Synthesis of enantiomerically enriched α-trifluoromethylated acids, esters and ketones

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Abstract

α-Trifluoromethylated carboxylic acids have been obtained with high optical purity by enzymatic hydrolysis. Further, the synthesis of optically active α-trifluoromethylated ketones by the thermolysis of diallyl alcohols, produced from the reaction of Grignard reagent and optically pure α-trifluoromethylated carboxylic acid ethyl esters, is described.

Introduction

The importance of trifluoromethyl substitution at the position α to the carbonyl moiety lies in its capacity to engender bioactive compounds [1, 2] and to serve as a diagnostic tool for functional materials [3, 4]. However, very little synthetic application of chiral materials with a trifluoromethyl group at the position α to the carbonyl moiety has been studied since the strongly electronegative nature of the trifluoromethyl group interferes with, or alters the course of, reactions when compared to the analogous reactions involving non-fluorinated reactants [5]. In particular, the presence of an active hydrogen at the position α to the carbonyl moiety has been one of the most significant factors in preventing the creation of chirality in α-trifluoromethylated carbonyl compounds by chemical methods. In fact, reported synthetic routes to α-trifluoromethylated ketones to data have been limited to (i) the radical addition of trifluoromethyl iodide to enamines [6], (ii) the nucleophilic reaction of the enolsilyl ether derived from 3,3,3-trifluoropropiophenone [7] and (iii) the synthesis of 2-(trifluoromethyl)-propiophenone via the oxidation of 1-phenyl-2-(trifluoromethyl)-1-propanol [8]. Accordingly, we have been studying simple synthetic methods for the preparation of optically active carbonyl compounds bearing an α-trifluoromethyl group.

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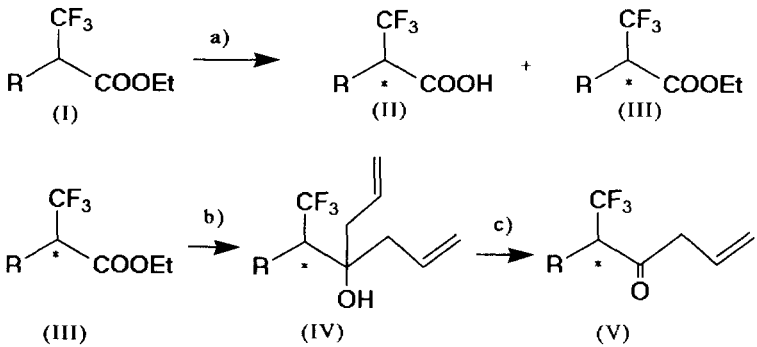
Results and discussion

The synthesis of optically active α-trifluoromethyl carboxylic acids (**II**) has been accomplished by the enantioselective enzymatic hydrolysis of α-trifluoromethyl esters (**I**) as shown in Scheme 1. Ethyl 2-(trifluoromethyl)-alkylates (**I**) obtained by the reported method [9] were employed as substrates, using lipase-PS (*Pseudomonas* sp.; Amano Seiyaku Co. Ltd.). The results obtained are listed in Table 1. Since the present biochemical method is a kinetic resolution, not only the hydrolyzed products (**II**) but also the unreacted esters (**III**) are optically active. Obviously, these facts demonstrate that the active hydrogen at the position α to the carboxy moiety is not removed



Scheme 1. a) Lipase PS, H_2O; b) allylmagnesium chloride, THF, 0 °C, 5 h; c) thermolysis at 400 °C with a liquid flow rate 0.5 ml min^{-1}.

