

REACTIONS OF TETRASULFUR TETRANITRIDE ANTIMONY PENTACHLORIDE COMPLEX ($S_4N_4 \cdot SbCl_5$) WITH PRIMARY β -ENAMINONES AND β -ENAMINO ESTERS: SYNTHESIS OF 4-SUBSTITUTED 3-AROYL- AND 3-ETHOXYCARBONYL-1,2,5-THIADIAZOLES

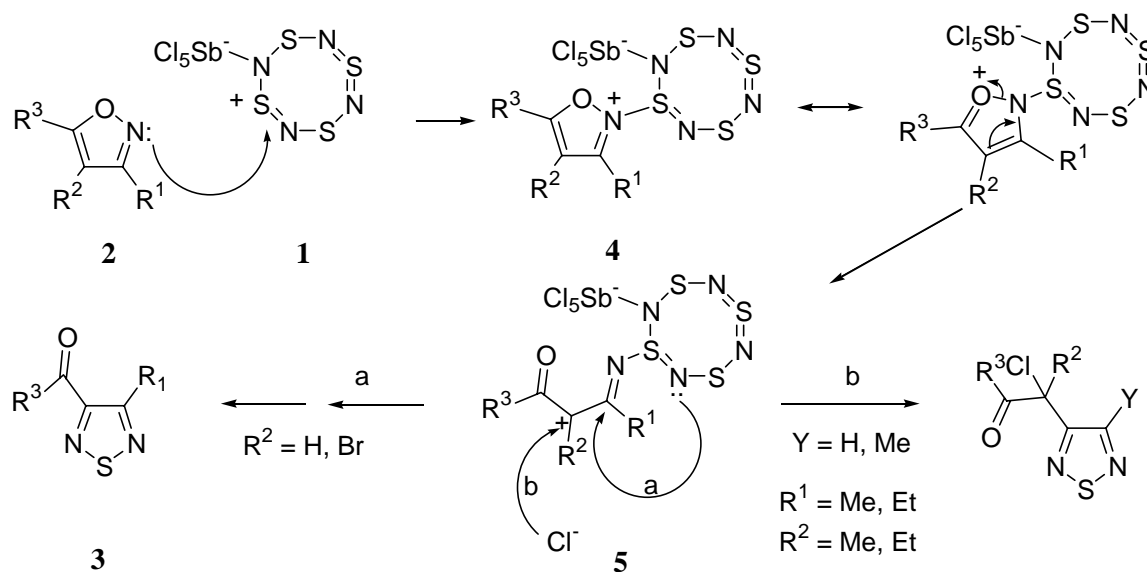
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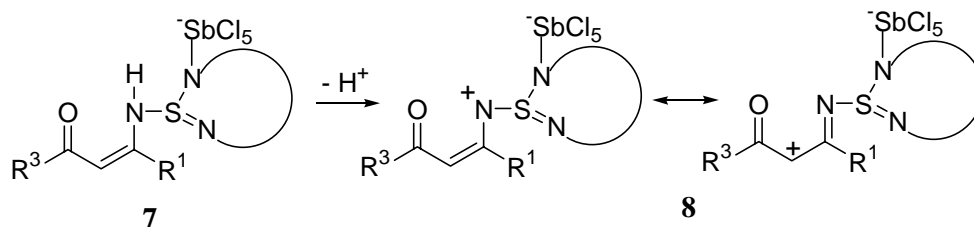
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Abstract - The reaction of tetrasulfur tetranitride antimony pentachloride complex ($S_4N_4 \cdot SbCl_5$) with 3-amino-3-alkyl-1-aryl-2-propenones and 3-amino-1,3-diaryl-2-propenones in toluene at 100 °C produced 4-substituted 3-aryl-1,2,5-thiadiazoles (**3a-p**) in 12 to 57% yields. Similarly treatment of β -enamino esters with $S_4N_4 \cdot SbCl_5$ complex under the same conditions as for the reaction with β -enaminones gave ethyl 3-aryl-1,2,5-thiadiazole-4-carboxylates (**3q-x**) in 41 to 54% yields. The formation of the products may be explained by the same mechanism as that proposed for the formation of 1,2,5-thiadiazoles from 5-substituted 3-alkyl- and 3-aryl-isoxazoles and $S_4N_4 \cdot SbCl_5$ complex.

It has been demonstrated that tetrasulfur tetranitride antimony pentachloride complex ($S_4N_4 \cdot SbCl_5$) (**1**), which is the most stable complex among the reported S_4N_4 -Lewis acid complexes,¹ possesses considerable synthetic potential, as exemplified by the ready conversion of sterically less hindered α -bromo ketones to α -chloro ketones² and complete regioselective formation of 4-substituted 3-acyl- and 3-aryl-1,2,5-thiadiazoles (**3a**) from 5-substituted 3-alkyl- and 3-aryl-isoxazoles (**2**).³ A mechanism was proposed by us for the latter reaction.³ The mechanism involves the nucleophilic attack of the nitrogen atom of isoxazoles (**2**) on a tetravalent sulfur atom of the complex (**1**), yielding a new complex (**4**), followed by cleavage of the N-O bond of the complex concomitant with electron delocalization (Scheme 1). This would give the cation (**5**), which undergoes different reactions, depending on the substituent R² at C-4 of isoxazoles. So a cation (**5**) is a key intermediate of the reaction. We examined the structure of the proposed key intermediate (**5**), in which the nitrogen of the ring-opened form of **2** is bonded to the sulfur of the complex (**1**). It is envisaged that a similar type of intermediate (**8**) possessing the same skeleton as



that of **5** may be obtained by deprotonation from the structure (**7**) which would be formed by the reaction of **1** with primary β -enaminones (Scheme 2). With this in mind, we have studied the reactions of primary β -enaminones with **1**. The study was extended to the reactions with β -enamino esters. The results are described herein.



RESULTS AND DISCUSSION

(A) Preparation of β -enamino ketones and β -enamino esters.

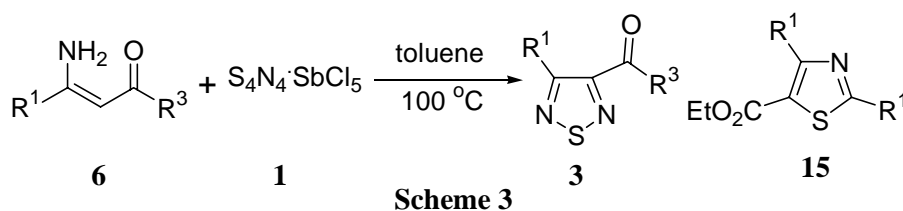
β -enamino ketones and β -enamino esters were prepared by treatment of 1,3-dicarbonyl compounds with ammonium acetate according to the procedure in the literature.⁴ When unsymmetrical 1,3-diketones such as 4-chlorobenzoyl-4-methoxybenzoylmethane and 1-(4-chlorophenyl)-4,5,5,6,6,6-heptafluorohexane-1,3-dione were subjected to the reported conditions, a mixture of regioisomers (**6e**) and (**6f**) was formed, respectively. The mixture could not be separated by chromatography. The ¹H NMR spectrum of the mixture (**6e**), exhibiting 3.83, 3.86 and 7.89 (d, $J = 8.8$ Hz), 7.91 (d, $J = 8.8$ Hz) ppm, assignable to methyl protons and C-3 protons of 4-chlorophenyl groups, respectively, indicated that **6e** consisted of 3-amino-1-(4-chlorophenyl)-3-(4-methoxyphenyl)-2-propenone and 3-amino-3-(4-chlorophenyl)-1-(4-methoxyphenyl)-2-propenone in the ratio of 1 : 2. The differentiation between two structural isomers was based on the GC-MS data in which the minor isomer exhibited a fragment with m/z 139 (14.6%), which

corresponded to $\text{ClC}_6\text{H}_4\text{CO}^+$, whereas the major isomer did not exhibit not only a fragment with m/z 135 ($\text{CH}_3\text{COC}_6\text{H}_4\text{CO}^+$) but also other fragments that could unambiguously give information about the structure. The MS data suggest that the minor isomer is 3-amino-3-(4-methoxyphenyl)-1-(4-chlorophenyl)-2-propenone. Similarly, **6f** was thought to be a mixture of 1-amino-1-(4-chlorophenyl)-4,4,5,5,6,6,6-heptafluoro-1-hexen-3-one and 3-amino-1-(4-chlorophenyl)-4,4,5,5,6,6,6-heptafluoro-2-hexenone (1 : 2.2) in view of the intensities of the peaks at 5.97, 6.17 and 7.81 (d, $J = 8.5$ Hz), 7.87 (d, $J = 8.5$ Hz) ppm, assignable to vinyl and aromatic (C-2) protons, respectively. The minor isomer of **6f** did not exhibit fragments giving information about the structure, whereas the major isomer exhibited fragments with m/z 180 (100%) and 151 (2.6%), which corresponded to the ions $\text{C}_9\text{H}_7\text{NOCl}^+$ and $\text{C}_8\text{H}_4\text{OCl}^+$, respectively. The MS data suggest that the major isomer is 3-amino-1-(4-chlorophenyl)-4,4,5,5,6,6,6-heptafluoro-2-hexenone. The prepared β -enaminones (**6a-n**) and β -enamino esters (**6o-v**) are all unknown except for 3-amino-1,3-diphenyl-2-propenone (**6a**)⁵ and 3-amino-1-phenyl-2-butenone (**6j**),⁵ which is listed in Table 1.

