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SYNTHESIS AND REACTION OF NOVEL SPIRO PYRAZOL-3-ONES CONTAINING OXIRANE MOIETY

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Abstract – An efficient synthesis and reaction of a series of spiro pyrazol-3-one derivatives containing oxirane moiety are described. The convenient substrates, three types of pyrazole-4,5-diones, were reacted with phenacyl bromides in the presence of triethylamine in ethanol at room temperature to give the corresponding spiro epoxide-pyrazol-3-ones in moderate to good yields. Furthermore, thermal treatment of spiro compounds with pyrrolidine in the presence of water caused ring transformation easily to afford the corresponding pyridazinone derivatives. These methods provide several advantages such as operational simplicity, shorter reaction time, and higher yields. All the synthesized compounds were characterized by spectroscopic analysis.

INTRODUCTION

Epoxide and its derivatives have been recognized as valuable intermediates in organic synthesis because of their ready availability and easy transformation.[1] They are also recognized not only as privileged skeletons with important biological activities,[2] but also important precursors in synthetic chemistry.[3] Concerning spiro compounds, representative natural spiro epoxides are important compounds; examples include lumacinin D and FR901464, which show potent antiangiogenic[4] and anticancer[5] activities (Figure 1). In this context, there have been many attempts to develop alternative methods for the synthesis of epoxide derivatives.[6]

Among nitrogen-containing heterocyclic compounds, the pyrazole unit is also an important pharmacophore, which is found in a large number of biologically active molecules. They are known to exhibit a wide spectrum of biological activities such as hypoglycemic, antihypertensive, anti-oxidant, and antitumor activities.[7] For the reasons given above, a large number of general methods for the preparation of pyrazole derivatives have recently reported.[8]

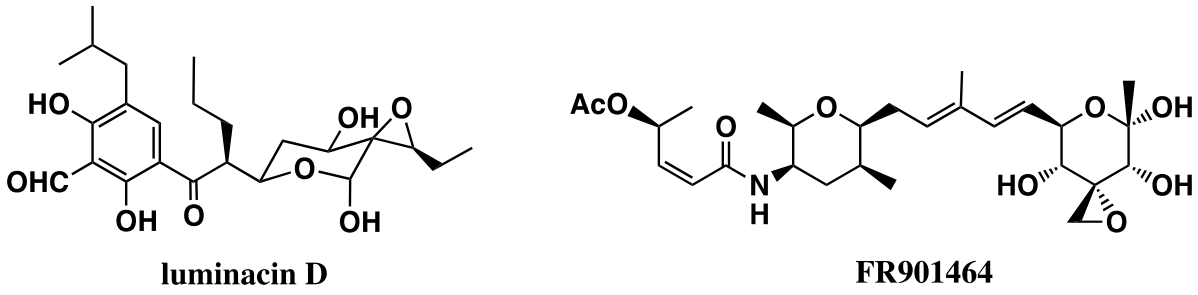


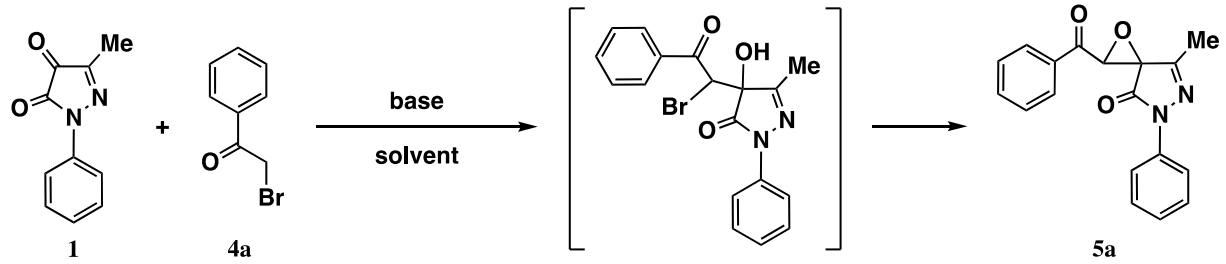
Figure 1. Structures of luminacin D and FR901464

