The Dakin–West Reaction of *N*-Alkoxycarbonyl-*N*-alkyl-α-amino Acids Employing Trifluoroacetic Anhydride

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The Dakin-West reaction of *N*-alkoxycarbonyl-*N*-alkyl-α-amino acids (1a—j) with trifluoroacetic anhydride in the presence of pyridine gave α-amido trifluoromethyl ketones (2a—j), in which probable intermediates were mesoionic 1,3-oxazolium-5-olates (munchnones). The diastereoselective reduction of 2a—f with $NaBH_4$ gave the *threo*-aminoalcohols (5a—f), which may be explained by the Felkin–Anh model. This was confirmed by converting 5a—f into *trans*-5-trifluoromethyl-2-oxazolidinones (6a—f) in good yields.

Key words trifluoromethyl ketone; α-aminoalcohol; Dakin–West reaction; α-amino acid; trifluoroacetic anhydride; 2-oxazolidinone

α-Amino trifluoromethyl ketones (ATFMKs) and the masked versions thereof are compounds which have found widespread use as an important class of inhibitors of hydrolytic enzymes including serine, cysteine and aspartyl proteases[1] and as precursors of physiologically important ethanolamine derivatives.[2]

Published methods for the preparation of ATFMKs are the Henry reaction followed by nitro reduction and oxidation,[3] the condensation of a CF_3ZnX, CF_3MgX, or CF_3SiMe_3 with an aldehyde followed by oxidation,[4] or the condensation of carboxylate dianions with trifluoroacetaldehyde hemiacetal followed by rearrangement and oxidation.[5] In general, the oxidation of trifluoromethyl alcohols to the corresponding ketones is difficult and requires the use of the relatively expensive Dess–Martin reagent.[6] In order to circumvent the oxidation of alcohols, two methods have recently been devised: i) addition of CF_3SiMe_3 to oxazolidin-5-ones followed by acid hydrolysis, which is somewhat limited by steric constraints[7] and ii) hydrolysis of 4-trifluoromethyl-Δ^3-imidazolines, which is limited by the fact that only glycine and phenylglycine derived ATFMKs are accessible.[8]

The Dakin–West (D–W) reaction of *N*-benzoyl α-amino acids with trifluoroacetic anhydride (TFAA) has been successfully implemented for the preparation of α-amino trifluoromethyl ketones.[9] The scope of the sequence seems to be narrow and only α-benzamido trifluoromethyl ketones could be obtained from the corresponding oxazolones.

On the other hand, treatment of *N*-acyl-*N*-alkyl-α-amino acids or *N*-acylprolines with TFAA under the D–W reaction conditions can lead to trifluoromethyl substituted oxazoles,[10] acyloins,[11] or morpholines,[12] depending on the nature of the *N*-substituents of the amino acids and/or reaction conditions. In these reactions, the D–W reaction products, ATFMKs, were not isolated. Recently, we also found that the reaction of *N*-alkoxycarbonylprolines with TFAA led unexpectedly, by way of a novel decarboxylative dehydration followed by trifluoroacetylation, to 4-trifluoroacetyl-2,3-dihydropyrroles.[13] In the reaction, the D–W reaction products 2-trifluoroacetylpyrrolidines were not obtained. As part of our studies on the reactivities of mesoionic 1,3-oxazolium-5-olates generated from secondary α-amino acids, we have investigated in detail the reaction of *N*-alkoxycarbonyl-*N*-alkyl-α-amino acids (**1**) with TFAA, which has not been previously reported in the literature. We now present a full account of this reaction. The reduction of the products, ATFMKs (**2**) with $NaBH_4$ provides the *threo*-aminoalcohols (**5**) which were converted to *trans*-5-trifluoromethyl-2-oxazolidinones (**6**).

Results and Discussion

First, we examined the D–W reaction of *N*-benzyl-*N*-methoxycarbonylglycine (**1a**) with TFAA under various conditions. The results are summarized in Table 1. As is shown in run 1, no reaction takes place in the absence of pyridine. Three eq of TFAA with respect to **1a** were needed to obtain a good yield of the product (**2a**) (runs 4, 7, and 8). Several *N*-alkoxycarbonyl-*N*-alkylamino acids (**1**) were subjected to the reaction under the optimum conditions (run 3). As is shown in Table 2, various amino acids (**1a**—**j**) of glycine, phenylalanine, alanine, leucine, and phenylglycine were transformed to the ATFMKs (**2a**—**j**). The yield of **2a** was dimin-

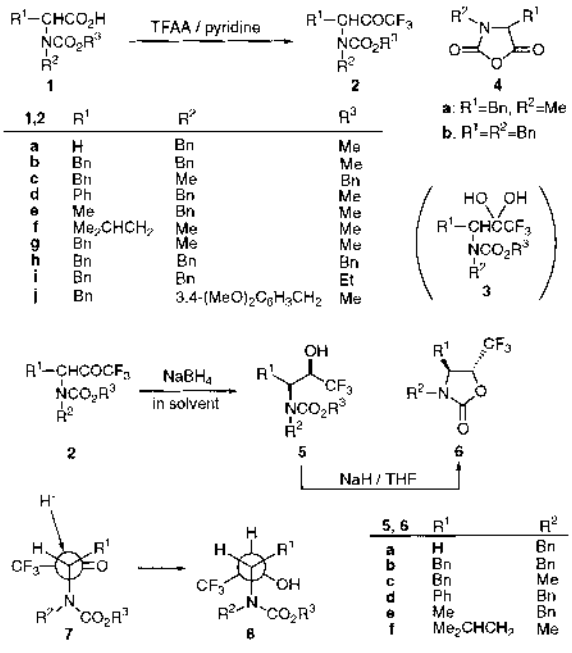

Chart 1

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Table 1. Reactions of *N*-Benzyl-*N*-methoxycarbonylglycine (**1a**) with TFAA[a)]

Run	Base (mol eq)[b)]	Solvent	Conditions[c)]	Yield of **2a** (%)
1	None	Benzene	r.t., 5 h	0
2	Pyridine (3)	Benzene	r.t., 5 h	34
3	Pyridine (3)	Benzene	r.t., 3 h	54
4	Pyridine (3)	Benzene	r.t., 1 h	49
5	Pyridine (3)	CH_2Cl_2	r.t., 1 h	52
6	Pyridine (3)	DMF	r.t., 1 h	16
7	Pyridine (6)	Benzene	r.t., 1 h	45
8	Pyridine (2)	Benzene	r.t., 1 h	44
9	Pyridine (3)	CH_2Cl_2	0 °C, 3 h	55

a) The reactions were carried out on a 1 mmol scale. *b*) Eq refers to molar equivalents with respect to **1a**. *c*) r.t.=room temperature.

