A New Convenient Synthetic Method for 3-Allyl-1,1,1-trifluoroacetylacetone and its Derivatives

Yasuhiro Kamitori, Masaru Hojo*, Ryōichi Masuda, Toshihiko Fujitani, Takashi Kobuchi, Takayuki Nishigaki

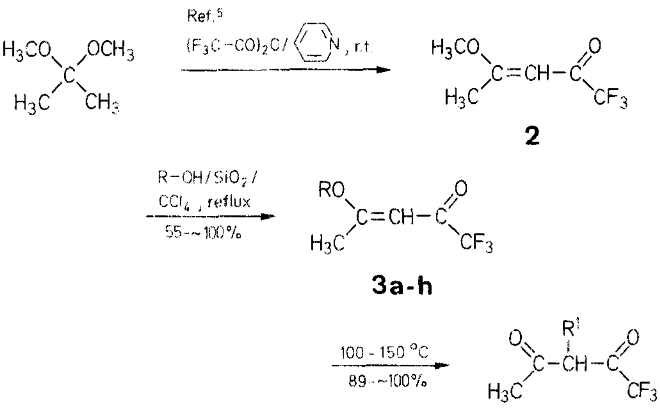
Department of Industrial Chemistry, Faculty of Engineering, Kobe University, Rokkodai, Kobe 657, Japan

Starting from the dimethyl acetal of acetone several 3-allyl-1,1,1-trifluoroacetylacetones (**1**) were synthesized in high yields by treatment with trifluoroacetic anhydride, ether exchange reaction of the resulting β-trifluoroacetyl-α-methylvinyl ether with allyl alcohols in the presence of silica gel, followed by Claisen rearrangement. Reaction of **1** with hydrazine hydrate gave an allyl-substituted pyrazole bearing a trifluoromethyl group in high yield.

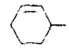
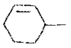
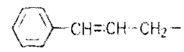
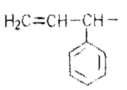
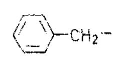
1,1,1-Trifluoroacetylacetone (**1**) has been known as a unique and useful chelating reagent to extract and separate various metal cations[1]. High solubility toward most organic solvents and readily sublimable nature of the metal chelates of **1** and its derivatives are particularly useful for L.C. and G.L.C. analysis of a variety of metal cations[2]. Compound **1** and its derivatives have also been utilized as new N.M.R. shift reagents[3]. At the same time **1** is expected to be an important intermediate to prepare various heterocyclic compounds bearing a trifluoromethyl group, and as for medicinal activity their specific nature attracts much attention in this field[4].

Recently, we reported that β-trifluoroacetylvinyl ether (**2**) can be readily prepared from the dimethyl acetal of acetone and trifluoroacetic anhydride in high yields[5]. Starting from **2**, we have found the title compounds **1** bearing various allylic groups can be prepared easily by ether exchange reaction followed by Claisen rearrangement of the intermediate allyloxy derivatives **3**.

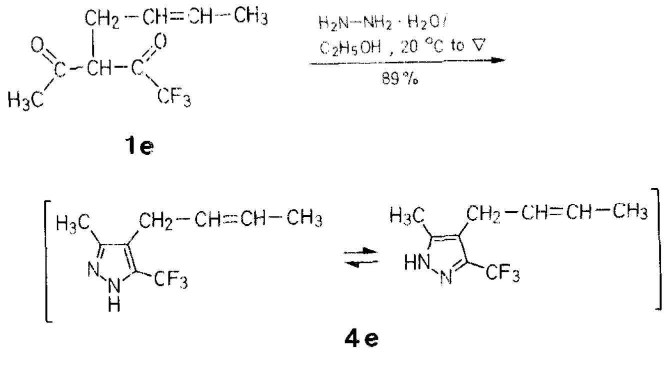
The ether exchange reaction (**2** → **3**) proceeded at the refluxing temperature of tetrachloromethane in the presence of silica gel and the methoxy group was easily replaced by the desired allyloxy groups to give the corresponding **3** in high yields (Table 1). This ether exchange can also be regarded as a vinylogous reaction of ester exchange of trifluoroacetates. In the cases of **3b**, **3d**, **3e**, and **3f** subsequent Claisen rearrangement (**3** → **1**) occurred to some extent, giving these products as mixtures with **1b**, **1d**, **1e**, and **1f**, respectively. It seems noteworthy that considerable amounts of sterically hindered diketone **1d** were produced under such a mild condition for this ether exchange reaction. Attempted reaction without added silica gel resulted in poorer yields of **3** and most of the starting material **2** was recovered together with the formation of some unidentified materials.



