USE OF THE TRIFLAMIDE GROUP FOR FRIEDEL-CRAFTS ACYLATION OF *N*-(β-PHENETHYL)AMINO ACIDS TO 3-BENZAZEPINE DERIVATIVES

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Abstract --- Triflamides of *N*-(β-phenethyl)amino acids (**1**) were treated with P_2O_5 under the Friedel-Crafts acylation conditions to give the 3-benzazepines in good yields. *N*-(β-Phenethyl)-*N*-triflylvaline (**1f**) and phenylglycine (**1g**) were efficiently prepared from the corresponding *N*-triflylamino acids and β-phenethyl alcohol *via* the Mitsunobu reaction.

2,3,4,5-Tetrahydro-1*H*-3-benzazepine derivatives substituted either on the benzene ring or on the azepine ring are of considerable medicinal interest.[1] In particular, the presence of both a 1-aryl substituent and a 7,8-dioxygenation pattern gives rise to 3-benzazepines as dopaminomimetic or antidopaminergic agents.[2] In our current work, we needed an easy access to 2-substituted 3-benzazepines. Though several procedures for the synthesis of these azacycles are already known,[3] a general synthetic approach to the 2-substituted 3-benzazepines has not been developed and not received as much attention. A route to 2-aryl-3-benzazepines that has been reported involves a ring expansion of the 1-substituted tetrahydroisoquinoline *via* the intermediate aziridine.[4]

On the other hand, the cyclization of the *N*-(β-phenethyl)amino acids of type (**1**) appears to be an obvious route to 2-substituted 3-benzazepines (**2**) (eq. 1). However, it has been reported that *N*-(β-phenethyl)glycines fail to give Friedel-Crafts acylation products unless the α-amino group is suitably protected.[5] This is due to the basicity of the nitrogen causing decarboxylation. The sulfonyl[6] and phosphoryl[7] groups were used in early work as the protecting group, but only the glycine derivatives appears to be synthetically useful. In one

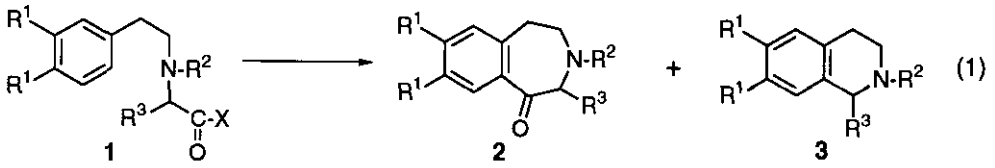
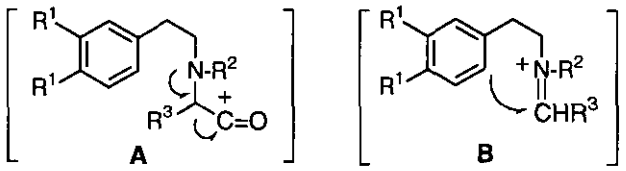


Table 1. Friedel-Crafts Acylation of *N*-(β-Phenethyl)amino Acids.

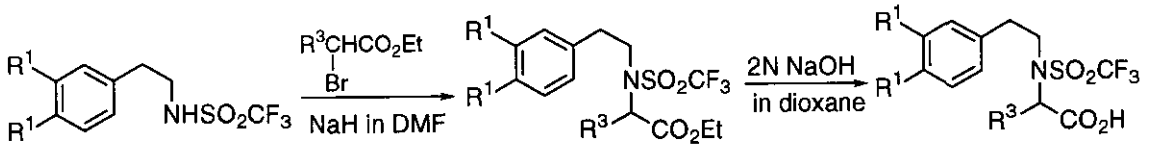
1	R^1	R^2	R^3	X	Reaction Conditions	Products, Yield (%)
a	H	Ts	Me	Cl	$AlCl_3$ in CH_2Cl_2, -70 °C	**2a** (40)[a]
b	MeO	Ms	Me	OH	P_2O_5 in DCE, 0 °C	**2b** (43) + **3** (38)
c	MeO	Tf	Me	OH	P_2O_5 in DCE, 0 °C	**2c** (81)
d	H	Tf	H	OH	P_2O_5 in DCE, 0 °C	**2d** (65)
e	MeO	Tf	H	OH	P_2O_5 in DCE, 0 °C	**2e** (84)
f	MeO	Tf	Me_2CH	OH	P_2O_5 in DCE, 0 °C	**2f** (64)
g	MeO	Tf	Ph	OH	P_2O_5 in DCE, 0 °C	**2g** (70)