Table 2. Reactions of *N*-Alkoxycarbonylamino Acids (**1**) with TFAA

Run	**1**	Product (yield, %)
1	**a**	**2a** (54)
2	**b**	**2b** (98)
3	**c**	**2c** (39), **4a** (43)
4	**d**	**2d** (43)
5	**e**	**2e** (53)
6	**f**	**2f** (93)
7	**g**	**2g** (93)
8	**h**	**2h** (47), **4b** (43)
9	**i**	**2i** (59)
10	**j**	**2j** (75)

ished by the longer reaction time (Table 1, runs 2—4), whereas the yields of ATFMKs (**2b**—**j**) were not influenced by the reaction time. *N*-Methoxycarbonyl (**1a**, **b**, **d**—**g**, and **j**) and *N*-ethoxycarbonyl (**1i**) derivatives worked well and gave the corresponding ATFMKs (**2a**, **b**, **d**—**g**, **i**, and **j**) in good yields. In the case of *N*-benzyloxycarbonyl derivatives (**1c** and **h**), *N*-carboxy α-amino acid anhydrides (**4a** and **b**) were also isolated (runs 3 and 8). The mechanism of formation of **4** is discussed later (Chart 2).

The ^{1}H-NMR spectra of ATFMKs (**2**) were complicated due to both the hindered rotation around the amide bond and the existence of the hydrates (**3**) and the trifluoromethyl ketones (**2**). The MS spectra of **2a**, **2e**, **2f**, and **2j** showed peaks as the hydrates (**3**), whereas those of other **2** showed peaks as the ketones. The IR spectra of **2** exhibited an absorption band due to keto (1760 cm^{-1}) forms.

Formation of the hydrate on silica gel, well known for TFMKs, is responsible for the lowering of the yield.[14)] As significant losses occur through hydration on the silica gel during chromatography, ATFMKs (**2**) can be used without purification as a starting material.

The reaction of **2b** with $NaBH_4$ in EtOH for 1 h afforded an easily separable mixture of alcohol (**5b**) and 2-oxazolidinone (**6b**) in 36% and 56% yields, respectively (Table 3, run 3). The formation of **6b** might be due to the cyclization of **5b** during the reaction. Prolonged reaction time (24 h) leads to the quantitative formation of oxazolidinone (**6b**) (run 4). Compound **5b** was found to be *syn* from the ^{1}H-NMR (J= 3.9 Hz for ring protons 4-H and 5-H) of the correponding oxazolidinone **6b** obtained by cyclization of **5b**, which may be explained by the Felkin–Anh model (**7**) (Chart 1).[15)] In the

Table 3. Reductions of **2** with $NaBH_4$

Run	**2**	Solvent	Conditions[a)]	Product (yield, %)
1	**a**	EtOH	r.t., 48 h	**5a** (26), **6a** (27)
2	**a**	MeOH	r.t., 24 h	**5a** (77)
3	**b**	EtOH	r.t., 1 h	**5b** (36), **6b** (56)
4	**b**	EtOH	r.t., 24 h	**6b** (99)
5	**c**	EtOH	r.t., 48 h	**6c** (91)
6	**d**	EtOH	r.t., 24 h	**5d** (45), **6d** (13)
7	**e**	EtOH	r.t., 24 h	**6e** (91)
8	**f**	EtOH	r.t., 24 h	**5f** (83)

a) r.t.=room temperature.

Table 4. Cyclization of α-Trifluoromethyl Alcohols (**5**) to 2-Oxazolidinones (**6**)

Run	**5**	Base (mol eq)[a)]	Solvent	Conditions[b)]	Product (yield, %)
1	**a**	NaH (1.2)	THF	r.t., 1.5 h	**6a** (71)
2	**a**	NaOEt (1)	EtOH	r.t., 24 h	**6a** (32)
3	**a**	*tert*-BuOK (1.5)	THF	r.t., 16 h	**6a** (61)
4	**a**	*tert*-BuOK (3)	THF	r.t., 6 h	**6a** (20)
5	**d**	NaH (1.3)	THF	r.t., 1 h	**6d** (54)
6	**f**	NaH (1.2)	THF	r.t., 1 h	**6f** (90)

a) Eq refers to molar equivalents with respect to **5**. *b*) r.t.=room temperature.

Felkin–Anh model (**7**), the *N*-alkoxycarbonyl-*N*-alkyl-amido group plays the role of 'large' substituent.[16)]

In order to prove the generality of the reaction, the process was further applied to **2a** and **c**—**f** (Table 3). Phenylalanine (**2c**) and alanine (**2e**) derivatives also worked well (runs 5 and 7). On the other hand, glycine (**2a**), phenylglycine (**2d**), and leucine (**2f**) derivatives failed to complete the cyclization of the alcohol (**5a**, **d**, and **f**) to oxazolidinone (**6a**, **d**, and **f**) under the similar conditions and these reactions afforded the mixture of **5** and **6** (runs 1 and 6). Cyclization of **5a** to **6a** was attempted under various conditions (Table 4). Among the following three bases examined, NaOEt, KOBu^t, and NaH, use of 1.2 mol equivalent of the last one proved to be most effective (runs 1—3). Under the optimum conditions (run 1), the alcohols (**5a**, **d**, and **f**) could be converted to the corresponding 2-oxazolidinone (**6a**, **d**, and **f**) in good yields (runs 1, 5, and 6). ^{1}H-NMR spectrum of **6a**—**f** exhibits a coupling constant $J_{H4\text{-}H5}$=4—5 Hz, reflecting a *trans* relationship between H4 and H5.[16,17)]

Mechanistic Consideration A plausible mechanism of the formation of **2** and **4** is suggested in Chart 2. The reaction involves mesoionic 1,3-oxazolium-5-olates (**11**), commonly known as munchnones, formed through the cyclodehydration of **1** by TFAA. Although munchnones obtained by cyclodehydration of *N*-acylamino acids are the most extensively studied class of mesoionic compounds,[18)] to our knowledge only one publication has been devoted to an attempt to form 2-alkoxy-substituted munchnones from *N*-alkoxycarbonylamino acids.[19)] In order to obtain 2-alkoxy-substituted munchnones, *N*-ethoxycarbonyl-*N*-phenylglycine was treated with $SOCl_2$, in which *N*-carbonylglycine anhydride and ethyl chloride were isolated. This suggests that ring closure to a munchnone actually occurred and that it underwent rapid deethylation.[19)] In our previous work, the reaction of *N*-benzyloxycarbonylproline with TFAA in a refluxing

