NOVEL FORMATION AND CRYSTAL STRUCTURE OF 2-(2,2,2-TRIFLUOROETHYLIDENE)-6-TRIFLUORO-METHYL-2,3-DIHYDRO-4*H*-1,4-OXAZIN-3-ONES FROM *N*-ACETYL-*N*-ALKYL-α-AMINO ACIDS

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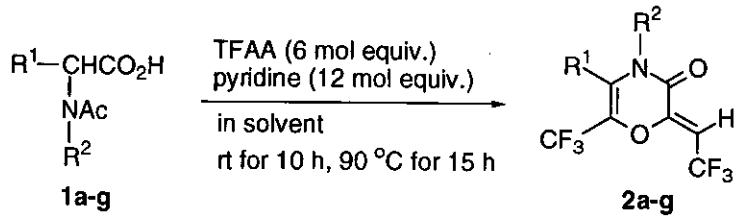
Abstract --- The title compounds (**2a-g**) were formed from *N*-acetyl-*N*-alkyl-α-amino acids (**1a-g**) on treatment with trifluoroacetic anhydride in the presence of pyridine. The structure of the product (**2a**) was determined by single crystal X-Ray analysis.

During the last two dacades, considerable attention has been devoted to find novel methods for preparing the trifluoromethyl substituted compounds because of their biological, chemical, and physical properties.[1] Recently we reported a novel synthesis of 5-trifluoromethyl-oxazoles[2] or α-trifluoromethylacyloins[3] by the reaction of *N*-acyl-*N*-alkyl-α-amino acids with trifluoroacetic anhydride (TFAA) under the Dakin-West (D-W) reaction conditions. These reactions proceeded through mesoionic 1,3-oxazolium-5-olates followed by ring cleavage. During the previous work,[2] we observed that the reaction is markedly influenced by the nature of *N*-substituents of α-amino acids. Thus, *N*-benzoyl-, *N*-pivaloyl-, and *N*-cinnamoyl-α-amino acids were easily transformed to the 5-trifluoromethyloxazoles in good yields. On the other hand, *N*-acetyl derivative afforded no oxazole derivative and any products could not be characterized. In our continuous studies in this field, we examined in more detail a reaction of *N*-acetyl-*N*-alkyl-α-amino acids with TFAA under the D-W reaction conditions, and a new 2-(α-trifluoromethylmethylene)-6-trifluoromethyl-1,4-oxazine derivative (**2a-g**) was obtained as a main product. Now we wish to report the results.

First, we examined the D-W reaction of *N*-acetyl-*N*-benzylphenylalanine (**1a**) with TFAA in the presence of pyridine under various conditions. Six equiv. of TFAA and twelve equiv. of pyridine to **1a** were needed to obtain a better yield of **2a**. The use of 3 equiv. of TFAA and six equiv. of pyridine to **1a** lowered the yield (**2a**, 6%). Both prolonged reaction time and a

Table 1. Reactions of *N*-acetyl-*N*-alkylamino acids (**1a-g**) with TFAA in the presence of pyridine.



1a-g **2a-g**

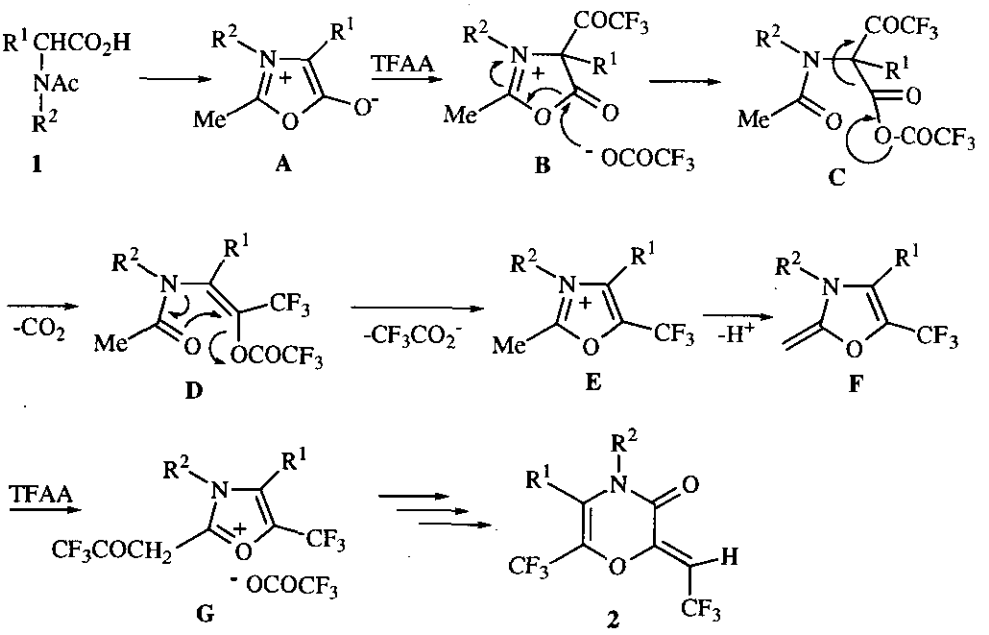
Entry	Compound	R^1	R^2	Solvent	Products, Yield (%)
1	**1a**	$PhCH_2$	$PhCH_2$	benzene	**2a** (29)
2	**1a**	$PhCH_2$	$PhCH_2$	DME	**2a** (27)
3	**1a**	$PhCH_2$	$PhCH_2$	$MeNO_2$	**2a** (31)
4	**1a**	$PhCH_2$	$PhCH_2$	THF	**2a** (31)
5	**1a**	$PhCH_2$	$PhCH_2$	DMF	**2a** (41)
6	**1a**	$PhCH_2$	$PhCH_2$	DCE	**2a** (43)
7	**1b**	$PhCH_2$	Me	DMF	**2b** (25)
8	**1b**	$PhCH_2$	Me	DCE	**2b** (17)
9	**1c**	Ph	$PhCH_2$	DMF	**2c** (24)
10	**1c**	Ph	$PhCH_2$	DCE	**2c** (17)
11	**1d**	Ph	Me	DMF	**2d** (18)
12	**1d**	Ph	Me	DCE	**2d** (8)
13	**1e**	Me_2CH	$PhCH_2$	DMF	**2e** (20)
14	**1e**	Me_2CH	$PhCH_2$	DCE	**2e** (26)
15	**1f**	Me_2CHCH_2	Me	DMF	**2f** (22)
16	**1f**	Me_2CHCH_2	Me	DCE	**2f** (16)
17	**1g**	Me	$PhCH_2$	DMF	**2g** (38)
18	**1g**	Me	$PhCH_2$	DCE	**2g** (26)

