Studies on Trifluoromethyl Ketones. VII.[1] Ene Reaction of Trifluoroacetaldehyde and Its Application for Synthesis of Trifluoromethyl Compounds[2]

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As an extension of our studies on the ene reaction of trifluoromethyl ketones, the ene reaction of trifluoroacetaldehyde was examined. The aldehyde reacted with various ene compounds as a good enophile in the presence of Lewis acids, among which methylaluminum dichloride worked best, though polymerization of the aldehyde caused by the Lewis acid often lowered the isolation yields of the ene reaction. The ene reaction products were successfully oxidized to trifluoromethyl β,γ-unsaturated ketones with Dess–Martin reagent. Reduction of the ene reaction products followed by oxidation with Jones reagent gave saturated trifluoromethyl ketones. The β,γ-unsaturated ketone rearranged on thermolysis to an α,β-unsaturated ketone. These ketones obtained were converted to other types of trifluoromethyl compounds. Thus, the ene reaction of trifluoroacetaldehyde provides a versatile method for synthesis of many types of trifluoromethyl compounds. During this derivatization, a trifluoromethyl group was found to behave as a much larger substituent than a decyl group.

Keywords trifluoroacetaldehyde; ene reaction; trifluoromethyl; homoallyl alcohol; methylaluminum dichloride; Dess–Martin reagent; ketone; Grignard reaction; Wittig reaction; steric effect

We have already reported the ene reaction[3] of trifluoromethyl ketones with ene compounds and derivatization[4] of the products, trifluoromethylated homoallyl alcohols, to various types of trifluoromethyl compounds (see Chart 1). During that research, we noticed that the alkyl groups of trifluoromethyl ketones show a strong steric effect on their reactivities. Thus, we planned to examine the ene reaction of trifluoroacetaldehyde, which has the smallest substituent, a hydrogen. We expected that this small steric effect would help us to understand the steric effect on this reaction and that, if the reaction proceeded, the products would be α-trifluoromethylated secondary homoallyl alcohols that might be converted to trifluoromethyl ketones by oxidation. These ketones could be versatile intermediates for the synthesis of various types of trifluoromethyl compounds (see Chart 1).

Only one report on the reaction of trifluoroacetaldehyde with olefins was published, by Pautrat's group,[5] before the name "ene reaction" became familiar. They used ferric chloride as a catalyst for the reaction with cyclohexene and obtained 3-(2,2,2-trifluoro-1-hydroxyethyl)cyclohexene in the yield of 40%, though its purity was only 70%. They described its reaction with some olefins, but most of the products were mixtures and the yields were low. Thus, their method has little practical utility, and no attention has been paid to it for a long time. We examined this reaction more extensively, hoping to develop it into a useful synthetic method. The results are summarized in Table I.

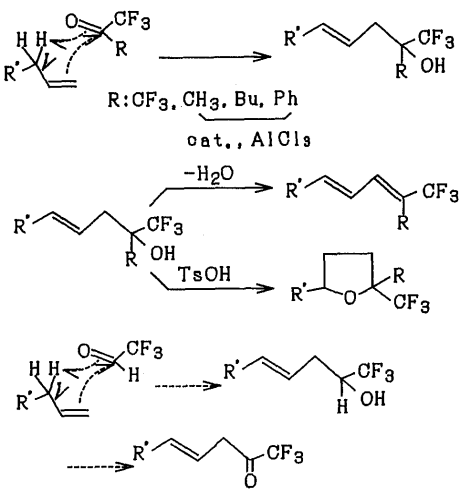
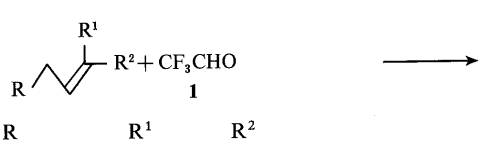
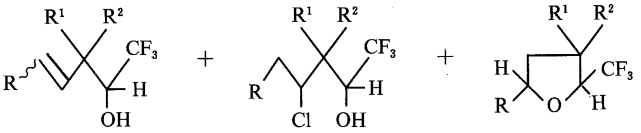


Chart 1

At first, 1-octene was heated with trifluoroacetaldehyde (**1**), which was generated from its hemiacetal, in the absence of a catalyst, but the olefin was recovered quantitatively. Hexafluoroacetone, which has two trifluoromethyl groups, reacts without a catalyst.[3a] The aldehyde (**1**) has only one trifluoromethyl group and is not reactive enough to react with an ene compound without a catalyst even though its steric hindrance may be small. The reaction in the presence of ferric chloride gave 1,1,1-trifluoro-4-decen-2-ol (**2**, 42%) with small amounts of 4-chloro-1,1,1-trifluoro-2-decanol (**3**, 1%) and 2-pentyl-5-(trifluoromethyl)tetrahydrofuran (**4**, 5%). The structure of **2** was determined by examination of the proton and fluorine nuclear magnetic resonance (^{1}H- and ^{19}F-NMR) spectra. Thus, a hydroxylic proton was observed at 2.20 ppm as a doublet, which disappeared on addition of D_2O. Usually, an alcoholic proton appears as a singlet. This splitting is characteristic of an α-trifluoromethyl alcohol. Two olefinic protons appeared at 5.33 and 5.69 ppm. The coupling constant between them was 15.4 Hz, which shows that the double bond is an *E*-form. Only one doublet was observed on ^{19}F-NMR. This suggests that the *Z*-isomer was not formed in an appreciable amount. Compound **3** showed a hydroxylic proton, two types of methylene protons and two methine protons, but no olefinic proton in its ^{1}H-NMR spectrum. Compound **4** is an isomer of **2**, but it does not have a hydroxyl group or olefinic protons. ^{19}F-NMR of **4** shows that it consists of two isomers, probably *cis* and *trans*. In this reaction, formation of polymers from **1** was significant and the yield of **2** was unsatisfactory. The ene reaction of trifluoromethyl ketones was catalyzed successfully with aluminum chloride at −78 °C.[3b,c] Thus, this condition was examined, but the yield of **2** was less than in the former case, and the yields

TABLE I. Ene Reaction of Trifluoroacetaldehyde





R	R^1	R^2							
Pen	H	H	$FeCl_3$, 80 °C	**2**	42%	**3**	1%	**4**	5%
			120 °C, 5 h		No reaction				
			$AlCl_3$, −78 °C		36%		6%		10%
			MADC, −78 °C		48%		1%		0.5%
$-(CH_2)_3-$		H	$AlCl_3$, −78 °C	**5**	9%	**6**[a]	12%		
			MADC, −78 °C		32%		2%		
			$(C_2H_5)_2AlCl_2$		No reaction				
Ph	H	H	$AlCl_3$, −78 °C	**7**	20%	**8**	17%	**9**	8%
			MADC, −78 °C		38%		14%		4%
Bu	Me	H	$FeCl_3$, 80 °C	**10**	22%				
			MADC, −78 °C		76%				
Hept	H	H	MADC, −78 °C	**11**	27%	**12**	1%		
			$AlCl_3$, −78 °C		77%		1%		

a) Concerning the structure, see text.

of the by-products were increased. Since polymerization of **1** seemed to be catalyzed by the Lewis acid, the reaction was carried out at −78 °C in the presence of methylaluminum dichloride (MADC), a weaker Lewis acid than $AlCl_3$. Now, the yield of **2** was improved to 48% and those of **3** and **4** were decreased remarkably. Formation of a chloro compound and a tetrahydrofuran compound was observed in the ene reaction of trifluoroacetone.[3b] Similar mechanisms are proposed. Compound **4** is formed by the cyclization of the ene reaction product (**2**), and **3** is formed from the transition state of the ene reaction. One to three equivalents of **1** were used in these experiments. Use of a large excess of **1** did not greatly improve the yield of **2**.