TABLE 1

Physical properties of optically active acids

Comp. No.	R	Hydrolysis		$[\alpha]_D^{21}$ (*c*) (MeOH)	Carboxylic acids		
		Time (h)	Conversion (%)		Opt. purity[a] (% *e.e.*)	^{19}F NMR[b]	
						δ (ppm)	J_{FH} (Hz)
IIa	C_2H_5	56	45	−10.9(1.01)	87	−10.7(d)	8.3
IIb	n-C_3H_7	40	31	−11.3(1.15)	71	−10.5(d)	7.5
IIc	allyl	10	19	−9.77(1.13)	94	−10.1(d)	7.3
IId	C_4H_9	48	40	−15.9(0.99)	>95	−9.9(d)	7.9
IIe	i-C_4H_9	78	40	−14.63(1.026)	91	−9.8(d)	7.5
IIf	$CH_2{=}CH(CH_2)_2$	14	15	−13.7(1.04)	>90	−10.5(d)	7.5
IIg	Ph	24	45	−5.77(1.48)	70	−10.7(d)	9.0
IIh	$PhCH_2$	20	45	−13.0(0.48)	80	−10.2(d)	9.4

[a]The optical purity was determined by GLC methods after conversion of the compound to its carbinol with $LiAlH_4$ and then to its diastereomeric ester with optically active MTPA. The analysis was undertaken via a Shimadzu GC-14A capillary gas chromatography using a ULBON HR-20M column.

[b]δ (ppm) from ext. CF_3COOH in $CDCl_3$.

TABLE 2

Physical properties of optically active ketones

R	Compound (IV)		Compound (V)				
	Yield (%)	B.p. (°C/mmHg)	Yield (%)	$[\alpha]_D^{21}$ (*c*) (MeOH)	O.p.[a] (% *e.e.*)	^{19}F NMR[b]	
						δ (ppm)	J_{FH} (Hz)
Et	37	78–80(35)	16	+8.90(1.01)	84	−11.4(d)	9.5
n-C_3H_7	44	94–96(31)	31	+9.70(1.14)	69	−13.0(d)	9.5
CH_2=$CHCH_2$	56	94–95(33)	31	+13.2(0.97)	91	−10.3(d)	9.0
n-C_4H_9	60	90–92(30)	35	+14.6(0.86)	89	−8.70(d)	7.9
$PhCH_2$	40	135–137(28)	36	+13.7(0.93)	78	−10.5(d)	7.7

[a]The optical purity was determined by ^{19}F NMR intensities using NMR shift reagent.
[b]δ (ppm) from ext. CF_3COOH in $CDCl_3$.

by lipase-PS under these reaction conditions. The optical purities of α-trifluoromethylated acids and esters were determined by GLC methods after conversion of the compounds to their carbinols with $LiAlH_4$ and then to their diastereomeric esters by optically active MTPA; however, their absolute configurations have not been determined at the present time.

In the next phase, a stereoselective synthetic approach to α-trifluoromethylated ketones has been studied. Firstly, bis(homoallyl)alkanols (**IV**) were prepared from the reaction of optically active ethyl 2-(trifluoromethyl)-alkylates (**III**) with allyl magnesium chloride at 0 °C. Then a mixture solution of diisopropyl ether and carbinol (**IV**) was fed into a Pyrex tube maintained at 400 °C, with a liquid flow rate of 0.5 ml min^{-1} [10], as shown in Scheme 1. The desired optically active 1-(trifluoromethyl)alkyl allyl ketones (**V**) were purified by column chromatography on silica gel. Although various other types of Grignard reagents were examined, the thermolysis of their alcohols did not produce the desired ketones. Some results are listed in Table 2.

Experimental

General procedures

The reaction products were analyzed by GC methods using a 3 mm i.d.×3 m column of 15% Silicone DC 200 on 60–80 mesh Celite 545. NMR spectra were recorded at 60 or 200 MHz for ^{1}H NMR and 56.4 MHz for ^{19}F NMR in $CDCl_3$. ^{19}F chemical shifts are reported in parts per million (ppm) relative to trifluoroacetic acid (δ 0.00) as an external standard.

