* isomers of **2** in a 40:60 ratio (overall yield = 91%) which can be converted into a 32:68 mixture of the *E*/*Z* isomers of the ethylthio compounds **3** (overall yield = 90%) (Scheme 2).

Treatment of acroleins **2** or **3** with an equimolar amount of primary alkyl- or aryl-amine or hydrazone in THF at room temperature leads to their complete transformation into (trifluoromethyl)-1-aza-1,3-dienes **4** or **5**. The latter (Table 1), in contrast to their non-fluorinated analogues [2], are very stable and can be readily purified by column chromatography over SiO_2.

Table 2
Reduction of 1-aza-1,3-dienes by $NaBH_4$ in MeOH



4 R = Cl
5 R = SEt

6 R = Cl
7 R = SEt

Entry	R group	R' group	Reaction time (h)	Yield (%)
a	Cl	CH_3	12	93
b	Cl	^{i}Bu	16	99
c	Cl	^{t}Bu	12	97
e	Cl	Ph	12	95
g	Cl	CH_2Ph	12	95
i	SEt	CH_3	12	89
k	SEt	propyl	12	92

Allylamines are both useful synthetic intermediates and common structural elements in natural products, but they are only available via a relatively limited number of procedures [4]. However, various syntheses of primary allylamines have been developed because of their synthetic potential, their presence in several natural products [4b] and their physiological activity [5]. Tertiary allylamines are more readily accessible but the secondary compounds are not very easy to prepare [6]. There has been no report of the synthesis of the trifluoro analogues of allylamines. Recently Mison et al. [7] proposed a few examples of the synthesis of primary trifluoro-allylamines and -allylamides. Since then we have tested the possibility of transforming our 1-aza-1,3-dienes into secondary allylamines. The reduction of 1-aza-1,3-dienes by sodium borohydride in methanol leads almost quantitatively, in all cases, to the formation of the corresponding secondary stable trifluoromethylated allylamines **6** or **7** (Table 2).

^1H, ^{19}F and ^{13}C NMR, IR and mass spectral data, together with elemental analyses, for the various (trifluoromethyl)-1-aza-1,3-dienes and trifluoromethylated allylamines prepared are listed in Tables 3–10, respectively.

3. Experimental details

3.1. General

^1H NMR spectra were recorded either on a Varian EM 360 (60 MHz), Bruker AC 200 (200.13 MHz) or

Table 3
IR and ^{19}F NMR spectra of 1-aza-1,3-dienes **4** and **5**

Entry	R group	R^1 group	IR spectrum (cm^{-1})	^{19}F NMR spectrum (ϕ, ppm; J, Hz)	
				Major (Z)	Minor (E)
a	Cl	CH_3	1635 (C=N); 1190, 1145 (C–F)	−60.6	−58.3 [d, $J(^1H–^{19}F)=1.6$]
b	Cl	^{t}Bu	1630 (C=N); 1180 (C–F)	−60.6	−58.5 [d, $J(^1H–^{19}F)=1.6$]
c	Cl	^{t}Bu	1640 (C=N); 1210 (C–F)	−59.5	−60.8 [d, $J(^1H–^{19}F)=1.9$]
d	Cl	$(CH_2)_2SH$	1630 (C=N)	−61.2	
e	Cl	Ph	1640 (C=N); 1180 (C–F)	−59.5	−60.8 [d, $J(^1H–^{19}F)=1.9$]
f	Cl	o-C_6H_4SH	1640 (C=N); 1210 (C–F)	−58.9	−61.6
g	Cl	CH_2Ph	1640 (C=N); 1230 (C–F)	−58.6	−60.1
h	Cl	$N(CH_3)_2$	1120 (C–F)	−56.1	−55.7
i	Cl	NHPh	3325 (N–H); 1610 (C=N); 1135 (C–F)	−58.2	−59.6
j	SEt	CH_3	1630 (C=N); 1190 (C–F)	−54.6	−57.3
k	SEt	propyl	1620 (C=N); 1180 (C–F)	−55.4	−55.7