(B) Reactions of β -enaminones and β -enamino esters with **1**

A solution containing a mixture of β -enaminones (**6**) and an equimolar amount of **1** in toluene was heated at 100 °C. The color of the solution started to turn from red to dark brown in 5 min. The progress of the reaction was monitored by the disappearance of a spot corresponding to **6** on TLC (silica gel, $R_f = 0.42$, EtOAc - *n*-hexane = 1 : 5). Chromatography (silica gel, 70 - 230 mesh, ASTM) of the reaction mixture gave **3** as a major product in addition to sulfur, S_4N_4 , and unknown mixtures. Reaction time, melting points, and yields of **3** are summarized in Table 1.

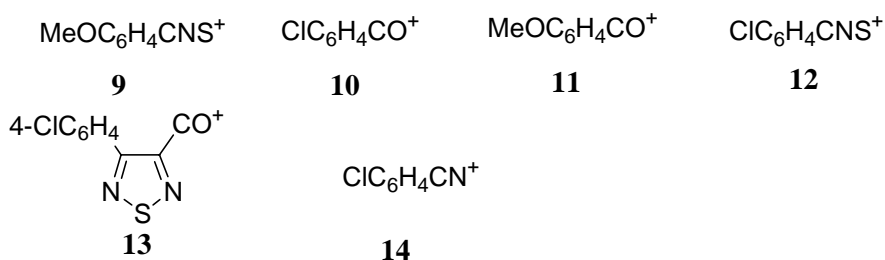
4-Substituted 3-acyl-1,2,5-thiadiazoles were reported to be synthesized for the first time by treatment of 1,3-diketones with S_4N_4 in refluxing toluene.⁶ Employment of either symmetric diaroylmethanes or unsymmetric 1,3-diketones such as aroylacetonates and aroyl-1,1,1-trifluoroacetones caused the formation of one of the two possible structural isomers. Recently, a new method involving 1,3-diketones and trithiazyl trichloride (NSCl)₃ in the presence of molecular sieves in CCl_4 at reflux under nitrogen was found to give the same type of products as for the reactions with S_4N_4 .⁷ However, the above two reactions limit their general use. One other method which is more useful for the preparation of 3-acyl- and 3-aryol-1,2,5-thiadiazoles involves the reaction of 3-alkyl- and 3-aryolisoxazoles with **1** in toluene between 90 °C and reflux temperature.³ Since the acyl and aroyl groups originate from the substituent of isoxazoles at C-5, only a single structural isomer is possible. Moreover, reaction times are much shorter than those previously reported,^{6,7} and yields are comparable to or better than those obtained from the other methods. The advantage of the present reactions involving β -enaminones is to produce only a single structural isomer, i.e., 4-substituted

Table 1. Reaction times, melting points, and yields of **3**

Entry	Compound	R ¹	R ³	Time(h)	Product	Yield ^a (%)	mp ^b (°C)	Product	Yield ^a (%)	mp ^b (°C)
1	6a	Ph	Ph	1	3a	50, (56) ³ , (40) ⁶ , (41) ⁷	80-81 (lit., ⁶ 81-82)			
2	6b	3-BrC ₆ H ₄	Ph	1	3b	50	106-107			
3	6c	4-ClC ₆ H ₄	4-ClC ₆ H ₄	1	3c	57, (61) ³	130-132 (lit., ³ 130-131)			
4	6d	4-MeOC ₆ H ₄	4-MeOC ₆ H ₄	1	3d	40, (18) ³	113-115			
5	6e^c	4-ClC ₆ H ₄	4-MeOC ₆ H ₄	1	3e	29	102-104			
		4-MeOC ₆ H ₄	4-ClC ₆ H ₄		3f	25	84-87			
6	6f^c	4-ClC ₆ H ₄	CF ₃ CF ₂ CF ₂	3	3g	12	liquid			
		CF ₃ CF ₂ CF ₂	4-ClC ₆ H ₄		3h	21	liquid			
7	6g	CF ₃	Ph	12	3i	51, (50) ⁶	liquid (lit., ⁶ liquid)			
8	6h	CF ₃	2-Naphthyl	8	3j	35	76-77			
9	6i	CF ₃	2-Thienyl	4	3k	28, (40) ⁶	52-54 (lit., ⁶ 51-53)			
10	6j	Me	Ph	1	3l	26, (43) ³ , (12) ⁶ , (25) ⁷	71-72 (lit., ⁶ 72-73)			
11	6k	Et	Ph	1	3m	29	44-45			
12	6l	<i>n</i> -Pr	Ph	1	3n	29	liquid			
13	6m	<i>n</i> -Pentyl	Ph	0.5	3o	<i>d</i>				
14	6n	PhCH ₂ CH ₂	Ph	1	3p	40	liquid			
15	6o	3-O ₂ NC ₆ H ₄	OEt	2	3q	50	110-111			
16	6p	Ph	OEt	1	3r	54 (23) ⁷	liquid	15a	15	104-105
17	6q	2-FC ₆ H ₄	OEt	1	3s	41	liquid	15b	23	118-119
18	6r	4-ClC ₆ H ₄	OEt	1	3t	51	80-81	15c	6	154-155
19	6s	4-MeC ₆ H ₄	OEt	1	3u	46	liquid	15d	15	89-90
20	6t	4-MeOC ₆ H ₄	OEt	0.5	3v	47	liquid			
21	6u	2-Naphthyl	OEt	1	3w	42	liquid			
22	6v	2-Thienyl	OEt	0.5	3x	47	liquid			

^a Isolated yields. Numbers in parentheses represent reported yields in the literature. ^b Solids (**3**) were recrystallized from *n*-hexane except for **3d**, **3t**, and **15b-c**, which were recrystallized from CH₂Cl₂/*n*-hexane and **3m** and **15d**, which were recrystallized from MeOH/*n*-hexane. ^c The enaminones (**6e**) and (**6f**) were a mixture of structural isomers. ^d The formation of compound (**3o**) was identified only by GC-MS data.

3-aryl-1,2,5-thiadiazoles. Yields of some products, i.e., **3a** (Entry 1), **3c** (Entry 3), and **3i** (Entry 7), are comparable but those of **3k** (Entry 9) and **3l** (Entry 10) are inferior to those in the literature. The reaction with a mixture of 3-amino-3-(4-chlorophenyl)-1-(4-methoxyphenyl)-2-propenone and 3-amino-1-(4-chlorophenyl)-3-(4-methoxyphenyl)-2-propenone under the same conditions gave a mixture of the corresponding 1,2,5-thiadiazoles (**3e**) and (**3f**) (Entry 5), which were separable by chromatography. It was hard to distinguish between the structure of **3e** and that of **3f** on the basis of ¹H NMR and IR spectroscopic data. However, it was possible to assign the structure (**3e**) in view of the major fragmentation pathways in the MS spectra of 1,2,5-thiadiazoles which give RCN⁺ and RCNS⁺, where R comprises substituents at C-3 and C-4. Subsequent loss of sulfur from the latter ion leads to the formation of a fragment RCN⁺.⁸ In fact, GC-MS data for **3f** exhibited fragments with m/z 165 (38.1%) and 139 (85.5%), which corresponded to the ions (**9**) and (**10**), respectively. The fragment with m/z 135, corresponding to ion (**11**), was not observed. This MS data suggests that compound (**3f**) has a 4-chlorobenzoyl group at C-3.