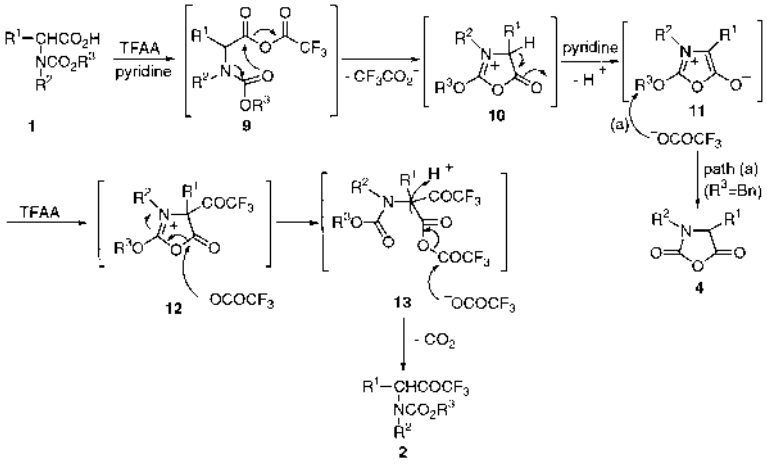

Chart 2

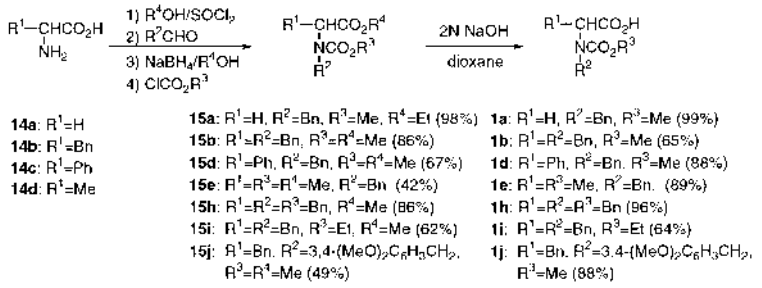

Chart 3

MeCN afforded proline and *N*-benzylacetamide.[13] Formation of the proline is presumably due to hydrolysis of *N*-carbonylproline anhydride, which was produced by the attack of trifluoroacetate ion on the munchnone intermediate. *N*-Ethoxycarbonyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylic acid was treated with TFAA in the presence of pyridine to give the D–W reaction product, 1-trifluoroacetyl-1,2,3,4-tetrahydroisoquinoline and 1-isoquinolone.[20] The 1-isoquinolone might be formed *via* autooxidation of a munchnone.[18] The above described results support the existence of intermediary 2-alkoxy-substituted munchnones (**11**). Thus, the cyclodehydration reaction of **1** to **10** could proceed efficiently in the presence of pyridine and the conversion of **10** to **11** occurred with proton abstraction of **10** by the base. Formation of **4** could be through the attack of trifluoroacetate ion on the munchnone (**11**). The intermediate (**11**) undergoes trifluoroacetylation followed by decarboxylation to give the trifluoroacetyl ketones (**2**): a similar mechanism has been postulated in the D–W reaction.[21]

In conclusion, we have shown for the first time that D–W reaction could be applied to *N*-alkoxycarbonyl-α-amino acids (**1**) and an efficient preparation of α-amido trifluoromethyl ketones (**2**) was developed. The hydrated form of these trifluoromethyl ketones (**2**) is stable and could be efficiently utilized as a synthon for the preparation of trifluoromethyl substituted compounds. 2-Oxazolidinones are an especially important class of compounds[22] due to a building block of β-aminoalcohols of biological interest.[2]

Experimental

General Methods All melting points were determined with a Yanagimoto hot-stage melting point apparatus and are uncorrected. ^{1}H-NMR spectra were measured on either a JEOL JNM-PMX60SI or a JEOL JNM-GSX500 spectrometer with tetramethylsilane (Me_4Si) as an internal reference and $CDCl_3$ as the solvent, unless otherwise noted. ^{13}C-NMR spectra were obtained on a JEOL JNM-GSX500 spectrometer (at 126 MHz). IR spectra were recorded on a JASCO IR810 spectrometer. Only pertinent IR peaks are given. Low- and high-resolution MS spectra were measured with a JEOL JMS-DS300 spectrometer with a direct inlet system at 70 eV. Combustion analyses were carried out in the microanalytical laboratory of this university. For column chromatography, SiO_2 (Merck, Art 9385) was used. In the preparation of *N*-alkoxycarbonyl-*N*-alkyl-α-amino acids (**1**), L-Phe, L-Ala, L-Leu, and DL-phenylglycine were used as the starting materials. Methyl *N*-methyl-*N*-benzyloxycarbonylphenylalaninate (**15c**) was prepared by the reported procedure.[23]

Preparation of *N*-Benzyl-*N*-methoxycarbonyl-α-amino Acid Esters (15a—j) Compounds (**15a**—**j**) were synthesized in good yields by methoxycarbonylation of *N*-benzylamino acids, which were prepared by the reported method (Chart 3).[24]

Ethyl *N*-Benzyl-*N*-methoxycarbonylglycinate (**15a**): Yield 98% (after column chromatography) (EtOAc : hexane=1 : 1), oil. IR (oil) cm^{-1}: 1745, 1705. ^{1}H-NMR ($CDCl_3$, 60 MHz) δ: 1.23 (t, 3H, J=7.0 Hz), 3.75 (s, 3H), 3.85 (br s, 2H), 4.15 (q, 2H, J=7.0 Hz), 4.55 (s, 2H), 7.23 (s, 5H). MS *m/z*: 251 (M^+, 8%), 91 (100%). HRMS Calcd for $C_{13}H_{17}NO_4$: 251.1157. Found: 251.1163.

Methyl *N*-Benzyl-*N*-methoxycarbonylphenylalaninate (**15b**): Yield 86% (after column chromatography) (EtOAc : hexane=1 : 1), oil. IR (oil) cm^{-1}: 1745, 1710. ^{1}H-NMR ($CDCl_3$, 60 MHz) δ: 2.88—3.33 (m, 2H), 3.50 (s, 3H), 3.67 (s, 3H), 3.90 (d, 1H, J=16.0 Hz), 4.00—4.57 (m, 1H), 4.47 (d, 1H, J=16.0 Hz), 6.67—7.35 (m, 10H). MS *m/z*: 327 (M^+, 1%), 91 (100%). HRMS Calcd for $C_{19}H_{21}NO_4$: 327.1470. Found: 327.1467.

Methyl *N*-Benzyl-*N*-methoxycarbonylphenylglycinate (**15d**): Yield 67% (after column chromatography) (EtOAc : hexane=1 : 1), oil. IR (oil) cm^{-1}: 1750, 1710. ^{1}H-NMR ($CDCl_3$, 60 MHz) δ: 3.70 (s, 3H), 3.74 (s, 3H), 4.17 (d, 1H, J=16.0 Hz), 4.71 (d, 1H, J=16.0 Hz), 5.70 (s, 1H), 6.68—7.48 (m, 10H). MS *m/z*: 313 (M^+, 0.3%), 91 (100%). HRMS Calcd for $C_{18}H_{19}NO_4$:

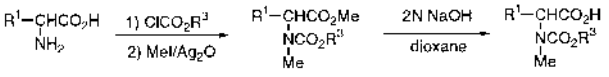

Chart 4

313.1314. Found: 313.1304.

Methyl *N*-Benzyl-*N*-methoxycarbonylalaninate (**15e**): Yield 42% (after column chromatography) (EtOAc : hexane=1 : 1), oil. IR (oil) cm^{-1}: 1745, 1710. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 1.36 (d, 3H, J=6.7 Hz), 3.65 (s, 3H), 3.74 (s, 3H), (4.11—4.12)+(4.54—4.55) (m, 1H), 4.42+4.62 (d, 2H, J=16.5 Hz), 7.24—7.32 (m, 5H). MS *m/z*: 251 (M^+, 5%), 91 (100%). HRMS Calcd for $C_{13}H_{17}NO_4$: 251.1158. Found: 251.1182.