Table 4
^{13}C NMR of 1-aza-1,3-dienes **4** and **5**

Entry	R group	R^1 group	Z/E ratio	^{13}C NMR spectrum (δ, ppm; J, Hz)
a	Cl	CH_3	59:41	Z: 47.8 (CH_3); 161.2 (CH) E: 47.6 (CH_3); 158.4 (CH)
b	Cl	^{t}Bu	62:38	Z: 20.97 (CH_3); 29.5 (CH); 46.9 (CH_2); 159.58 (CH) E: 20.90 (CH_3); 27.0 (CH); 46.9 (CH_2); 156.97 (CH)
c	Cl	^{t}Bu	60:40	Z:29.8 (CH_3); 117.5 [q, ^1J(C–F)=278, CF_3]; 156.25 (CH) E: 29.8 (CH_3); 117.5 [q, ^1J(C–F)=278, CF_3]; 159.40 (CH)
d	Cl	$(CH_2)_2SH$	69:31	Z: 34.8 (CH_2); 62.1 (CH_2); 119.8 [q, ^1J(C–F)=276, CF_3)]; 162.1 (CH) E: 35.2 (CH_2); 64.2 (CH_2); 120.6 [q, ^1J(C–F)=276, CF_3]; 164.3 (CH)
e	Cl	Ph	80:20	Z: 122.0 [q, J(C–F)=276, CF_3)]; 127–132 (m); 156.1 (CH) E: 124.1 [q, J(C–F)=276, CF_3]; 127–132 (m); 154.0 (CH)
f	Cl	o-C_6H_4SH	65:35	– –
g	Cl	CH_2Ph	75:25	Z: 51.8 (CH_2); 120–126 (m); 160.4 (CH) E: 53.1 (CH_2); 120–126 (m); 161.3 (CH)
h	Cl	$N(CH_3)_2$	71:29	– –
i	Cl	NHPh	58:43	– –
j	SEt	CH_3	75:25	Z: 15.2 (CH_3); 30.72 (CH_2); 118–124 (m); 159.8 (CH) E: 15.2 (CH_3); 31.2 (CH_2); 118–124 (m); 157.7 (CH)
k	SEt	propyl	73:27	Z: 11.74 (CH_3); 14.59 (CH_3); 23.78 (CH_2); 30.85 (CH_2); 60.04 (CH_2); 123.25 [q, ^1J(C–F)=275.5, CF_3]; 127–132 (m); 136.59 (Cq phenyl); 152.59 (Cq); 162.32 (CH) E: 11.63 (CH_3); 14.31 (CH_3); 23.69 (CH_2); 28.78 (CH_2); 64.19 (CH_2); 123.56 [q, ^1J(C–F)=276.9, CF_3]; 127–132 (m); 137.44 (Cq phenyl); 150.90 (Cq); 159.13 (CH)