Next, the reaction of cyclohexene, a 1,2-disubstituted ene compound, was examined in the presence of aluminum chloride to give 3-(2,2,2-trifluoro-1-hydroxyethyl)cyclohexene (**5**, 9%) and 1-chloro-1-(2,2,2-trifluoro-1-hydroxyethyl)-cyclohexane (**6**, 12%), whereas in the presence of MADC, the yields of **5** and **6** were 32% and 2%, respectively. Here, polymerzation of **1** proceeded preferentially to the ene reaction. Thus, we tried diethylaluminum chloride as a catalyst, but no ene reaction product was formed, *i.e.*, diethylaluminum chloride is not effective for this reaction. The structure of **5** was determined from the following NMR data: six methylene protons, two olefinic protons at 5.66 and 6.03 ppm, one methine proton around 2.6 ppm, another methine proton at 3.76 ppm (qdd) and one OH proton at 2.31 ppm (d). One doublet was observed on ^{19}F-NMR. The ^{1}H-NMR spectrum of **6** showed only one methine proton (dq, changed to q with D_2O). Its ^{13}C-NMR spectrum showed five methylenes. These data support the structure of **6**. Formation of this product suggests a two-step mechanism through a carbocation, in contrast with the formation of **3**. Since no stereoisomer of **5** was detected, the ene reaction itself seems to be a concerted reaction.

The same reaction of allylbenzene with **1** in the presence of $AlCl_3$ gave 1,1,1-trifluoro-5-phenyl-4-penten-2-ol (**7**, 20%), 4-chloro-1,1,1-trifluoro-5-phenylpentanol (**8**, 17%) and 2-phenyl-5-(trifluoromethyl)tetrahydrofuran (**9**, 8%). The yields of **8** and **9** were quite large. Therefore, MADC was examined as a catalyst. The yield of **7** was slightly improved, but the by-products were still formed in fairly large amounts. This may be due to the high stability of a benzylic cation or a benzenonium ion.

The ene reaction of hexafluoroacetone with a 1,2-disubstituted olefin, 2-octene, hardly proceeded,[3a] while trifluoroacetone reacted with 2-octene in the presence of aluminum chloride.[3b] The difference of the reactivities seems to be attributable to the difference of steric effects of a methyl and a trifluoromethyl group. Thus, reaction of **1** with 2-octene was examined in the presence of $FeCl_3$ and MADC. While the former catalyst gave a poor yield of 3-methyl-1,1,1-trifluoro-4-nonen-2-ol (**10**, 22%), the latter gave a much better yield of **10** (76%). The ^{1}H-NMR spectrum of **10** shows two methyl protons, a doublet and a triplet, and two olefinic protons. This fact shows that a proton was abstracted not from the methyl group, but from the methylene part, though a methyl proton is abstracted in the usual ene reaction of 2-octene with non-fluorinated enophiles. No isomer of **10** was observed on ^{19}F-NMR. Thus, this reaction is highly regio- and steroselective. These selectivities will be discussed in the last part in this report. In the ene reaction of trifluoromethyl ketones, the reactivity of 2-octene is rather low. The high yield of **10** may be due to the lower steric hindrance of the hydrogen of trifluoroacetaldehyde than of other alkyl groups of trifluoromethyl ketones.

Finally, to investigate derivatization of trifluoromethyl compounds from the ene reaction product, a product of low volatility was required. For this purpose, the ene reaction of 1-decene was examined. MADC did not give a satisfactory result. As mentioned above, $AlCl_3$ seems to cause **1** to polymerize. Therefore, $AlCl_3$ was added gradually to a solution of 1-decene and **1** in CH_2Cl_2 at −78 °C, and 1,1,1-trifluoro-4-dodecen-2-ol(**11**, 77%) was obtained together with a very small amount of a chloro compound (**12**). The structure of **11** was determined by comparison of the spectral data with those of **2**.

Next, we planned to convert the ene reaction products, the secondary trifluoromethylated homoallyl alcohols, to other types of trifluoromethyl compounds. For this purpose, we chose **11** as a model compound, since the volatility of

the product was expected to be low enough to allow accurate estimation of the yield of reactions. Oxidation of **11** to a trifluoromethyl ketone was examined first. A trifluoromethyl carbinol is usually very stable, and in this case, we could not obtain the objective ketone by usual methods of oxidation, such as the use of Jones reagent, probably because the olefinic part reacted faster than the alcohol part. However, by means of Dess–Martin reagent,[6] **11** was oxidized smoothly to 1,1,1-trifluoro-4-dodecen-2-one (**13**, 74%). If **11** was hydrogenated first in the presence of Pd–C to 1,1,1-trifluoro-2-dodecanol (**14**, 99%), the latter was oxidized by Jones reagent to 1,1,1-trifluoro-2-dodecanone (**15**, 62%). Further, heating of **13** without a solvent at 180 °C afforded 1,1,1-trifluoro-3-dodecen-2-one (**16**) quantitatively. Thus, we could obtain three kinds of trifluoromethyl ketones from the ene reaction products of trifluoroacetaldehyde (see Chart 2). Oxidation of **2** gave 1,1,1-trifluoro-4-decen-2-one, but its isolation from methylene chloride was difficult due to the high volatility of the fluorine compound.

Next, some reactions of these carbonyl compounds for the introduction of carbon functions were examined.

Grignard reagents reacted with these ketones as normal carbonyl compounds. Thus, methyl magnesium iodide or phenyl magnesium bromide reacted with **13** to give 1,1,1-trifluoro-2-methyl-4-dodecen-2-ol (**17**, 60%) or 1,1,1-trifluoro-2-phenyl-4-dodecen-2-ol (**18**, 65%) without intervention of a fluorine as a halogen or the trifluoromethyl group as a pseudo halogen.[7] Similarly, **15** and **16** reacted to give trifluoromethylated tertiary alcohols (**19**, **20** and **21**). In the last case, no product of 1,4-addition reaction was detected, even in the presence of copper(I) iodide. The strong inductive effect of the trifluoromethyl group seems to make the alpha position highly electrophilic (see Chart 3).

As another reaction for carbon-chain elongation of the carbonyl group, the Wittig reaction was examined. When the ketone (**15**) was treated with benzyltriphenylphosphonium bromide in the presence of sodium ethoxide in ethanol, (1*E*)-1-phenyl-2-(trifluoromethyl)-1-dodecene (**22**) was obtained in only 9% yield. Ordinary ketones give good yields of olefins under this condition. The poor yield of the above reaction might be attributed to the fact that the high electronegativity of the trifluoromethyl group makes the carbonyl group highly electrophilic and that **15** forms a hemiacetal in ethanol. To avoid this acetal formation, the reaction was carried out in benzene in the presence of sodium hydride to give a 72% yield of **22**. The stereochemistry was determined from the coupling between the vinylic hydrogen and the trifluoromethyl fluorines in NMR. The reaction of **15** with triphenylphosphonium butylide gave 5-(trifluoromethyl)-4-pentadecene (**23**, 92%), which consisted of about 75% of (4*Z*) and about 25% of (4*E*) isomers. ^{19}F-NMR showed a singlet at −4.62 and a broad doublet at 2.60 (ratio 3 : 1). A small coupling of the latter with the olefinic hydrogen shows that this signal is attributable to the (4*E*) isomer.[4b] Namely, the (4*Z*) isomer was formed preferentially. In the Wittig reaction of ketones, a stable ylide such as benzyl ylide is reported to give a *trans* isomer preferentially for a larger substituent and an unstable ylide such as butyl ylide yields a *cis* isomer preferentially. If we apply this rule to our results, a trifluoromethyl group is larger than a decyl group. The ketone **13** gave a similar result to **15** (see Chart 3).