Meanwhile, the MS data of **3e** exhibited fragments with m/z 169 (3.0%) and 135 (100%), corresponding to the ions (**12**) and (**11**), respectively, which suggest that compound (**3e**) has a 4-methoxybenzoyl group at C-3. Similarly the MS fragmentation of compound (**3g**) exhibited fragments with m/z 223 (100%) and 137 (9.87%), corresponding to the ions (**13**), and (**14**), respectively, whereas those of **3h** exhibited a fragment with m/z 139 (100%), indicative of the ion (**10**). Based on these fragments with characteristic mass numbers, it was possible to distinguish between the structures (**3g**) and (**3h**). It seems that the reaction conditions leading to 3-aryl-1,2,5-thiadiazoles are incompatible with those for the preparation of 3-acyl-1,2,5-thiadiazoles in view of the complex mixture resulting from the reaction with 4-amino-3-penten-2-one (R¹ = R³ = Me). However, when R³ = CF₃CF₂CF₂, 2,2,3,3,4,4,4-heptafluorobutanoyl-1,2,5-thiadiazole (**3g**) was isolated, albeit in low yield (Entry 6). When R¹ becomes a longer alkyl chain such as the *n*-pentyl group (Entry 13), the reaction proceeded quickly but was complicated. GC-MS data for the reaction mixture exhibited a fragment corresponding to the molecular ion of compound (**3o**) (R¹ = *n*-pentyl, R³ = Ph). However, the product (**3o**) could not be successfully isolated. Table 1 shows that treatment of 3-aminocinnamic ester (R¹ = Ph, R³ = EtO) and its analogs (R¹ = aryl, R³ = EtO) produced 3-

aryl-4-ethoxycarbonyl-1,2,5-thiadiazoles (**3q-x**) in comparable yield to that of **3a** and ethyl 2,4-diarylthiazoles (**15**) as minor products. Compounds (**15**) which have never been reported are formed depending on the structures of enamino esters. Although a few 3-alkoxycarbonyl-4-aryl-1,2,5-thiadiazoles such as **3r**⁷ have been prepared, yields were low and they were obtained as a byproduct. Consequently, this is the first general method for the preparation of 4-aryl-1,2,5-thiadiazoles possessing an alkoxycarbonyl group at C-3. In contrast, the reaction with ethyl 3-aminocrotonate ($R^1 = \text{Me}$, $R^3 = \text{EtO}$) produced only tarry material, and the reaction with ethyl 3-amino-1,1,1-trifluorocrotonate ($R^1 = \text{CF}_3$, $R^3 = \text{EtO}$), in spite of 3 days of prolonged reaction time, did not proceed with recovery of the ester in 82% yield. These results indicate that the reaction of **1** with β -enamino esters occurs to give the desired compound in cases where aryl groups, without regard to the electronic effects of the substituent, are bonded to the β -carbon of the β -enamino esters. The structures of **15** were unambiguously determined based on X-Ray crystallographic analysis of **15b**. Figure 1 shows the molecular structure of **15b**.

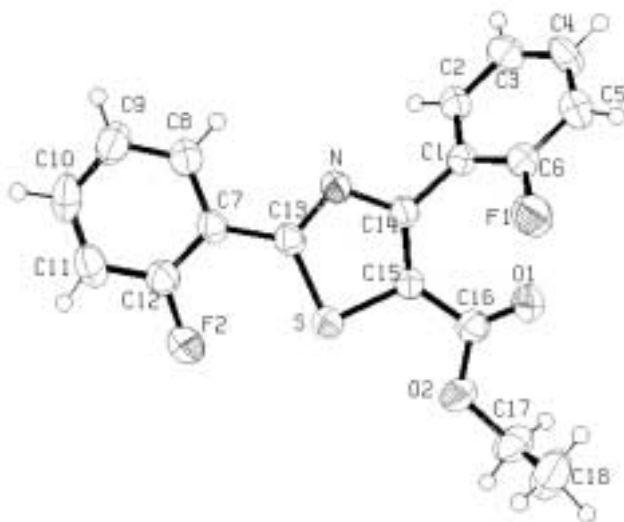


Figure 1 ORTEP view of compound (**15b**)

In summary, the reaction of $\text{S}_4\text{N}_4\text{SbCl}_5$ complex with primary β -enaminones, which are characterized by an aryl or perfluoroalkyl group bonded at the carbonyl carbon, and alkyl or aryl group at β -position gave 3-acyl (or aroyl)-4-aryl-1,2,5-thiadiazoles. A similar reaction with primary β -enamino esters having an aryl group at β -position produced 3-aryl-4-ethoxycarbonyl-1,2,5-thiadiazoles which have been seldom reported in the literature in addition to ethyl 2,4-diarylthiazoles. The formation of 1,2,5-thiadiazoles can be understood as the result of the same mechanism proposed previously for the formation of 1,2,5-thiadiazoles from 3,5-disubstituted isoxazoles and $\text{S}_4\text{N}_4\text{SbCl}_5$ complex.

EXPERIMENTAL

The ^1H NMR spectra were recorded at 300 MHz in CDCl_3 solution containing tetramethylsilane as an internal standard. IR spectra were recorded in KBr or as thin films on KBr plates. GC-MS spectra were obtained by electron impact at 70 eV. Elemental analyses were determined by the Korea Basic Science Institute. Column chromatography was performed using silica gel (70-230 mesh, Merck). Melting points are uncorrected. Tetrasulfur tetranitride⁷ and tetrasulfur tetranitride antimony pentachloride complex ($\text{S}_4\text{N}_4\cdot\text{SbCl}_5$) (**1**)¹ were prepared according to procedures in the literature. Primary β -enaminones (**6a-p**) were prepared by treatment of 1,3-diketones with ammonium acetate according to the literature.⁴ 3-Amino-1,3-diphenyl-2-propenone (**6a**), mp 81-82 °C (*n*-hexane) (lit.,⁵ 82°C), 3-amino-1-phenyl-2-butenone (**6j**), mp 140-142 °C(CH_2Cl_2 - *n*-hexane) (lit.,⁵ 142°C).

3-Amino-3-(4-bromophenyl)-1-phenyl-2-propenone (6b): mp 56-57°C (*n*-hexane); ^1H NMR (CDCl_3 , δ , ppm) 5.61 (1H, s, NH), 6.08 (1H, s, =C₂H), 7.31 (1H, t, J = 4.7 Hz, ArH), 7.42 - 7.46 (3H, m, ArH), 7.53 (1H, d, J = 4.4 Hz, ArH), 7.61 (1H, d, J = 4.1 Hz, ArH), 7.75 (1H, s, ArH), 7.92 (2H, d, J = 4.8 Hz, ArH), 10.25 (1H, s, NH); IR (KBr) (ν , cm^{-1}) 3360, 3136, 1593, 1523, 1472, 1379, 1318, 1084, 1008, 832, 761; MS (EI) m/z 303 (M^+ , 47%), 302 (100), 224 (8), 146 (79), 117 (11.7), 103 (24). *Anal.* Calcd for $\text{C}_{15}\text{H}_{12}\text{NOBr}$: C, 59.62; H, 4.00; N, 4.64. Found: C, 59.72; H, 4.16; N, 4.62.

3-Amino-1,3-di(4-chlorophenyl)-2-propenone (6c): mp 100-102°C (CCl_4); ^1H NMR (CDCl_3 , δ , ppm) 6.01 (1H, s, =C₂H), 7.19 - 7.66 (6H, m, ArH), 7.84 (2H, d, J = 8.1 Hz, ArH); IR (KBr) (ν , cm^{-1}) 3360, 3136, 1590, 1523, 1472, 1379, 1318, 1084, 1008, 832; MS (EI) m/z 291 (M^+ , 42%), 290 (100), 180 (34), 139 (12), 111 (14). *Anal.* Calcd for $\text{C}_{15}\text{H}_{11}\text{NOCl}_2$: C, 61.67; H, 3.79; N, 4.79. Found: C, 61.58; H, 3.55; N, 4.62.