Methyl *N*-Benzyl-*N*-benzyloxycarbonylphenylalaninate (**15h**): Yield 86% (after column chromatography) (EtOAc : hexane=1 : 2), oil. IR (oil) cm^{-1}: 1745, 1710. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: (3.01—3.06)+(3.18—3.22) (m, 1H), 3.25—3.38 (m, 1H), 3.38+3.59 (s, 3H), 3.89+3.93 (d, 1H, J=16.0 Hz), (4.16—4.19)+(4.34—4.37) (m, 1H), 4.48+4.58 (d, 1H, J=16.0 Hz), 5.09—5.23 (m, 2H), 6.96—7.39 (m, 15H). MS *m/z*: 403 (M^+, 1%), 91 (100%). HRMS Calcd for $C_{25}H_{25}NO_4$: 403.1784. Found: 403.1782.

Methyl *N*-Benzyl-*N*-ethoxycarbonylphenylalaninate (**15i**): Yield 62% (after column chromatography) (EtOAc : hexane=1 : 1), oil. IR (oil) cm^{-1}: 1740, 1700. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 1.25—1.27 (m, 3H), (3.05—3.10)+(3.16—3.21) (m, 1H), 3.31—3.34 (m, 1H), 3.57+3.60 (s, 3H), 3.91+3.99 (d, 1H, J=15.3 Hz), (4.19—4.21)+(4.40—4.42) (m, 1H), 4.21 (q, 2H, J=7.0 Hz), 4.47+4.57 (d, 1H, J=15.3 Hz), 7.08—7.28 (m, 10H). MS *m/z*: 341 (M^+, 3%), 91 (100%). HRMS Calcd for $C_{20}H_{23}NO_4$: 341.1627. Found: 341.1627.

Methyl *N*-Methoxycarbonyl-*N*-(3,4-dimethoxyphenylmethyl)phenylalaninate (**15j**): Yield 49% (after column chromatography) (EtOAc : hexane=1 : 1), oil. IR (oil) cm^{-1}: 1735, 1700. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: (3.03—3.07)+(3.17—3.22) (m, 1H), 3.30—3.33 (m, 1H), 3.61+3.64 (s, 3H), 3.76—3.79 (m, 1H), 3.76 (s, 3H), 3.79 (s, 3H), 3.85 (s, 3H), (4.12—4.14)+(4.26—4.28) (m, 1H), 4.43—4.51 (d, 1H, J=15.1 Hz), 6.56—6.73 (m, 3H), 7.02—7.08 (m, 2H), 7.19—7.27 (m, 3H). MS *m/z*: 387 (M^+, 17%), 151 (100%). HRMS Calcd for $C_{21}H_{25}NO_6$: 387.1682. Found: 387.1705.

Preparation of *N*-Methoxycarbonyl-*N*-methyl-α-amino Acid Esters (15f and g) Compounds (**15f** and **g**) were synthesized by methylation of *N*-methoxycarbonylamino acids with methyl iodide and silver oxide (Chart 4).[23]

Methyl *N*-Methoxycarbonyl-*N*-methylleucinate (**15f**): Yield 80% (after column chromatography) (EtOAc : hexane=1 : 1), oil. IR (oil) cm^{-1}: 1740, 1700. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 0.88—0.94 (m, 6H), 1.47—1.55 (m, 1H), 1.62—1.71 (m, 2H), 2.79+2.83 (s, 3H), 3.69+3.71 (s, 6H), 4.65—4.70+4.87—4.94 (m, 1H). MS *m/z*: 217 (M^+, 0.5%), 158 (100%). HRMS Calcd for $C_{10}H_{19}NO_4$: 217.1314. Found: 217.1320.

Methyl *N*-Methoxycarbonyl-*N*-methylphenylalaninate (**15g**): Yield 99% (after column chromatography) (EtOAc : hexane=2 : 1), oil. IR (oil) cm^{-1}: 1750, 1710. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 2.77+2.82 (s, 3H), 2.95—3.06 (m, 1H), 3.28—3.38 (m, 1H), 3.57+3.65 (s, 3H), 3.74 (s, 3H), (4.74—4.80)+(4.97—5.03) (m, 1H), 7.16—7.33 (m, 5H). MS *m/z*: 251 (M^+, 1%), 160 (100%). HRMS Calcd for $C_{13}H_{17}NO_4$: 251.1157. Found: 251.1163.

Hydrolysis of Methyl α-Amino Acid Esters (15a—j) A solution of methyl ester (10 mmol) and 2 N NaOH (7.5 ml, 15 mmol) in dioxane (7.5 ml) was stirred at 65 °C for 2 h. The reaction mixture was diluted with Et_2O (50 ml) and H_2O (50 ml). The aqueous layer was acidified with conc. HCl and extracted with AcOEt (80 ml×2) followed by standard workup to give the desired acids (**1a**—**j**) in high yields. *N*-Benzyl-*N*-methoxycarbonylglycine (**1a**): Yield 99%, oil. IR (oil) cm^{-1}: 3370—2770, 1700. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 3.77+3.81 (s, 3H), 3.90+3.99 (s, 2H), 4.55+4.59 (s, 2H), 7.21—7.35 (m, 5H). MS *m/z*: 223 (M^+, 20%), 91 (100%). HRMS Calcd for $C_{11}H_{13}NO_4$: 223.0845. Found: 223.0837.

N-Benzyl-*N*-methoxycarbonylphenylalanine (**1b**): Yield 65%, mp 102—104 °C (AcOEt–hexane). IR (Nujol) cm^{-1}: 3400—2500, 1740, 1670. ^{1}H-NMR ($CDCl_3$, 60 MHz) δ: 2.98—3.48 (m, 2H), 3.77 (s, 3H), 3.79 (d, 1H, J=14.5 Hz), 4.00—4.43 (m, 1H), 4.55 (d, 1H, J=14.5 Hz), 6.83—7.40 (m, 10H), 9.19 (s, 1H). MS *m/z*: 313 (M^+, 1%), 91 (100%). *Anal*. Calcd for $C_{18}H_{19}NO_4$: C, 69.00; H, 6.11; N, 4.47. Found: C, 69.16; H, 6.18; N, 4.58.

