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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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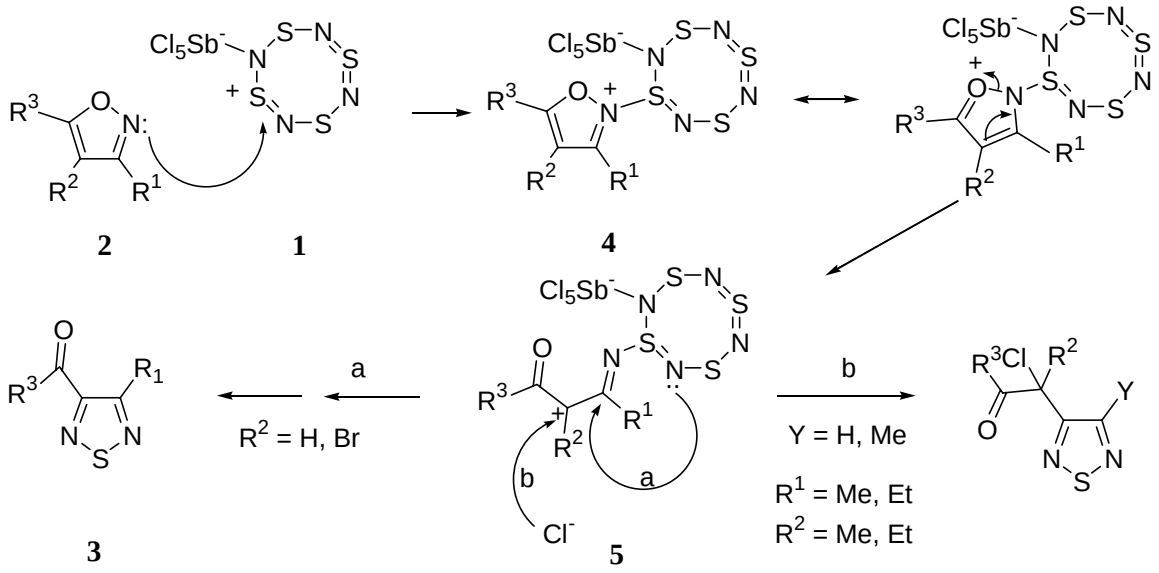
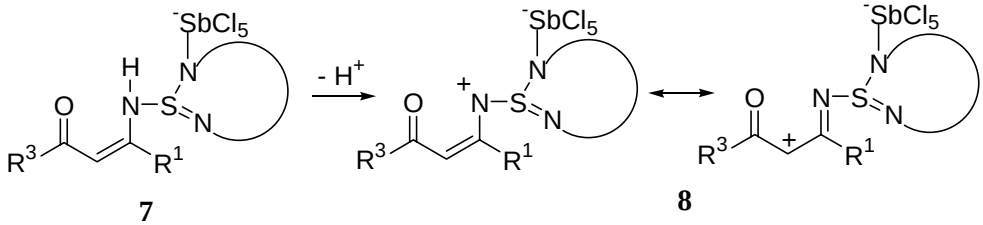
Abstract - The reaction of tetrasulfur tetranitride antimony pentachloride complex ($S_4N_4 \cdot SbCl_5$) with 3-amino-3-alkyl-1-aryl-2-propenones and 3-amino-1,3-diaryl-2-propenones in toluene at 100 °C produced 4-substitued 3-aroyl-1,2,5-thiadiazoles (**3a**-**p**) in 12 to 57% yields. Similarly treatment 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-thiadizole-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-thiadizoles from 5-substitued 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 ketones[2] and complete regioselective formation of 4-substituted 3-acyl- and 3-aroyl-1,2,5-thiadiazoles (**3a**) from 5-substituted 3-alkyl- and 3-arylisoxazoles (**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 R^2 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



Scheme 1

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.