3-Amino-1,3-di(4-methoxyphenyl)-2-propenone (6d): mp 61-63°C (*n*-hexane); ^1H NMR (CDCl_3 , δ , ppm) 3.82 (6H, s, OCH_3), 6.07 (1H, s, =C₂H), 6.73 - 7.17 (4H, m, ArH), 7.55 (2H, d, J = 9.0 Hz, ArH), 7.92 (2H, d, J = 9.1, ArH); IR (KBr) (ν , cm^{-1}) 3360, 1593, 1555, 1484, 1452, 1321, 1248, 1171, 1024, 777; MS (EI) m/z 283 (M^+ , 40), 282 (100), 267 (3), 239 (4), 176 (13). *Anal.* Calcd for $\text{C}_{17}\text{H}_{17}\text{NO}_3$: C, 72.07; H, 6.05; N, 4.94. Found: C, 71.98; H, 6.25; N, 4.72.

3-Amino-4,4,4-trifluoro-1-phenyl-2-butenone (6g): mp 80-81°C (*n*-hexane); ^1H NMR (CDCl_3 , δ , ppm) 6.24 (1H, s, =C₂H), 7.25 - 7.52 (3H, m, ArH), 7.93 (2H, d, J = 6.9 Hz, ArH); IR (KBr) (ν , cm^{-1}) 3376, 3264, 1635, 1545, 1499, 1328, 1289, 1234, 1129, 1014, 769, 697; MS (EI) m/z 215 (M^+ , 40%), 214 (100), 194 (21), 138 (40), 105 (35), 77 (41). *Anal.* Calcd for $\text{C}_{10}\text{H}_8\text{NOF}_3$: C, 55.82; H, 3.75; N, 6.51. Found: C, 57.72; H, 3.96; N, 6.62.

3-Amino-4,4,4-trifluoro-1-(2-naphthyl)-2-butenone (6h): mp 103-105°C (*n*-hexane); ^1H NMR (CDCl_3 , δ , ppm) 6.33 (1H, s, =C₂H), 7.50 - 7.57 (2H, m, ArH), 7.84 - 8.00 (4H, m, ArH), 8.42 (1H, s, ArH); IR (KBr) (ν , cm^{-1}) 3408, 3296, 1635, 1545, 1456, 1350, 1308, 1193, 1126, 1190; MS (EI) m/z 265 (M^+ ,

28%), 264 (100), 244 (10), 167 (10), 155 (10), 138 (11), 127 (13). *Anal.* Calcd for C₁₄H₁₀NOF₃: C, 63.40; H, 3.80; N, 5.2. Found: C, 61.74; H, 3.91; N, 5.32.

3-Amino-3-trifluoromethyl-1-(2-thienyl)-2-propenone (6i): mp 106-10 °C (CH₂Cl₂); ¹H NMR (DMSO-d₆, δ, ppm) 6.18 (1H, s, =C₂H), 7.15 - 7.19 (1H, m, ArH), 7.94 (2H, s, ArH); IR (KBr) (ν, cm⁻¹) 3360, 3264, 3188, 1628, 1542, 1408, 1315, 1248, 1136, 1046, 985, 854, 781; MS (EI) m/z 221 (M⁺, 35%), 220 (100), 200 (11), 188 (82), 168 (10), 138 (12), 111 (41), 96 (7). *Anal.* Calcd for C₈H₆NOF₃S : C, 43.44; H, 2.73; N, 6.33; S, 14.50. Found: C, 43.36; H, 2.71; N, 6.29; S, 14.34.

3-Amino-1-phenyl-2-pentenone (6k): mp 100-101°C (CH₂Cl₂ - *n*-hexane); ¹H NMR (CDCl₃, δ, ppm) 1.24 (3H, t, *J* = 7.5 Hz, CH₃), 2.29 (2H, q, *J* = 7.6 Hz, CH₂), 5.29 (1H, s, NH), 5.76 (1H, s, =C₂H), 7.37 - 7.46 (3H, m, ArH), 7.88 (2H, d, *J* = 7.4 Hz, ArH), 10.29 (1H, s, NH); IR (KBr) (ν, cm⁻¹) 3312, 3132, 1596, 1545, 1523, 1404, 1324, 1273, 1216, 1065, 748; MS (EI) m/z 175 (M⁺, 65%), 174 (100), 159 (15), 146 (8), 105 (23), 98 (51), 77 (26). *Anal.* Calcd for C₁₁H₁₃NO: C, 75.40; H, 7.48; N, 7.99. Found: C, 75.33; H, 7.51; N, 7.90.

3-Amino-1-phenyl-2-hexenone (6l): mp 90-91°C (CH₂Cl₂ - *n*-hexane); ¹H NMR (CDCl₃, δ, ppm) 0.99 (3H, t, *J* = 7.3 Hz, CH₃), 1.60 - 1.75 (2H, m, CH₂), 2.23 (2H, t, *J* = 7.3 Hz, CH₂), 5.29 (1H, s, NH), 5.74 (1H, s, =C₂H), 7.37 - 7.46 (3H, m, ArH), 7.88 (2H, d, *J* = 7.3 Hz, ArH), 10.28 (1H, s, NH); IR (KBr) (ν, cm⁻¹) 3280, 3137, 1590, 1555, 1520, 1404, 1315, 1280, 1216, 1065, 753; MS (EI) m/z 189 (M⁺, 99%), 174 (80), 160 (37), 146 (13), 112 (50), 105 (100), 77 (49). *Anal.* Calcd for C₁₂H₁₅O: C, 76.16; H, 7.99; N, 7.40. Found: C, 76.09; H, 7.89; N, 7.51.

3-Amino-1-phenyl-2-octenone (6m): liquid; ¹H NMR (CDCl₃, δ, ppm) 0.92 (3H, t, *J* = 6.3 Hz, CH₃), 1.34-1.36 (4H, m, CH₂CH₂), 1.64 - 1.66 (2H, m, CH₂), 2.26 (2H, t, *J* = 7.4 Hz, CH₂), 5.47 (1H, s, NH), 5.76 (1H, s, =C₂H), 7.28 - 7.48 (3H, m, ArH), 7.88 (2H, d, *J* = 7.9 Hz, ArH), 10.35 (1H, s, NH); IR (KBr) (ν, cm⁻¹) 3344, 3184, 3056, 2944, 1606, 1558, 1523, 1315, 1270, 1177, 742, 691; MS (EI) m/z 217 (M⁺, 17.8%), 174 (54), 161 (36), 133 (19), 105 (100), 77 (29). *Anal.* Calcd for C₁₄H₁₉NO: C, 77.38; H, 8.81; N, 6.45. Found: C, 77.26; H, 8.91; N, 6.51.

3-Amino-1,5-diphenyl-2-pentenone (6n): liquid; ¹H NMR (CDCl₃, δ, ppm) 2.58 (2H, t, *J* = 8.3 Hz, CH₃), 2.97 (2H, t, *J* = 8.3 Hz, CH₂), 5.31 (1H, s, NH), 5.78 (1H, s, =C₂H), 7.23 - 7.36 (5H, m, ArH), 7.40 - 7.49 (3H, m, ArH), 7.89 (2H, d, *J* = 7.4 Hz, ArH), 10.23 (1H, s, NH); IR (neat) (ν, cm⁻¹) 3328, 3168, 1596, 1564, 1520, 1280, 1072, 742; MS (EI) m/z 51 (M⁺, 100%), 234 (24), 174 (29), 159 (63), 146 (48), 105 (90), 91 (84), 77 (50). *Anal.* Calcd for C₁₇H₁₇NO: C, 81.24; H, 6.82; N, 5.57. Found: C, 81.12; H, 6.94; N, 5.44.

Ethyl 3-Amino-3-(3-nitrophenyl)-2-propenoate (6o): mp 68-69°C (CH₂Cl₂ - *n*-hexane); ¹H NMR

(CDCl₃, δ , ppm) 1.33 (3H, t, $J = 7.1$ Hz, CH₃), 4.22 (2H, q, $J = 7.1$ Hz, CH₂), 5.04 (1H, s, =C₂H), 7.63 (1H, t, $J = 8.0$ Hz, ArH), 7.99 (1H, d, $J = 7.0$ Hz, ArH), 8.31 (1H, d, $J = 8.0$ Hz, ArH), 8.44 (1H, s, ArH); IR (KBr) (ν , cm⁻¹) 3455, 3312, 1664, 1619, 1538, 1507, 1353, 1308, 1180, 1081, 1033, 774; MS (EI) m/z 236 (M⁺, 33%), 208 (8), 191 (79), 164 (100), 146 (35), 117 (16), 89 (9). *Anal.* Calcd for C₁₁H₁₂N₂O₄: C, 55.93; H, 5.12; N, 11.86. Found: C, 55.90; H, 5.09; N, 11.79.