2 **3a-h** **1a-g**

1,3	R →	R^1 (in **1**)
a	$H_2C=CH-CH_2-$	$H_2C=CH-CH_2-$
b	$H_3C-CH=CH-CH_2-$	$H_2C=CH-CH(CH_3)-$
c	$H_2C=C(CH_3)-CH_2-$	$H_2C=C(CH_3)-CH_2-$
d	$(H_3C)_2C=CH-CH_2-$	$H_2C=CH-C(CH_3)_2-$
e	$H_2C=CH-CH(CH_3)-$	$H_3C-CH=CH-CH_2-$
f		
g		
h		—

Claisen rearrangement of **3a**–**3g** proceeded cleanly at 100–150 °C and afforded the corresponding products **1a**–**1g** quantitatively (Table 2). Diketones **1a**, **1c** and **1e** exist partially as enols **1a′**, **1c′** and **1e′**), respectively (by ^{1}H-



1e **4e**

Table 1. Ether Exchange Reaction of **2** with Allyl Alcohols in the Presence of Silica Gel

Substrate	Product (Ratio)	Yield [%]	b.p. [°C]/torr[a] or m.p. [°C]	Molecular Formula[b]	^{1}H-N.M.R.[c,d] ($CDCl_3/TMS_{int}$) δ [ppm]
2a	**3a**	97	80°/10	$C_8H_9F_3O_2$ (194.2)	5.15–6.33 (m, 4H, CH=); 4.47 (d, 2H, CH_2); 2.40 (s, 3H, CH_3)
2b	**3b** + **1b** (4 : 1)[e]	~100	110°/7	$C_9H_{11}F_3O_2$ (208.2)	5.33–6.10 (m, 2H, CH=); 4.37 (d, 2H, CH_2); 2.40 (s, 3H, CH_3); 1.76 (s, 3H, CH_3)
2c	**3c**	99	130°/25	$C_9H_{11}F_3O_2$ (208.2)	5.70 (s, 1H, CH=); 5.09 (s, 2H, CH_2=); 4.40 (s, 2H, CH_2); 2.44 (s, 3H, CH_3); 1.81 (s, 3H, CH_3)
2d	**3d** + **1d** (1 : 1)[e]	64	100°/50	$C_{10}H_{13}F_3O_2$ (222.2)	5.67 (s, 1H, CH=); 5.40 (t, 1H, CH=); 4.47 (d, 2H, CH_2); 2.40 (s, 3H, CH_3); 1.70, 1.77 (br, 6H, CH_3)
2e	**3e** + **1e** (1 : 4)[e]	77	100°/9	$C_9H_{11}F_3O_2$ (208.2)	4.85–5.82 (m, 4H, CH= and CH); 2.40 (s, 3H, CH_3); 1.25 (d, 3H, CH_3)
2f	**3f** + **1f** (5 : 3)[e]	55	100°/9	$C_{11}H_{13}F_3O_2$ (234.2)	5.50–5.90 (m, 3H, CH=); 4.80 (br, 1H, CH); 2.40 (s, 3H, CH_3); 1.13–2.20 (m, 6H, CH_2)
2g	**3g**	73	95°	$C_{14}H_{13}F_3O_2$ (270.3)	7.33 (s, 5H_{arom}); 5.98–6.95 (m, 3H, CH=); 4.63 (d, 2H, CH_2); 2.43 (s, 3H, CH_3)
2h	**3h**	71	130°/15	$C_{12}H_{11}F_3O_2$ (244.2)	7.34 (s, 5H_{arom}); 5.80 (s, 1H, CH=); 4.93 (s, 2H, CH_2); 2.44 (s, 3H, CH_3)

[a] Oven temperature of ball-tube distillation.