Table 5
^{1}H NMR spectra of 1-aza-1,3-dienes **4** and **5**

Entry	R group	R^1 group	^{1}H NMR spectrum (δ, ppm; J, Hz)		$CH{=}NR^1$
a	Cl	CH_3	*Z*: 3.30 (s, CH_3); 6.88–7.42 (m, 5H) *E*: 3.28 (s, CH_3); 6.88–7.42 (m, 5H)		*Z*: 8.56 (s) *E*: 8.40 [q, J(H–F) = 1.6]
b	Cl	^{t}Bu	*Z*: 0.84 (t, 3H, J = 6.71); 1.9 (m, 1H); 3.3 (t, 2H, J = 6.71); *E*: 1.05 (t, 3H, J = 6.64; 2.1 (m, 1H); 3.1 (t, 2H, J = 6.64);	7–7.6 (m, 5H)	*Z*: 8.30 (s) *E*: 8.50 [q, J(H–F) = 1.2]
c	Cl	^{t}Bu	*Z*: 1.21 (s, 9H); 6.8–7.5 (m, 5H) *E*: 1.10 (s, 9H; 6.8–7.5 (m, 5H)		*Z*: 8.72 (s) *E*: 8.52 [q, J(H–F) = 1.3]
d	Cl	$(CH_2)_2SH$	*Z*: 2.75 (t, 2H, J = 8); 3.20 (t, 2H, J = 8); 5.9 (s, sH); *E*: 2.81 (t, 2H, J = 8); 3.22 (t, 2H, J = 8); 5.9 (s, SH);	7.1–7.6 (m, 5H)	*Z*: 8.81 (s) *E*: 8.62 [q, J(H–F) = 1.3]
e	Cl	Ph	*Z*: 7.1–7.7 (m, 10H) *E*: 7.1–7.7 (m, 10H)		*Z*: 9.0 (s) *E*: 8.8 [q, J(H–F) = 1.4]
f	Cl	*o*-C_6H_4SH	4.42 (s, SH); 7.25–8.0 (m, 10H)		8.10(s)
g	Cl	CH_2Ph	3.78 (s, 2H); 7.00–7.7 (m, 10H)		8.78(s)
h	Cl	$N(CH_3)_2$	2.93 (s, 6H); 7.00–7.46 (m, 6H)		
i	Cl	NHPh	6.55–7.50 (m, 10H); 8.0 (s, NH)		8.8 (s)
j	SEt	CH_3	*Z*: 1.2 (t, 3H, J = 7.0); 2.6 (q, 2H, J = 7.0); 3.48 (s, 3H); *E*: 1.4 (t, 3H, J = 7.0); 2.95 (q, 2H, J = 7.0); 3.48 (s, 3H);	7.1–7 (m, 5H)	*Z*: 9.2 (s) *E*: 8.75 (m)
k	SEt	propyl	*Z*: 0.86 (t, 3H, J = 7.3); 1.34 (t, 3H, J = 7.3); 1.59 (sext, 2H, J = 7.3); 2.84 (q, 2H, J = 7.3); 3.55 (t, 2H, J = 7.3); 7.1–7.4 (m, 5H). *E*: 0.86 (t, 3H, J = 7.3); 1.09 (t, 3H, J = 7.3); 1.59 (sext, 2H, J = 7.3); 2.64 (q, 2H, J = 7.3); 3.51 (t, 2H, J = 7.3); 7.1–7.4 (m, 5H).		*Z*: 8.89 (s) *E*: 8.45 [q, J(H–F) = 1.35]

Table 6
IR and ^{19}F NMR spectra of allylamines **6** and **7**

Entry	R group	R^1 group	IR spectrum (cm^{-1})	^{19}F spectrum (ϕ, ppm)	
				Major (*Z*)	Minor (*E*)
a	Cl	CH_3	3325 (N–H); 1210–1180 (C–F)	−60.00	−58.83
b	Cl	^{i}Bu	3330 (N–H); 1190–1170 (C–F)	−60.6	−58.5
c	Cl	^{t}Bu	3335 (N–H); 1220 (C–F)	−60.83	−59.50
d	Cl	Ph	3300 (N–H); 1210–1190 (C–F)	−62.0	−60.8
e	Cl	CH_2Ph	3300 (N–H); 1210–1180 (C–F)	−60.1	−58.6
f	SEt	CH_3	3335 (N–H); 1200–1180 (C–F)	−56.16	−58.14
g	SEt	propyl	3410 (N–H)	−55.7	−55.4

Bruker AM 300 (300.13 MHz) spectrometer. ^{13}C NMR spectra were registered on a Bruker AC 200 (50.32 MHz) or Bruker AM 300 (74.47 MHz) spectrometer and are reported in δ units (ppm) with tetramethylsilane as internal standard and $CDCl_3$ as solvent. ^{19}F NMR spectra were measured on a Bruker WP 80 (75.38 MHz) spectrometer in $CDCl_3$ and are reported in ϕ units upfield from internal $CFCl_3$. Coupling constants are recorded in Hertz. IR spectra were recorded (ν cm^{-1}) in $CHCl_3$ (unless otherwise stated) on a Perkin-Elmer 297 infrared spectrometer or on a Specord M80 (Carl Zeiss).