Ethyl 3-Amino-3-phenyl-2-propenoate (6p): liquid; ¹H NMR (CDCl₃, δ , ppm) 1.30 (3H, t, $J = 7.1$ Hz, CH₃), 4.19 (2H, q, $J = 7.1$ Hz, CH₂), 4.97 (1H, s, =C₂H), 7.40 - 7.44 (3H, m, ArH), 7.54 (2H, d, $J = 7.0$ Hz, ArH); IR (neat) (ν , cm⁻¹) 3440, 3328, 1664, 1619, 1555, 1494, 1315, 1177, 1094, 1027, 774; MS (EI) m/z 191 (M⁺, 46.7%), 146 (92), 119 (100), 104 (59), 91 (23), 77 (17). *Anal.* Calcd for C₁₁H₁₃NO₂: C, 69.09; H, 6.85; N, 7.32. Found: C, 68.89; H, 6.62; N, 7.54.

Ethyl 3-Amino-3-(2-fluorophenyl)-2-propenoate (6q): liquid; ¹H NMR (CDCl₃, δ , ppm) 1.26 (3H, t, $J = 7.1$ Hz, CH₃), 4.13 (2H, q, $J = 7.1$ Hz, CH₂), 4.84 (1H, s, =C₂H), 7.06 - 7.17 (2H, m, ArH), 7.34-7.36 (1H, m, ArH), 7.43 (1H, t, $J = 7.5$ Hz, ArH); IR (neat) (ν , cm⁻¹) 3440, 3328, 2976, 1660, 1612, 1555, 1484, 1315, 1254, 1180, 1091, 1024, 758; MS (EI) m/z 209 (M⁺, 37%), 164 (79), 137 (100), 122 (52), 109 (15), 102 (11). *Anal.* Calcd for C₁₁H₁₂NO₂F: C, 63.15; H, 5.78; N, 6.69. Found: C, 62.98; H, 5.81; N, 6.54.

Ethyl 3-Amino-3-(4-chlorophenyl)-2-propenoate (6r): liquid; ¹H NMR (CDCl₃, δ , ppm) 1.29 (3H, t, $J = 7.1$ Hz, CH₃), 4.18 (2H, q, $J = 7.1$ Hz, CH₂), 4.93 (1H, s, =C₂H), 7.39 (2H, d, $J = 8.3$ Hz, ArH), 7.48 (2H, d, $J = 8.3$ Hz, ArH); IR (neat) (ν , cm⁻¹) 3440, 3328, 2976, 1664, 1619, 1552, 1494, 1312, 1184, 1094, 1011, 838, 790; MS (EI) m/z 225 (M⁺, 52%), 180 (82), 153 (100), 138 (52), 117 (21), 102 (7), 89 (15). *Anal.* Calcd for C₁₁H₁₂NO₂Cl: C, 58.54; H, 5.36; N, 6.21. Found: C, 58.65; H, 5.33; N, 6.11.

Ethyl 3-Amino-3-(4-tolyl)-2-propenoate (6s): liquid; ¹H NMR (CDCl₃, δ , ppm) 1.26 (3H, t, $J = 7.1$ Hz, CH₃), 2.34 (3H, s, CH₃), 4.13 (2H, q, $J = 7.1$ Hz, CH₂), 4.93 (1H, s, =C₂H), 7.16 (2H, d, $J = 8.1$ Hz, ArH), 7.40 (2H, d, $J = 8.1$ Hz, ArH); IR (neat) (ν , cm⁻¹) 3456, 3344, 2992, 1654, 1609, 1555, 1315, 1174, 1091, 1030, 823, 787; MS (EI) m/z 205 (M⁺, 58.4%), 160 (75), 133 (100), 118 (59), 105 (6), 91 (14). *Anal.* Calcd for C₁₂H₁₅NO₂: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.33; H, 7.40; N, 6.88.

Ethyl 3-Amino-3-(4-methoxyphenyl)-2-propenoate (6t): liquid; ¹H NMR (CDCl₃, δ , ppm) 1.26 (3H, t, $J = 7.0$ Hz, CH₃), 3.75 (3H, s, OCH₃), 4.12 (2H, q, $J = 7.1$ Hz, CH₂), 4.91 (1H, s, =C₂H), 6.85 (2H, d, $J = 7.2$ Hz, ArH), 7.44 (2H, d, $J = 7.3$ Hz, ArH); IR (neat) (ν , cm⁻¹) 3455, 3328, 2960, 1660, 1606, 1555, 1315, 1254, 1174, 1091, 1030, 841, 790; MS (EI) m/z 221 (M⁺, 67%), 176 (65), 149 (100), 134 (59), 104 (10), 91 (5), 77 (4). *Anal.* Calcd for C₁₂H₁₅NO₃: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.23; H, 6.72; N, 6.44.

Ethyl 3-Amino-3-(2-naphthyl)-2-propenoate (6u): liquid; ¹H NMR (CDCl₃, δ , ppm) 1.26 (3H, t, $J = 7.1$ Hz, CH₃), 4.15 (2H, q, $J = 7.1$ Hz, CH₂), 5.06 (1H, s, =C₂H), 7.40 - 7.51 (3H, m, ArH), 7.52 - 7.77 (3H, m, ArH), 7.93 (1H, s, ArH); IR (neat) (ν , cm⁻¹) 3472, 3328, 2960, 3040, 2976, 1657, 1609, 1548, 1363, 1302, 1171, 1088, 1030, 793; MS (EI) m/z 241 (M⁺, 59%), 212 (5), 196 (52), 169 (100), 154 (54), 139 (12), 127

(19), 115 (7), 83 (11). *Anal.* Calcd for C₁₅H₁₅NO₃: C, 74.67; H, 6.28; N, 5.81. Found: C, 74.88; H, 6.31; N, 5.88.

Ethyl 3-Amino-3-(2-thienyl)-2-propenoate (6v): liquid; ¹H NMR (CDCl₃, δ, ppm) 1.26 (3H, t, *J* = 7.2 Hz, CH₃), 4.15 (2H, q, *J* = 7.1 Hz, CH₂), 5.07 (1H, s, =C₂H), 6.54 (2H, s, NH), 7.01 - 7.03 (1H, m, ArH), 7.32 (1H, d, *J* = 4.0 Hz, ArH), 7.66 (1H, d, *J* = 3.9 Hz, ArH); IR (neat) (ν, cm⁻¹) 3456, 3328, 3104, 2990, 1737, 1657, 1616, 1510, 1289, 1255, 1168, 1043, 851; MS (EI) *m/z* 197 (M⁺, 58%), 152 (70), 125 (100), 109 (30), 97 (17), 68 (7). *Anal.* Calcd for C₉H₁₁NO₂S: C, 54.80; H, 5.62; N, 7.10; S, 16.26. Found: C, 54.99; H, 5.53; N, 7.21; S, 16.46.

A Mixture of 3-Amino-3-(4-chlorophenyl)-1-(4-methoxyphenyl)-2-propenone and 3-Amino-1-(4-chlorophenyl)-3-(4-methoxyphenyl)-2-propenone (6e): For the major, ¹H NMR (CDCl₃, δ, ppm) 3.86 (3H, s, OCH₃), 5.78 (1H, s, NH), 6.05 (1H, s, =C₂H), 6.92 (2H, d, *J* = 8.7 Hz, ArH), 7.38 (2H, d, *J* = 8.5 Hz, ArH), 7.59 (2H, d, *J* = 8.4 Hz, ArH), 7.91 (2H, d, *J* = 8.8 Hz, ArH), 10.29 (1H, s, NH); IR (neat) (ν, cm⁻¹) 3360, 3134, 3050, 1594, 1523, 1479, 1452, 1320, 1024, 832; MS (EI) *m/z* 287 (M⁺, 41%), 286 (100), 242 (3), 171 (13), 137 (7), 112 (5), 77 (13).