We have already reported derivatization of trifluoromethylated dienes from the ene reaction products of trifluoromethyl ketones by dehydration.[4b] Now, the ene reaction products were dehydrated similarly to the trifluoromethylated dienes with a hydrogen on the trifluoromethylated olefinic carbon. Thus, **11** was treated with phosphoryl chloride in pyridine to give (2*E*,4*E*)-1,1,1-

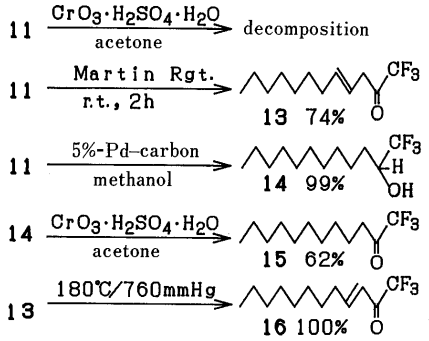


Chart 2

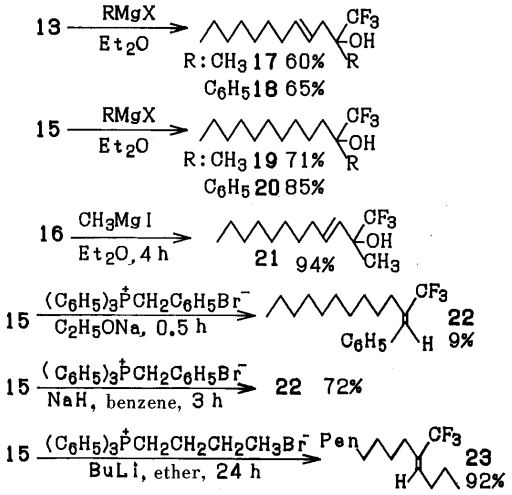


Chart 3

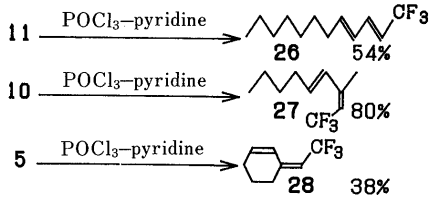


Chart 4

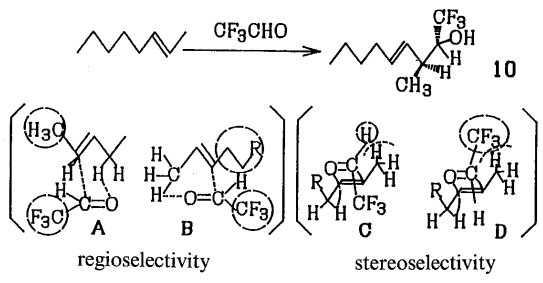


Chart 5

trifluoro-2,4-dodecadiene (**26**, 54%), which included very small amouts of its (2*Z*,4*E*)-isomer and the chlorination product of **11**. A similar reaction of **10** gave 1,1,1-trifluoro-3-methyl-2,4-nonadiene (**27**) selectively. Its stereochemistry was determined as (2*Z*,4*E*) based on the low chemical shift of the trifluoromethyl fluorine on ^{19}F-NMR and the small coupling constants between the methyl protons and the trifluoromethyl fluorines (see Chart 4). A similar dehydration of **5** gave predominantly (*Z*)-3-[(trifluoromethyl)methylene]cyclohexene (**28**), the structure of which was determined from the nuclear Overhauser effect (NOE) interaction between the *exo*-olefinic proton and the 4-methylene protons. A small amount of *E*-isomer was isolated and showed NOE interaction between the olefinic protons (see Chart 4).

As we have reported, this reaction proceeds predominantly through an anti-elimination.[4b] Therefore, these results shows that the stereochemistry of **10** and **5** is *l* (based on *l-u*: *like-unlike* notation.[8]) The regioselectivity is explained by a comparison of transition states A and B. Repulsion between the trifluoromethyl group and the pentyl group in B is larger than that between the trifluoromethyl group and the methyl group in A. The stereoselectivity can be explained similarly: repulsion between the olefinic hydrogen and the methyl group in trasition state C is smaller than that between the trifluoromethyl group and the methyl group in transition state D. Thus, **10** was formed through C (see Chart 5).

In conclusion, trifluoroacetaldehyde was found to react as a good enophile in the presence of a Lewis acid, though it also polymerizes in the presence of the Lewis acid. Therefore, the catalyst should be chosen carefully. The product was oxidized to a trifluoromethyl ketone, which was further converted to other types of trifluoromethyl compounds. In some of these transformations, it was found that a trifluoromethyl group behaves as a larger substituent than a decyl group.

Experimental

Gerneral Procedures Trifluoroacetaldehyde was obtained as follows. Trifluoroacetaldehyde ethyl hemiacetal was added dropwise to concentrated H_2SO_4 at 120 °C under stirring, and trifluoroacetaldehyde (**1**) was collected through a reflux condenser in a trap cooled at −78 °C. ^{1}H-NMR spectra were obtained on JNM-FX90Q and JNM-GX400 spectrometers. ^{19}F-NMR spectra were recorded on the JNM-FX90Q spectrometer, using benzotrifluoride as an internal standard (upper field taken as plus).