N-Benzyloxycarbonyl-*N*-methylphenylalanine (**1c**): Yield 92%, oil. IR (oil) cm^{-1}: 3000, 1760, 1640. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 2.79+2.86 (s, 3H), 3.02+3.11 (dd, 1H, J=14.3, 11.0 Hz), 3.32+3.37 (dd, 1H, J=14.3, 4.9 Hz), 4.88+4.93 (dd, 1H, J=11.0, 4.9 Hz), 5.03+5.11 (s, 2H), 7.11—7.36 (m, 10H). MS *m/z*: 313 (M^+, 1%), 91 (100%). HRMS Calcd for $C_{18}H_{19}NO_4$: 313.1314. Found: 313.1305.

N-Benzyl-*N*-methoxycarbonylphenylglycine (**1d**): Yield 88%, mp 116—118 °C (AcOEt–hexane). IR (Nujol) cm^{-1}: 3270—2660, 1730, 1655. ^{1}H-NMR ($CDCl_3$, 60 MHz) δ: 3.73 (s, 3H), 4.13 (d, 1H, J=16.0 Hz), 4.75 (d, 1H, J=16.0 Hz), 5.57 (s, 1H), 6.75—7.33 (m, 10H), 9.20 (s, 1H). MS *m/z*: 299 (M^+, 1%), 91 (100%). *Anal*. Calcd for $C_{17}H_{17}NO_4$: C, 68.22; H, 5.72; N, 4.68. Found: C, 68.33; H, 5.82; N, 4.80.

N-Benzyl-*N*-methoxycarbonylalanine (**1e**): Yield 89%, oil. IR (oil) cm^{-1}: 3670—2400, 1700. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 1.37—1.38 (m, 3H), 3.76 (s, 3H), 4.24—4.25 (m, 1H), 4.43 (d, 1H, J=16.3 Hz), 4.65 (d, 1H, J=16.3 Hz), 7.26—7.38 (m, 5H). MS *m/z*: 237 (M^+, 5%), 91 (100%). HRMS Calcd for $C_{12}H_{15}NO_4$: 237.1001. Found: 237.1009.

N-Methoxycarbonyl-*N*-methylleucine (**1f**): Yield 99%, oil. IR (oil) cm^{-1}: 3600—2500, 1740, 1705, 1670. ^{1}H-NMR ($CDCl_3$, 60 MHz) δ: 0.83—1.17 (m, 6H), 1.53—1.93 (m, 3H), 2.83 (s, 3H), 3.67 (s, 3H), 4.50—5.10 (m, 1H), 9.53 (br s, 1H). MS *m/z*: 203 (M^+, 0.3%), 158 (100%). HRMS Calcd for $C_9H_{17}NO_4$: 203.1158. Found: 203.1154.

N-Methoxycarbonyl-*N*-methylphenylalanine (**1g**): Yield 99%, oil. IR (oil) cm^{-1}: 3000 (OH), 1745, 1665. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 2.76+2.84 (s, 3H), 3.00—3.14 (m, 1H), 3.32—3.41 (m, 1H), 3.60+3.68 (s, 3H), 4.81—4.94 (m, 1H), 7.17—7.32 (m, 5H). MS *m/z*: 237 (M^+, 1%), 146 (100%). HRMS Calcd for $C_{12}H_{15}NO_4$: 237.1001. Found: 237.0987.

N-Benzyl-*N*-benzyloxycarbonylphenylalanine (**1h**): Yield 96%, oil. IR (oil) cm^{-1}: 3100, 1745, 1660. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 3.20—3.35 (m, 2H), 3.68+3.73 (d, 1H, J=15.5 Hz), 4.05—4.18 (m, 1H), 4.51+4.65 (d, 1H, J=15.5 Hz), 5.17—5.26 (t, 2H, J=12.5 Hz), 6.92—7.38 (m, 15H). MS *m/z*: 389 (M^+, 0.4%), 91 (100%). HRMS Calcd for $C_{24}H_{23}NO_4$: 389.1627. Found: 389.1640.

N-Benzyl-*N*-ethoxycarbonylphenylalanine (**1i**): Yield 64%, oil. IR (oil) cm^{-1}: 3680—2400, 1700. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 1.18 (t, 3H, J=6.3 Hz), (2.99—3.04)+(3.14—3.19) (m, 1H), 3.23—3.26 (m, 1H), 3.62+3.70 (d, 1H, J=15.3 Hz), 3.98+4.08 (m, 1H), 4.15—4.16 (m, 2H), 4.41+4.55 (d, 1H, J=15.3 Hz), 6.99—7.19 (m, 10H). MS *m/z*: 327 (M^+, 2%), 91 (100%). HRMS Calcd for $C_{19}H_{21}NO_4$: 327.1471. Found: 327.1462.

N-Methoxycarbonyl-*N*-(3,4-dimethoxyphenylmethyl)phenylalanine (**1j**): Yield 88%, oil. IR (oil) cm^{-1}: 3670—2310, 1700. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: (3.07—3.12)+(3.23—3.28) (m, 1H), 3.28—3.33 (m, 1H), 3.64 (d, 1H, J=15.0 Hz), 3.76+3.77 (s, 3H), 3.80 (s, 3H), 3.85 (s, 3H), 4.07—4.13 (m, 1H), 4.44+4.55 (d, 1H, J=15.0 Hz), 6.54—6.72 (m, 3H), 7.02—7.18 (m, 2H), 7.20—7.29 (m, 3H). MS *m/z*: 373 (M^+, 36%), 151 (100%). HRMS Calcd for $C_{20}H_{23}NO_6$: 373.1526. Found: 373.1533.

General Procedure for the Reaction of *N*-Alkoxycarbonyl-*N*-alkyl-α-amino Acids (1a—j) with TFAA TFAA (0.42 ml, 3 mmol) was added to a solution of an *N*-alkoxycarbonyl-*N*-alkylamino acid (**1**) (1 mmol) and pyridine (0.24 ml, 3 mmol) in dry CH_2Cl_2 (5 ml) at 0 °C and the mixture was stirred for 5 h. The reaction mixture was diluted with 1% HCl (20 ml) with cooling and extracted with EtOAc (30 ml×2). The combined extracts were washed successively with brine (30 ml), 3% Na_2CO_3 (30 ml), and brine (30 ml). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure at 40 °C using a rotary evaporator. The residue was chromatographed on a column of silica gel with AcOEt–hexane as the eluent to give the product (**2**). In the reactions of **1c** and **1h**, after the evaporation of the extracts, the precipitated solid was collected and recrystallized to give **4a** and **4b**, respectively. The filtrate was evaporated and the residue was purified by column chromatography to give **2c** and **2h**, respectively. The results are summarized in Table 2.