*(−)-2-(Trifluoromethyl)butanoic acid (**IIa**)*

A suspension of ethyl 2-(trifluoromethyl)butyrate (**I**, R=C_2H_5) (9.2 g, 50 mmol) and lipase-PS (10 g, 3×10^4 unit g^{-1}; Amano Seiyaku Co. Ltd.) in distilled water (20 ml) was stirred at 40 °C. The mixture was maintained

at pH 7 by adding 0.1 N NaOH aqueous solution and the hydrolysis was carried to less than 45% conversion. The unreacted ester was isolated from the aqueous phase by extraction with diisopropyl ether. The aqueous solution was acidified by adding 1 N HCl aqueous solution, and the optically active acid was then extracted with diisopropyl ether. The extract was washed with saturated aqueous NaCl and dried over Na_2SO_4. After removal of the solvent, the acid product was carefully chromatographed on silica gel, using a mixture of n-hexane/dichloromethane (5:1) as an eluent to give **IIa** in 23% yield; ^{19}F NMR $CDCl_3$ δ: −10.7 (d, J_{FH} = 8.3 Hz) ppm. ^1H NMR $CDCl_3$ δ: 0.97 (CH_3, t, J_{HH} = 7.0 Hz); 1.95–2.09 (CH_2, m); 3.07 ($CHCF_3$, m); 10.6 (COOH) ppm. IR KBr cm^{-1} 1720 (C=O). High-resolution MS: Calcd. for $C_5H_7O_2F_3$, 156.0398. Found, 156.0409.

*(−)-2-(Trifluoromethyl)pentanoic acid (**IIb**)*

With the same procedure as above, ethyl 2-(trifluoromethyl)pentanate (50 mmol) and lipase-PS (10 g) were used and the mixture worked-up similarly. (−)-2-(Trifluoromethyl)pentanoic acid (**IIb**) was obtained in 44% yield. ^{19}F NMR $CDCl_3$ δ: −10.5 (d, J_{FH} = 7.5 Hz ppm). ^1H NMR $CDCl_3$ δ: 0.94 (CH_3, t, J_{HH} = 7.0 Hz); 1.40–1.95 (4H, m); 3.06 ($CHCF_3$, m); 10.8 (COOH) ppm. IR KBr cm^{-1}: 3445 (COOH); 1760 (C=O). High-resolution MS: Calcd. for $C_6H_9O_2F_3$, 170.0555. Found, 170.0547.

*(−)-2-(Trifluoromethyl)-4-pentenoic acid (**IIc**)*

With the same procedure as above, ethyl 2-(trifluoromethyl)-4-pentenate (50 mmol) and lipase-PS (10 g) were used and the mixture worked-up similarly. (−)-2-(Trifluoromethyl)-4-pentenoic acid (**IIc**) was obtained in 55% yield. ^{19}F NMR $CDCl_3$ δ: −10.1 (d, J_{FH} = 7.3 Hz) ppm. ^1H NMR $CDCl_3$ δ: 2.55 (2H, d, J_{HH} = 6.0 Hz); 3.15 ($CHCF_3$, m); 5.08–5.34 (=CH_2, m); 5.58–5.90 (CH=, m) ppm. IR KBr cm^{-1} 3445 (COOH); 1770 (C=O). High-resolution MS: Calcd. for $C_6H_7O_2F_3$, 163.0398. Found, 168.0387.

*(−)-2-(Trifluoromethyl)hexanoic acid (**IId**)*

With the same procedure as above, ethyl 2-(trifluoromethyl)hexanate (50 mmol) and lipase PS (10 g) were used and the mixture worked-up similarly. (−)-2-(Trifluoromethyl)hexanoic acid (**IId**) was obtained in 25.5% yield. ^{19}F NMR $CDCl_3$ δ: −9.9 (d, J_{FH} = 7.9 Hz) ppm. ^1H NMR $CDCl_3$ δ: 0.92 (CH_3, t, J_{FH} = 6.0 Hz); 1.37–1.78 (6H, m); 3.03 ($CHCF_3$, m); 10.8 (COOH) ppm. IR KBr cm^{-1} 3440 (COOH); 1770 (C=O). High-resolution MS: Calcd. for $C_7H_{11}O_2F_3$, 184.0711. Found, 184.0724.