Reaction of 1 with 1-Octene 1) In the Presence of $FeCl_3$: $FeCl_3$ (0.1 g, 0.6 mmol), 1-octene (3.0 g, 27 mmol) and CH_2Cl_2 (10 ml) were put in a stainless steel tube, the tube was cooled to −78 °C, and **1** (3.3 ml) was introduced into the tube using a vacuum line. The tube was sealed and shaken at 80 °C for 5 h. After being cooled to room temperature, the tube was opened and the contents were treated with 10% NH_4OH (5 ml) and CH_2Cl_2 (10 ml). The mixture was filtered through a Celite layer. The filter cake was washed with CH_2Cl_2. The filtrate and washings were combined and extracted with CH_2Cl_2. The CH_2Cl_2 layer was dried over $MgSO_4$ and concentrated under vacuum. The residue was separated by a column chromatography (SiO_2, hexane–CH_2Cl_2, 4:1 to 1:1) to give 1,1,1-trifluoro-4-decen-2-ol (**2**, 2.43 g, 42%), 2-pentyl-5-(trifluoromethyl)tetrahydrofuran (**4**, 0.28 g, 5%) and 4-chloro-1,1,1-trifluoro-2-decanol (**3**, 0.07 g, 1%). **2**: A colorless oil. Mass spectrum (MS) *m/z*: 210 (M^+). High resolution MS (HRMS) Calcd for $C_{10}H_{17}F_3O$: 210.123. Found: 210.124. ^{1}H-NMR ($CDCl_3$) δ: 0.94 (3H, t, J=5.1 Hz), 1.07—1.57 (6H, m), 1.83—2.11 (2H, m), 2.20 (1H, d, J=5.9 Hz), 2.33—2.64 (2H, m), 3.68—4.17 (1H, m), 5.33 (1H, ddd, J=6.2, 6.7, 15.4 Hz), 5.69 (1H, td, J=5.7, 15.4 Hz). ^{19}F-NMR ($CDCl_3$) ppm: 15.06 (d, J=6.8 Hz). **3**: A colorless oil. MS *m/z*: 246 (M^+) HRMS Calcd for $C_{10}H_{18}ClF_3O$: 246.100. Found: 246.100. ^{1}H-NMR($CDCl_3$) δ: 0.97 (3H, m), 1.11—1.60 (11H, m), 1.62—1.84 (2H, m), 1.84—2.07 (2H, m), 2.45 (1H, d, J=6.2 Hz, disappeared on addition of D_2O), 3.92—4.61 (2H, m), ^{19}F-NMR ($CDCl_3$) ppm: 15.64 (d, J=6.8 Hz). **4**: A colorless oil. MS *m/z*: 210 (M^+). HRMS Calcd for $C_{10}H_{17}F_3O$: 210.123. Found: 210.124. ^{1}H-NMR ($CDCl_3$) δ: 0.81 (6H, t, J=5.1 Hz), 0.94—1.61 (12H, m), 1.72—2.24 (2H, m), 3.49—4.46 (2H, m). ^{19}F-NMR ($CDCl_3$) ppm: 14.40 (d, J=7.3 Hz), 14.55 (d, J=7.3 Hz) (ratio 1:1).

2) Thermal Reaction without a Catalyst: A solution of 1-octene (1.0 g, 9 mmol) in CH_2Cl_2 (10 ml) were sealed in a stainless steel tube and **1** (1.5 ml) was added as above. The tube was shaken at 120 °C for 5 h, and the mixture was treated as above. The analysis of the product by gas-liquid chromatography (GLC) showed only recovery of 1-octene. (The aldehyde **1** polymerized to an insoluble solid.)

3) In the Presence of $AlCl_3$: To a mixture of $AlCl_3$ (2.3 g, 17 mmol) and 1-octene (1.0 g, 9 mmol) in CH_2Cl_2 (10 ml), **1** (2.3 ml) was added through a cannula at −78 °C in an atmosphere of argon. The mixture was stirred at this temperature for 2 h, then poured into a mixture of 10% HCl and ice, and extracted with CH_2Cl_2. The CH_2Cl_2 layer was washed with H_2O and dried over $MgSO_4$. A similar separation to that descibed in section 1) gave **2** (1.57 g, 36%), **3** (0.31 g, 6%) and **4** (0.44 g, 10%).

4) In the Presence of MADC: In an atmosphere of Ar, **1** (6 ml) and CH_3AlCl_2 (MADC, 20 wt%/hexane, 16 ml) were added in that order at −78 °C to a solution of 1-octene (5.0 g, 45 mmol) in CH_2Cl_2 (28 ml), and the mixture was stirred at this temperature for 3 h. The mixture was treated as described in sec 1) to give **2** (4.5 g, 48%), **3** (0.11 g, 1%) and **4** (0.05 g, 0.5%).

Reaction of 1 with Cyclohexene 1) In the Presence of $AlCl_3$: In an atmosphere of Ar, cyclohexene (3.5 g, 42 mmol and **1** (11.5 g) were added to a suspension of $AlCl_3$ (12.0 g, 90 mmol) in CH_2Cl_2 (21 ml) at −78°C, and the mixture was stirred at this temperature for 1 h, then poured into a mixture of 10% HCl and ice, and extracted with CH_2Cl_2. The CH_2Cl_2 layer was washed with H_2O and dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by a column chromatography (SiO_2, hexane–CH_2Cl_2, 4:1) to give 3-(2,2,2-trifluoro-1-hydroxyethyl)cyclohexene (**5**, 0.72 g, 9%) and 1-chloro-1-(2,2,2-trifluoro-1-hydroxyethyl)cyclohexane (**6**, 1.09 g, 12%). **5**: A colorless oil. bp 122 °C/100 mmHg. MS *m/z*: 180 (M^+). HRMS Calcd for $C_8H_{11}F_3O$: 180.076. Found 180.075. ^{1}H-NMR ($CDCl_3$) δ: 1.34—1.88 (4H, m), 1.88—2.17 (2H, m), 2.31 (1H, d, J=8.2 Hz), 2.44—2.84 (1H, m), 3.76 (1H, qdd, J=8.0, 8.2, 4.3 Hz), 5.66 (1H, bd, J=7.7 Hz), 6.03 (1H, dm, J=7.7 Hz). ^{19}F-NMR ($CDCl_3$) ppm: 12.31 (d, J=8.0 Hz). **6**: A colorless oil. MS *m/z*: 215 (M−1). HRMS Calcd for $C_8H_{12}ClF_3O$: 215.045. Found: 215.046. ^{1}H-NMR ($CDCl_3$) δ: 1.16—1.35 (1H, m), 1.61—1.86 (7H, m), 2.06—2.22 (2H, m), 2.98 (1H, d, J=9.2 Hz, disappeared on addition of D_2O), 3.76 (1H, qd, J=7.0, 9.2 Hz, q on addition of D_2O). ^{13}C-NMR ($CDCl_3$): 124.18 (CF_3), 76.43 (CF_3-C), 75.58 (C-Cl), 37.07, 34.64, 25.03, 21.66, 21.52 ($CH_2\times5$). ^{19}F-NMR ($CDCl_3$) ppm: 6.78 (d, J=7.0 Hz).

2) In the Presence of $(C_2H_5)_2$ AlCl: In a stream of Ar, **1** (2.3 ml) was added to a solution of cyclohexene (1.2 g, 15 mmol) in dry CH_2Cl_2 (7 ml). To this solution, 10% $(C_2H_5)_2AlCl$ (10 ml) was added at −78°C and the mixture was stirred at this temperature for 3 h, then worked up as above. Analysis by GLC showed that cyclohexene was recovered completely.

3) In the Presence of MADC: In an atmosphere of Ar, **1** (2.3 ml) and MADC (20 wt%/hexane, 17 ml) were added to a solution of cyclohexene (1.2 g, 15 mmol) in dry CH_2Cl_2 (7 ml) at −78 °C. The mixture was stirred at this temperature for 4 h, then poured into a mixture of 10% HCl and ice, and extracted with CH_2Cl_2. The organic layer was washed with H_2O and dried over $MgSO_4$. After evaporation of the solvent, the residue was separated by column chromatography (SiO_2, hexane–CH_2Cl_2, 4:1) to give **5** (0.84 g, 32%) and **6** (0.06 g, 2%).