[b] The microanalyses were in satisfactory agreement with the calculated values: C ±0.35, H ±0.21, F ±0.40.

[c] *All ^{1}H-N.M.R. spectra were recorded at 60 MHz on JEOL PMX 60SI.*

[d] In the case of mixture (**b**, **d**, **e**, and **f**), chemical shifts for **3b**, **3d**, **3e**, and **3f** are recorded here.

[e] These were calculated on the basis of the ^{1}H-N.M.R. spectra.

Table 2. Claisen Rearrangement of **3** to **1**

Substrate	Products (Ratio)	Yield [%]	b.p. [°C]/torr[a]	Molecular[b] Formula	^{1}H-N.M.R.[c] ($CDCl_3/TMS_{int}$) δ [ppm]
3a	**1a** + **1a′** (4 : 1)[d]	99	80°/55	$C_8H_9F_3O_2$ (194.2)	16.07 (s, enol OH); 4.80–6.03 (m, CH=); 4.13 (t, keto CH); 3.13 (d, enol CH_2); 2.61 (t, keto CH_2); 2.41 (s, enol CH_3); 2.23 (s, keto CH_3)
3b	**1b**	96	80°/13	$C_9H_{11}F_3O_2$ (208.2)	4.83–6.06 (m, 3H, CH=); 4.11 (d, 1H, CH); 2.76–3.47 (m, 1H, CH); 2.25, 2.30 (s, 3H, CH_3); 1.12, 1.09 (d, 3H, CH_3)[e]
3c	**1c** + **1c′** (1 : 1)[d]	98	120°/20	$C_9H_{11}F_3O_2$ (208.2)	16.05 (s, enol OH); 4.70 (br, keto CH_2=); 4.61 (br, enol CH_2=); 4.27 (t, keto CH); 3.01 (s, enol CH_2); 2.59 (d, keto CH_2); 2.25 (s, keto CH_3); 2.19 (s, enol CH_3); 1.75 (s, keto CH_3); 1.43 (s, enol CH_3)
3d	**1d**	98	150°/80	$C_{10}H_{13}F_3O_2$ (222.2)	4.80–6.30 (m, 3H, CH=); 4.13 (s, 1H, CH); 2.23 (s, 3H, CH_3); 1.20 (s, 6H, CH_3)
3e	**1e** + **1e′** (1 : 4)[d]	96	90°/15	$C_9H_{11}F_3O_2$ (208.2)	16.21 (s, enol OH); 5.17–5.85 (m, CH=); 4.09 (t, keto CH); 3.00 (br, enol CH_2); 2.58 (t, keto CH_2); 2.26 (s, CH_3); 1.62 (d, CH_3)
3f	**1f**	99	130°/15	$C_{11}H_{13}F_3O_2$ (234.2)	5.17–6.03 (m, 2H, CH=); 4.04, 4.08 (d, 1H, CH)[e]; 2.83–3.40 (br, 1H, CH); 2.28 (s, 3H, CH_3); 1.17–2.22 (m, 6H, CH_2)
3g	**1g**	89	160°/10	$C_{14}H_{13}F_3O_2$ (270.3)	7.16–7.27 (m, 5H_{arom}); 5.66–6.21 (m, 1H, CH=); 4.92–5.25 (m, 2H, CH_2=); 4.66 (d, 1H, CH); 4.00–4.33 (m, 1H, CH); 2.32, 1.82 (s, 3H, CH_3)[e]

[a] Oven temperature of ball tube distillation.