All new compounds in this paper were chromatographically homogeneous (TLC) and gave analytical data (IR, ^{1}H, ^{19}F, ^{13}C NMR, mass spectrometry and/or elemental analysis) in accord with their assigned structures. Column chromatography purifications were carried out on silica gel (Merck, 230–400 mesh) using

Table 7
^{13}C NMR spectra of allylamines **6** and **7**

Entry	R group	R^1 group	^{13}C NMR spectrum (δ, ppm; J, Hz)
a	Cl	CH_3	*Z*: 35.01 (NH–*C*H_3); 55.25 (*C*H_2–NH); 120.9 [*C*F_3, J(C–F) = 274.26]; 127.0–130.0 (m, *C o, m, p*); 135.95 (*C*q); 145.4 [q, J(C–F) = 2.29] *E*: 34.77 (NH–*C*H_3); 52.29 (*C*H_2–NH); 121.4 [*C*F_3, J(C–F) = 274.26]; 127.0–130.0 (m, *C o, m, p*); 137.47 (*C*q); 145.4 (*C*q)
b	Cl	^{i}Bu	*Z*: 20.97 (s, *C*H_3); 28.78 (s, *C*H); 58.07 (s, *C*H_2); 58.29 (s, *C*H_2) *E*: 20.90 (s, *C*H_3); 29.80 (s, *C*H); 56.96 (s, *C*H_2); 56.81 (s, *C*H_2)
c	Cl	^{t}Bu	*Z*: 28.70 (s, *C*H_3); 48.22 (s, *C*H_2); 155.0 (*C*q) *E*: 29.03 (s, *C*H_3); 48.22 (s, *C*H_2); 154.6 (*C*q)
d	Cl	Ph	*Z*: 52.4 (s, *C*H_2) *E*: 51.8 (s, *C*H_2)
e	Cl	CH_2Ph	52.72 (s, *C*H_2); 53.46 (s, *C*H_2); 120.54 [1, *C*F_3, J(C–F) = 274]; 127.0–128.7 (m, *C o, m, p*); 136.42 (*C*q); 139.52 (*C*q); 146.4 [*C*q, J(C–F) = 2]
f	SEt	CH_3	*Z*: 14.51 (s, CH_2–*C*H_3); 29.77 [q, S*C*H_2, J(C–F) = 1.1]; 35.43 (s, NH–*C*H_3); 56.90 (s, *C*H_2–NH); 123.50 [q, *C*F_3, J(C–F) = 271.0]; 128–132 (m, *C o, m, p*); 139.11 (*C*q); 158.14 (*C*q) *E*: 14.23 (s, CH_2–*C*H_3); 29.00 [q, S*C*H_2, J(C–F) = 1.2]; 35.16 (s, NH–*C*H_3); 53.5 (s, *C*H_2–NH); 127.50 [q, *C*F_3, J(C–F) = 271.0]; 128–132 (m, *C o, m, p*); 140.16 (*C*q); 158.50 (*C*q)
g	SEt	propyl	*Z*: 11.65 (s, *C*H_3); 14.55 (s, *C*H_3); 23.04 (s, *C*H_2); 29.78 (s, *C*H_2); 50.46 (s, *C*H_2); 122.86 [q, *C*F_3, J = 276] *E*: 11.59 (s, *C*H_3); 14.29 (s, *C*H_3); 29.00 (s, *C*H_2); 29.95 (s, *C*H_2); 54.94 (s, *C*H_2); 123.40 [q, *C*F_3, J = 276]

Table 8
^{1}H NMR spectra of allylamines **6** and **7**

Entry	R group	R^1 group	^{1}H NMR spectrum (δ, ppm; J, Hz)
a	Cl	CH_3	*Z*: 1.84 (s, NH); 2.40 (s, 3H); 3.81 (s, 2H); 7.2–7.6 (m, 5H) *E*: 1.84 (s, NH); 2.35 (s, 3H); 3.81 (s, 2H); 7.2–7.6 (m, 5H)
b	Cl	^{i}Bu	*Z*: 0.85 (d, 6H, J = 7); 1.65 (m, 1H); 3.7 (d, 2H, J = 7); 7.1–7.6 (m, 5H) *E*: 0.95 (d, 6H, J = 7); 1.85 (m, 1H); 3.5 (d, 2H, J = 7); 7.1–7.6 (m, 5H)
c	Cl	^{t}Bu	*Z*: 1.15 (s, 9H); 3.4 (s, 2H); 7.1–7.6 (m, 6H) *E*: 1.20 (s, 9H); 3.6 (s, 2H); 7.1–7.6 (m, 6H)
d	Cl	Ph	*Z*: 1.76 (NH); 3.44 (s, 2H); 7.1–8.1 (m, 10H) *E*: 1.76 (NH); 3.37 (s, 2H); 7.1–8.1 (m, 10H)
e	Cl	CH_2Ph	1.70 (s, NH); 3.68 (s, CH_2); 3.76 (s, CH_2); 7.08–7.50 (m, 10H)
f	SEt	CH_3	*Z*: 1.31 (t, 3H, J = 7.3); 2.32 (s, 3H); 2.84 (q, 2H, J = 7.3); 3.94 (s, 2H); 7.1–7.4 (m, 5H) *E*: 1.06 (t, 3H, J = 7.4); 2.29 (s, 3H); 2.49 (q, 2H, J = 7.4); 3.74 (s, 2H); 7.1–7.4 (m, 5H)
g	SEt	propyl	*Z*: 0.83 (t, 3H, J = 7.4); 1.33 (t, 3H, J = 7.4); 1.4 (sext, 2H, J = 7.4); 2.50 (t, 2H, J = 7.4); 2.84 (q, 2H, J = 7.4); 3.99 (q, 2H, J = 1.2); 7.1–7.4 (m, 5H) *E*: 0.79 (t, 3H, J = 7.4); 1.21 (t, 3H, J = 7.4); 1.4 (sext, 2H, J = 7.4); 2.50 (t, 2H, J = 7.4); 2.84 (q, 2H, J = 7.4); 3.79 (q, 2H, J = 1.6); 7.1–7.4 (m, 5H)