high temperature (90 °C) were needed and no product was characterized at rt in spite of long reaction time (7 days). However, the stirring at rt for 10 h was necessary prior to the heating to obtain good results. The best result was obtained when 1,2-dichloroethane (DCE) or DMF was used as a solvent. The results are summarized in Table 1 (Entries1-6).

Several *N*-acetyl-*N*-alkyl-α-amino acids (**1b-g**) reacted by a similar procedure to Entry 5 or 6. As shown in Table 1, various *N*-acetyl-*N*-alkyl-α-amino acids of alanine, phenylalanine, phenylglycine, leucine, and valine were transformed to the 2-(α-trifluoromethylmethylene)-6-trifluoromethyl-1,4-oxazine derivative (**2**). In these reactions, the starting materials (**1**) were not recovered and several polar materials were detected by TLC, but none of them were

characterized. Isolation of the product (**2**) from reaction mixture was easily performed by silica gel chromatography eluting with AcOEt-hexane (1:5).

The structure of **2a** was unequivocally confirmed by X-Ray diffraction study of single crystals (Figure 1). In the crystal, 6- and 7-CF_3 groups were found to have rotational disorder (*vide infra*). The X-Ray structure analysis indicates that the methylene moiety has the (Z)-stereochemistry. The ^{1}H NMR spectrum of **2a** exhibited the signal of the vinyl proton at δ 6.20 (quartet, $J_{H\text{-}F}$=8.2 Hz) and other products (**2b-g**) showed the characteristic vinyl protons at the almost same position (Table 3). The precise assignments of the carbon signals in **2a** were easily performed on the basis of the long-range ^{13}C-^{19}F coupling (Table 4). Thus, $J_{C\text{-}F}$ is measured up to three bonds in ^{1}H-decoupled ^{13}C NMR spectra: δ 101.02 (<u>C</u>HCF$_3$, $^2J_{C\text{-}F}$=37.2 Hz), 120.34 (CF$_3$, $^1J_{C\text{-}F}$=272.1 Hz), 122.42 (CF$_3$, $^1J_{C\text{-}F}$=270.0 Hz), 122.69 (C-5, $^3J_{C\text{-}F}$=4.2 Hz), 126.33 (C-6, $^2J_{C\text{-}F}$=42.0 Hz), and 146.20 (C-2, $^3J_{C\text{-}F}$=4.2 Hz).



Scheme 1

Although it is premature to discuss the precise mechanism at the present stage, the most plausible reaction route for the product (**2**) is illustrated in Scheme 1. A mesoionic 1,3-oxazolium-5-olate (**A**) initially formed by cyclodehydration of **1** undergoes trifluoroacetylation followed by decarboxylation to give the enol trifluoroacetate (**D**). The further cyclization of **D** leads to the oxazolium salt (**E**), the posturated common intermediate for the reaction of *N*-acyl-*N*-alkyl-α-amino acids with TFAA.[2,3] Intermediate (**E**) isomerizes to **F** which undergoes trifluoroacetylation to give **G**. A similar type of trifluoroacetylation has been reported in the

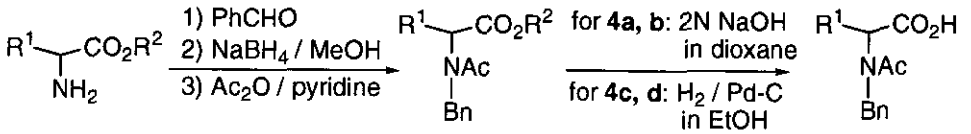
reaction of other vinyl ethers with TFAA in the presence of pyridine.[4] However, it is difficult to get a definitive explanation for the ring expansion of **G** to **2**.