*(−)-2-(Trifluoromethyl)-4-methylpentanoic acid (**IIe**)*

With the same procedure as above, ethyl 2-(trifluoromethyl)-4-methylpentanate (50 mmol) and lipase-PS (10 g) were used and the mixture worked-up similarly. (−)-2-(Trifluoromethyl)-4-methylpentanoic acid (**IIe**) was obtained in 20% yield. ^{19}F NMR $CDCl_3$ δ: −9.8 (d, J_{FH} = 7.5 Hz) ppm. ^1H NMR $CDCl_3$ δ: 0.95 (CH_3, t, J_{HH} = 6.0 Hz); 1.63 (2H, m); 2.01 (1H, m); 3.08

($CHCF_3$, m); 10.7 (COOH) ppm. IR KBr cm^{-1} 3445 (COOH); 1760 (C=O). High-resolution MS: Calcd. for $C_7H_{11}O_2F_3$, 184.0711. Found, 184.0709.

(−)-2-(Trifluoromethyl)-5-hexenoic acid ***(IIf)***

With the same procedure as above, ethyl 2-(trifluoromethyl)-5-hexenate (50 mmol) and lipase-PS (10 g) were used and the mixture worked-up similarly. (−)-2-(Trifluoromethyl)-5-hexenoic acid (**IIf**) was obtained in 24% yield. ^{19}F NMR $CDCl_3$ δ: −9.5 (d, J_{FH}=7.5 Hz) ppm. ^1H NMR $CDCl_3$ δ: 2.07–2.20 (4H, m); 3.10 ($CHCF_3$, m); 5.00–5.15 (CH_2=, m); 5.90 (=CH, m); 10.7 (COOH) ppm. IR KBr cm^{-1}: 3450 (COOH); 1760 (C=O). High-resolution MS: Calcd. for $C_7H_9O_2F_3$, 182.0555. Found, 182.0549.

(−)-2-(Trifluoromethyl)-2-phenylacetic acid ***(IIg)***

With the same procedure as above, ethyl 2-(trifluoromethyl)-2-phenylacetate (50 mmol) and lipase-PS (10 g) were used and the mixture worked-up similarly. (−)-2-(Trifluoromethyl)-2-phenylacetic acid (**IIg**) was obtained in 35% yield. ^{19}F NMR $CDCl_3$ δ: −10.5 (d, J_{FH}=9.5 Hz) ppm. ^1H NMR $CDCl_3$ δ: 3.08 ($CHCF_3$, m); 7.05–7.24 (Ar–H); 10.9 (COOH) ppm. IR KBr cm^{-1} 3445 (COOH); 1755 (C=O). High-resolution MS: Calcd. for $C_9H_7O_2F_3$, 204.0398. Found, 204.0391.

(−)-2-(Trifluoromethyl)-3-phenylpropanoic acid ***(IIh)***

With the same procedure as above, ethyl 2-(trifluoromethyl)-3-phenylpropanate (50 mmol) and lipase-PS (10 g) were used and the mixture worked-up similarly. (−)-2-(Trifluoromethyl)-3-phenylpropanoic acid (**IIh**) was obtained in 41% yield. ^{19}F NMR $CDCl_3$ δ: −10.1 (d, J_{FH}=9.5 Hz) ppm. ^1H NMR $CDCl_3$ δ: 3.04–3.21 (3H, m); 7.06–7.27 (Ar–H); 10.9 (COOH) ppm. IR KBr cm^{-1} 3450 (COOH); 1750 (C=O). High-resolution MS: Calcd. for $C_{10}H_9O_2F_3$, 218.0555. Found, 218.0564.

Hydrolysis using lipase P (*Pseudomonas* sp., Amano Seiyaku Co. Ltd.) in the above mentioned reactions gave similar results.