Scheme 2

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 ^{1}H 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

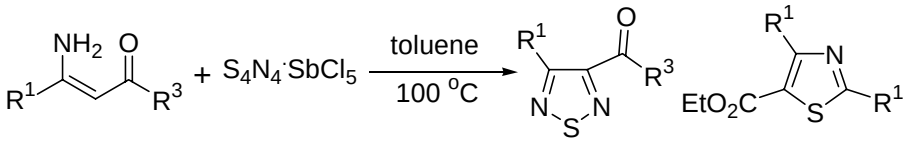
corresponded to $ClC_6H_4CO^+$, whereas the major isomer did not exhibit not only a fragment with m/z 135 ($CH_3COC_6H_4CO^+$) but also other fragments that could unambiguously give information about the structure. The MS data suggest that the minor isomer is 3-amino-3-(4-methoxyphenyl)-1-(4-chlorophenyl)-2-propenone. 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 $C_9H_7NOCl^+$ and $C_8H_4OCl,^+$ 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-aroyl-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 aroylacetones 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-aroyl-1,2,5-thiadiazoles involves the reaction of 3-alkyl- and 3-aroylisoxazoles 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**



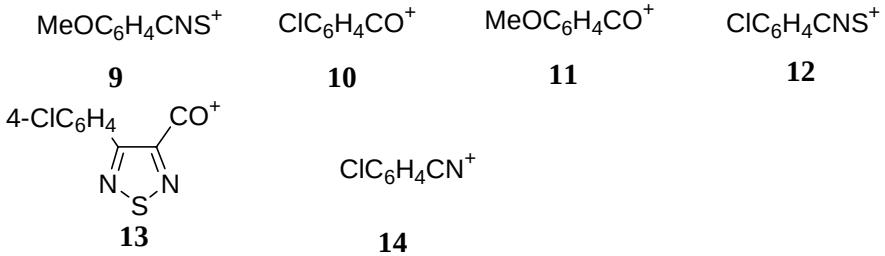
6 **1** **3** **15**

Scheme 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_6H_4	Ph	1	**3b**	50	106-107			
3	**6c**	4-ClC_6H_4	4-ClC_6H_4	1	**3c**	57, (61)[3]	130-132 (lit.,[3] 130-131)			
4	**6d**	4-$MeOC_6H_4$	4-$MeOC_6H_4$	1	**3d**	40, (18)[3]	113-115			
5	**6e**[c]	4-ClC_6H_4	4-$MeOC_6H_4$	1	**3e**	29	102-104			
		4-$MeOC_6H_4$	4-ClC_6H_4		**3f**	25	84-87			
6	**6f**[c]	4-ClC_6H_4	$CF_3CF_2CF_2$	3	**3g**	12	liquid			
		$CF_3CF_2CF_2$	4-ClC_6H_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**	*n*-Pr	Ph	1	**3n**	29	liquid			
13	**6m**	*n*-Pentyl	Ph	0.5	**3o**	*d*				
14	**6n**	$PhCH_2CH_2$	Ph	1	**3p**	40	liquid			
15	**6o**	3-$O_2NC_6H_4$	OEt	2	**3q**	50	110-111			
16	**6p**	Ph	OEt	1	**3r**	54 (23)[7]	liquid	**15a**	15	104-105
17	**6q**	2-FC_6H_4	OEt	1	**3s**	41	liquid	**15b**	23	118-119
18	**6r**	4-ClC_6H_4	OEt	1	**3t**	51	80-81	**15c**	6	154-155
19	**6s**	4-MeC_6H_4	OEt	1	**3u**	46	liquid	**15d**	15	89-90
20	**6t**	4-$MeOC_6H_4$	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 CH_2Cl_2/*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-aroyl-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 ^{1}H 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 $RCN^{+\cdot}$.[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-aroyl-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 ($R^1 = R^3 = Me$). However, when $R^3 = CF_3CF_2CF_2$, 2,2,3,3,4,4,4-heptafluorobutanoyl-1,2,5-thiadiazole (**3g**) was isolated, albeit in low yield (Entry 6). When R^1 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**) (R^1 = *n*-pentyl, R^3 = Ph). However, the product (**3o**) could not be successfully isolated. Table 1 shows that treatment of 3-aminocinnamic ester (R^1 = Ph, R^3 = EtO) and its analogs (R^1 = aryl, R^3 = 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 = Me, R^3 = EtO) produced only tarry material, and the reaction with ethyl 3-amino-1,1,1-trifluorocrotonate (R^1 = CF_3, R^3 = 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**.