This unique 1,4-oxazine formation from *N*-acetyl-*N*-alkyl-α-amino acids was not anticipated but the reaction is general as evidenced by the examples indicated in Table 1. In all cases the yields are modest, however this is offset by the fact that these compounds are available in one pot from cheap and readily-available α-amino acid derivatives.

EXPERIMENTAL

Melting points are uncorrected. ^{1}H NMR spectra were measured at 60, 270, or 500 MHz with tetramethylsilane (Me_4Si) as an internal reference and $CDCl_3$ as the solvent. Low and high resolution mass spectra (MS) were obtained with a direct inlet system at 70 eV. Elemental analyses were performed in the Microanalytical Laboratory of Josai University. Standard workup means that the organic layers were finally dried over Na_2SO_4, filtered, and concentrated *in vacuo* below 45 °C using a rotary evaporator. In preparation of **1a**, **b**, **e**, and **f**, L-Phe, L-Val, and L-Leu were used as the starting materials, respectively. DL-Ala and DL-phenylglycine were employed for the preparation of **1c**, **d**, and **g**. Analytical and physical data of all new products are presented in Table 2.

Preparation of *N*-Acetyl-*N*-benzyl-α-amino Acid Esters (4): Compounds (**4**) were synthesized in good yields by acetylation of *N*-benzylamino acids, which were prepared by the reported method (Scheme 2).[5]

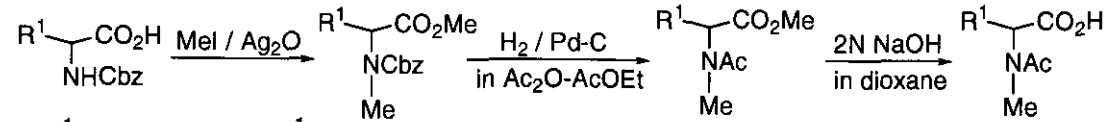


3a: R^1=Bn, R^2=Me
3b: R^1=Ph, R^2=Me
3c: R^1=Me_2CH, R^2=Bn
3d: R^1=Me, R^2=Bn

4a: R^1=Bn, R^2=Me (82%)
4b: R^1=Ph, R^2=Me (88%)
4c: R^1=Me_2CH, R^2=Bn (78%)
4d: R^1=Me, R^2=Bn (67%)

1a: R^1=Bn (95%)
1c: R^1=Ph (93%)
1e: R^1=Me_2CH (91%)
1g: R^1=Me (95%)

Scheme 2



5a: R^1=Bn
5b: R^1=Me_2CHCH_2

6a: R^1=Bn (96%)
6b: R^1=Me_2CHCH_2 (91%)

7a: R^1=Bn (93%)
7b: R^1=Me_2CHCH_2 (93%)

1b: R^1=Bn (94%)
1f: R^1=Me_2CHCH_2 (97%)

Scheme 3

Table 2. Physical and analytical data of new compounds.