[a] Literature data [6a]



experiment, the Friedel-Crafts type cyclization of alanine derivative (**1a**) was tried and the yield of **2a** was poor.[6a] Based on these results, it is considered that a more electron-withdrawing, nitrogen-protecting group would inhibit decarboxylation. We selected a trifluoromethanesulfonyl (triflyl, symbolized as Tf) group,[8] which is one of the most powerful electron-withdrawing group, as the nitrogen-protecting group. Initially, we attempted the cyclization of *N*-methanesulfonylalanine derivative (**1b**) by heating with PPA or treating its chloride with aluminum chloride in CH_2Cl_2 in the cold, but in vain. In these studies, we found that 2-methyl-3-benzazepinone (**2b**) could be obtained in 43% yield from **1b** with P_2O_5 in 1,2-dichloroethane (DCE) accompanying isoquinoline (**3**) (38%), which could be formed *via* intermediate (**A**) followed by **B**. Still, there is substantial decarboxylation. In this reaction, five equiv. of P_2O_5 to **1b** were needed to obtain good results, and the use of two equiv. of P_2O_5 failed to give the products. Finally, this method was applied to the cyclization of *N*-triflylalanine derivative (**1c**).

It was found that, by using triflyl function, Friedel-Crafts type cyclization of **1c** succeeded to produce 2-methyl-3-benzazepines (**2c**) in 81% yield. No isoquinoline derivative was detected in the reaction. The procedure was simple: a solution of **1c** in DCE was added for 0.5 h to a stirred solution of P_2O_5 (5 mol equiv) in DCE with ice-cooling. The reaction mixture was stirred overnight in an ice bath. Usual workup and isolation by silica gel column chromatography afforded 3-benzazepine (**2c**). The structure of **2c** was confirmed by spectroscopic analysis. Various *N*-triflylamino acid derivatives were reacted in this way to produce 3-benzazepines in good yields and the results are presented in Table 1. The reaction was then extended to the *N*-(β-phenethyl)amino acids of glycine, alanine, valine, and phenylglycine.



4a: R^1=MeO
4b: R^1=H

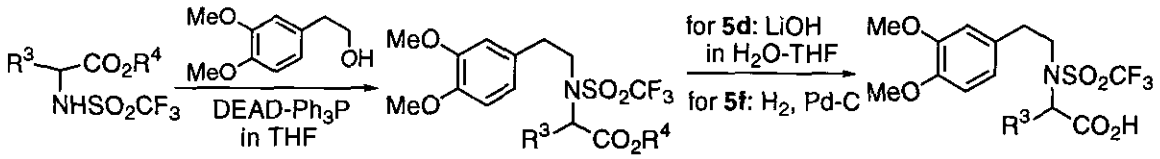
5a: R^1=MeO, R^3=Me (72%)
5b: R^1=R^3=H (85%)
5c: R^1=MeO, R^3=H (91%)

1c: R^1=MeO, R^3=Me (82%)
1d: R^1=R^3=H (91%)
1e: R^1=MeO, R^3=H (93%)