A Mixture of 1-Amino-1-(4-chlorophenyl)-4,4,5,5,6,6,6-heptafluorohexen-3-one and 3-Amino-1-(4-chlorophenyl)-4,4,5,5,6,6,6-heptafluoro-2-hexenone (6f): mp 94-125°C; For the major, ¹H NMR (CDCl₃, δ, ppm) 6.17 (1H, s, =C₂H), 7.34 (2H, d, *J* = 8.5 Hz, ArH), 7.87 (2H, d, *J* = 8.5 Hz, ArH); IR (neat) (ν, cm⁻¹) 3312, 3184, 1695, 1612, 1532, 1478, 1338, 1228, 1111, 1008, 934, 780; MS (EI) *m/z* 349 (M⁺, 17%), 330 (3), 180 (100), 137 (22), 117 (15), 90 (9).

General Procedure for the Synthesis of 4-Substituted 3-Aroyl- and 3-Ethoxycarbonyl-1,2,5-thiadiazoles (3)

To a solution of **6** (0.61-1.51 mmol) in toluene (30 mL) was added **1** (0.64-1.51 mmol), which was heated at 100°C for an appropriate time. The color of the solution started to turn from red to dark brown in 5 min. The reaction mixture was cooled to rt when a spot corresponding to **6** (*R_f* = 0.25, *n*-hexane - EtOAc = 10 : 1) had disappeared on TLC. After removal of the solvent *in vacuo*, the residue was chromatographed on a silica gel column (2 x 10 cm). Elution with *n*-hexane gave a trace amount of sulfur and tetrasulfur tetranitride. Elution with a mixture of *n*-hexane and benzene (1 : 1) gave 4-substituted 3-aroylethyl-1,2,5-thiadiazoles (**3a**), (**3d**) and (**3l-n**). Compounds (**3b-c**), (**3e-i**), and (**3o**) were eluted with a mixture of EtOAc and *n*-hexane (1 : 20). Compound (**3k**) was eluted with carbon tetrachloride. Chromatography of the reaction mixture obtained from S₄N₄ and β-enamino esters with a mixture of *n*-hexane and benzene (1 : 1) as an eluent gave ethyl 2,4-diarylthiazoles (**15**) containing a small amount of **3**, which was separated by repeated chromatography using the same solvent mixture (2 : 1), yielding **3s**. Compounds (**3q-r**) and (**3u**) were eluted with a mixture of EtOAc and *n*-hexane (1 : 20). Compounds (**3t**) and (**3v-x**) were eluted with a mixture of *n*-hexane and CH₂Cl₂ (2 : 1).

3-Benzoyl-4-(3-bromophenyl)-1,2,5-thiadiazole (3b): ^1H NMR (CDCl_3 , δ , ppm) 7.06 (1H, d, $J = 7.9$ Hz, ArH), 7.31 - 7.47 (3H, m, ArH), 7.64 - 7.70 (3H, m, ArH), 7.97 (1H, d, $J = 7.4$ Hz, ArH), 8.27 (1H, s, ArH); IR (KBr) (ν , cm^{-1}) 1625, 1590, 1555, 1324, 1270, 1068, 902, 780, 680; MS (EI) m/z 346 ($\text{M}^+ + 2$, 30%), 344 (M^+ , 30.5), 317 (9), 315 (9), 265(12), 105 (100), 77 (50). *Anal.* Calcd for $\text{C}_{15}\text{H}_9\text{N}_2\text{OS}$: C, 52.19; H, 2.63; N, 8.11; S, 9.29. Found: C, 51.14; H, 2.40; N, 8.21; S, 9.48.

3-(4-Chlorophenyl)-4-(4-methoxybenzoyl)-1,2,5-thiadiazole (3e): ^1H NMR (CDCl_3 , δ , ppm) 3.91 (3H, s, OCH_3), 6.99 (2H, d, $J = 8.7$ Hz, ArH), 7.56 (2H, d, $J = 8.4$ Hz, ArH), 7.68 (2H, d, $J = 8.4$ Hz, ArH), 7.97 (2H, d, $J = 8.8$ Hz, ArH); IR (KBr) (ν , cm^{-1}) 1654, 1590, 1561, 1497, 1417, 1257, 1155, 1088, 1011, 896, 822; MS (EI) m/z 330 (M^+ , 26.3%), 313 (3), 169 (3), 147 (5), 135 (100), 107 (9), 92 (14), 77 (18). *Anal.* Calcd for $\text{C}_{16}\text{H}_{11}\text{N}_2\text{O}_2\text{ClS}$: C, 58.09; H, 3.35; N, 8.47; S, 9.69. Found: C, 58.25; H, 3.22; N, 8.25; S, 9.49.

4-(4-Chlorobenzoyl)-3-(4-methoxyphenyl)-1,2,5-thiadiazole (3f): ^1H NMR (CDCl_3 , δ , ppm) 3.84 (3H, s, OCH_3), 6.94 (2H, d, $J = 8.8$ Hz, ArH), 7.49 (2H, d, $J = 8.5$ Hz, ArH), 7.67 (2H, d, $J = 8.7$ Hz, ArH), 7.94 (2H, d, $J = 8.5$ Hz, ArH); IR (KBr) (ν , cm^{-1}) 1654, 1596, 1577, 1440, 1372, 1251, 1177, 1084, 896, 827, 771; MS (EI) m/z 330 (M^+ , 100%), 315 (4), 165 (38), 139 (86), 111(39). *Anal.* Calcd for $\text{C}_{16}\text{H}_{11}\text{N}_2\text{O}_2\text{ClS}$: C, 58.09; H, 3.35; N, 8.47; S, 9.69. Found: C, 58.21; H, 3.20; N, 8.22; S, 9.80.

3-(4-Chlorophenyl)-4-(2,2,3,3,4,4,4-heptafluorobutanoyl)-1,2,5-thiadiazole (3g): ^1H NMR (CDCl_3 , δ , ppm) 7.50 (2H, d, $J = 8.6$ Hz, ArH), 7.63 (2H, d, $J = 8.6$ Hz, ArH); IR (KBr) (ν , cm^{-1}) 3056, 1728, 1593, 1436, 1401, 1340, 1228, 1120, 1094, 864, 825; MS (EI) m/z 392 (M^+ , 32%), 223 (100), 196 (4), 169 (10), 137 (10), 86 (41). *Anal.* Calcd for $\text{C}_{12}\text{H}_4\text{N}_2\text{OCIF}_7\text{S}$: C, 36.70; H, 1.03; N, 7.13; S, 8.17. Found: C, 36.54; H, 1.01; N, 7.27; S, 8.34.

3-(4-Chlorobenzoyl)-4-(1,1,2,2,3,3,3-heptafluoropropyl)-1,2,5-thiadiazole (3h): ^1H NMR (CDCl_3 , δ , ppm) 7.52 (2H, d, $J = 8.5$ Hz, ArH), 7.84 (2H, d, $J = 8.5$ Hz, ArH); IR (KBr) (ν , cm^{-1}) 3056, 1680, 1580, 1424, 1340, 1228, 1209, 1120, 1088, 857; MS (EI) m/z 392 (M^+ , 21.2%), 373 (10), 139 (100), 111 (31), 75 (10). *Anal.* Calcd for $\text{C}_{12}\text{H}_4\text{N}_2\text{OCIF}_7\text{S}$: C, 36.70; H, 1.03; N, 7.13; S, 8.17. Found: C, 36.66; H, 0.99; N, 7.25; S, 8.36.

3-Trifluoromethyl-4-(2-naphthoyl)-1,2,5-thiadiazole (3j): ^1H NMR (CDCl_3 , δ , ppm) 7.61 (1H, t, $J = 6.8$ Hz, ArH), 7.70 (1H, t, $J = 6.8$ Hz, ArH), 7.94 - 8.02 (3H, m, ArH), 8.15 (1H, d, $J = 8.6$ Hz, ArH), 8.48 (1H, s, ArH); IR (KBr) (ν , cm^{-1}) 3056, 1670, 1616, 1472, 1353, 1276, 1184, 1152, 1056, 966, 924, 806, 758; MS (EI) m/z 308 (M^+ , 70%), 289 (3), 155 (100), 127 (88). *Anal.* Calcd for $\text{C}_{14}\text{H}_7\text{N}_2\text{OF}_3\text{S}$: C, 54.54; H, 2.29; N, 9.09; S, 10.40. Found: C, 54.29; H, 2.40; N, 9.21; S, 10.18.