Compound	Formula	mp (°C) (solvent) [a]	Found (%) (requires) C	H	N	IR, ν_{max} (cm^{-1})	MS, m/z (%), M^+ and base peak
1a	$C_{18}H_{19}NO_3$	151-153 (A-H)	72.47 (72.71)	6.60 (6.44)	4.47 (4.71)	3000 (br) 1730, 1610	297 (4) 91
1b	$C_{12}H_{15}NO_3$	141-142 (A)	65.01 (65.14)	6.87 (6.83)	6.21 (6.33)	3000 (br) 1720, 1600	221 (4) 88
1c	$C_{17}H_{17}NO_3$	140-141 (A)	72.15 (72.07)	6.29 (6.05)	4.93 (4.94)	3000 (br) 1720, 1590	283 (6) 91
1d	$C_{11}H_{13}NO_3$	120-123 (A-H)	63.63 (63.76)	6.26 (6.32)	6.67 (6.76)	2500 (br) 1725, 1590	207 (0.2) 106
1e	$C_{14}H_{19}NO_3$	111-113 (A-H)	67.57 (67.45)	7.53 (7.68)	5.44 (5.62)	3000 (br) 1730, 1610	249 (7) 91
1f	$C_9H_{17}NO_3$	103-104 (A-H)	57.95 (57.73)	8.99 (9.15)	7.46 (7.48)	3000 (br) 1730, 1610	187 (3) 100
1g	$C_{12}H_{15}NO_3$	112-113 (A-H)	65.24 (65.14)	6.80 (6.83)	6.18 (6.33)	3000 (br) 1740, 1610	221 (7) 91
2a	$C_{21}H_{15}NO_2F_6$	153-154 (E-H)	59.18 (59.02)	3.29 (3.54)	3.18 (3.28)	1690, 1665	427 (11) 91
2b	$C_{15}H_{11}NO_2F_6$	oil	351.0696 (351.0694)			1710,1690, 1660	351 (100)
2c	$C_{20}H_{13}NO_2F_6$	oil	413.0844 (413.0850)			1690, 1665	413 (37) 91
2d	$C_{14}H_9NO_2F_6$	oil	337.0535 (337.0538)			1695, 1670	337 (80) 118
2e	$C_{17}H_{15}NO_2F_6$	oil	379.0999 (379.1007)			1680, 1650	379 (4) 91
2f	$C_{12}H_{13}NO_2F_6$	oil	317.0845 (317.0851)			1685, 1660	317 (74) 206
2g	$C_{15}H_{11}NO_2F_6$	115-116 (H)	51.06 (51.29)	3.26 (3.16)	4.01 (3.99)	1695, 1670	351 (14) 91
4a	$C_{19}H_{21}NO_3$	oil	311.1526 (311.1522)			1745, 1660	311 (3) 91
4b	$C_{18}H_{19}NO_3$	oil	297.1376 (297.1365)			1745, 1640	297 (1) 91
4c	$C_{21}H_{25}NO_3$	oil	339.1828 (339.1834)			1735, 1650	339 (7) 91
4d	$C_{19}H_{21}NO_3$	oil	311.1512 (311.1521)			1740, 1650	311 (4) 91
6b	$C_{16}H_{23}NO_4$	oil	293.1631 (293.1628)			1735, 1700	293 (3) 91
7a	$C_{13}H_{17}NO_3$	oil	235.1205 (235.1208)			1740, 1640	235 (1) 102
7b	$C_{10}H_{19}NO_3$	oil	201.1374 (210.1365)			1740, 1650	201 (5) 100
7c	$C_{18}H_{19}NO_3$	oil	297.1361 (297.1365)			1745, 1650	297 (4) 120

[a] A=AcOEt, E=Et_2O, H=hexane.

Table 3. ^{1}H NMR data of new compounds.