light petroleum ether (b.p. 45–65 °C) or light petroleum ether/diethyl ether (9:1).

3.2. Vilsmeier reaction: general procedure

Dimethylformamide (25 ml) was added dropwise to 14 ml (150 mmol) of phosphorus oxychloride while keeping the temperature below 30 °C. After stirring for 15 min, the keto compound was added dropwise while keeping the temperature below 65 °C. The reaction mixture was stirred for 3 h at 65 °C and then hydrolyzed with a saturated solution of AcONa. The ethereal layers were washed with a solution of $NaHCO_3$ until basic, dried over $MgSO_4$ and concentrated. The crude reaction product was purified either by column chromatography or by distillation under vacuum.

Table 9
Elemental analyses and mass spectra of 1-aza-1,3-dienes **4** and **5**

Entry	Elemental analyses		Mass spectra *m/z* (%)
	Calc. (%)	Found (%)	
$C_{11}H_9NClF_3$ **(4a)**	C, 53.44; H, 3.64; N, 5.66; F, 23.08	C, 53.32; H, 3.38 N, 5.72; F, 22.81	247 ($M^{+\cdot}$); 212 (100); 77 (5); 69 (11)
$C_{14}H_{15}NClF_3$ **(4b)**	C, 58.13; H, 5.19; N, 4.84; F, 19.72	C, 57.89; H, 5.02; N, 4.81; F, 19.22	289 ($M^{+\cdot}$); 254 (100); 232 (42); 69 (8)
$C_{14}H_{15}NClF_3$ **(4c)**	C, 58.13; H, 5.19; N, 4.84; F, 19.72	C, 57.82; H, 4.97; N, 4.77; F, 19.44	289 ($M^{+\cdot}$); 254 (22); 232 (100); 69 (12)
$C_{12}H_{11}NSClF_3$ **(4d)**	C, 49.15; H, 3.75; N, 4.78; F, 19.45	–	293 ($M^{+\cdot}$); 258 (100); 260 (22); 69 (5)
$C_{16}H_{11}NClF_3$ **(4e)**	C, 62.14; H, 3.56; N, 4.53; F, 18.45	–	309 ($M^{+\cdot}$); 274 (100); 232 (13); 69 (7)
$C_{16}H_{11}NSClF_3$ **(4f)**	C, 56.30; H, 3.23; N, 4.10; F, 16.71	–	341 ($M^{+\cdot}$); 306 (100); 77 (8); 69 (12)
$C_{17}H_{13}NClF_3$ **(4g)**	C, 63.17; H, 4.02; N, 4.33; F, 17.25	–	323 ($M^{+\cdot}$); 278 (100); 232 (23); 69 (11)
$C_{16}H_{12}N_2ClF_3$ **(4h)**	C, 52.17; H, 4.35; N, 10.14; F, 20.65	–	276 ($M^{+\cdot}$); 241 (100); 232 (34); 69 (17)
$C_{16}H_{12}N_2ClF_3$ **(4i)**	C, 59.26; H, 3.70 N, 8.64; F, 17.59	–	326 ($M^{+\cdot}+2$); 234 ($M^{+\cdot}$); 289 (100); 69 (8)
$C_{13}H_{14}NSF_3$ **(5j)**	C, 57.14; H, 5.13; N, 5.13; F, 20.88	–	273 ($M^{+\cdot}$); 231 (100); 212 (66); 69 (13)
$C_{15}H_{18}NSF_3$ **(5k)**	C, 59.80; H, 5.98; N, 4.65; F, 18.94	C, 59.52; H, 5.52; N, 4.53; F, 18.61	301 ($M^{+\cdot}$); 240 (47); 231 (100); 69 (9)