Scheme 1

The starting carboxylic acids (**1c-e**) were prepared by the routes as outlined in Scheme 1. The triflamides (**4a** and **b**) were prepared in good yields by reacting β-phenethylamines with triflyl chloride in CH_2Cl_2 in the presence of triethylamine at -78 °C. Treatment of triflamides (**4**) with NaH followed by addition of ethyl 2-bromopropionate or ethyl bromoacetate gave *N*-triflylalanine derivative (**5a**, 72%) and glycine derivatives (**5b**, 85%; **5c**, 91%), respectively. Subsequent hydrolysis of **5a-c** with 2N NaOH in dioxane at 60 °C yielded the corresponding carboxylic acids (**1c-e**) in high yields. However, valine derivative (**1f**) and phenylglycine derivative (**1g**) were difficult to prepare in a similar manner for the preparation of **1c-e**. Alkylation of **4a** with ethyl 2-bromoisovaleric ester or methyl α-bromophenylacetate failed and the starting materials were recovered. After several trial, we next turned to another route. Thus, following a recent report that *N*-benzyltriflamide is usable as a nucleophile in a Mitsunobu reaction,[9] we were successful in condensation of *N*-triflyl-α-amino acids (**6**) with *3,4-dimethoxyphenethyl alcohol under the Mitsunobu reaction condition using diethyl* azodicarboxylate (DEAD) and triphenylphosphine in THF and the desired esters (**5d-f**) were obtained in good yields. Attempted hydrolysis of **5d** or **5e** with 2N NaOH failed to occur and more vigorous conditions led to a decomposition of the starting material. However, treatment of **5d** with LiOH[10] in aqueous THF at 25 °C afforded the desired carboxylic acid (**1f**) (60%) and the recovered starting material (35%). On the other hand, treatment of **5e** with

LiOH gave no carboxylic acid and unreacted ester was recovered unchanged. Consequently, instead of **5e**, benzyl ester (**5f**) was subjected to catalytic hydrogenation and the desired carboxylic acid (**1g**) was obtained in 78% yield (Scheme 2).



6a: R^3=Me_2CH, R^4=Et
6b: R^3=Ph, R^4=Et
6c: R^3=Ph, R^4=Bn

5d: R^3=Me_2CH, R^4=Et (73%)
5e: R^3=Ph, R^4=Et (74%)
5f: R^3=Ph, R^4=Bn (81%)

1f: R^3=Me_2CH (65%)
1g: R^3=Ph (78%)

Scheme 2

In conclusion, we have demonstrated that the triflyl function can inhibit the decarboxylation in the Friedel-Crafts acylation of *N*-(β-phenethyl)amino acids. As the starting *N*-(β-phenethyl)-amino acids can be readily prepared from *N*-triflylamino acids *via* the Mitsunobu reaction, the synthetic route is suitable for the preparation of variously 2-substituted 3-benzazepines.

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. *N*-Triflamides (**4a,b and 6a-c**) were prepared by the reported method.[9] In the preparation of **6c**, Tf_2O was used instead of TfCl. Analytical and physical data of all new products are presented in Tables 2 and 3.

General Procedure for the Alkylation of *N*-Triflamides (4): A solution of *N*-triflamide (**4**)(5 mmol) in DMF (5 mL) was added to a suspension of NaH (240 mg, 60% dispersion in mineral oil, 6 mmol) in DMF (5 mL) at 0 °C under an Ar atmosphere. After the reaction mixture was stirred for 0.5 h, a solution of ethyl 2-bromopropionate (1.08 g, 6 mmol) or ethyl bromoacetate (1.01 g, 6 mmol) in DMF (3 mL) was added at 0 °C. The resulting mixture was stirred for 3 h at rt, and then diluted with brine (60 mL) and AcOEt (80 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 alkylation products (**5a-c**).

Table 2. Physical and analytical data of new compounds.