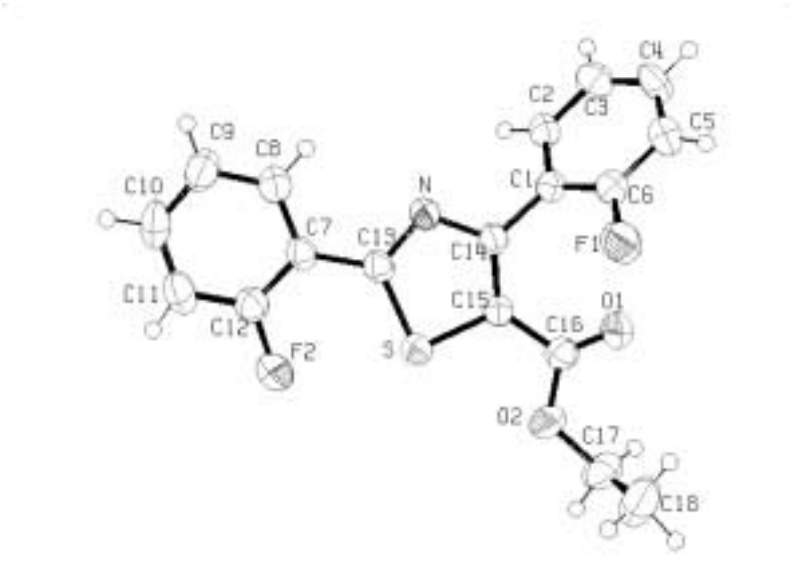


Figure 1 ORTEP view of compound (**15b**)

In summary, the reaction of $S_4N_4{\cdot}SbCl_5$ 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 $S_4N_4{\cdot}SbCl_5$ complex.