Table 10
Elemental analyses and mass spectra of allylamines **6** and **7**

Entry	Elemental analyses		Mass spectra *m/z* (%)
	Calc. (%)	Found (%)	
$C_{11}H_{11}NClF_3$ **(6a)**	C, 53.01; H, 4.42; N, 5.62; F, 22.89	C, 52.62; H, 4.17; N, 5.51; F, 22.47	249 ($M^{+\cdot}$); 214 (22); 205 (100); 77 (8)
$C_{14}H_{17}NClF_3$ **(6b)**	C, 57.73; H, 5.84; N, 4.81; F, 19.59	C, 57.61; H, 5.58 N, 4.72; F, 19.46	291 ($M^{+\cdot}$); 256 (100); 207 (42); 77 (5)
$C_{14}H_{17}NClF_3$ **(6c)**	C, 57.73; H, 5.84; N, 4.81; F, 19.59	C, 57.42; H, 5.62; N, 4.56; F, 19.34	291 ($M^{+\cdot}$); 256 (100); 207 (33); 69 (4)
$C_{16}H_{13}NClF_3$ **(6e)**	C, 61.74; H, 4.18; N, 4.50; F, 18.33	–	311 ($M^{+\cdot}$); 276 (14); 205 (100); 69 (8)
$C_{17}H_{15}NClF_3$ **(6g)**	C, 62.77; H, 4.61; N, 4.31; F, 17.54	–	325 ($M^{+\cdot}$); 280 (42); 205 (100); 69 (7)
$C_{13}H_{16}NSF_3$ **(7j)**	C, 56.73; H, 5.82; N, 5.09; F, 20.73	–	275 ($M^{+\cdot}$); 260 (34); 214 (100); 69 (16)
$C_{15}H_{20}NSF_3$ **(7k)**	C, 59.40; H, 6.60; N, 4.62; F, 18.81	C, 59.31; H, 6.32; N, 4.51; F, 18.33	303 ($M^{+\cdot}$); 260 (44); 242 (27); 231 (100)

2-Phenyl-3-chloro-4,4,4-trifluoro-but-2-en-1-al (**2**): the crude reaction product was purified by distillation (b.p. 62 °C/0.35 mmHg). Yield (weight) = 91%. IR (cm^{-1}): 1690 (C=O); 1140–1190 (C–F).

2*Z* (60%): ^1H NMR δ: 7.0–7.6 (m, 5H, C_6H_5); 10.5 (s, 1H, CHO) ppm. ^{13}C NMR δ: 120.4 [q, CF_3, $^1J(C-F) = 276$ Hz]; 134.8 [q, C–CF_3, $^2J(C-F) = 37.4$ Hz]; 129.1–132.0 (m, C_6H_5); 142.1 (s, C_2); 189.6 (s, CHO) ppm. ^{19}F NMR ϕ: −62.0 (s, 3F, CF_3) ppm.

2*E* (40%): ^1H NMR δ: 7.0–7.6 (m, 5H, C_6H_5); 10.2 [q, 1H, CHO, $J(H-F) = 2$ Hz] ppm. ^{13}C NMR δ: 120.8 [q, CF_3, $^1J(C-F) = 276.1$ Hz]; 128.7–131.9 (m, C_6H_5);

134.9 [q, C–CF_3, ^2J(C–F) = 40.4 Hz]; 145.6 [q, C_2, ^3J(C–F) = 1.8 Hz); 186.8 [q, CHO, ^4J(C–F) = 4.1 Hz]. ^{19}F NMR ϕ: −58.3 [d, 3F, CF_3, J(H–F) = 2 Hz].