1a	2.14 (s, 3H), 3.03-3.35 (m, 2H), 3.71 (d, 1H, J=16.8), 4.12 (d, 1H, J=8.5), 4.13 (d, 1H, J=8.5), 4.39 (d, 1H, J=16.8), 7.08-7.14 (m, 4H), 7.22 (m, 6H)
1b[a]	1.77+2.03 (s, 3H), 2.81+2.93 (s, 3H), 2.98-3.04+3.12-3.19 (m, 1H), 3.33-3.41 (m, 1H), 4.57-4.60+5.00-5.10 (m, 1H), 5.90-6.30 (br, 1H), 7.15-7.32 (m, 5H)
1c	2.13 (s, 3H), 4.43 (d, 1H, J=17.7), 4.68 (d, 1H, J=17.7), 5.00-5.40 (br, 1H), 5.82 (s, 1H), 7.01 (d, 2H, J=6.7), 7.16-7.31 (m, 8H)
1d	2.14 (s, 3H), 2.81 (s, 3H), 6.34 (s, 1H), 7.26-7.44 (m, 5H)
1e	0.89 (d, 3H, J=6.7), 1.00 (d, 3H, J=6.7), 2.23 (s, 3H), 2.64-2.72 (m, 1H), 3.73 (d, 1H, J=10.4), 4.42 (d, 1H, J=16.5), 4.74 (d, 1H, J=16.5), 7.20 (d, 2H, J=7.3), 7.31 (t, 1H, J=7.3), 7.37 (t, 2H, J=7.3)
1f[a]	0.92-0.99 (m, 6H), 1.45-1.58 (m, 1H), 1.70-1.83 (m, 2H), 2.16+2.17 (s, 3H), 2.85-2.95 (s, 3H), 4.39-4.42+5.24-5.37 (m, 1H), 5.60-6.25 (br, 1H)
1g	1.40 (d, 3H, J=7.3), 2.16 (s, 3H), 4.54 (d, 1H, J=17.7), 4.60 (q, 1H, J=7.3), 4.68 (d, 1H, J=17.7), 7.27 (d, 2H, J=7.6), 7.30 (t, 1H, J=7.6), 7.38 (t, 2H, J=7.6)
2a	3.75 (s, 2H), 4.80 (s, 2H), 6.20 (q, 1H, $J_{H\text{-}F}$=8.2), 7.09 (d, 2H, J=7.4), 7.17 (d, 2H, J=7.4), 7.32-7.36 (m, 2H), 7.36-7.41 (m, 4H)
2b	3.11 (s, 3H), 3.92 (s, 2H), 6.11 (q, 1H, $J_{H\text{-}F}$=8.2), 7.19 (d, 2H, J=7.3), 7.30 (t, 1H, J=7.3), 7.38 (t, 2H, J=7.3)
2c	4.68 (s, 2H), 6.25 (q, 1H, $J_{H\text{-}F}$=8.2), 6.78 (d, 2H, J=7.4), 7.05 (d, 2H, J=7.4), 7.13-7.21 (m, 2H), 7.30-7.46 (m, 4H)
2d	2.90 (s, 3H), 6.17 (q, 1H, $J_{H\text{-}F}$=8.2), 7.28-7.33 (m, 2H), 7.46-7.55 (m, 3H)
2e	1.26 (d, 6H, J=7.3), 3.17-3.31 (m, 1H), 5.11 (s, 2H), 6.06 (q, 1H, $J_{H\text{-}F}$=8.2), 7.12 (d, 2H, J=7.3), 7.28 (t, 1H, J=7.3), 7.36 (t, 2H, J=7.3)
2f	1.00 (d, 6H, J=6.7), 1.71-1.86 (m, 1H), 2.43 (d, 2H, J=7.3), 3.32 (s, 3H), 6.07 (q, 1H, $J_{H\text{-}F}$=8.2)
2g	2.09 (q, 3H, $J_{H\text{-}F}$=1.8), 5.07 (s, 2H), 6.15 (q, 1H, $J_{H\text{-}F}$=8.2), 7.18 (d, 2H, J=8.2), 7.32 (t, 1H, J=8.2), 7.37 (t, 2H, J=8.2)
4a[a]	1.99+2.09 (s, 3H), 3.19-3.36 (m, 2H), 3.34+3.63 (s, 3H), 3.85 (d, 1H, J=16.8), 4.37-4.59 (m, 1H), 4.42 (d, 1H, J=16.8), 7.11-7.16 (m, 4H), 7.21-7.31 (m, 6H)
4b	2.11 (s, 3H), 3.75 (s, 3H), 4.43 (d, 1H, J=17.7), 4.65 (d, 1H, J=17.7), 6.01 (s, 1H), 6.97 (d, 2H, J=6.7), 7.18 (d, 2H, J=7.3), 7.14-7.24 (m, 6H)
4c[a]	0.83+0.90 (d, 3H, J=6.7), 0.96+0.97 (d, 3H, J=6.7), 2.05+2.28 (s, 3H), 2.29-2.41 (m, 1H), 3.97-4.94 (m, 5H), 7.12-7.35 (m, 10H)
4d	1.38 (d, 3H, J=7.0), 2.07 (s, 3H), 4.43-4.60 (m, 2H), 4.67 (q, 1H, J=7.0), 5.07 (s, 2H), 7.17 (br s, 5H), 7.23 (br s, 5H)
6b[a]	0.84-0.97 (m, 6H), 1.49-1.57 (m, 1H), 1.64-1.74 (m, 2H), 2.86+2.88 (s, 3H), 3.66+3.71 (s, 3H), 4.71-4.75+4.92-4.96 (m, 1H), 5.15+5.17 (s, 2H), 7.28-7.38 (m, 5H)
7a[a]	1.75+1.99 (s, 3H), 2.82+2.89 (s, 3H), 2.96-3.08+3.28-3.40 (m, 2H), 3.73+3.77 (s, 3H), 4.53-4.56+5.26-5.30 (m, 1H), 7.14-7.32 (m, 5H)
7b[a]	0.91-0.99 (m, 6H), 1.43-1.59 (m, 1H), 1.65-1.82 (m, 2H), 2.14+2.16 (s, 3H), 2.82+2.93 (s, 3H), 3.70+3.74 (s, 3H), 4.37-4.41+5.34-5.37 (m, 1H)
7c	2.16 (s, 3H), 2.79 (s, 3H), 5.11-5.37 (m, 2H), 6.51 (s, 1H), 7.17-7.32 (m, 10H)

[a] The multiplicity of the signals suggests two conformers due to hindered rotation of the amide bond.

Preparation of *N*-Benzyloxycarbonyl-*N*-methyl-α-amino Acid Esters (6): Compounds (**6a**)[6] and (**6b**) were synthesized by methylation of *N*-benzyloxycarbonylamino acids with methyl iodide and silver oxide (Scheme 3).[6]

One-pot Procedure for the Conversion of *N*-Benzyloxycarbonylamino Acids (6) to *N*-Acetylamino Acids (7a and b): A mixture of **6** (20 mmol) and 10% Pd-C (500 mg) in acetic anhydride (2.8 mL, 30 mmol) and AcOEt (50 mL) was stirred under a H_2 atmosphere at rt for 1 h. The mixture was filtered and the filtrate was concentrated under reduced pressure. The residue was diluted with AcOEt (100 mL) and 5% Na_2CO_3 (50 mL). After standard workup, the residue was chromatographed on a column of silica gel with AcOEt-hexane (1:3) as the eluent to give the *N*-acetyl derivatives (**7 a** and **b**).