Compound	Yield (%)	Formula	mp (°C) (solvent)[a]	Found (%) (requires) C	H	N	IR, ν_{max} (cm^{-1})	MS, m/z (%), M^+ and base peak
4a	71	$C_{11}H_{14}NO_4F_3S$	111-112 (C-H)	42.26 (42.17)	4.43 (4.50)	4.47 (4.47)	-	313 (19) 151
4b	96	$C_9H_{10}NO_2F_3S$	oil	253.0386 (253.0385)			-	253 (23) 91
5a	72	$C_{16}H_{22}NO_6F_3S$	oil	413.1110 (413.1120)			1750	413 (15) 151
5b	85	$C_{13}H_{17}NO_4F_3S$	oil	340.0819 (M^++1)[b] (340.0830)			1755	340[b] (M^++1,100)
5c	91	$C_{15}H_{20}NO_6F_3S$	oil	399.0937 (399.0963)			1755	399 (14) 151
5d	73	$C_{18}H_{26}NO_6F_3S$	oil	441.1432 (441.1432)			1740	441 (19) 151
5e	74	$C_{21}H_{24}NO_6F_3S$	oil	475.1268 (475.1277)			1745	475 (26) 151
5f	81	$C_{26}H_{26}NO_6F_3S$	oil	537.1420 (537.1433)			1750	537 (61) 151
6a	67	$C_8H_{14}NO_4F_3S$	oil	278.0670 (M^++1)[b] (278.0674)			3200, 1720	278[b] (M^++1,100)
6b	85	$C_{11}H_{12}NO_4F_3S$	oil	311.0439 (311.0440)			3250, 1740	311 (4) 238
6c	62	$C_{16}H_{14}NO_4F_3S$ $1/2H_2O$	73-75 (E-H)	50.33 (50.12)	3.76 (3.95)	3.73 (3.65)	3270, 1735 1710	373 (0.1) 91
1b	95	$C_{14}H_{21}NO_6S$	oil	331.1086 (331.1090)			3525, 3250 1730	331 (21) 151
1c	82	$C_{14}H_{18}NO_6F_3S$	115-116 (A-H)	43.76 (43.64)	4.83 (4.71)	3.61 (3.63)	3225, 1750	385 (14) 151
1d	91	$C_{11}H_{12}O_4NF_3S$	149-151 (A-H)	42.23 (42.44)	3.84 (3.89)	4.65 (4.50)	3050, 1720	311 (0.1) 104
1e	93	$C_{13}H_{16}NO_6F_3S$	112-113 (A-H)	42.19 (42.05)	4.29 (4.34)	3.66 (3.77)	3050, 1715	371 (17) 151
1f	65	$C_{16}H_{22}NO_6F_3S$	oil	413.1118 (413.1119)			3600-2500 1730	413 (17) 151
1g	78	$C_{19}H_{20}NO_6F_3S$	oil	447.0956 (447.0964)			3500-2500 1740	447 (21) 151
2b	43	$C_{14}H_{19}NO_5S$	165-166 (A-H)	53.52 (53.66)	6.07 (6.11)	4.29 (4.47)	1670	313 (31) 234
2c	81	$C_{14}H_{16}NO_5F_3S$	102-103 (E)	45.71 (45.78)	4.38 (4.39)	3.86 (3.81)	1680	367 (32) 234
2d	65	$C_{11}H_{10}NO_3F_3S$	76 (E-H)	44.94 (45.05)	3.46 (3.44)	4.78 (4.78)	1690	293 (8) 160
2e	84	$C_{13}H_{14}NO_5F_3S$	158-160 (C-H)	43.91 (44.19)	3.97 (3.99)	3.98 (3.96)	1670	353 (49) 220
2f	64	$C_{16}H_{20}NO_5F_3S$	oil	395.1011 (395.1018)			1680	395 (19) 262
2g	70	$C_{19}H_{18}NO_5F_3S$	175-178 (A-H)	53.11 (53.14)	4.29 (4.23)	3.30 (3.26)	1680	429(12) 296