Synthesis of optically active ketones

In other asymmetric hydrolyses carried out as reported above, the ethyl ester was hydrolyzed to more than 75%, and then the residual (+)-ethyl ester purified by column chromatography on silica gel.

(+)-Allyl 1-(trifluoromethyl)propyl ketone ***(Va)***

(a) Reaction of allylmagnesium chloride with ethyl 2-(trifluoromethyl)butyrate — To the solution of a Grignard reagent prepared from magnesium (0.48 g, 20 mmol) and allyl chloride (1.50 g, 20 mmol) in tetrahydrofuran (40 ml), (+)-ethyl 2-(trifluoromethyl)butyrate (1.84 g, 10 mmol) in tetrahydrofuran (10 ml) was added at 0 °C. The reaction mixture was agitated for 5 h at 0 °C and stirred overnight at room temperature. The mixture was quenched with saturated NH_4Cl solution (50 ml) and the oily materials then extracted with diisopropyl ether. The extracts were washed

with water and then dried over anhydrous sodium sulfate. On removal of the solvent, distillation gave the corresponding carbinol (**IV**, R = Et) in 37% yield, b.p., 78–80 °C/35 mmHg. ^{19}F NMR $CDCl_3$ δ: −15.2 (d, J_{FH} = 9.6 Hz) ppm. ^1H NMR $CDCl_3$ δ: 1.05 (CH_3, t, J_{HH} = 7.0 Hz); 1.88 (3H, m); 2.39 (4H, d, J_{HH} = 7.2 Hz); 2.70 ($CHCF_3$, m); 5.00–5.30 (=CH_2, m); 5.60–5.90 (CH=, m) ppm. IR KBr cm^{-1} 3550 (OH); 1630 (C=C).

(b) Thermolysis of carbinol (IV, R = Et) – A diisopropyl ether solution (5 ml) of the above carbinol (**IV**, R = Et) (1.0 g) was fed into a vertical unpacked pyrex tube maintained at 400 °C, with a liquid flow rate of 0.5 g ml min^{-1} [10]. On removal of the solvent, the residues were purified by column chromatography on silica gel, eluant a mixture of n-hexane/dichloromethane (8:2) to give (+)-allyl 1-(trifluoromethyl)propyl ketone (**Va**) in 16% yield. ^{19}F NMR $CDCl_3$ δ: −11.4 (d, J_{FH} = 9.5 Hz) ppm. ^1H NMR $CDCl_3$ δ: 0.95 (CH_3, t, J_{HH} = 7.0 Hz); 1.90 (2H, m); 3.05 ($CHCF_3$, m); 3.35 (2H, d, J_{HH} = 6.0 Hz); 5.0–5.35 (CH_2=, m); 5.60–5.90 (=CH, m) ppm. IR KBr cm^{-1} 1720 (C=O); 1620 (C=C). High resolution MS: Calcd. for $C_8H_{11}OF_3$, 180.0762. Found, 180.0754.

*(+)-Allyl 1-(trifluoromethyl)butyl ketone (**Vb**)*

(a) Reaction of allylmagnesium chloride with ethyl 2-(trifluoromethyl)pentanate – In the above reaction, allylmagnesium chloride prepared from magnesium (0.48 g, 20 mmol) and allyl chloride (1.50 g, 20 mmol) in tetrahydrofuran (40 ml) and (+)-ethyl 2-(trifluoromethyl)pentanate (1.96 g, 10 mmol) was used. After 5 h stirring at 0 °C, the mixture was worked-up similarly. Distillation gave the corresponding carbinol (**IV**, R = Pr) in 44% yield, b.p., 107–109 °C/31 mmHg. ^{19}F NMR $CDCl_3$ δ: −20.4 (d, J_{FH} = 7.5 Hz) ppm. ^1H NMR $CDCl_3$ δ: 0.95 (CH_3, t, J_{HH} = 6.0 Hz); 1.40–2.50 (10H, m); 5.12–5.34 (=CH_2, m); 5.75–6.10 (CH=, m) ppm. IR KBr cm^{-1} 3555 (OH); 1640 (C=C).