3-(*N*-Benzyl-*N*-methoxycarbonylamido)-1,1,1-trifluoro-2-propanone (**2a**): Yield 54% (after column chromatography) (EtOAc : hexane=1 : 2), oil. IR (oil) cm^{-1}: 3600—2900, 1775, 1670. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 3.55+4.25+4.33 (s, 2H), 3.74+3.82+3.83 (s, 3H), 4.53+4.57+4.61 (s, 2H), 7.20 (d, 2H, J=7.0 Hz), 7.28—7.36 (m, 3H). MS *m/z*: 293 (M^+, 0.3%),

91 (100%). HRMS Calcd for $C_{12}H_{14}NO_4F_3$ (hydrate form): 293.0875. Found: 293.0864.

3-(*N*-Benzyl-*N*-methoxycarbonylamido)-4-phenyl-1,1,1-trifluoro-2-butanone (**2b**): Yield 98% (after column chromatography) (EtOAc : hexane=1 : 2), oil. IR (oil) cm^{-1}: 1760, 1700. ^{1}H-NMR (DMSO-d_6+D_2O, 500 MHz) δ: 2.68—2.77 (m, 1H), 3.07—3.14 (m, 1H), 3.35+3.40 (s, 3H), 4.47—4.59 (m, 2H), 4.83+5.05 (d, 1H, J=11.3 Hz), 6.76—7.27 (m, 10H). MS *m/z*: 365 (M^+, 0.1%), 91 (100%). HRMS Calcd for $C_{19}H_{18}NO_3F_3$ (keto form): 365.1239. Found: 365.1238.

3-(*N*-Benzyloxycarbonyl-*N*-methylamido)-4-phenyl-1,1,1-trifluoro-2-butanone (**2c**) and 4-Benzyl-3-methyloxazolidine-2,5-dione (**4a**): **2c**: Yield 39% (after column chromatography) (EtOAc : hexane=1 : 3), oil. IR (oil) cm^{-1}: 3410, 1760, 1665. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 2.44+2.70+2.75 (s, 3H), 3.00—3.46 (m, 2H), 4.80—4.98 (m, 1H), 5.10+5.13+5.24+5.26 (s, 2H), 7.05—7.42 (m, 10H). MS *m/z*: 365 (M^+, 0.2%), 91 (100%). HRMS Calcd for $C_{19}H_{18}NO_3F_3$ (keto form): 365.1238. Found: 365.1224. **4a**: Yield 43%, mp 133—134 °C (CH_2Cl_2–hexane). IR (Nujol) cm^{-1}: 1835, 1770. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 2.93 (s, 3H), 3.21 (d, 2H, J=4.9 Hz), 4.41 (t, 1H, J=4.9 Hz), 7.13—7.16 (m, 2H), 7.27—7.34 (m, 3H). MS *m/z*: 205 (M^+, 4%), 91 (100%). *Anal*. Calcd for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.17; H, 5.42; N, 6.74.

3-(*N*-Benzyl-*N*-methoxycarbonylamido)-3-phenyl-1,1,1-trifluoro-2-propanone (**2d**): Yield 43% (after column chromatography) (EtOAc : hexane=1 : 2), oil. IR (oil) cm^{-1}: 1770, 1680. ^{1}H-NMR (DMSO-d_6+D_2O, 500 MHz) δ: 3.41+3.64 (s, 3H), 3.46+3.51 (s, 1H), 3.99—4.06 (m, 1H), 4.46—4.63 (m, 1H), 7.20—7.59 (m, 10H). MS *m/z*: 351 (M^+, 1%), 91 (100%). HRMS Calcd for $C_{18}H_{16}NO_3F_3$ (keto form): 351.1083. Found: 351.1089.

3-(*N*-Benzyl-*N*-methoxycarbonylamido)-1,1,1-trifluoro-2-butanone (**2e**): Yield 53% (after column chromatography) (EtOAc : hexane=1 : 2), oil. IR (oil) cm^{-1}: 1770, 1670. ^{1}H-NMR (DMSO-d_6+D_2O, 500 MHz) δ: 1.06 (d, 3H, J=7.0 Hz), 3.56 (s, 3H), 3.74—3.84 (m, 1H), 4.47—4.68 (m, 2H), 7.13—7.32 (m, 5H). MS *m/z*: 307 (M^+, 0.03%), 91 (100%). HRMS Calcd for $C_{13}H_{16}NO_4F_3$ (hydrate form): 307.1031. Found: 307.1030.

3-(*N*-Methoxycarbonyl-*N*-methylamido)-5-methyl-1,1,1-trifluoro-2-hexanone (**2f**): Yield 93% (after column chromatography) (EtOAc : hexane=1 : 2), oil. IR (oil) cm^{-1}: 1760, 1700. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 0.90—0.97 (m, 6H), 1.50—1.70 (m, 3H), 2.81+2.86 (s, 3H), 3.70+3.71+3.72 (s, 3H), 4.87—4.49+5.13—5.16 (m, 1H). MS *m/z*: 256 (M^+, 2.5%), 158 (100%). HRMS Calcd for $C_{13}H_{16}NO_4F_3$ (hydrate form): 307.1031. Found: 307.1030.

3-(*N*-Methoxycarbonyl-*N*-methylamido)-4-phenyl-1,1,1-trifluoro-2-butanone (**2g**): Yield 93% (after column chromatography) (EtOAc : hexane=1 : 3), oil. IR (oil) cm^{-1}: 3350, 1765, 1700, 1670. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 2.42+2.68+2.73 (s, 3H), 3.00—3.48 (m, 2H), 3.63+3.70+3.75+3.81 (s, 3H), 4.70—5.16 (m, 1H), 7.14—7.32 (m, 5H). MS *m/z*: 289 (M^+, 5%), 192 (100%). HRMS Calcd for $C_{13}H_{14}NO_3F_3$ (keto form): 289.0926. Found: 289.0931.

3-(*N*-Benzyl-*N*-benzyloxycarbonylamido)-4-phenyl-1,1,1-trifluoro-2-butanone (**2h**) and 3,4-Bis(benzyl)oxazolidine-2,5-dione (**4b**): **2h**: Yield 47% (after column chromatography) (EtOAc : hexane=1 : 5), oil. IR (oil) cm^{-1}: 3400, 1765, 1690, 1665. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 3.00—5.32 (m, 7H), 6.80—7.40 (m, 15H). MS *m/z*: 441 (M^+, 0.2%), 91 (100%). HRMS Calcd for $C_{25}H_{22}NO_3F_3$ (keto form): 441.1551. Found: 441.1564. **4b**: Yield 43%, mp 71—72 °C (AcOEt–hexane). IR (Nujol) cm^{-1}: 1855, 1770. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 3.15+3.20 (dd, 2H, J=5.0 Hz), 3.98 (d, 1H, J=15.2 Hz), 4.24 (t, 1H, J=5.0 Hz), 5.03 (d, 1H, J=15.2 Hz), 7.11—7.15 (m, 4H), 7.31—7.37 (m, 6H). MS *m/z*: 281 (M^+, 3%), 91 (100%). *Anal*. Calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.37; N, 4.98. Found: C, 72.62; H, 5.60; N, 4.85.