3-Benzoyl-4-ethyl-1,2,5-thiadiazole (3m): ^1H NMR (CDCl_3 , δ , ppm) 1.39 (3H, t, $J = 7.5$ Hz, CH_3), 3.21 (2H, q, $J = 7.5$ Hz, CH_2), 7.51 (2H, t, $J = 7.8$ Hz, ArH), 7.63 (1H, t, $J = 7.4$ Hz, ArH), 8.10 (2H, d, $J = 9.6$

Hz, ArH); IR (KBr) (ν , cm^{-1}) 1651, 1590, 1440, 1328, 1289, 1216, 905, 825, 720, 678; MS (EI) m/z 217 (M^+ , 100%), 203 (87), 189 (17), 158 (11), 105 (87), 86 (12), 77 (88). *Anal.* Calcd for $\text{C}_{11}\text{H}_{10}\text{N}_2\text{OS}$: C, 60.53; H, 4.62; N, 12.83; S, 14.69. Found: C, 60.63; H, 4.59; N, 12.78; S, 14.51.

3-Benzoyl-4-(*n*-propyl)-1,2,5-thiadiazole (3n): ^1H NMR (CDCl_3 , δ , ppm) 1.03 (3H, t, $J = 7.3$ Hz, CH_3), 1.86 (2H, q, $J = 6.9$ Hz, CH_2), 3.18 (2H, t, $J = 6.8$ Hz, CH_2), 7.54 (2H, t, $J = 7.4$ Hz, ArH), 7.66 (1H, t, $J = 7.7$ Hz, ArH), 8.11 (2H, d, $J = 7.0$, ArH); IR (neat) (ν , cm^{-1}) 1664, 1600, 1456, 1401, 1280, 1257, 1129, 921, 828; MS (EI) m/z 232 (M^+ , 50%), 203 (100), 139 (10), 105 (42), 77 (47). *Anal.* Calcd for $\text{C}_{12}\text{H}_{12}\text{N}_2\text{OS}$: C, 62.04; H, 5.21; N, 12.06; S, 13.80. Found: C, 62.11; H, 5.31; N, 12.01; S, 13.58.

3-Benzoyl-4-phenethyl-1,2,5-thiadiazole (3p): ^1H NMR (CDCl_3 , δ , ppm) 3.16 (2H, t, $J = 7.5$ Hz, CH_2), 3.54 (2H, t, $J = 7.5$ Hz, CH_2), 7.21 - 7.29 (5H, m, ArH), 7.51 (2H, t, $J = 8.6$ Hz, ArH), 7.65 (1H, d, $J = 7.4$ Hz, ArH), 8.05 (2H, d, $J = 8.2$ Hz, ArH); IR (neat) (ν , cm^{-1}) 1651, 1590, 1443, 1395, 1267, 1116, 905, 688; MS (EI) m/z 294 (M^+ , 56%), 203 (49), 189 (19), 105 (25), 91 (100), 77 (36). *Anal.* Calcd for $\text{C}_{17}\text{H}_{14}\text{N}_2\text{OS}$: C, 69.36; H, 4.79; N, 9.52; S, 10.89. Found: C, 69.44; H, 4.61; N, 9.33; S, 10.69.

Ethyl 4-(3-Nitrophenyl)-1,2,5-thiadiazole-3-carboxylate (3q): ^1H NMR (CDCl_3 , δ , ppm) 1.39 (3H, t, $J = 7.1$ Hz, CH_3), 4.45 (2H, q, $J = 7.1$ Hz, CH_2), 7.68 (1H, t, $J = 7.9$ Hz, ArH), 8.10 (1H, d, $J = 7.8$ Hz, ArH), 8.35 (1H, d, $J = 7.9$ Hz, ArH), 8.63 (1H, s, ArH); IR (KBr) (ν , cm^{-1}) 3072, 2992, 1715, 1523, 1491, 1436, 1408, 1347, 1264, 1168, 1088, 1030, 739; MS (EI) m/z 279 (M^+ , 56%), 262 (22), 251 (25), 234 (100), 218 (11), 204 (20), 180 (40), 149 (29), 134 (12), 102 (11). *Anal.* Calcd for $\text{C}_{11}\text{H}_9\text{N}_3\text{O}_4\text{S}$: C, 47.31; H, 3.25; N, 16.05; S, 11.98. Found: C, 47.27; H, 3.19; N, 14.98; S, 11.69.

Ethyl 4-Phenyl-1,2,5-thiadiazole-3-carboxylate (3r): ^1H NMR (CDCl_3 , δ , ppm) 1.35 (3H, t, $J = 7.1$ Hz, CH_3), 4.41 (2H, q, $J = 7.2$ Hz, CH_2), 7.26-7.50 (3H, m, ArH), 7.69 - 7.72 (2H, m, ArH); IR (neat) (ν , cm^{-1}) 3056, 2976, 1724, 1456, 1401, 1276, 1254, 1136, 1014, 755; MS (EI) m/z 234 (M^+ , 100%), 205 (32), 189 (69), 162 (19), 135 (98), 103 (23), 86 (34), 76 (13). *Anal.* Calcd for $\text{C}_{11}\text{H}_{10}\text{N}_2\text{O}_2\text{S}$: C, 56.39; H, 4.30; N, 11.96; S, 13.69. Found: C, 56.27; H, 4.16; N, 12.08; S, 13.40.

Ethyl 4-(2-Fluorophenyl)-1,2,5-thiadiazole-3-carboxylate (3s): ^1H NMR (CDCl_3 , δ , ppm) 1.31 (3H, t, $J = 7.1$ Hz, CH_3), 4.39 (2H, q, $J = 7.1$ Hz, CH_2), 7.17 (1H, t, $J = 9.1$ Hz, ArH), 7.29 (1H, t, $J = 7.5$ Hz, ArH), 7.47 - 7.49 (1H, m, ArH), 7.60 (1H, t, $J = 7.4$ Hz, ArH); IR (neat) (ν , cm^{-1}) 3056, 2976, 1737, 1662, 1580, 1462, 1420, 1289, 1248, 1142, 1100, 1020, 761; MS (EI) m/z 252 (M^+ , 100%), 224 (25), 207 (89), 180 (22), 153 (90), 121 (34), 86 (37). *Anal.* Calcd for $\text{C}_{11}\text{H}_9\text{N}_2\text{O}_2\text{FS}$: C, 52.37; H, 3.60; N, 11.10; S, 12.71. Found: C, 52.24; H, 3.71; N, 11.08; S, 11.94.

Ethyl 4-(4-Chlorophenyl)-1,2,5-thiadiazole-3-carboxylate (3t): ^1H NMR (CDCl_3 , δ , ppm) 1.34 (3H, t, $J = 7.1$ Hz, CH_3), 4.39 (2H, q, $J = 7.1$ Hz, CH_2), 7.46 (2H, d, $J = 8.4$ Hz, ArH), 7.71 (2H, d, $J = 8.4$ Hz, ArH); IR (neat) (ν , cm^{-1}) 2973, 1715, 1376, 1289, 1151, 1088, 1020, 992, 820; MS (EI) m/z 268 (100%, M^+), 239 (19.0), 223 (47.3), 196 (13.8), 169 (92.9), 137 (30.7), 102 (14.5), 86 (33.3). *Anal.* Calcd for

C₁₁H₉N₂O₂ClS: C, 49.17; H, 3.38; N, 10.42; S, 11.93. Found: C, 49.11; H, 3.41; N, 10.33; S, 12.11.

Ethyl 4-(4-Tolyl)-1,2,5-thiadiazole-3-carboxylate (3u): ¹H NMR (CDCl₃, δ, ppm) 1.35 (3H, t, *J* = 7.1 Hz, CH₃), 2.41 (3H, s, CH₃), 4.42 (2H, q, *J* = 7.2 Hz, CH₂), 7.27 (2H, d, *J* = 7.9 Hz, ArH), 7.60 (2H, d, *J* = 7.9 Hz, ArH); IR (neat) (ν, cm⁻¹) 3050, 2976, 1731, 1456, 1408, 1273, 1251, 1136, 1020, 816; MS (EI) *m/z* 248 (M⁺, 100%), 219 (19), 203 (32), 174 (9), 149 (80), 117 (18), 86 (17). *Anal.* Calcd for C₁₂H₁₂N₂O₂S: C, 58.05; H, 4.87; N, 11.28; S, 12.91. Found: C, 52.20; H, 4.71; N, 11.18; S, 13.17.