3.3. Addition of EtSH: general procedure

To a suspension of 288 mg of NaH (12 mmol) in 20 ml of THF, 744 mg of EtSH were added dropwise with stirring. After 15 min, the aldehyde (10 mmol) as a solution in 10 ml of THF was added dropwise at 0 °C. The reaction mixture was stirred at room temperature for 5 h and then poured into iced water. The sulfur derivative was extracted with ether (3×50 ml). The ethereal layers were dried ($MgSO_4$), filtered and the ether removed. The crude product was purified by distillation.

2-Phenyl-3-ethylthio-4,4,4-trifluoromethyl-but-2-en-1-al (**3**): b.p. 73 °C/0.15 mmHg. Yield = 90%. IR (cm^{-1}): 1680 (C=O); 1130–1170 (C–F). Mass spectrum: 170 (100%); 260 ($M^{+\cdot}$).

3*Z* (68%): ^{1}H NMR δ: 1.4 (t, 3H, CH_3, J = 7.4 Hz); 3.0 (q, 2H, CH_2, J = 7.4 Hz); 7.0–7.1 (m, 2H, phenyl); 7.4–7.5 (m, 3H, phenyl); 10.5 (s, CHO) ppm. ^{13}C NMR δ: 14.7 (s, CH_3); 31.0 [q, CH_2, ^4J(C–F) = 1.6]; 122.6 [q, CF_3, ^1J(C–F) = 277.5 Hz]; 128.1–129.0 (m, C_6H_5); 133.5 (s, C–C_6H_5); 139.5 [q, C–CF_3, ^2J(C–F) = 32.4 Hz]; 150.5 [q, C_2, ^3J(C–F) = 2.4 Hz]; 191.0 (s, CHO) ppm. ^{19}F NMR ϕ: −58.7 (s, 3F, CF_3) ppm.

3*E* (32%): ^{1}H NMR δ: 1.1 (t, 3H, CH_3, J = 7.4 Hz); 2.4 (q, 2H, CH_2, J = 7.4 Hz); 7.1–7.2 (m, 2H, phenyl); 7.4–7.5 (m, 3H, phenyl); 10.2 [q, CHO, ^4J(H–F) = 3 Hz] ppm. ^{13}C NMR δ: 14.1 (s, CH_3); 28.5 [q, CH_2, ^4J(C–F) = 1.9 Hz]; 122.8 [q, CF_3, ^1J(C–F) = 278.4 Hz]; 128.6–129.4 (m, C_6H_5); 133.5 (s, C–C_6H_5); 188.1 [q, CHO, ^4J(C–F) = 3.9 Hz] ppm. ^{19}F NMR ϕ: −54.7 [d, 3F, CF_3, J(H–F) = 3 Hz] ppm.

3.4. 1-Aza-1,3-dienes 4 and 5: general procedure

To a solution of aldehyde **2** or **3** in THF was added 1 equiv. of primary alkyl- (or aryl-) amine at 0 °C with stirring. Stirring was continued at room temperature (see Table 1). The reaction mixture was dissolved in ether and washed with water. The ethereal layer was dried ($MgSO_4$) and concentrated under vacuum. Compounds **4** and **5** were purified by column chromatography over SiO_2.

3.5. Allylamines 6 and 7: general procedure

A solution of 1-aza-1,3-diene **4** or **5** in MeOH was treated with 1 equiv. of $NaBH_4$ at room temperature. Stirring was continued at room temperature (see Table 2). The reaction mixture was hydrolyzed with iced water and extracted with ether. The ethereal layer was dried ($MgSO_4$) and concentrated under vacuum to give the almost pure compounds **6** or **7**.

4. Conclusions

A general synthesis of (trifluoromethyl)-1-aza-1,3-dienes has been developed. After reduction, these compounds lead very cleanly (and almost quantitatively) to secondary (trifluoromethyl)-allylamines. By a judicious choice of substituents (captodative groups) such azadienes should provide very interesting synthons for Diels–Alder syntheses. Furthermore, the allylamines should be of interest for pharmaceutical purposes.

Acknowledgments

This work was partially supported by a grant from Centre National de la Recherche Scientifique to A. Selmi.

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