3-(*N*-Benzyl-*N*-ethoxycarbonylamido)-4-phenyl-1,1,1-trifluoro-2-butanone (**2i**): Yield 59% (after column chromatography) (EtOAc : hexane=1 : 4), oil. IR (oil) cm^{-1}: 1760, 1660. ^{1}H-NMR (DMSO-d_6+D_2O, 500 MHz) δ: 0.80+1.00 (t, 3H, J=7.0 Hz), 2.71+2.76 (d, 1H, J=14.7 Hz), 3.08+3.13 (d, 1H, J=14.7 Hz), 3.81 (s, 3H), 4.45—4.59 (m, 2H), 4.87+5.05 (d, 1H, J=11.3 Hz), 6.76—7.27 (m, 10H). MS *m/z*: 379 (M^+, 10%), 91 (100%). HRMS Calcd for $C_{20}H_{20}NO_3F_3$ (keto form): 379.1395. Found: 379.1394.

3-(*N*-(3,4-Dimethoxyphenylmethyl)-*N*-methoxycarbonylamido)-4-phenyl-1,1,1-trifluoro-2-butanone (**2j**): Yield 75%, mp 87—91 °C (hexane). IR (Nujol) cm^{-1}: 3420, 1660. ^{1}H-NMR (DMSO-d_6+D_2O, 500 MHz) δ: 2.75—2.83 (m, 1H), 3.06—3.14 (m, 1H), 3.36+3.44 (s, 3H), 3.41 (s, 3H), 3.65 (s, 3H), 4.00—4.54 (m, 2H), 4.82+5.05 (d, 1H, J=11.3 Hz), 6.40—7.12 (m, 8H). MS *m/z*: 425 (M^+, 37%), 151 (100%). *Anal*. Calcd for $C_{21}H_{24}NO_6F_3$ (hydrate form): C, 56.88; H, 5.46; N, 3.16. Found: C, 56.90; H, 5.45; N, 3.05.

General Procedure for the Reduction of ATFMKs (2a—f) with $NaBH_4$ $NaBH_4$ (37 mg, 1 mmol) was added to a stirred solution of **2** (1 mmol) in dry EtOH (5 ml) at 0 °C, and the mixture was stirred at 25 °C for 1—48 h, then diluted with H_2O (20 ml) and 2 N H_2SO_4 (5 ml). The mixture was extracted with AcOEt (30 ml×2) and the extracts were washed with brine (30 ml), and dried over Na_2SO_4. After evaporation of the solvents, the residue was chromatographed on a column of silica gel with AcOEt–hexane as the eluent to give the products (**5** and/or **6**). The results are summarized in Table 3.

3-Benzyl-5-trifluoromethyloxazolidin-2-one (**6a**) and 3-(*N*-Benzyl-*N*-methoxycarbonylamide)-1,1,1-trifluoro-2-propanol (**5a**): **6a**: 27% yield from the less polar fraction (EtOAc : hexane=1 : 2), oil. IR (oil) cm^{-1}: 1760. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 3.43 (dd, 1H, J=9.8, 4.9 Hz), 3.60 (dd, 1H, J=9.8, 9.5 Hz), 4.39 (d, 1H, J=15.1 Hz), 4.46 (d, 1H, J=15.1 Hz), 4.68—4.75 (m, 1H), 7.31—7.36 (m, 5H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ: 43.23 (CH, $^3J_{C\text{-}F}$=2.1 Hz), 48.17 (CH_2), 69.00 (CH, $^2J_{C\text{-}F}$=35.2 Hz), 122.78 (CF_3, $^1J_{C\text{-}F}$=280.3 Hz), 127.93 (CH), 128.30 (CH), 128.97 (CH), 134.48 (C), 155.76 (C). MS *m/z*: 245 (M^+, 100%). HRMS Calcd for $C_{11}H_{10}NO_2F_3$: 245.0664. Found: 245.0673. **5a**: 26% yield from the more polar fraction (EtOAc : hexane=1 : 2), oil. IR (oil) cm^{-1}: 3350, 1670. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 3.37—3.40 (m, 1H), 3.64—3.69 (m, 1H), 3.79 (s, 3H), 4.04—4.09 (m, 1H), 4.43—4.59 (m, 2H), 7.19 (d, 2H, J=7.0 Hz), 7.27—7.35 (m, 3H). MS *m/z*: 277 (M^+, 3%), 91 (100%). HRMS Calcd for $C_{12}H_{14}NO_3F_3$: 277.0925. Found: 277.0927.

trans-3,4-Bis(benzyl)-5-trifluoromethyloxazolidin-2-one (**6b**) and 3-(*N*-Benzyl-*N*-methoxycarbonyl)-4-phenyl-1,1,1-trifluoro-2-butanol (**5b**): **6b**: 56% yield from the less polar fraction (EtOAc : hexane=1 : 3), oil. IR (oil) cm^{-1}: 1770. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 2.85 (dd, 1H, J=14.0, 7.7 Hz), 3.09 (dd, 1H, J=14.0, 5.1 Hz), 3.85 (ddd, 1H, J=7.7, 5.1, 3.7 Hz), 4.12 (d, 1H, J=15.3 Hz), 4.44 (dq, 1H, J=6.1, 3.7 Hz), 4.99 (d, 1H, J=15.3 Hz), 7.10 (d, 2H, J=6.7 Hz), 7.23 (d, 2H, J=6.1 Hz), 7.32—7.43 (m, 6H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ: 38.10 (CH_2), 46.51 (CH_2), 55.04 (CH), 73.30 (CH, $^2J_{C\text{-}F}$=34.1 Hz), 122.49 (CF_3, $^1J_{C\text{-}F}$=280.4 Hz), 127.73 (CH), 128.07 (CH), 128.40 (CH), 128.97 (CH), 129.15 (CH), 129.22 (CH), 133.81 (C), 134.36 (C), 155.66 (C). MS *m/z*: 335 (M^+, 10%), 91 (100%). HRMS Calcd for $C_{18}H_{16}NO_2F_3$: 335.1133. Found: 335.1122. **5b**: 36% yield from the more polar fraction (EtOAc : hexane=1 : 3), oil. IR (oil) cm^{-1}: 3260, 1665. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 2.43—2.45 (m, 1H), 3.52—3.57 (m, 2H), 3.77—3.84 (m, 1H), 3.94 (s, 3H), 3.97 (d, 1H, J=15.0 Hz), 5.02 (d, 1H, J=15.0 Hz), 6.92 (d, 2H, J=6.1 Hz), 7.21—7.27 (m, 3H), 7.38 (d, 2H, J=6.7 Hz), 7.41—7.49 (m, 3H). MS *m/z*: 367 (M^+, 5%), 91 (100%). HRMS Calcd for $C_{19}H_{20}NO_3F_3$: 367.1395. Found: 367.1395.