Reaction of 1 with Allylbenzene 1) In the Presence of $AlCl_3$: In an atmosphere of Ar, **1** (2.2 ml) was added to a mixture of $AlCl_3$ (2.5 g, 19 mmol) and allylbenzene (1.5 g, 13 mmol) in dry CH_2Cl_2 (10 ml) at −78 °C, and the mixture was stirred at this temperature for 3 h, then poured into a mixture of 10% HCl and ice, and extracted with CH_2Cl_2. The CH_2Cl_2 layer was washed with H_2O and dried over $MgSO_4$. The solvent was evaporated off under vacuum, and the residue was separated by column chromatography (SiO_2, hexane–CH_2Cl_2, 4:1 to 1:1) to give 1,1,1-trifluoro-5-phenyl-4-penten-2-ol (**7**, 0.56 g, 20%), 4-chloro-1,1,1-trifluoro-5-phenylpentan-2-ol (**8**, 0.54 g, 17%) and 2-phenyl-5-(trifluoromethyl)tetrahydrofuran (**9**, 0.22 g, 8%). **7**: A colorless oil, bp 120 °C/20 mmHg, which solidified on standing. MS *m/z*: 216 (M^+). HRMS Calcd for $C_{11}H_{11}F_3O$: 216.076. Found: 216.076. ^{1}H-NMR ($CDCl_3$) δ: 2.29 (1H, d, J=6.7 Hz), 2.37—2.74 (2H, m), 3.80—4.29 (1H, m), 6.20 (1H,

ddd, J=15.9, 6.4, 6.4 Hz), 6.52 (1H, d, J=15.9 Hz), 6.74—7.57 (5H, m). ^{19}F-NMR ($CDCl_3$) ppm: 15.08 (d, J=6.8 Hz). **9**: A colorless oil. MS m/z: 216 (M^+). HRMS Calcd for $C_{11}H_{11}F_3O$: 216.076. Found: 216.076. ^{1}H-NMR ($CDCl_3$) δ: 1.67—2.73 (7H, m), 3.56 (1H, qdd, J=6.6, 7.2, 7.2 Hz), 3.89 (1H, m), 4.20—4.70 (2H, m), 4.86—5.19 (1H, m), 7.09—7.47 (10H, m). ^{19}F-NMR ($CDCl_3$) ppm: 14.02 (d, J=6.6 Hz), 14.34 (d, J=7.8 Hz). (ratio 2 : 1).

2) In the Presence of MADC: In an atmosphere of Ar, **1** (2.3 ml) and MADC (20 wt%/hexane, 5 ml) were added to a solution of allylbenzene (1.2 g, 10 mmol) in dry CH_2Cl_2 (7 ml) at −78 °C, and the mixture was stirred at this temperature for 2 h, then poured into a mixture of 10% HCl and ice, and extracted with CH_2Cl_2. The CH_2Cl_2 layer was washed with H_2O and dried over $MgSO_4$. After evaporation of the solvent, the residue was separated by column chromatography (SiO_2, hexane–CH_2Cl_2, 4 : 1 to 1 : 1) to give **7** (0.83 g, 38%), **8** (0.36 g, 14%) and **9** (0.09 g, 4%).

Reaction of 1 with 2-Octene 1) In the Presence of $FeCl_3$: Ferric chloride (0.1 g, 0.6 mmol), 2-octene (3.0 g, 27 mmol) and CH_2Cl_2 (10 ml) were placed in a stainless steel tube, and **1** (3.3 ml) was added at −78 °C under vacuum. The sealed tube was shaken at 80 °C for 4 h, then the mixture was worked up as in the case of the reaction of 1-octene and separated by column chromatography (SiO_2, hexane–CH_2Cl_2, 4 : 1 to 1 : 1) to give 3-methyl-1,1,1-trifluoro-4-nonen-2-ol (**10**, 1.25 g, 22%). **10**: A colorless oil. MS m/z: 210 (M^+). HRMS Calcd for $C_{10}H_{17}F_3O$: 210.123. Found: 210.124. ^{1}H-NMR ($CDCl_3$) δ: 0.89 (3H, t, J=6.2 Hz), 1.16 (3H, d, J=7.5 Hz), 1.21—1.45 (4H, m), 1.77—2.23 (2H, m), 2.48 (1H, s), 2.67 (1H, qdd, J=7.5, 7.2, 5.4 Hz), 3.76 (1H, qd, J=6.8, 5.4 Hz), 5.40 (1H, dd, J=15.4, 7.2 Hz), 5.53—5.87 (1H, m). ^{19}F-NMR ($CDCl_3$) ppm: 11.82 (d, J=6.8 Hz).

2) In the Presence of MADC: In an atmosphere of Ar, **1** (3.3 ml) and MADC (20wt%/hexane, 3 ml) were added to a solution of 2-octene (3.0 g, 27 mmol) in dry CH_2Cl_2 (10 ml) at −78 °C and the mixture was stirred at this temperature for 1.5 h. The reaction mixture was worked up as usual and the product was purified by column chromatography (SiO_2, hexane–CH_2Cl_2, 4 : 1 to 1 : 1) to give **10** (4.28 g, 76%).

Reaction of 1-Decene In an atomosphere of Ar, **1** (8.0 ml) was added through a cannula to a solution of 1-decene (5.0 g, 36 mmol) in dry CH_2Cl_2 (50 ml) at −78 °C. To this solution, $AlCl_3$ (5.0 g, 38 mmol) was added in small portions at −78 °C. The mixture was stirred at this temperature for 3 h, then poured into a mixture of 10% HCl and ice, and extracted with CH_2Cl_2. The CH_2Cl_2 layer was washed with H_2O and dried over $MgSO_4$. The solvent was evaporated off under vacuum, and the residue was purified by column chromatography (SiO_2, hexane–CH_2Cl_2, 4 : 1 to 1 : 1) to give 1,1,1-trifluoro-4-dodecen-2-ol (**11**, 6.61 g, 77%). **11**: A colorless oil. bp 130 °C/26 mmHg. MS m/z: 238 (M^+). HRMS Calcd for $C_{12}H_{21}F_3O$: 238.155. Found: 238.155. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, t, J=5.1 Hz), 1.06—1.61 (10H, m), 1.85—2.17 (3H, m), 2.23—2.53 (2H, m), 5.34 (1H, ddd, J=15.2, 7.2, 6.4 Hz), 5.63 (1H, td, J=5.1, 15.2 Hz). ^{19}F-NMR ($CDCl_3$ ppm: 15.14 (d, J=6.6 Hz). A chloro compound (**12**, 1%) was detected on GLC-MS.

1,1,1-Trifluoro-4-dodecen-2-one (13) Compound **11** (6.6 g, 28 mmol) was added to a solution of Dess–Martin reagent (29.2 g, 69 mmol) in dry CH_2Cl_2 (312 ml). The mixture was stirred at room temperature for 2 h, then treated with saturated $NaHCO_3$ (300 ml) containing $Na_2S_2O_3$ (68.2 g) and extracted with CH_2Cl_2. The CH_2Cl_2 layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by column chromatography (SiO_2, pentane) to give 1,1,1-trifluoro-4-dodecen-2-one (**13**, 4.8 g, 74%). **13**: bp 105 °C/20 mmHg. MS m/z: 236 (M^+) HRMS Calcd for $C_{12}H_{19}F_3O$: 236.139. Found 236.139. ^{1}H-NMR ($CDCl_3$) δ: 0.90 (3H, t, J=5.1 Hz), 1.08—1.46 (10H, m), 1.78—2.17 (2H, m), 3.44 (2H, d, J=5.7 Hz), 5.51 (1H, td, J=5.1, 15.1 Hz), 6.28 (1H, td, J=5.5, 15.1 Hz). ^{19}F-NMR ($CDCl_3$) ppm: 14.47 (s).