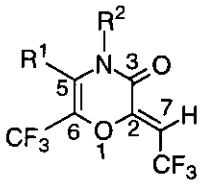
Preparation of Benzyl N-Acetyl-N-methylphenylglycinate (7c): A solution of benzyl phenylglycinate (**3e**)[7] (3.8 g, 15.8 mmol) and paraformaldehyde (581 mg, 19.4 mmol) in benzene (30 mL) was refluxed for 3 h, using a Dean-Stark apparatus. After the reaction, formic acid (6.6 mL, 17.5 mmol) was added to the reaction mixture and then $NaBH_3CN$ (1.99 g, 31.6 mmol) was added under ice cooling. The mixture was stirred at rt for 15 h and the solvent was evaporated under reduced pressure. The residue was diluted with $CHCl_3$ (100 mL) and 10% Na_2CO_3 (50 mL). After standard workup, the residue was dissolved in CH_2Cl_2 (30 mL), and then acetic anhydride (2.1 mL, 22.3 mmol) and pyridine (3.7 mL, 45.7 mmol) were added to the solution under ice cooling. The mixture was stirred at rt for 20 h and the solvent was evaporated under reduced pressure. The residue was diluted with 5% HCl (40 mL) and extracted with EtOAc (80 mL x 2). The combined extracts were washed successively with brine (40 mL), 5% Na_2CO_3 (40 mL), and brine (40 mL). After standard workup, the residue was chromatographed on a column of silica gel with AcOEt-hexane (2:3) as the eluent to give **7 c** (2.5 g, 53%) as a colorless oil.

Hydrolysis of Methyl α-Amino Acid Esters (4a, 4b, 7a, and 7b): A solution of methyl ester (**4a, 4b, 7a,** or **7b**) (10 mmol) and 2N 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 x 2) followed by standard workup to give the desired acids (**1 a, b, c,** and **f**) in high yields.

Catalytic Hydrogenation of Benzyl α-Amino Acid Esters (4c, 4d, and 7c): A mixture of benzyl ester (**4c, 4d,** or **7c**) (20 mmol) and 10% Pd-C (500 mg) in EtOH (60 mL) was stirred under a H_2 atmosphere at rt for 0.5 h. The mixture was filtered and the filtrate was concentrated *in vacuo* to give the desired acids (**1 d, e,** and **g**) in high yields.

General Procedure for the Reaction of *N*-Acetyl-*N*-alkylamino Acids (1a-g) with TFAA: Pyridine (0.97 mL, 12 mmol) was added to a solution of TFAA (0.84 mL, 6 mmol) in DCE or DMF (5 mL) at 0 °C under an Ar atmosphere and then an *N*-acetyl-*N*-alkylamino acid (**1**) (1 mmol) was added. The mixture was stirred at rt for 10 h and then at 90 °C for 15 h. The reaction mixture was diluted with 1% HCl (20 mL) and extracted with EtOAc (30 mL x 2). The combined extracts were washed successively with brine (30 mL), 3% Na_2CO_3 (30 mL), and brine (30 mL). After standard work-up, the residue was chromatographed on a column of silica gel with AcOEt-hexane (1:5) as the eluent to give 2-(2,2,2-trifluoroethylidene)-6-trifluoromethyl-2,3-dihydro-4*H*-1,4-oxazin-3-ones (**2a-g**). The results are summarized in Table 1. ^1H- and ^{13}C NMR data are collected in Tables 3 and 4, respectively.

Table 4. ^{13}C NMR data of 1,4-oxazines (**2**).



Compound	C-2	C-3	C-5	C-6	C-7	others
2a	146.20 (q) (J=4.2)	155.24	122.69 (q) (J=4.2)	126.33 (q) (J=42.0)	101.02 (q) (J=37.2)	31.24 (CH_2), 45.68 (CH_2), 120.34(q)(CF_3, J=272.1), 122.42 (q)(CF_3, J=270.0), 125.84 (CH), 127.17 (CH), 127.74 (CH), 128.08 (CH), 129.27 (CH), 129.52 (CH), 134.78 (C), 135.53 (C)
2b	146.21 (q) (J=5.2)	154.92	122.91 (q) (J=3.1)	126.10 (q) (J=37.3)	100.22 (q) (J=36.2)	29.77 (CH_3), 31.83 (CH_2), 120.38(q)(CF_3, J=271.0), 122.43 (q)(CF_3, J=270.0), 127.37 (CH), 127.63 (CH), 129.37 (CH), 134.51 (C)
2c	146.64 (q) (J=5.1)	154.79	125.56 (q) (J=3.1)	125.20 (q) (J=38.3)	100.99 (q) (J=37.2)	47.09 (CH_2), 119.58(q)(CF_3, J=272.1),122.46 (q) (CF_3, J=270.0), 127.01 (CH), 127.82 (CH), 128.27 (CH), 128.51 (CH), 128.57 (CH), 130.49 (CH), 132.04 (C), 135.48 (C)
2d	146.55 (q) (J=5.7)	154.49	125.61 (q) (J=3.1)	124.88 (q) (J=32.1)	100.28 (q) (J=36.2)	31.50 (CH_3), 120.30(q)(CF_3, J=270.0), 122.45 (q) (CF_3, J=269.0), 129.06 (CH), 129.85 (CH), 130.55 (CH), 133.03 (C)
2e	146.30 (q) (J=5.2)	155.93	123.41 (q) (J=2.1)	125.43 (q) (J=33.1)	100.65 (q) (J=37.2)	20.42 (CH_3 x 2), 26.67 (CH), 47.76 (CH_2),120.60(q) (CF_3, J=271.0), 122.34 (q)(CF_3, J=269.0), 125.56 (CH), 127.69 (CH), 128.97 (CH), 135.35 (C)
2f	146.31 (q) (J=5.2)	155.33	124.40 (q) (J=2.1)	125.24 (q) (J=37.2)	99.92 (q) (J=37.2)	21.72 (CH_3 x 2), 27.42 (CH_2), 30.16 (CH), 33.79 (CH_3), 120.39(q)(CF_3, J=271.0), 122.44 (q) (CF_3, J=270.0)
2g	146.41 (q) (J=5.2)	155.03	121.55 (q) (J=3.1)	124.59 (q) (J=37.2)	100.54 (q) (J=37.2)	12.40 (q)(CH_3, J=3.1), 46.04 (CH_2), 120.45(q) (CF_3, J=271.0), 122.48 (q)(CF_3, J=269.0), 126.32 (CH), 128.14 (CH), 129.24 (CH), 135.36 (C)