trans-4-Benzyl-3-methyl-5-trifluoromethyloxazolidin-2-one (**6c**): Yield 91% (after column chromatography) (EtOAc : hexane=1 : 1), oil. IR (oil) cm^{-1}: 1770. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 2.83 (dd, 1H, J=14.0, 7.3 Hz), 2.85 (s, 3H), 3.03 (dd, 1H, J=14.0, 5.2 Hz), 3.92 (ddd, 1H, J=7.3, 5.2, 4.0 Hz), 4.34 (dq, 1H, J=6.2, 4.0 Hz), 7.11 (m, 2H), 7.23—7.31 (m, 3H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ: 29.55 (CH_2), 37.89 (CH_3), 58.07 (CH), 72.88 (CH, $^2J_{C\text{-}F}$=34.2 Hz), 122.57 (CF_3, $^1J_{C\text{-}F}$=280.4 Hz), 127.66 (CH), 129.09 (CH), 129.22 (CH), 133.69 (C), 155.48 (C). MS *m/z*: 259 (M^+, 2%), 168 (100%). HRMS Calcd for $C_{12}H_{12}NO_2F_3$: 259.0820. Found: 259.0823.

trans-3-Benzyl-4-phenyl-5-trifluoromethyloxazolidin-2-one (**6d**) and 3-(*N*-Benzyl-*N*-methoxycarbonyl)-3-phenyl-1,1,1-trifluoro-2-propanol (**5d**): **6d**: 13% yield from the less polar fraction (EtOAc : hexane=1 : 4), oil. IR (oil) cm^{-1}: 1770. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 3.71 (d, 1H, J=15.0 Hz), 4.52 (d, 1H, J=4.9 Hz), 4.57—4.62 (m, 1H), 4.95 (d, 1H, J=15.0 Hz), 7.12—7.15 (m, 2H), 7.22—7.24 (m, 2H), 7.35—7.37 (m, 3H), 7.47—7.48 (m, 3H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ: 45.92 (CH_2), 58.41 (CH), 76.98 (CH, $^2J_{C\text{-}F}$=34.1 Hz), 122.62 (CF_3, $^1J_{C\text{-}F}$=280.4 Hz), 126.80 (CH), 128.18 (CH), 128.27 (CH), 128.89 (CH), 129.69 (CH), 129.78 (CH), 134.18 (C), 135.71 (C), 155.60 (C). MS *m/z*: 321 (M^+, 34%), 172 (100%). HRMS Calcd for $C_{17}H_{14}NO_2F_3$: 321.0977. Found: 321.0975. **5d**: 45% yield from the more polar fraction (EtOAc : hexane=1 : 4), oil. IR (oil) cm^{-1}: 3460, 1680. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 3.73 (s, 3H), 4.07—4.16 (m, 1H), 4.58—4.74 (m, 3H), 7.07—7.33 (m, 10H). MS *m/z*: 353 (M^+, 1%), 91 (100%). HRMS Calcd for $C_{18}H_{18}NO_3F_3$: 353.1239. Found: 353.1247.

trans-3-Benzyl-4-methyl-5-trifluoromethyloxazolidin-2-one (**6e**): Yield 91% (after column chromatography) (EtOAc : hexane=2 : 3), oil. IR (oil) cm^{-1}: 1765. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 1.30 (d, 3H, J=6.1 Hz), 3.65—3.70 (m, 1H), 4.09 (d, 1H, J=15.3 Hz), 4.26—4.31 (m, 1H), 4.81 (d, 1H, J=15.3 Hz), 7.22—7.24 (m, 2H), 7.29—7.36 (m, 3H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ: 18.61 (CH_3), 45.81 (CH_2), 50.27 (CH, $^3J_{C\text{-}F}$=2.1 Hz), 76.17 (CH, $^2J_{C\text{-}F}$=34.1 Hz), 122.68 (CF_3, $^1J_{C\text{-}F}$=280.3 Hz), 127.84 (CH), 128.27 (CH), 128.98 (CH), 134.60 (C), 155.44 (C). MS *m/z*: 259 (M^+, 92%), 91

(100%). HRMS Calcd for $C_{12}H_{12}NO_2F_3$: 259.0820. Found: 259.0816.

3-(*N*-Methoxycarbonyl-*N*-methyl)-5-methyl-1,1,1-trifluoro-2-hexanol (**5f**): Yield 83% (after column chromatography) (EtOAc : hexane=1 : 3), oil. IR (oil) cm^{-1}: 3400 (br), 1680. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 0.90—0.96 (m, 6H), 1.50—1.65 (m, 3H), 1.90—2.08 (m, 1H), 2.92 (br s, 3H), 3.70 (s, 3H), 3.90 (br s, 1H). MS *m/z*: 321 (M^+, 34%), 172 (100%). HRMS Calcd for $C_{17}H_{14}NO_2F_3$: 321.0977. Found: 321.0975.

General Procedure for the Cyclization of α-Trifluoromethyl Alcohols (5a, d, and f) into 2-Oxazolones (6a, d, and f) A solution of **5** (1 mmol) in dry THF (2 ml) was added dropwise to a stirred solution of NaH (60% oil dispersion) (48 mg, 1.2 mmol) in dry THF (3 ml) at 0 °C, and the mixture was stirred at 25 °C for 1—1.5 h, then diluted with H_2O (25 ml). The mixture was extracted with AcOEt (30 ml×2) and the extracts were washed with brine (30 ml), and dried over Na_2SO_4. After evaporation of the solvents, the residue was chromatographed on a column of silica gel with AcOEt–hexane as the eluent to give the product (**6**). The results are summarized in Table 4.

trans-3-Methyl-4-(2-methylpropyl)-5-trifluoromethyloxazolidin-2-one (**6f**): Yield 90% (after column chromatography) (EtOAc : hexane=1 : 3), oil. IR (oil) cm^{-1}: 1780. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 0.89 (d, 3H, J=6.3 Hz), 0.93 (d, 3H, J=6.3 Hz), 1.38—1.47 (m, 1H), 1.56—1.66 (m, 2H), 2.82 (s, 3H), 3.66 (dt, 1H, J=3.7, 6.6 Hz), 4.33 (dq, 1H, J=3.7, 6.3 Hz); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ: 21.42 (CH_3), 23.29 (CH_3), 23.76 (CH_2), 29.09 (CH), 41.07 (CH_3), 55.59 (CH), 74.36 (CH, $^2J_{C\text{-}F}$=34.1 Hz), 122.77 (CF_3, $^1J_{C\text{-}F}$=281.4 Hz), 155.33 (C). MS *m/z*: 225 (M^+, 8%), 168 (100%). HRMS Calcd for $C_9H_{14}NO_2F_3$: 225.0976. Found: 225.0981.

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