1,1,1-Trifluoro-2-dodecanol (14) A solution of **11** (4.0 g, 17 mmol) in MeOH (200 ml) was shaken with 5% Pd–C (0.2 g) in a stream of H_2. After removel of the catalyst by filtration, the reaction mixtue was concentrated under vacuum and purified by column chromatography (SiO_2, pentane to give 1,1,1-trifluoro-2-dodecanol **14**. 4.0 g, 99%). **14**: A colorless oil. MS m/z: 240 (M^+). HRMS Calcd for $C_{12}H_{23}F_3O$: 240.170. Found: 240.171. ^{1}H-NMR ($CDCl_3$) δ: 0.91 (3H, t, J=5.14 Hz), 1.15—1.43 (16H, br s), 1.49—1.78 (2H, m), 1.95 (1H, s), 3.70—4.10 (1H, m). ^{19}F-NMR ($CDCl_3$) ppm: 15.83 (d, J=6.84 Hz).

1,1,1-Trifluoro-2-dodecanone (15) Jones reagent (32 ml) was added to a solution of **14** (1.4 g, 5.8 mmol) in acetone (150 ml) added at 0 °C under stirring. Stirring was continued for a further 24 h. Isopropanol was then added dropwise till the red–brown color disappeared. Ice water was added to the mixture and the whole was extracted with CH_2Cl_2. The CH_2Cl_2 layer was washed with H_2O and dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by column chromatography (SiO_2, pentane) to give 1,1,1-trifluoro-2-dodecanone (**15**, 0.83 g, 62%). **15**: A colorless oil. MS m/z: 238 (M^+). HRMS Calcd for $C_{12}H_{21}F_3O$: 238.155. Found: 238.155. ^{1}H-NMR ($CDCl_3$) δ: 0.89 (3H, t, J=5.14 Hz), 1.09—1.47 (14 H, br s), 1.48—1.87 (2H, m), 2.73 (2H, t, J=7.46 Hz). ^{19}F-NMR ($CDCl_3$) ppm: 15.11 (s).

1,1,1-Trifluoro-3-dodecen-2-one (16) Heating of **13** without any solvent at 180 °C and purification by column chromatography (SiO_2, pentane) gave 1,1,1-trifluoro-3-dodecen-2-one (**16**) quantitatively. **16**: A colorless oil. bp 105 °C/20 mmHg. MS m/z: 236 (M^+). HRMS Calcd for $C_{12}H_{19}F_3O$: 236.139. Found: 236.139. ^{1}H-NMR ($CDCl_3$) δ: 0.91 (3H, t, J=5.1 Hz), 1.14—1.48 (12 H, m), 2.06—2.49 (2H, m), 6.43 (1H, d, J=15.9 Hz), 7.16—7.58 (1H, m). ^{19}F-NMR ($CDCl_3$) ppm: 13.23 (s).

1,1,1-Trifluoro-2-methyl-4-dodecen-2-ol (17) A solution of **13** (0.3 g, 1.3 mmol) in dry Et_2O (5 ml) was added to a solution of MeMgI, which was prepared from Mg (113 mg, 4.7 mmol) and MeI (600 mg, 4.2 mmol) in dry Et_2O (15 ml), in an atmosphere of Ar. The mixture was stirred at room temperature for 4h, then poured into a mixture of 10% NH_4Cl and ice, and extracted with Et_2O. The Et_2O layer was washed with H_2O and dried over $MgSO_4$. After the evaporation of the solvent under vacuum, the residue was purified by column chromatography (SiO_2, hexane–CH_2Cl_2, 4 : 1) to give 1,1,1-trifluoro-2-methyl-4-dodecen-2-ol (**17**, 0.19 g, 60%). **17**: A colorless oil. MS m/z: 252 (M^+). HRMS Calcd for $C_{13}H_{23}F_3O$: 252.170. Found: 252.170. ^{1}H-NMR ($CDCl_3$) δ: 0.89 (3H, t, J=4.9 Hz), 1.05—1.49 (13H, m), 1.90—2.16 (2H, m), 2.12 (1H, s, disappeared on addition of D_2O), 2.26 (1H, dd, J=9.6, 7.4 Hz), 2.50 (1H, dd, J=9.6, 7.4 Hz), 5.36 (1H, ddd, J=7.4, 9.6, 15.1 Hz), 5.49 (1H, td, J=5.8, 15.1 Hz). ^{19}F-NMR ($CDCl_3$) ppm: 17.87 (s).

1,1,1-Trifluoro-2-phenyl-4-dodecen-2-ol (18) A solution of **13** (0.5 g, 2 mmol) in dry Et_2O (5 ml) was added to a solution of PhMgBr, which was prepared from Mg (160 mg, 6.6 mmol) and PhBr (1.0 g, 6.4 mmol) in dry Et_2O (30 ml) in an atmosphere of Ar. The mixture was stirred at room temperature for 3 h, then poured into 10% NH_4Cl and ice, and extracted with Et_2O. The Et_2O layer was washed with H_2O and dried over $MgSO_4$. After evaporation of the solvent under vacuum, the residue was purified by column chromatography (SiO_2, hexane–CH_2Cl_2, 4 : 1) to give 1,1,1-trifluoro-2-phenyl-4-dodecen-2-ol (**18**, 0.43 g, 65%). **18**: A colorless oil. MS m/z: 314 (M^+). HRMS Calcd for $C_{18}H_{25}F_3O$: 314.186. Found: 314.185. ^{1}H-NMR ($CDCl_3$) δ: 0.90 (3H, t, J=5.14 Hz), 1.06—1.48 (10H, m), 1.79—2.14 (2H, m), 2.63 (1H, s), 2.87 (2H, d, J=6.9 Hz), 5.14 (1H, td, J=6.7, 14.8 Hz), 5.66 (1H, td, J=6.4, 14.8 Hz), 7.23—7.71 (5H, m), ^{19}F-NMR ($CDCl_3$) ppm: 14.68 (s).

1,1,1-Trifluoro-2-methyl-2-dodecanol (19) A solution of **15** (0.3 g, 1.3 mmol) in dry Et_2O (5 ml) was added to a solution of MeMgI which was obtained by the reaction of Mg (113 mg, 4.7 mmol) and MeI (512 mg, 3.6 mmol) in dry Et_2O (15 ml) in atmosphere of Ar. The mixture was stirred at room temperature for 2 h, then poured into 10% NH_4Cl and ice, and extracted with Et_2O. The Et_2O layer was washed with H_2O and dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by column chromatography (SiO_2, hexane–CH_2Cl_2, 4 : 1) to give 1,1,1-trifluoro-2-methyl-2-dodecanol (**19**, 229 mg, 71 %). **19**: A colorless oil. MS m/z: 254 (M^+). HRMS Calcd for $C_{13}H_{25}F_3O$: 254.186. Found: 254.186. ^{1}H-NMR ($CDCl_3$) δ: 0.92 (3H, t, J=5.1 Hz), 1.09—1.45 (21H, m), 1.74 (1H, s). ^{19}F-NMR ($CDCl_3$) 18.83 (s).