EXPERIMENTAL

The ^{1}H 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 tetranitride[7] and tetrasulfur tetranitride antimony pentachloride complex ($S_4N_4{\cdot}SbCl_5$) (**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); ^{1}H NMR ($CDCl_3$, δ, ppm) 5.61 (1H, s, NH), 6.08 (1H, s, $=C_2H$), 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) (υ, 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 $C_{15}H_{12}NOBr$: 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); ^{1}H NMR ($CDCl_3$, δ, ppm) 6.01 (1H, s, $=C_2H$), 7.19 - 7,66 (6H, m, ArH), 7.84 (2H, d, *J* = 8.1 Hz, ArH); IR (KBr) (υ, 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 $C_{15}H_{11}NOCl_2$: 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); ^{1}H NMR ($CDCl_3$, δ, ppm) 3.82 (6H, s, OCH_3), 6.07 (1H, s, $=C_2H$), 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) (υ, 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 $C_{17}H_{17}NO_3$: 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); ^{1}H NMR ($CDCl_3$, δ, ppm) 6.24 (1H, s, $=C_2H$), 7.25 - 7.52 (3H, m, ArH), 7.93 (2H, d, *J* = 6.9 Hz, ArH); IR (KBr) (υ, 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 $C_{10}H_8NOF_3$: 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); ^{1}H NMR ($CDCl_3$, δ, ppm) 6.33 (1H, s, $=C_2H$), 7.50 - 7.57 (2H, m, ArH), 7.84 - 8.00 (4H, m, ArH), 8.42 (1H, s, ArH); IR (KBr) (υ, 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 $C_{14}H_{10}NOF_3$: 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 (CH_2Cl_2); ^1H NMR (DMSO-d_6, δ, ppm) 6.18 (1H, s, $=C_2H$), 7.15 - 7.19 (1H, m, ArH), 7.94 (2H, s, ArH); IR (KBr) (υ, 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 $C_8H_6NOF_3S$: 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 (CH_2Cl_2 - *n*-hexane); ^1H NMR ($CDCl_3$, δ, ppm) 1.24 (3H, t, *J* = 7.5 Hz, CH_3), 2.29 (2H, q, *J* = 7.6 Hz, CH_2), 5.29 (1H, s, NH), 5.76 (1H, s, $=C_2H$), 7.37 - 7.46 (3H, m, ArH), 7.88 (2H, d, *J* = 7.4 Hz, ArH), 10.29 (1H, s, NH); IR (KBr) (υ, 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 $C_{11}H_{13}NO$: 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 (CH_2Cl_2 - *n*-hexane); ^1H NMR ($CDCl_3$, δ, ppm) 0.99 (3H, t, *J* = 7.3 Hz, CH_3), 1.60 - 1.75 (2H, m, CH_2), 2.23 (2H, t, *J* = 7.3 Hz, CH_2), 5.29 (1H, s, NH), 5.74 (1H, s, $=C_2H$), 7.37 - 7.46 (3H, m, ArH), 7.88 (2H, d, *J* = 7.3 Hz, ArH), 10.28 (1H, s, NH); IR (KBr) (υ, 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 $C_{12}H_{15}O$: 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 ($CDCl_3$, δ, ppm) 0.92 (3H, t, *J* = 6.3 Hz, CH_3), 1.34-1.36 (4H, m, CH_2CH_2), 1.64 - 1.66 (2H, m, CH_2), 2.26 (2H, t, *J* = 7.4 Hz, CH_2), 5.47 (1H, s, NH), 5.76 (1H, s, $=C_2H$), 7.28 - 7.48 (3H, m, ArH), 7.88 (2H, d, *J* = 7.9 Hz, ArH), 10.35 (1H, s, NH); IR (KBr) (υ, 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 $C_{14}H_{19}NO$: 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 ($CDCl_3$, δ, ppm) 2.58 (2H, t, *J* = 8.3 Hz, CH_3), 2.97 (2H, t, *J* = 8.3 Hz, CH_2), 5.31 (1H, s, NH), 5.78 (1H, s, $=C_2H$), 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) (υ, 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 $C_{17}H_{17}NO$: C, 81.24; H, 6.82; N, 5.57. Fouund: C, 81.12; H, 6.94; N, 5.44.

Ethyl 3-Amino-3-(3-nitrophenyl)-2-propenoate (6o): mp 68-69°C (CH_2Cl_2 - *n*-hexane); ^1H NMR

($CDCl_3$, δ, ppm) 1.33 (3H, t, *J* = 7.1 Hz, CH_3), 4.22 (2H, q, *J* = 7.1 Hz, CH_2), 5.04 (1H, s, =C_2H), 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) (υ, 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 $C_{11}H_{12}N_2O_4$: 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; ^{1}H NMR ($CDCl_3$, δ, ppm) 1.30 (3H, t, *J* = 7.1 Hz, CH_3), 4.19 (2H, q, *J* = 7.1 Hz, CH_2), 4.97 (1H, s, =C_2H), 7.40 - 7.44 (3H, m, ArH), 7.54 (2H, d, *J* = 7.0 Hz, ArH); IR (neat) (υ, 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 $C_{11}H_{13}NO_2$: 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; ^{1}H NMR ($CDCl_3$, δ, ppm) 1.26 (3H, t, *J* = 7.1 Hz, CH_3), 4.13 (2H, q, *J* = 7.1 Hz, CH_2), 4.84 (1H, s, =C_2H), 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) (υ, 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 $C_{11}H_{12}NO_2F$: 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; ^{1}H NMR ($CDCl_3$, δ, ppm) 1.29 (3H, t, *J* = 7.1 Hz, CH_3), 4.18 (2H, q, *J* = 7.1 Hz, CH_2), 4.93 (1H, s, =C_2H), 7.39 (2H, d, *J* = 8.3 Hz, ArH), 7.48 (2H, d, *J* = 8.3 Hz, ArH); IR (neat) (υ, 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 $C_{11}H_{12}NO_2Cl$: C, 58.54; H, 5.36; N, 6.21. Found: C, 58.65; H, 5.33; N, 6.11.