[b] The microanalyses were in satisfactory agreement with the calculated values: C ±0.41, H ±0.32, F ±0.37.

[c] All ^{1}H-N.M.R. spectra were recorded on JEOL PMX 60SI.

[d] *These were calculated on the basis of ^{1}H-N.M.R. spectra.*

[e] These products were the 1 : 1 mixtures of two diastereomers.

N.M.R.). The product **1e** (containing 29% of **1e′**) was successfully converted to pyrazole **4e** in high yield by treating it with hydrazine.

Ether Exchange Reaction of 2 with Allyl Alcohol; Typical Procedure:
Commercial grade silica gel (Wakogel C300, for column chromatography) is dried at 150–170 °C for 3 h under reduced pressure (5 torr). To a suspension of dry silica gel thus prepared (1.0 g) in dry carbon tetrachloride (8 ml), **2** (840 mg, 5 mmol) and allyl alcohol (1.45 g, 25 mmol) are added and the mixture is stirred for 48 h at the reflux temperature of tetrachloromethane. After silica gel is filtered off and washed thoroughly with dichloromethane/diethyl ether (1/1, 30 ml), washings and the filtrates are combined. Removal of the solvent and ball tube distillation (oven temperature 80 °C/10 torr) of the residual material afford pure **3a**; yield: 941 mg (97%).

$C_8H_9F_3O_2$	calc.	C 49.49	H 4.67	F 29.36
(194.2)	found	49.14	4.87	29.70

In the case of the reaction of **2** with cinnamyl alcohol to yield **3g**, the raw product is purified by silica gel column chromatography (benzene) followed by recrystallization from carbon tetrachloride.

Claisen Rearrangement of 3a; Typical Procedure:

In a nitrogen-flushed sealed tube, **3a** (194 mg, 1 mmol) is heated for 18 h at 150 °C. The raw product **1a** is essentially pure by ^{1}H-N.M.R. Further purification for microanalysis is carried out by ball tube distillation (oven temperature 80 °C/55 torr) to afford pure **1a**, yield: 192 mg (99%).

$C_8H_9F_3O_2$	calc.	C 49.49	H 4.67	F 29.36
(194.2)	found	49.21	4.42	29.55

Pyrazole 4e:

To a solution of **1e** (250 mg, 1.201 mmol) in dry ethanol (10 ml) is added hydrazine hydrate (60.1 mg, 1.201 mmol). The mixture is stirred for 40 min at 20 °C and for another 2 h at the reflux temperature. After cooling the mixture is poured onto saturated aqueous sodium chloride (100 ml) and the organic layer is extracted with diethyl ether (2 × 20 ml). The ether layer is dried with magnesium sulfate and the solvent is removed by evaporation. Ball tube distillation (oven temperature 130 °C/6 torr) affords pure **4e**; yield: 218 mg (89%).

$C_9H_{11}F_3N_2$	calc.	C 52.94	H 5.43	N 13.72	F 27.91
(204.2)	found	52.75	5.64	13.62	27.99

^{1}H-N.M.R. ($CDCl_3$): δ = 1.16 (br, 3H); 2.19 (s, 3H); 3.04–3.30 (br, 2H); 5.34–5.48 (m, 2H); 7.42 ppm (br, 1H).

Received: July 16, 1985

---

[1] For instance see: Scribner, W.G., Treat, W.J., Weis, J.D., Moshier, R.W. *Anal. Chem.* **1965**, *37*, 1136.

[2] Sievers, R.E., Ponder, B.W., Morris, M.L., Moshier, R.W. *Inorg. Chem.* **1963**, *2*, 693.

[3] Sanders, J.K.M., Hanson, S.W., Williams, D.H. *J. Am. Chem. Soc.* **1972**, *94*, 5325.

[4] Reviews: Filler, R. in: *Organofluorine Chemicals and Their Industrial Applications*, Banks, R.E., Ed., Ellis Horwood, London, 1979.

[5] Hojo, M., Masuda, R., Okada, E. *Synthesis*, in press.