Ethyl 4-(4-Methoxyphenyl)-1,2,5-thiadiazole-3-carboxylate (3v): ¹H NMR (CDCl₃, δ, ppm) 1.37 (3H, t, *J* = 7.1 Hz, CH₃), 3.85 (3H, s, OCH₃), 4.42 (2H, q, *J* = 7.2 Hz, CH₂), 6.98 (2H, d, *J* = 8.8 Hz, ArH), 7.69 (2H, d, *J* = 8.8 Hz, ArH); IR (neat) (ν, cm⁻¹) 2976, 2848, 1721, 1609, 1574, 1513, 1459, 1256, 1136, 1020, 812; MS (EI) *m/z* 264 (M⁺, 100%), 235 (6), 219 (13), 165 (60), 150 (10), 133 (19), 86 (9). *Anal.* Calcd for C₁₂H₁₂N₂O₃S: C, 54.53; H, 4.58; N, 10.60; S, 12.13. Found: C, 54.42; H, 4.62; N, 10.44; S, 12.33.

Ethyl 4-(2-Naphthyl)-1,2,5-thiadiazole-3-carboxylate (3w): ¹H NMR (CDCl₃, δ, ppm) 1.33 (3H, t, *J* = 7.1 Hz, CH₃), 4.40 (2H, q, *J* = 7.1, CH₂), 7.47 - 7.54 (2H, m, ArH), 7.76 (1H, d, *J* = 6.8 Hz, ArH), 7.83 - 7.91 (3H, m, ArH), 8.21 (1H, s, ArH); IR (neat) (ν, cm⁻¹) 3056, 2992, 1734, 1408, 1260, 1232, 1145, 1120, 1036, 819; MS (EI) *m/z* 284 (M⁺, 100%), 255 (6), 239 (11), 185 (61), 153 (42), 140 (10), 126 (9), 86 (5). *Anal.* Calcd for C₁₅H₁₂N₂O₂S: C, 63.36; H, 4.25; N, 9.85; S, 11.28. Found: C, 63.24; H, 4.11; N, 9.89; S, 11.44.

Ethyl 4-(2-Thienyl)-1,2,5-thiadiazole-3-carboxylate (3x): ¹H NMR (CDCl₃, δ, ppm) 1.44 (3H, t, *J* = 7.1 Hz, CH₃), 4.51 (2H, q, *J* = 7.1 Hz, CH₂), 7.08 - 7.13 (1H, m, ArH), 7.50 (1H, d, *J* = 4.7 Hz, ArH), 7.98 (1H, d, *J* = 4.5 Hz, ArH); IR (neat) (ν, cm⁻¹) 3104, 2976, 1731, 1536, 1385, 1251, 1129, 1049, 1011, 844, 710; MS (EI) *m/z* 240 (M⁺, 100%), 212 (9), 195 (29), 168 (11), 141 (81), 109 (16), 86 (16). *Anal.* Calcd for C₉H₈N₂O₂S₂: C, 44.98; H, 3.36; N, 11.66; S, 26.69. Found: C, 44.82; H, 3.41; N, 11.76; S, 16.50.

Ethyl 2,4-Diphenylthiazole-5-carboxylate (15a): ¹H NMR (CDCl₃, δ, ppm) 1.33 (3H, t, *J* = 7.4 Hz, CH₃), 4.30 (2H, q, *J* = 7.1 Hz, CH₂), 7.45 - 7.68 (6H, m, ArH), 7.81 - 7.84 (2H, m, ArH), 8.02 - 8.06 (2H, m, ArH); IR (neat) (ν, cm⁻¹) 3056, 2992, 1713, 1513, 1475, 1420, 1318, 1257, 1136, 1081, 755; MS (EI) *m/z* 309 (M⁺, 100%), 280 (48), 264 (32), 237 (38), 178 (2), 134 (41), 89 (50). *Anal.* Calcd for C₁₈H₁₅NO₂S: C, 69.88; H, 4.89; N, 4.53; S, 10.36. Found: C, 69.91; H, 4.87; N, 4.62; S, 10.18.

Ethyl 2,4-Di(2-fluorophenyl)thiazole-5-carboxylate (15b): ¹H NMR (CDCl₃, δ, ppm) 1.26 (3H, t, *J* = 7.1 Hz, CH₃), 4.39 (2H, q, *J* = 7.1 Hz, CH₂), 7.16-7.29 (4H, m, ArH), 7.42 - 7.47 (2H, m, ArH), 7.62 (1H, t, *J* = 4.8 Hz, ArH), 8.38 (1H, t, *J* = 4.8 Hz); IR (neat) (ν, cm⁻¹) 3056, 2960, 1712, 1606, 1574, 1523, 1481, 1404, 1318, 1248, 1091, 809, 755; MS (EI) *m/z* 345 (M⁺, 100%), 316 (18), 300 (49), 273 (33), 151 (47), 139 (6), 123 (8), 107 (53). *Anal.* Calcd for C₁₈H₁₃NO₂F₂S: C, 62.60; H, 3.79; N, 4.06; S, 9.28. Found: C, 62.54; H, 3.71; N, 4.11; S, 9.36.

Ethyl 2,4-Di(4-chlorophenyl)thiazole-5-carboxylate (15c): ¹H NMR (CDCl₃, δ, ppm) 1.29 (3H, t, *J* =

7.1 Hz, CH₃), 4.32 (2H, q, $J = 7.1$ Hz, CH₂), 7.40 - 7.45 (4H, m, ArH), 7.78 (2H, d, $J = 8.5$ Hz, ArH), 7.96 (2H, d, $J = 7.8$ Hz, ArH); IR (KBr) (ν , cm⁻¹) 2976, 1712, 1468, 1430, 1338, 1315, 1264, 1136, 1081, 1011, 819, 778; MS (EI) m/z 378 (M⁺, 23%), 377 (100), 348 (26), 332 (26), 305 (34), 167 (40), 139 (15), 123 (35). *Anal.* Calcd for C₁₈H₁₃NO₂Cl₂S: C, 57.15; H, 3.46; N, 3.70; S, 8.48. Found: C, 57.25; H, 3.41; N, 3.76; S, 8.59.

Ethyl 2,4-Di(4-tolyl)thiazole-5-carboxylate (15d): ¹H NMR (CDCl₃, δ , ppm) 1.31 (3H, t, $J = 7.1$ Hz, CH₃), 2.39 (6H, s, CH₃), 4.29 (2H, q, $J = 7.1$ Hz, CH₂), 7.23 - 7.28 (4H, m, ArH), 7.73 (2H, d, $J = 8.1$ Hz, ArH), 7.92 (2H, d, $J = 8.1$ Hz, ArH); IR (neat) (ν , cm⁻¹); 2976, 1718, 1523, 1481, 1430, 1318, 1248, 1225, 1139, 1078, 812; MS (EI) m/z 337 (M⁺, 100%), 308 (36), 292 (20), 265 (38), 147 (38), 135 (6), 103 (17), 77 (6). *Anal.* Calcd for C₂₀H₁₉NO₂S: C, 71.19; H, 5.68; N, 4.15; S, 9.50. Found: C, 71.23; H, 5.71; N, 4.19; S, 9.62.

X-Ray Structure Determination of Compound (15b). – Crystal data: C₁₈H₁₃NO₂F₂S, $M = 345.35$, triclinic, space group P $\bar{1}$, $a = 7.222(1)$, $b = 8.145(2)$, $c = 15.208(2)$ Å, $\alpha = 88.00(1)^\circ$, $\beta = 81.29(1)^\circ$, $\gamma = 64.65(1)^\circ$, $V = 798.7(2)$ Å³, $Z = 2$, $D_x = 1.436$ mg m⁻³, $\mu(\text{Mo-K}\alpha) = 0.71070$ Å, Data were measured on an Enraf-Nomius CAD-4 diffractometer with graphite-monochromate Mo-K α radiation using $\omega/2$ scan for 1479 reflection with having $I > 2\sigma(I)$. Crystals were grown from *n*-hexane-CH₂Cl₂. Positional parameters and their estimated standard deviations, and bond distances and angles, have been deposited at the Cambridge Crystallographic Data centre.

ACKNOWLEDGEMENT

The authors are grateful for the financial support by the Korea Research Foundation made in the program year 1998.

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