In the course of our interest to develop new methods for the synthesis of spiro pyrazole derivatives, we have shown the synthesis of spiro cyclopropane-pyrazol-3-ones,[9] spiro epoxide-pyrazol-3-ones,[10] spiro iminolactone-pyrazol-3-ones,[11] and spiro cyclobutathiazole-pyrazol-3-ones.[12] On the basis of the above experimental results together with some literature reports, we herein describe an efficient synthesis and reaction of a series of spiro pyrazol-3-one derivatives containing oxirane moiety, which might have useful biological activities, starting from pyrazole-4,5-diones.

RESULTS AND DISCUSSION

For the synthesis of the desired spiro epoxide-pyrazol-3-one **5a**, we examined the optimization process of the Darzens-type reaction with pyrazole-4,5-dione **1** and phenacyl bromide **4a** in the presence of a base as model reactants (Table 1). The substrate **1** could be easily prepared according to the method reported procedure.[13] We carried out several experiments on **5a**, testing different reaction conditions, *e.g.* the ratio of the substrate **1** to **4a** and base, solvents, and reaction temperature. When this transformation was carried out using various solvents such as EtOH, MeCN, and toluene conditions, the desired transformation was accomplished in 81, 19, and 42%, respectively (entries 2, 4, and 5). Therefore, EtOH was found to be a suitable solvent. It was found that the use of 2 equiv. of both **4a** and Et_3N was optimal (entries 1–3). In addition, the results suggested that a lower reaction temperature such as at room temperature could lead to higher yield of **5a**, whereas conducting the reaction under stronger reaction conditions such as in boiling solvent proved decrease to the yield of **5a** (entries 2 and 6). Furthermore, it was observed that this transformation proceeded smoothly in the presence of Et_3N, DBU, or K_2CO_3 as a base (entries 2, 7, and 8). On the basis of these results, the optimized reaction conditions of 2 equiv. of phenacyl bromides and 2 equiv. of Et_3N in EtOH at room temperature were used for further investigation (entry 2).

Table 1. Optimization of the reaction conditions[a]



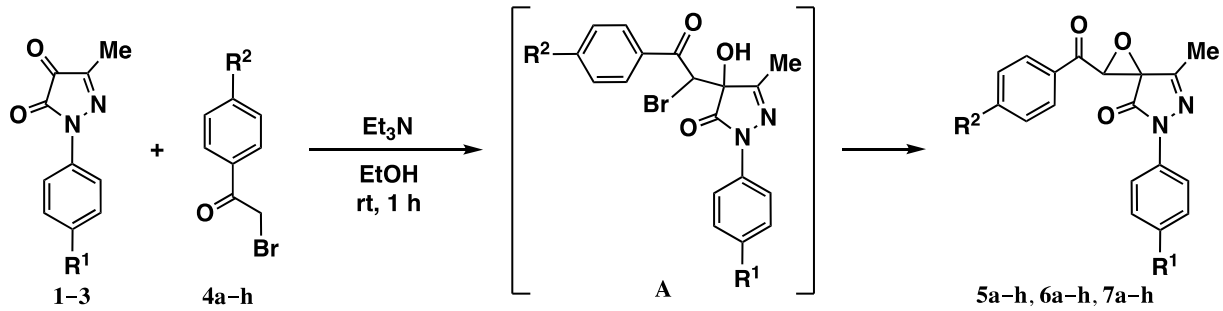
Entry	**4a** (equiv.)	Base (equiv.)	Solvent	Temp.	Time (h)	Yield (%)[b]
1	1.2	Et_3N (1.2)	EtOH	rt	1	60
2	2.0	Et_3N (2.0)	EtOH	rt	1	81
3	3.0	Et_3N (3.0)	EtOH	rt	1	76
4	2.0	Et_3N (2.0)	MeCN	rt	1	19
5	2.0	Et_3N (2.0)	toluene	rt	1	42
6	2.0	Et_3N (2.0)	EtOH	reflux	1	-
7	2.0	DBU (2.0)	EtOH	rt	1	76
8	2.0	K_2CO_3 (2.0)	EtOH	rt	1	73
9	2.0	Na_2CO_3 (2.0)	EtOH	rt	1	58
10	2.0	NaOEt (2.0)	EtOH	rt	1	29

[a]Reactions were carried out with **1** (1 mmol) as the substrate. [b]Isolated yield.