Ethyl 3-Amino-3-(4-toly)-2-propenoate (6s): liquid; ^{1}H NMR ($CDCl_3$, δ, ppm) 1.26 (3H, t, *J* = 7.1 Hz, CH_3), 2.34 (3H, s, CH_3), 4.13 (2H, q, *J* = 7.1 Hz, CH_2), 4.93 (1H, s, =C_2H), 7.16 (2H, d, *J* = 8.1 Hz, ArH), 7.40 (2H, d, *J* = 8.1 Hz, ArH); IR (neat) (υ, 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 $C_{12}H_{15}NO_2$: 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; ^{1}H NMR ($CDCl_3$, δ, ppm) 1.26 (3H, t, *J* = 7.0 Hz, CH_3), 3.75 (3H, s, OCH_3), 4.12 (2H, q, *J* = 7.1 Hz, CH_2), 4.91 (1H, s, =C_2H), 6.85 (2H, d, *J* = 7.2 Hz, ArH), 7.44 (2H, d, *J* = 7.3 Hz, ArH); IR (neat) (υ, 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 $C_{12}H_{15}NO_3$: 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; ^{1}H NMR ($CDCl_3$, δ, ppm) 1.26 (3H, t, *J* = 7.1 Hz, CH_3), 4.15 (2H, q, *J* = 7.1 Hz, CH_2), 5.06 (1H, s, =C_2H), 7.40 - 7.51 (3H, m, ArH), 7.52 - 7.77 (3H, m, ArH), 7.93 (1H, s, ArH); IR (neat) (υ, 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 $C_{15}H_{15}NO_3$: 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; ^{1}H NMR ($CDCl_3$, δ, ppm) 1.26 (3H, t, *J* = 7.2 Hz, CH_3), 4.15 (2H, q, *J* = 7.1 Hz, CH_2), 5.07 (1H, s, $=C_2H$), 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) (υ, 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 $C_9H_{11}NO_2S$: 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, ^{1}H NMR ($CDCl_3$, δ, ppm) 3.86 (3H, s, OCH_3), 5.78 (1H, s, NH), 6.05 (1H, s, $=C_2H$), 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) (υ, 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, ^{1}H NMR ($CDCl_3$, δ, ppm) 6.17 (1H, s, $=C_2H$), 7.34 (2H, d, *J* = 8.5 Hz, ArH), 7.87 (2H, d, *J* = 8.5 Hz, ArH) ; IR (neat) (υ, 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 teterasulfur tetranitride. Elution with a mixture of *n*-hexane and benzene (1 : 1) gave 4-substituted 3-aroyl-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 S_4N_4 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 CH_2Cl_2 (2 : 1).

3-Benzoyl-4-(3-bromophenyl)-1,2,5-thiadiazole (3b): ^{1}H 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) (υ, cm^{-1}) 1625, 1590, 1555, 1324, 1270, 1068, 902, 780, 680; MS (EI) m/z 346 (M^++2, 30%), 344 (M^+, 30.5), 317 (9), 315 (9), 265(12), 105 (100), 77 (50). *Anal.* Calcd for $C_{15}H_9N_2OS$: 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): ^{1}H 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) (υ, 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 $C_{16}H_{11}N_2O_2ClS$: 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): ^{1}H 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) (υ, 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 $C_{16}H_{11}N_2O_2ClS$: 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): ^{1}H 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) (υ, 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 $C_{12}H_4N_2OClF_7S$: 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): ^{1}H 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) (υ, 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 $C_{12}H_4N_2OClF_7S$: 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): ^{1}H 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) (υ, 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 $C_{14}H_7N_2OF_3S$: 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): ^{1}H 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) (υ, 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 $C_{11}H_{10}N_2OS$: 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) (υ, 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 $C_{12}H_{12}N_2OS$: 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) (υ, 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 $C_{17}H_{14}N_2OS$: 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) (υ, 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 $C_{11}H_9N_3O_4S$: 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) (υ, 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 $C_{11}H_{10}N_2O_2S$: 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) (υ, 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 $C_{11}H_9N_2O_2FS$: 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) (υ, 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