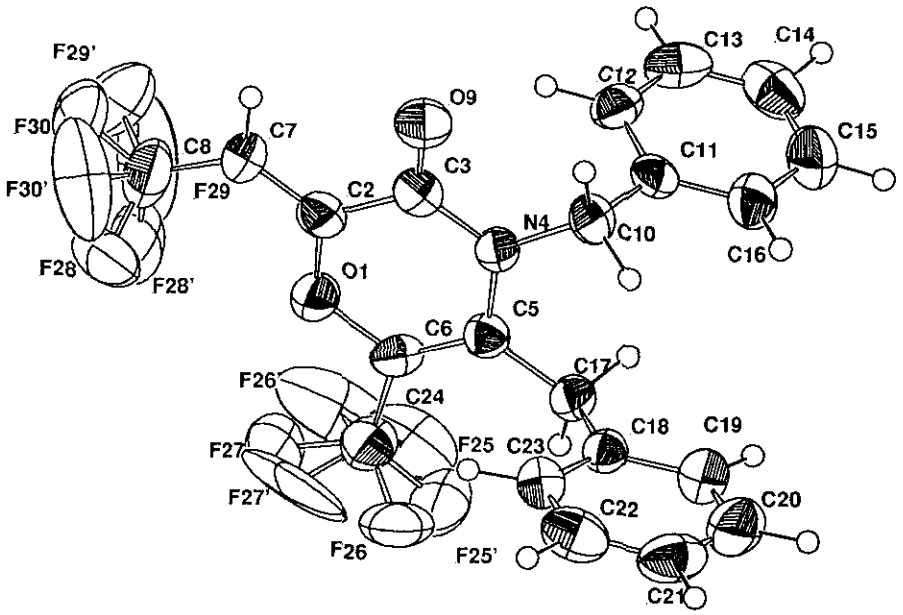


Figure 1. X-Ray structure drawing of 2a

X-Ray Analysis of 2a

$C_{21}H_{15}NO_2F_6$ F.W.=427, mp 153-154 °C (Et_2O-hexane).

Crystal data: a=7.855(4) Å, b=20.860(9) Å, c=12.521(5) Å, α=90 °, β=110.87(4) °, γ=90 °, V=1917(1) Å^3, monoclinic, $P2_1/a$, Z=4, D_x=1.481 g/cm^3, F(000)=872, μ(CuKα)=2.89 cm^{-1}.

The diffraction experiment was carried out using a colorless transparent single crystal with dimension of 0.4 x 0.4 x 0.4 mm. The diffractometer Rigaku AFC-5 was used with graphite-monochromated Cu Kα radiation (λ=1.5418 Å). The unit cell dimensions were determined from 19 2θ values in the range of 30-36 °. 3522 unique reflections (2θ≤130 °) were measured, of which 2384 with $F_o \geq 3\sigma(F_o)$ were considered as observed. The data were applied for Lp corrections but not for absorption and extinction. The structure was solved by the direct method. Successive difference Fourier map showed the F atoms on C8 might be in rotational disorder. Thus, the F28-F30 and F28'-F30' were set to be occupancy factors 0.5 each. At the final stage of refinement a difference Fourier map showed small peaks between F25-F27. Refinement assuming F25-F27 and F25'-F-27' of occupancy factors 0.8 and 0.2, respectively, gave the best R factor. The refinement of atomic parameters assuming anisotropic thermal displacement were applied for all non-H atoms, while H atoms were fixed at calculated position with an isotropic thermal parameter 1.25 and 1.5 times of that of the host atom for sp^2 and sp^3 carbon atoms, respectively. The final R value is 0.067

Table 5. Atomic coordinates and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for **2a**.