(b) Thermolysis of carbinol (IV, R = Pr) – The carbinol (**IV**, R = Pr) (1.0 g) in diisopropyl ether (5 ml) was fed in, and the mixture then worked-up similarly giving (+)-allyl 1-(trifluoromethyl)butyl ketone in 31% yield. ^{19}F NMR $CDCl_3$ δ: −16.0 (d, J_{FH} = 9.0 Hz) ppm. ^1H NMR $CDCl_3$ δ: 0.95 (CH_3, t, J_{HH} = 6.0 Hz); 1.46–1.90 (4H, m); 2.24–2.41 (2H, m); 3.10 ($CHCF_3$, m); 5.10–5.34 (CH_2=, m); 5.75–6.00 (=CH, m) ppm. IR KBr cm^{-1} 1720 (C=O); 1620 (C=C). High-resolution MS: Calcd. for $C_9H_{13}OF_3$, 194.0918. Found, 194.0914.

*(+)-Allyl 1-(trifluoromethyl)-3-butenyl ketone (**Vc**)*

(a) Reaction of allylmagnesium chloride with ethyl 2-(trifluoromethyl)-4-pentenate – To the solution of allylmagnesium chloride prepared from magnesium (0.48 g, 20 mmol) and allyl chloride (1.50 g, 20 mmol) in tetrahydrofuran (40 ml), (+)-ethyl 2-(trifluoromethyl)-4-pentenate (1.95 g, 10 mmol) in freshly dried tetrahydrofuran (20 ml) was added at 0 °C.

After 5 h stirring at 0 °C, the mixture was worked-up similarly. Distillation gave the corresponding carbinol (**IV**, R = allyl) in 56% yield, b.p., 94–95 °C/33 mmHg. ^{19}F NMR $CDCl_3$ δ: −15.3 (d, J_{FH} = 9.2 Hz) ppm. ^1H NMR $CDCl_3$ δ: 2.25–2.60 (7H, m); 2.70–3.00 (1H, m); 5.00–5.40 (=CH_2, m); 5.50–5.90 (CH=, m) ppm. IR KBr cm^{-1} 3500 (OH); 1630 (C=C).

(b) Thermolysis of carbinol (IV, R = allyl) — The carbinol (**IV**, R = allyl) (1.0 g) in diisopropyl ether (5 ml) was fed in, and the mixture was worked-up similarly giving (+)-allyl 1-(trifluoromethyl)-3-butenyl ketone in 31% yield. ^{19}F NMR $CDCl_3$ δ: −10.3 (d, J_{FH} = 9.0 Hz) ppm. ^1H NMR $CDCl_3$ δ: 2.60 (2H, m); 3.20 ($CHCF_3$, m); 3.37 (2H, d, J_{HH} = 6.0 Hz); 5.10–5.40 (CH_2=, m); 5.60–5.90 (=CH, m) ppm. IR KBr cm^{-1} 1720 (C=O); 1620 (C=C). High-resolution MS: Calcd. for $C_9H_{11}OF_3$, 192.0762. Found, 192.0771.