[a] A=AcOEt, C=CH_2Cl_2, E=Et_2O, H=hexane. [b] CIMS

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

4a	2.85 (t, 2H, J=6.7), 3.47-3.57 (m, 2H), 3.87 (s, 3H), 3.88 (s, 3H), 4.89 (br s, 1H), 6.69 (d, 1H, J=1.8), 6.74 (dd, 1H, J=1.8, 7.2), 6.83 (d, 1H, J=7.2)
4b	2.83 (t, 2H, J=7.0), 3.07-3.73 (m, 2H), 4.97 (br s, 1H), 7.10 (s, 5H)
5a	1.30 (t, 3H, J=7.0), 1.57 (d, 3H, J=7.3), 2.85-2.94 (br, 1H), 2.95-3.08 (br, 1H), 3.42-3.50 (m, 1H), 3.64-3.72 (m, 1H), 3.86 (s, 3H), 3.88 (s, 3H), 4.23 (q, 2H, J=7.0), 4.61 (q, 1H, J=7.3), 6.70 (d, 1H, J=1.8), 6.73 (dd, 1H, J=1.8, 8.2), 6.81 (d, 1H, J=8.2)
5b	1.29 (t, 3H, J=7.0), 2.95 (t, 2H, J=7.6), 3.65-3.82 (br, 2H), 3.90-4.10 (br, 2H), 4.23 (q, 2H, J=7.0), 7.18 -7.22 (m, 2H), 7.24-7.28 (m, 1H), 7.30-7.35 (m, 2H)
5c	1.29 (t, 3H, J=7.3), 2.90 (t, 2H, J=7.6), 3.62-3.78 (br, 1H), 3.87 (s, 3H), 3.88 (s, 3H), 3.90-4.07 (br, 1H), 4.23 (q, 2H, J=7.6), 6.70-6.75 (m, 2H), 6.82 (d, 1H, J=8.2)
5d	1.02 (d, 3H, J=6.7), 1.09 (d, 3H, J=6.7), 1.31 (t, 3H, J=7.3), 2.24-2.32 (m, 1H), 2.88-3.03 (m, 2H), 3.51-3.58 (m, 1H), 3.75-3.80 (br, 1H), 3.86 (s, 3H), 3.89 (s, 3H), 4.05 (d, 1H, J=10.4), 4.20-4.29 (m, 2H), 6.72 (d, 1H, J=1.8), 6.76 (dd, 1H, J=1.8, 8.2), 6.81 (d, 1H, J=8.2)
5e	1.27 (t, 3H, J=7.0), 2.50-2.97 (m, 1H), 3.30-3.60 (m, 2H), 3.60-3.90 (m, 1H), 3.70 (s, 3H x2), 4.20 (q, 2H, J=7.0), 5.67 (s, 1H), 6.13 (s, 1H), 6.23 (d, 1H, J=8.0), 6.57 (d, 1H, J=8.0), 7.33 (br s, 5H)
5f	2.68-2.73 (m, 1H), 3.40-3.70 (m, 2H), 3.70-3.90 (br s, 1H), 3.78 (s, 3H), 3.80 (s, 3H), 5.26 (s, 2H), 5.84 (br s, 1H), 6.24 (s, 1H), 6.30 (d, 1H, J=8.0), 6.67 (d, 1H, J=8.0), 7.28-7.36 (m, 7H), 7.42-7.49 (m, 3H)
6a	0.93 (d, 3H, J=7.0), 1.05 (d, 3H, J=7.0), 1.31 (t, 3H, J=7.3), 2.18-2.25 (m, 1H), 4.04-4.05 (br, 1H), 4.28 (t, 2H, J=7.3), 5.63 (br s, 1H)
6b	1.43 (t, 3H, J=7.3), 4.40 (q, 2H, J=7.3), 5.17 (s, 1H), 7.33-7.57 (m, 3H), 7.77-8.00 (m, 2H)
6c	5.16 (d, 1H, J=2.2), 5.23 (d, 1H, J=2.2), 5.31 (s, 1H), 6.34 (br s, 1H), 7.16-7.19 (m, 2H), 7.27-7.32 (m, 5H), 7.34-7.38 (m, 3H)
1b	1.54 (d, 3H, J=7.3), 2.82-2.89 (m, 1H), 2.92 (s, 3H), 3.00-3.05 (m, 1H), 3.19-3.26 (m, 1H), 3.48-3.54 (m, 1H), 3.86 (s, 3H), 3.88 (s, 3H), 4.66 (q, 1H, J=7.3), 6.72-6.75 (m, 2H), 6.80 (d, 1H, J=7.9)