1,1,1-Trifluoro-2-phenyl-2-dodecanol (20) A solution of **15** (0.5 g, 2 mmol) in dry Et_2O (5 ml) was added to a solution of PhMgBr, which was obtained by the reaction of Mg (160 mg, 6.6 mmol) and PhBr (1.0 g, 6.4 mmol) in dry Et_2O (20 ml), in an atmosphere of Ar. The mixture was stirred at room temperature for 2 h, then poured into a mixture of 10% NH_4Cl and ice, and extracted with Et_2O. The Et_2O layer was washed with H_2O and dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by column chromatograhy (SiO_2, hexane–CH_2Cl_2, 4 : 1) to give 1,1,1-trifluoro-2-phenyl-2-dodecanol (**20**, 0.57 g, 85%). **20**: A colorless oil. MS m/z: 316 (M^+). HRMS Calcd for $C_{18}H_{27}F_3O$: 316.202. Found: 316.201. ^{1}H-NMR ($CDCl_3$) δ: 0.89 (3H, t, J=5.1 Hz), 1.07—1.37 (18H, m), 2.33 (1H, s), 7.23—7.64 (5H, m). ^{19}F-NMR ($CDCl_3$) ppm: 15.83 (s).

1,1,1-Trifluoro-2-methyl-3-dodecen-2-ol (21) A solution of **16** (0.3 g, 1.3 mmol) in dry Et_2O (5 ml) was added to a solution of MeMgI, which was obtained by the reaction of Mg (113 mg, 4.7 mmol) and MeI (600 mg, 4.2 mmol) in dry Et_2O (15 ml), in an atmosphere of Ar. The mixture was stirred at room temperature for 4 h, then poured into 10% NH_4Cl and ice, and extracted with Et_2O. The Et_2O layer was washed with H_2O and dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by column chromatography (SiO_2, hexane–CH_2Cl_2, 4 : 1) to give

1,1,1-trifluoro-2-methyl-3-dodecen-2-ol (**21**, 0.31 g, 94%). **21**: A colorless oil. MS *m/z*: 252 (M^+). HRMS Calcd. for $C_{13}H_{23}F_3O$: 252.170. Found: 252.170. ^{1}H-NMR ($CDCl_3$) δ: 0.60—1.01 (3H, m), 1.10—1.42 (15H, m), 1.93—2.05 (3H, m), 5.59 (1H, d, J=15.9 Hz), 5.80—6.13 (1H, m). ^{19}F-NMR ($CDCl_3$) ppm: 18.41 (s).

(1*E*)-1-Phenyl-2-(trifluoromethyl)-1-dodecene (22) a) In EtOH: Sodium (110 mg, 4.8 mmol) was dissolved in EtOH (10 ml) and benzyltriphenylphosphonium bromide (1.65 g) was added to this solution in an atmosphere of Ar under vigous stirring. After 20 minutes' stirring, a solution of **15** (0.5 g, 2 mmol) in EtOH (5 ml) was added, and the whole was stirred at room temperature for a further 0.5 h then poured into ice-water and extracted with Et_2O. The Et_2O layer was washed with H_2O and dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by column chromatography (SiO_2, hexane) to give (1*E*)-1-phenyl-2-(trifluoromethyl)-1-dodecene (**22**, 63 mg, 9%). **22**: A colorless oil. MS *m/z*: 312 (M^+). HRMS Calcd for $C_{19}H_{27}F_3$: 312.207. Found: 312.207. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, t, J=5.1 Hz), 1.09—1.40 (16H, m), 2.23—2.51 (2H, m), 6.99—7.09 (1H, m), 7.24—7.41 (5H, m). ^{19}F-NMR ($CDCl_3$) ppm: 2.24 (d, J=1.7 Hz). A very small singlet (less than 5%) observed at 5.20 ppm is attributed to the (1*Z*) isomer.

b) In Benzene: A suspension of benzyltriphenylphosphonium bromide (1.1 g) and NaH (about 60%, 0.13 g) in dry C_6H_6 (20 ml) was stirred at room temperature for 0.5 h in an atmosphere of Ar, and a solution of **15** (0.5 g, 2 mmol) in dry C_6H_6 (5 ml) was added to this suspension. Stirring was continued at room temperature for 3 h, then the reaction mixture was poured into ice-water and extracted with Et_2O. The Et_2O layer was washed with H_2O and dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by column chromatography (SiO_2, hexane) to give **22** (0.52 g, 72%), which contained a trace of the (1*Z*) isomer.

(4*Z*)-5-(Trifluoromethyl)-4-pentadecene (23) BuLi (0.6 mmol/ml in hexane, 2.4 ml) was added to a suspension of butyltriphenylphosphonium bromide (1.4 g) in dry Et_2O (30 ml), and the mixture was stirred at room temperature for 2 h. A solution of **15** (0.5 g, 2 mmol) in dry Et_2O (5 ml) was added to the above mixture. The whole was stirred at room temperature for 24 h, then poured into ice-water and extracted with Et_2O. The Et_2O layer was washed with H_2O and dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by column chromatography (SiO_2, hexane) to give (4*Z*)-5-(trifluoromethyl)-4-pentadecene (**23**, 0.54 g, 92%). **23**: A colorless oil. MS *m/z*: 278 (M^+). HRMS Calcd for $C_{16}H_{29}F_3$: 278.222. Found: 278.222. ^{1}H-NMR ($CDCl_3$) δ: 0.77—1.04 (6H, m), 1.08—1.54 (18H, m), 1.94—2.33 (4H, m), 5.66 (1H, t, J=7.7 Hz). Another small olefinic proton signal was observed at 6.05 (m). ^{19}F-NMR ($CDCl_3$) ppm: −4.62 (s), 2.60 (br d, J=1.4 Hz, ratio 3:1).

(1*E*,4*E*)-1-Phenyl-2-(trifluoromethyl)-1,4-dodecadiene (24) A solution of **13** (0.5 g, 2 mmol) in dry C_6H_6 (5 ml) was added to a solution of triphenylphosphonium benzylide, which was obtained by the reaction of benzyltriphenylphosphonium bromide (1.1 g) with NaH (about 60%, 0.13 g) in dry C_6H_6 (25 ml) at room temperature for 0.5 h in an atmosphere of Ar. The mixture was stirred at room temperature for 3 h, then poured into ice water and extracted with Et_2O. The Et_2O layer was washed with H_2O and dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by column chromatography (SiO_2, hexane) to give (1*E*,4*E*)-1-phenyl-2-(trifluoromethyl)-1,4-dodecadiene (**24**, 82 mg, 12%). **24**: A colorless oil. MS *m/z*: 326 (M^+). HRMS Calcd for $C_{19}H_{25}F_3O$: 326.186. Found: 326.185. ^{1}H-NMR ($CDCl_3$) δ: 0.90 (3H, t, J=5.1 Hz), 1.05—1.46 (12H, br s), 1.88—2.28 (2H, m), 5.78—6.37 (2H, m), 7.03 (1H, d, J=2.2 Hz). 7.25—7.57 (5H, m). ^{19}F-NMR ($CDCl_3$) ppm: −0.10 (d, J=2.2 Hz).