*(+)-Allyl 1-(trifluoromethyl)pentyl ketone (**Vd**)*

(a) Reaction of allylmagnesium chloride with ethyl 2-(trifluoromethyl)hexanate — To the solution of a Grignard reagent prepared from magnesium (0.48 g, 20 mmol), and allyl chloride (1.50 g, 20 mmol) in tetrahydrofuran (40 ml), (+)-ethyl 2-(trifluoromethyl)hexanate (2.08 g, 10 mmol) in freshly dried tetrahydrofuran (20 ml) was added at 0 °C. After 5 h stirring at 0 °C, the mixture was worked-up similarly. Distillation gave the corresponding carbinol (**IV**, R = Bu) in 60% yield, b.p., 90–92 °C/30 mmHg. ^{19}F NMR $CDCl_3$ δ: −11.0 (d, J_{FH} = 8.5 Hz) ppm. ^1H NMR $CDCl_3$ δ: 0.93 (CH_3, t, J_{HH} = 6.0 Hz); 1.20–1.40 (4H, m); 1.70–1.90 (2H, m); 2.20–2.60 (6H, m); 5.10–5.30 (=CH_2, m); 5.60–5.90 (CH=, m) ppm. IR KBr cm^{-1} 3500 (OH); 1630 (C=C).

(b) Thermolysis of carbinol (IV, R = Bu) — The carbinol (**IV**, R = Bu) (1.0 g) in diisopropyl ether (5 ml) was fed in, and then the mixture was worked-up similarly giving (+)-allyl 1-(trifluoromethyl)pentyl ketone in 35% yield. ^{19}F NMR $CDCl_3$ δ: −8.7 (d, J_{FH} = 8.0 Hz) ppm. ^1H NMR $CDCl_3$ δ: 0.95 (CH_3, t, J_{HH} = 6.0 Hz); 1.30–1.60 (4H, m); 1.70–1.90 (2H, m); 3.10 ($CHCF_3$, m); 3.35 (2H, d, J_{HH} = 7.0 Hz); 5.05–5.35 (=CH_2, m); 5.60–5.90 (CH=, m) ppm. IR KBr cm^{-1} 1720 (C=O); 1620 (C=C). High-resolution MS: Calcd. for $C_{10}H_{15}OF_3$, 208.1076. Found, 208.1069.

*(+)-Allyl 1-(trifluoromethyl)-2-phenylethyl ketone (**Vh**)*

(a) Reaction of allylmagnesium chloride with ethyl 2-(trifluoromethyl)-3-phenylpropanate — To the solution of a Grignard reagent prepared from magnesium (0.48 g, 20 mmol) and allyl chloride (1.50 g, 20 mmol) in tetrahydrofuran (40 ml), (+)-ethyl 2-(trifluoromethyl)-3-phenylpropanate (2.46 g, 10 mmol) in freshly dried tetrahydrofuran (20 ml) was added at 0 °C. After 5 h stirring at 0 °C, the mixture was worked-up similarly. Distillation gave the corresponding carbinol (**IV**, R = CH_2Ph) in 36% yield, b.p., 135–137 °C/28 mmHg. ^{19}F NMR $CDCl_3$ δ: −15.5 (d, J_{FH} = 9.0 Hz) ppm. ^1H NMR $CDCl_3$ δ: 2.50 (4H, d, J_{HH} = 7.0 Hz); 2.70–3.30 (3H, m); 5.10–5.30 (=CH_2,

m); 5.60–6.00 (CH=, m); 7.25 (Ar–H) ppm. IR KBr cm^{-1} 3500 (OH); 1615 (C=C).

(b) Thermolysis of carbinol (IV, R=CH_2Ph) – The carbinol (**IV**, R=CH_2Ph, 1.0 g) in diisopropyl ether (5 ml) was fed in, and then the mixture was worked-up similarly giving (+)-allyl 1-(trifluoromethyl)-2-phenylethyl ketone in 36% yield. ^{19}F NMR $CDCl_3$ δ: −10.5 (d, J_{FH}=7.7 Hz) ppm. ^1H NMR $CDCl_3$ δ: 3.00–3.20 (4H, m); 3.60 ($CHCF_3$, m); 4.90–5.10 (=CH_2, m); 5.50–5.70 (CH=, m); 7.15–7.25 (Ar–H) ppm. IR KBr cm^{-1} 1720 (C=O); 1640 (C=C). High-resolution MS: Calcd. for $C_{13}H_{13}OF_3$, 242.0919. Found, 242.0913.

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