1c	1.63 (d, 3H, J=7.6), 2.83-2.95 (br, 1H), 2.95-3.10 (br, 1H), 3.41-3.52 (m, 1H), 3.65-3.75 (m, 1H), 3.86 (s, 3H), 3.88 (s, 3H), 4.67 (q, 1H, J=7.6), 6.69 (d, 1H, J=1.8), 6.72 (dd, 1H, J=1.8, 8,2), 6.81 (d, 1H, J=8.2)
1d	2.96 (t, 2H, J=7.9), 3.73 (br s, 2H), 4.06 (br s, 2H), 7.19-7.21 (m, 2H), 7.25-7.28 (m, 1H), 7.32-7.35 (m, 2H)
1e	2.90 (t, 2H, J=7.6), 3.65-3.78 (br, 2H), 3.87 (s, 3H), 3.88 (s, 3H), 3.96-4.10 (br, 2H), 6.71 (d, 1H, J=1.8), 6.74 (dd, 1H, J=1.8, 8.2), 6.82 (d, 1H, J=8.2)
1f	1.10 (d, 3H, J=6.4), 1.13 (d, 3H, J=6.4), 2.20-2.32 (m, 1H), 2.88-2.97 (m, 1H), 2.98-3.07 (m, 1H), 3.53-3.61 (m, 1H), 3.70-3.82 (m, 1H), 3.86 (s, 3H), 3.88 (s, 3H), 4.10-4.16 (m, 1H), 6.71 (d, 1H, J=1.8), 6.74 (dd, 1H, J=1.8, 7.9), 6.80 (d, 1H, J=7.9)
1g	2.67-2.76 (m, 1H), 3.35-3.52 (br, 1H), 3.55-3.70 (br, 1H), 3.73-3.84 (br, 1H), 3.79 (s, 3H), 3.80 (s, 3H), 5.75-5.85 (br, 1H), 6.26 (s, 1H), 6.32 (d, 1H, J=8.0), 6.68 (d, 1H, J=8.0), 7.40-7.50 (br s, 2H), 7.50-7.56 (br s, 3H)
2b	1.64 (d, 3H, J=7.3), 2.45 (s, 3H), 2.88-2.96 (m, 1H), 3.03-3.13 (m, 1H), 3.58-3.65 (m, 1H), 3.83-3.93 (m, 1H), 3.90 (s, 3H), 3.94 (s, 3H), 4.76 (q, 1H, J=7.3), 6.70 (s, 1H), 7.16 (s, 1H)
2c	1.69 (d, 3H, J=7.3), 2.90-2.99 (m, 1H), 3.08-3.17 (m, 1H), 3.60-3.78 (m, 1H), 3.91 (s, 3H), 3.95 (s, 3H), 3.93-4.12 (m, 1H), 4.73 (q, 1H, J=7.3), 6.68 (s, 1H), 7.18 (s, 1H)
2d	3.12 (t, 2H, J=6.5), 3.83 (br s, 2H), 4.33 (br s, 2H), 7.26 (dd, 1H, J=1.2, 7.6), 7.44 (dt, 1H, J=1.2, 7.6), 7.56 (dt, 1H, J=1.2, 7.6), 7.77 (dd, 1H, J=1.2, 7.6)
2e	3.10 (br s, 2H), 3.82 (br s, 2H), 3.93 (s, 3H), 3.96 (s, 3H), 4.32 (br s, 2H), 6.70 (s, 1H), 7.34 (s, 1H)
2f	1.14 (d, 3H, J=6.7), 1.18 (d, 3H, J=6.7), 2.30-2.40 (m, 1H), 2.93-3.00 (m, 1H), 3.20-3.30 (m, 1H), 3.64-3.76 (br, 1H), 3.91 (s, 3H), 3.95 (s, 3H), 3.97-4.07 (br, 1H), 4.14-4.35 (br, 1H), 6.64 (s, 1H), 7.28 (s, 1H)
2g	2.57 (m, 1H), 2.84-2.93 (m, 1H), 3.45-3.54 (br, 1H), 3.90-3.98 (br, 1H), 3.95 (s, 3H), 3.97 (s, 3H), 6.00-6.08 (br s, 1H), 6.63 (s, 1H), 7.34 (d, 2H, J=7.3), 7.40 (t, 1H, J=7.3), 7.45 (t, 2H, J=7.3), 7.50 (s, 1H)