The scope and generality of the present protocol were then examined by employing various substituted pyrazole-4,5-diones **1**–**3** and phenacyl bromides **4a**–**h**. The results are summarized in Table 2. The reaction tolerates both electron donating as well as electron withdrawing substituents (4-Me and 4-Cl) on the pyrazole component without any significant deviation in yields. Additionally, the reactions with **4b**–**d** and **4g**,**h** having electron withdrawing substituents (F, Cl, Br, CF_3, and NO_2) proceeded smoothly to afford the desired products in good yields. In the case of the use of **4f**, the somewhat lower yields of **5f** and **6f** would be caused by an electron-donating effect of the 4-methoxy group (entries 6 and 14). In these reactions, none of the possible key intermediate adducts **A** could be detected.

These products **5**–**7** gave satisfactory elemental analyses and spectroscopic data (IR, ^{1}H NMR, ^{13}C NMR, and MS) consistent with their assigned structures (see experimental section). For example, IR spectrum of **5a** displays bands two bands at 1713 and 1690 cm^{-1} because of two carbonyl groups. The ^{1}H NMR spectrum of **5a** exhibits a three-proton singlet at δ 1.88 assignable to the methyl protons and a one-proton singlet at δ 4.80 assignable to the methine proton. The ^{13}C NMR spectrum of **5a** shows a signal at δ 14.5 because of the methyl carbon, a signal at δ 62.4 because of the spiro carbon, a signal at δ 64.2 because of the methine carbon, and two signals at δ 164.8 and 189.3 because of two carbonyl carbons.

Table 2. Substrate scope of the synthesis for spiro epoxide-pyrazol-3-ones **5**-**7**[a]



Entry	Substrate	R^1	R^2	Product	Yield (%)[b]
1	**1**	H	H	**5a**	81
2	**1**	H	F	**5b**	84
3	**1**	H	Cl	**5c**	89
4	**1**	H	Br	**5d**	91
5	**1**	H	Me	**5e**	77
6	**1**	H	OMe	**5f**	56
7	**1**	H	CF_3	**5g**	79[c]
8	**1**	H	NO_2	**5h**	90
9	**2**	Me	H	**6a**	88
10	**2**	Me	F	**6b**	83
11	**2**	Me	Cl	**6c**	84
12	**2**	Me	Br	**6d**	87
13	**2**	Me	Me	**6e**	70
14	**2**	Me	OMe	**6f**	53
15	**2**	Me	CF_3	**6g**	85[c]
16	**2**	Me	NO_2	**6h**	92
17	**3**	Cl	H	**7a**	89
18	**3**	Cl	F	**7b**	90
19	**3**	Cl	Cl	**7c**	90
20	**3**	Cl	Br	**7d**	89
21	**3**	Cl	Me	**7e**	94
22	**3**	Cl	OMe	**7f**	88
23	**3**	Cl	CF_3	**7g**	81[c]
24	**3**	Cl	NO_2	**7h**	92