(4*Z*,7*E*)-5-(Trifluoromethyl)-4,7-pentadecadiene (25) A solution of **13** (0.2 g, 0.8 mmol) in dry Et_2O (2 ml) was added to a solution which was obtained by the reaction of butyltriphenylphosphonium bromide (350 mg) and BuLi (0.6 ml) in dry Et_2O (7.6 ml) at room temperature for 2 h in an atmosphere of Ar. The mixture was stirred at room temperature for 24 h, then poured into ice water and extracted with Et_2O. The Et_2O layer was washed with H_2O and dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by column chromatography (SiO_2, hexane) to give (4*Z*,7*E*)-5-(trifluoromethyl)-4,7-pentadecadiene (**25**, 29 mg, 12%). **25**: A colorless oil. MS *m/z*: 276 (M^+). HRMS Calcd for $C_{16}H_{27}F_3$: 276.206. Found: 276.205. ^{1}H-NMR ($CDCl_3$) δ: 0.81—0.98 (6H, m), 1.18—1.43 (12H, m), 1.95—2.29 (4H, m), 2.88 (2H, d, J=5.1 Hz), 5.28—5.52 (2H, m), 6.12 (1H, t, J=7.2 Hz). ^{19}F-NMR ($CDCl_3$) ppm: −4.29 (s).

1,1,1-Trifluoro-2,4-dodecadiene (26) A mixture of 1,1,1-trifluoro-4-dodecen-2-ol (**11**, 0.5 g, 2.1 mmol) in pyridine (1.12 ml) and $POCl_3$ (323 mg) was treated as above. After evaporation of the solvent, the residue was purified by a bulb-to-bulb distillation to give 1,1,1-trifluoro-2,4-dodecadiene (**26**, 0.25 g, 54%). **26**: A colorless oil. MS *m/z*: 220 (M^+). HRMS Calcd for $C_{12}H_{19}F_3$: 220.143. Found: 220.143. ^{1}H-NMR ($CDCl_3$) δ: 0.94 (3H, t, J=4.9 Hz), 1.07—1.50 (10H, m), 1.91—2.32 (2H, m), 5.61 (1H, qd, J=7.3, 15.4 Hz), 5.73—6.52 (2H, m), 6.55—6.97 (1H, m). ^{19}F-NMR ($CDCl_3$) ppm: −6.57 (d, J=8.5 Hz), −0.85 (d, J=7.3 Hz), 10.37 (d, J=6.1 Hz) ratio 1:14:1. The first peak is attributed to the (2*Z*,4*E*) isomer of **26**, the second to the (2*E*,4*E*) isomer, and the last to a chlorinated derivative of **11**.

1,1,1-Trifluoro-3-methyl-2,4-nonadiene (27) $POCl_3$ (250 mg) was added to a solution of 1,1,1-trifluoro-3-methyl-4-nonen-2-ol (**10**, 333 mg, 1.6 mmol) in pyridine (0.8 ml) at 0 °C, and the mixture was stirred at 110 °C for 48 h. After cooling, the mixture was treated with ice water and extracted with Et_2O. The Et_2O layer was washed with dilute HCl, H_2O and saturated $NaHCO_3$, and dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by a bulb-to-bulb distillation to give (**27**, 0.24 g, 80%). **27**: A colorless oil. MS *m/z*: 192 (M^+). HRMS Calcd for $C_{10}H_{15}F_3$: 192.113. Found: 192.113. ^{1}H-NMR ($CDCl_3$) δ: 0.78—1.09 (3H, m), 1.12—1.54 (4H, m), 1,80—2.01 (3H, m), 2.03—2.36 (2H, m), 5.39 (1H, q, J=8.5 Hz), 5.98 (1H, td, J=5.7, 15.7 Hz), 6.54 (1H, d, J=15.7 Hz). ^{19}F-NMR ($CDCl_3$) ppm: −8.87 (dqd, J=8.5, 2.1, 2.1 Hz).

3-[(Trifluoromethyl)methylene]cyclohexene (28) A mixture of **5** (833 mg, 4.6 mmol), $POCl_3$ (1.45 g, 9.5 mmol) and pyridine (2 ml) was heated at 110 °C for 66 h. After usual work-up, the residue was distilled to give a colorless oil (371 mg, 50%), which was found to consist of three components (ratio 12:3:1) by gas liquid chromatography (GLC) (15% DEGS 4 mm × 2 m, 60 °C, carrier, N_2 at 30 ml/min), and ^{19}F-NMR analyses. The two main components were obtained by preparative GLC (15% DEGS 4 mm × 2 m, 25 °C, carrier, He at 30 ml/min). The major product: (*Z*)-3-[(Trifluoromethyl)methylene]cyclohexene (**28**): A colorless oil. MS *m/z*: 162 (M^+). ^{1}H-NMR ($CDCl_3$) δ: 1.73—1.82 (2H, m), 2.16—2.24 (2H, m), 2.33—2.40 (2H, m), 5.26 (1H, q, J=8.7 Hz), 6.17 (1H, dqd, J=10.3, 4.0, 1.5 Hz), 6.57 (1H, dqd, J=10.3, 2.0, 1.0 Hz). NOE interaction between the vinylic proton alpha to CF_3 at 5.26 ppm and the protons at 2.33 ppm was observed (1.3%). which shows that stereochemistry of the new double bond is *Z*. ^{19}F-NMR ($CDCl_3$) ppm: −7.38 (dd, J=8.7, 2.0 Hz). The minor product: (*E*)-3-[(Trifluoromethyl)methylene]cyclohexene: A colorless oil. MS *m/z*: 162 (M^+). ^{1}H-NMR ($CDCl_3$) δ: 1.74 (2H, tt, J=6.3, 6.3 Hz), 2.12—2.22 (2H, m), 2.53—2.60 (2H, m), 5.35 (1H, q, J=9.0 Hz), 6.06 (1H, d, J=12.1 Hz), 6.13 (1H, dt, J=12.1, 4.0 Hz). ^{19}F-NMR ($CDCl_3$) ppm: 6.65 (d, J=9.0 Hz). NOE interaction was observed between the two olefinic protons (16%).

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References and Notes

1) Part VI: T. Nagai, K. Ogawa, M. Morita, M. Koyama, A. Ando, T. Miki, and I. Kumadaki, *Chem. Pharm. Bull.*, **37**, 1751 (1989).
2) Parts of this work were presented at the 109th and 110th Annual Meetings of the Pharmaceutical Society of Japan, Nagoya and Sapporo, 1989 and 1990.
3) *a*) Y. Kobayashi, T. Nagai, and I. Kumadaki, *Chem. Pharm. Bull.*, **32**, 5031 (1984); *b*) T. Nagai, I. Kumadaki, T. Miki, Y. Kobayashi, and G. Tomizawa, *ibid.*, **34**, 1546 (1986); *c*) T. Nagai, T. Miki, and I. Kumadaki, *ibid.*, **34**, 4782 (1986).
4) *a*) T. Nagai, T. Miki, and I. Kumadaki, *Chem. Pharm. Bull.*, **35**, 3620 (1987); *b*) T. Nagai, M. Hama, M. Yoshioka, M. Yuda, N. Yoshida, A. Ando, M. Koyama, T. Miki, and I. Kumadaki, *ibid.*, **37**, 177 (1989).
5) R. Pautrat, J. Marteau, and R. Cheritat, *Bull. Soc. Chim. Fr.*, **1968**, 1182.
6) D. B. Dess and J. C. Martin, *J. Org. Chem.*, **48**, 4156 (1983).
7) A trifluoromethyl group is easily replaced as it is a pseudo-halogen. See Y. Kobayashi, and I. Kumadaki, *Accounts Chem. Research*, **11**, 197 (1978).
8) D. Seebach and V. Prelog, *Angew. Chem. Int. Ed. Engl.*, **21**, 654 (1982).