General Procedure for the Mitsunobu Reaction of *N*-Triflamide (6): A solution of *N*-triflamide (**6**)(5 mmol), 2-(3,4-dimethoxyphenyl)ethyl alcohol (0.91 g, 5 mmol), triphenylphosphine (1.44 g, 5.5 mmol), and diethyl azodicarboxylate (0.87 mL, 5.5 mmol) in dry THF (25 mL) was stirred at rt for 15 h. The mixture was then evaporated and the residue was diluted with AcOEt (80 mL) and H_2O (60 mL). The organic layer was separated and washed successively with 3% HCl (50 mL), H_2O (50 mL), 3% Na_2CO_3 (50 mL), and brine (50 mL). After standard workup, the residue was chromatographed on a column of silica gel with AcOEt-hexane (1:1) as the eluent to give the products (**5d-f**).

General Procedure for the Hydrolysis of *N*-Triflamide Esters (5a-c): A solution of *N*-triflamide ester (**5**)(5 mmol) and 2N NaOH (3.75 mL, 7.5 mmol) in dioxane (7 mL) was stirred at 65 °C for 2 h. The reaction mixture was diluted with Et_2O (40 mL) and H_2O (30 mL). The aqueous layer was acidified with conc. HCl and extracted with AcOEt (40 mL x 2) followed by standard workup.

Hydrolysis of Ethyl *N*-[2-(3,4-Dimethoxyphenyl)ethyl]-*N*-trifluoromethanesulfonylvalinate (5d) with LiOH: A solution of LiOH (96 mg, 4 mmol) in H_2O (2 mL) was added to a solution of **5d** (882 mg, 2 mmol) in THF (5 mL) and the mixture was stirred at rt for 24 h. The mixture was diluted with Et_2O (30 mL) and 2% Na_2CO_3 (20 mL). The aqueous layer was acidified with conc. HCl and extracted with AcOEt (40 mL x 2). The standard workup gave *N*-[2-(3,4-dimethoxyphenyl)ethyl]-*N*-trifluoromethanesulfonylvaline (**1f**)(495.6 mg, 60%) which was used without further purification. The starting material (**5d**)(309 mg, 35%) was recovered from the Et_2O layer.

Catalytic Hydrogenation of Benzyl *N*-[2-(3,4-Dimethoxyphenyl)ethyl]-*N*-trifluoromethanesulfonylphenylglycinate (5f): A mixture of **5f** (805.5 mg, 15 mmol) and 10% Pd-C (30 mg) in EtOH (5 mL) was stirred under a H_2 atmosphere at rt for 0.3 h. The mixture was filtered and the filtrate was concentrated *in vacuo* to give *N*-[2-(3,4-dimethoxyphenyl)ethyl]-*N*-trifluoromethanesulfonyl phenylglycine (**1g**)(523.0 mg, 78%).

General Procedure for the Friedel-Crafts Type Acylation of *N*-Triflylamino Acids (1): A solution of **1** (1 mmol) in $ClCH_2CH_2Cl$ (7 mL) was added to a solution of P_2O_5 (710 mg, 5 mmol) in $ClCH_2CH_2Cl$ (5 mL) at 0 °C under an Ar atomosphere and the mixture was stirred for 24 h. The reaction mixture was diluted with 3% NaOH (40 mL) and CH_2Cl_2 (80 mL). After standard workup, the residue was chromatographed on a column of silica gel to give the 3-benzazepinones (**2**). The results are summarized in Table 1 and ^{13}C NMR data are collected in Table 4.

Table 4. ^{13}C NMR data of 3-benzazepines (**2**).