$C_{11}H_9N_2O_2ClS$: 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): ^{1}H NMR ($CDCl_3$, δ, ppm) 1.35 (3H, t, *J* = 7.1 Hz, CH_3), 2.41 (3H, s, CH_3), 4.42 (2H, q, *J* = 7.2 Hz, CH_2), 7.27 (2H, d, *J* = 7.9 Hz, ArH), 7.60 (2H, d, *J* = 7.9 Hz, ArH); IR (neat) (υ, 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 $C_{12}H_{12}N_2O_2S$: 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): ^{1}H NMR ($CDCl_3$, δ, ppm) 1.37 (3H, t, *J* = 7.1 Hz, CH_3), 3.85 (3H, s, OCH_3), 4.42 (2H, q, *J* = 7.2 Hz, CH_2), 6.98 (2H, d, *J* = 8.8 Hz, ArH), 7.69 (2H, d, *J* = 8.8 Hz, ArH); IR (neat) (υ, 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), 8.6 (9). *Anal.* Calcd for $C_{12}H_{12}N_2O_3S$: 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): ^{1}H NMR ($CDCl_3$, δ, ppm) 1.33 (3H, t, *J* = 7.1 Hz, CH_3), 4.40 (2H, q, *J* = 7.1, CH_2), 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) (υ, 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 $C_{15}H_{12}N_2O_2S$: 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): ^{1}H NMR ($CDCl_3$, δ, ppm) 1.44 (3H, t, *J* = 7.1 Hz, CH_3), 4.51 (2H, q, *J* = 7.1 Hz, CH_2), 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) (υ, 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 $C_9H_8N_2O_2S_2$: 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): ^{1}H NMR ($CDCl_3$, δ, ppm) 1.33 (3H, t, *J* = 7.4 Hz, CH_3), 4.30 (2H, q, *J* = 7.1 Hz, CH_2), 7.45 - 7.68 (6H, m, ArH), 7.81 - 7.84 (2H, m, ArH), 8.02 - 8.06 (2H, m, ArH); IR (neat) (υ, 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 $C_{18}H_{15}NO_2S$: 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): ^{1}H NMR ($CDCl_3$, δ, ppm) 1.26 (3H, t, *J* = 7.1 Hz, CH_3), 4.39 (2H, q, *J* = 7.1 Hz, CH_2), 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) (υ, 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 $C_{18}H_{13}NO_2F_2S$: 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): ^{1}H NMR ($CDCl_3$, δ, ppm) 1.29 (3H, t, *J* =

7.1 Hz, CH_3), 4.32 (2H, q, J = 7.1 Hz, CH_2), 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) (υ, 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 $C_{18}H_{13}NO_2Cl_2S$: 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): ^{1}H NMR ($CDCl_3$, δ, ppm) 1.31 (3H, t, J = 7.1 Hz, CH_3), 2.39 (6H, s, CH_3), 4.29 (2H, q, J = 7.1 Hz, CH_2), 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) (υ, 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 $C_{20}H_{19}NO_2S$: 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: $C_{18}H_{13}NO_2F_2S$, M = 345.35, triclinic, space group $P\bar{1}$, a = 7.222(1), b = 8.145(2), c = 15.208(2) Å, α = 88.00(1)°, β = 81.29(1)°, γ = 64.65(1)°, V = 798.7(2) $Å^3$, Z = 2, Dx = 1.436 mg m^{-3}, μ(Mo-Kα) = 0.71070 Å, Data were measured on an Enraf-Nomius CAD-4 diffractometer with graphite-monochromate Mo-Kα radiation using $\omega/2\theta$ scan for 1479 reflection with having $I > 2\sigma(I)$. Crystals were grown from *n*-hexane-CH_2Cl_2. Positional parameters and their estimated standard deviations, and bond distances and angles, have been deposited at the Cambridge Crystallographic Data centre.

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