	x/a	y/b	z/c	U_{eq}*		x/a	y/b	z/c	U_{eq}*
O1	.0771(4)	.6450(2)	.4013(2)	55(2)	C19	.6420(7)	.5710(3)	.8588(4)	62(4)
C2	-.0624(7)	.6086(2)	.4080(4)	49(4)	C20	.7526(8)	.5186(3)	.8971(5)	81(5)
C3	-.0435(7)	.5777(2)	.5197(4)	52(4)	C21	.7662(8)	.4737(3)	.8220(6)	76(5)
N4	.1082(5)	.5926(2)	.6122(3)	42(3)	C22	.6638(8)	.4799(3)	.7069(5)	75(4)
C5	.2524(6)	.6292(2)	.6003(4)	42(3)	C23	.5500(7)	.5322(3)	.6664(4)	55(4)
C6	.2308(7)	.6529(2)	.4982(4)	45(3)	C24	.3682(10)	.6923(4)	.4660(7)	65(6)
C7	-.2147(7)	.6019(2)	.3181(4)	56(4)	F25	.392(2)	.7492(6)	.515(1)	124(9)
C8	-.2504(14)	.6307(6)	.2054(6)	76(7)	F26	.529(1)	.6650(5)	.498(1)	90(6)
O9	-.1631(4)	.5425(2)	.5255(3)	73(2)	F27	.320(2)	.6996(8)	.357(1)	118(8)
C10	.1156(6)	.5695(2)	.7240(4)	46(3)	F25'	.519(6)	.708(4)	.549(3)	114(30)
C11	.0772(7)	.6217(2)	.7980(4)	47(3)	F26'	.289(9)	.751(2)	.428(7)	186(43)
C12	-.0702(7)	.6633(2)	.7528(4)	51(4)	F27'	.399(11)	.678(4)	.380(6)	222(65)
C13	-.1082(7)	.7077(2)	.8232(5)	61(4)	F28	-.129(4)	.619(2)	.157(2)	135(18)
C14	-.0004(9)	.7118(3)	.9370(5)	80(5)	F29	-.276(10)	.690(1)	.206(2)	173(24)
C15	.1458(8)	.6716(3)	.9826(4)	76(5)	F30	-.395(4)	.607(3)	.127(2)	156(26)
C16	.1855(7)	.6264(2)	.9135(4)	59(4)	F28'	-.135(4)	.669(3)	.193(2)	148(23)
C17	.4200(6)	.6376(2)	.7043(4)	45(3)	F29'	-.401(3)	.660(2)	.170(3)	130(20)
C18	.5357(6)	.5781(2)	.7425(4)	42(3)	F30'	-.282(9)	.585(2)	.129(2)	187(24)

* U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

Table 6. Selected bond lengths(Å) and angles(°), and dihedral angles(°) around C2-C7 bond for **2a**.

O1-C2	1.361(7)	C11-C12	1.396(7)	C2-O1-C6	118.8(4)
O1-C6	1.383(5)	C11-C16	1.395(6)	O1-C2-C3	119.0(4)
C2-C3	1.498(8)	C12-C13	1.381(8)	O1-C2-C7	120.6(5)
C2-C7	1.326(6)	C13-C14	1.376(8)	C3-C2-C7	120.4(5)
C3-N4	1.369(5)	C14-C15	1.372(9)	C2-C3-N4	117.3(5)
C3-O9	1.215(7)	C15-C16	1.389(9)	C2-C3-O9	119.6(4)
N4-C5	1.417(7)	C17-C18	1.512(6)	N4-C3-O9	123.0(5)
N4-C10	1.462(6)	C18-C19	1.405(6)	C3-N4-C5	121.4(4)
C5-C6	1.324(7)	C18-C23	1.383(7)	C3-N4-C10	117.5(4)
C5-C17	1.496(5)	C19-C20	1.371(8)	C5-N4-C10	121.2(3)
C6-C24	1.52(1)	C20-C21	1.36(1)	N4-C5-C6	118.1(4)
C7-C8	1.47(1)	C21-C22	1.383(8)	N4-C5-C17	117.4(4)
C10-C11	1.527(7)	C22-C23	1.387(8)	C6-C5-C17	124.5(5)
				O1-C6-C5	125.0(5)
				O1-C6-C24	108.2(5)
				C5-C6-C24	126.8(5)
O1-C2-C7-C8	0(1)			C2-C7-C8	125.4(6)
C3-C2-C7-C8	178.8(7)			N4-C10-C11	113.4(4)
				C5-C17-C18	115.0(4)

(R_w=0.049, S=6.506). The minimum and maximum peaks on the final difference Fourier map were -0.3 and 0.3*e* Å^{-3} (the maximum peak is located in the center of the 1,4-oxazine ring of **2a**). All the calculations were carried out using *Xtal* 3.2[8] on a Hewlett Packerd 735/125 of Josai University. Atomic parameters, bond lengths and angles, and selected dihedral angles are collected in Tables 5 and 6.

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Received, 22nd July, 1997