Compound	C-1	C-2	C-4	C-5	CF_3	others
2b	205.75 (C)	60.24 (CH)	42.48 (CH_2)	32.31 (CH_2)	-	14.49 (CH_3), 39.76 (CH_3), 56.07 (CH_3), 56.13 (CH_3), 111.33 (CH), 111.63 (CH), 130.61 (C), 130.62 (C), 148.27 (C), 152.59 (C)
2c	204.07 (C)	61.63 (CH)	43.11 (CH_2)	31.93 (CH_2)	119.59 (q) (J=320.6)	13.77 (CH_3), 56.11 (CH_3), 56.16 (CH_3), 111.64 (CH), 111.68 (CH), 129.41 (C), 129.86 (C), 148.53 (C), 152.93 (C)
2d	200.20 (C)	55.18 (CH_2)	47.59 (CH_2)	32.16 (CH_2)	119.51 (q) (J=322.8)	128.36 (CH), 129.32 (CH), 129.43 (CH), 133.86 (CH), 136.05 (C), 136.15 (C)
2e	198.08 (C)	55.08 (CH_2)	47.40 (CH_2)	32.36 (CH_2)	119.68 (q) (J=322.8)	56.12 (CH_3), 56.20 (CH_3), 111.66 (CH), 112.01 (CH), 128.41 (C), 131.03 (C), 148.80 (C), 153.80 (C)
2f	210.37 (C)	72.37 (CH)	44.47 (CH_2)	32.55 (CH_2)	119.32 (q) (J=321.7)	19.52 (CH_3), 21.23 (CH_3), 27.36 (CH), 55.98 (CH_3), 56.04 (CH_3), 111.63 (CH), 112.59 (CH), 129.54 (C), 130.18 (C), 148.34 (C), 152.92 (C)
2g	218.00 (C)	68.64 (CH)	45.05 (CH_2)	31.50 (CH_2)	119.47 (q) (J=288.6)	56.11 (CH_3), 56.14 (CH_3), 111.78 (CH), 112.35 (CH), 127.09 (CH), 128.68 (C), 128.87 (C), 129.38 (CH x 2), 131.26 (C), 148.60 (C), 153.75 (C)

Preparation of *N*-[2-(3,4-Dimethoxyphenyl)ethyl]-*N*-methanesulfonylalanine (1b): **1b** was synthesized in two steps from *N*-[2-(3,4-dimethoxyphenyl)ethyl]methanesulfonamide[11] by the same procedure as described in the preparation of **1d-f**. **Ethyl *N*-[2-(3,4-dimethoxyphenyl)ethyl]-*N*-methanesulfonylalaninate**: Yield 81% (after column chromatography)(AcOEt-hexane, 1:2): oil, ^1H NMR δ 1.29 (t, 3H, J=7.0), 1.49 (d, 3H, J=7.3), 2.82-2.90 (m, 1H), 2.93 (s, 3H), 2.98-3.05 (m, 1H), 3.16-3.25 (m, 1H), 3.44-3.53 (m, 1H), 3.86 (s, 3H), 3.88 (s, 3H), 4.20 (q, 2H, J=7.0), 4.62 (q, 1H, J=7.3), 6.72-6.76 (m, 2H), 6.81 (d, 1H); IR ν_{max}/neat (cm^{-1}) 1735; MS m/z 359 (M^+, 16), 59 (100). HRMS Calcd for $C_{16}H_{25}NO_6S$: 359.1402, Found 359.1396.

Friedel-Crafts Type Acylation of 1b: The procedure was same as described in the general procedure for the Friedel-Crafts type reaction. The product was purified by silica gel column chromatography. First elution with AcOEt-hexane (1:1) afforded **3** (108.3 mg, 38%). mp 105-106 °C (AcOEt-hexane). ^1H NMR δ 1.55 (d, 3H, J=6.7), 2.66-2.70 (m, 1H), 2.81 (s, 3H), 2.92-2.99 (m, 1H), 3.41-3.49 (m, 1H), 3.85 (s, 3H), 3.86 (s, 3H), 3.88-3.96 (m, 1H), 4.92 (q, 1H, J=6.7), 6.56 (s, 1H), 6.59 (s, 1H); MS m/z 285 (M^+, 17), 270 (100). Anal. Calcd for $C_{13}H_{19}NO_4S$: C, 54.44; H, 6.58; N, 4.80. Found C, 54.72; H, 6.71; N, 4.91. Second elution with AcOEt-hexane (3 : 1) afforded **2b** (150.2 mg, 43%) whose ^{13}C NMR data are collected in Table 4.

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Received, 17th March, 1997