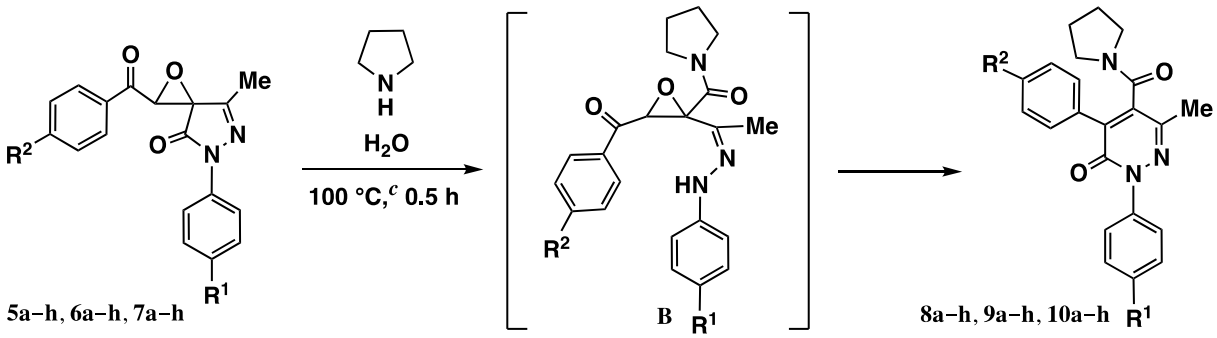
[a]Reactions were carried out with **1**□**3** (1 mmol), **4** (2 mmol), and Et_3N (2 mmol). [b] Isolated yield.
[c]Reaction for 0.5 h.

To expand the scope application of reactions of spiro epoxide-pyrazol-3-ones **5**–**7**, we next examined the ring transformation of **5a** in detail. Fortunately, we found the reaction condition under which pyridazinone derivative **8a** could be isolated. Indeed, thermal treatment of **5a** with pyrrolidine as the reagent and solvent in order to simplify the reaction caused a ring opening/recyclization to give pyridazinone **8a** in 66% yield (Table 3, entry 1). To get the optimized reaction conditions, we carried out several experiments on **8a**, testing different reaction conditions, for example, substrate/reactant molar ratio, solvent, reaction temperature, and reaction time. Best result was obtained when a mixture of **5a** and pyrrolidine in the presence of H_2O as a proton source under solvent-free conditions was stirred at 100 ˚C for 0.5 h. In this case, the reaction in the absence of H_2O resulted in the ring transformation of **5a** with 38% lower yield. The use of other bases such as morpholine and piperidine was not successful and the reaction was not clean. It makes us believe that this reaction could only be promoted by using the pyrrolidine/H_2O condition. With the optimal reaction conditions in hand, we constructed a series of pyridazinone derivatives. Consequently, **5b**–**g**, **6a**–**g**, and **7a**–**g** were reacted with pyrrolidine under the optimized conditions, affording the expected compounds **8b**–**g**, **9a**–**g**, and **10a**–**g** with 24–80% isolated yields (Table 3). In the case of **5b**,**h**, **6b**,**h**, and **7b**,**h** as the substrates, the expected products **8b**,**h**, **9b**,**h**, and **10b**,**h** were not detected at all and the reaction was not clean (entries 2, 8, 10, 16, 18, and 24). It is assumed that an intramolecular nucleophilic addition of secondary amino group of the ring-opening intermediate **B** to carbonyl group may be less likely to occur due to the influence of fluorine, nitro, or trifluoromethyl substituent as electron withdrawing substituent.

By comparison of the IR spectra, ^{1}H NMR spectra, ^{13}C NMR spectra, and MS spectra, and elemental analyses of **8a**–**g**, **9a**–**g**, and **10a**–**g**, it seems that the structural assignments given to these compounds are correct (see experimental section). For example, IR spectrum of **8a** displays bands two bands at 1618 and 1609 cm^{-1} because of two carbonyl groups. The ^{1}H NMR spectrum of **8a** exhibits a three-proton singlet at δ 2.44 assignable to the methyl protons. The ^{13}C NMR spectrum of **8a** shows a signal at δ 19.7 because of the methyl carbon, four signals at δ 24.6, 25.9, 45.7, and 46.3 because of pyrrolidine carbons, and two signals at δ 164.7 and 165.1 because of two carbonyl carbons.

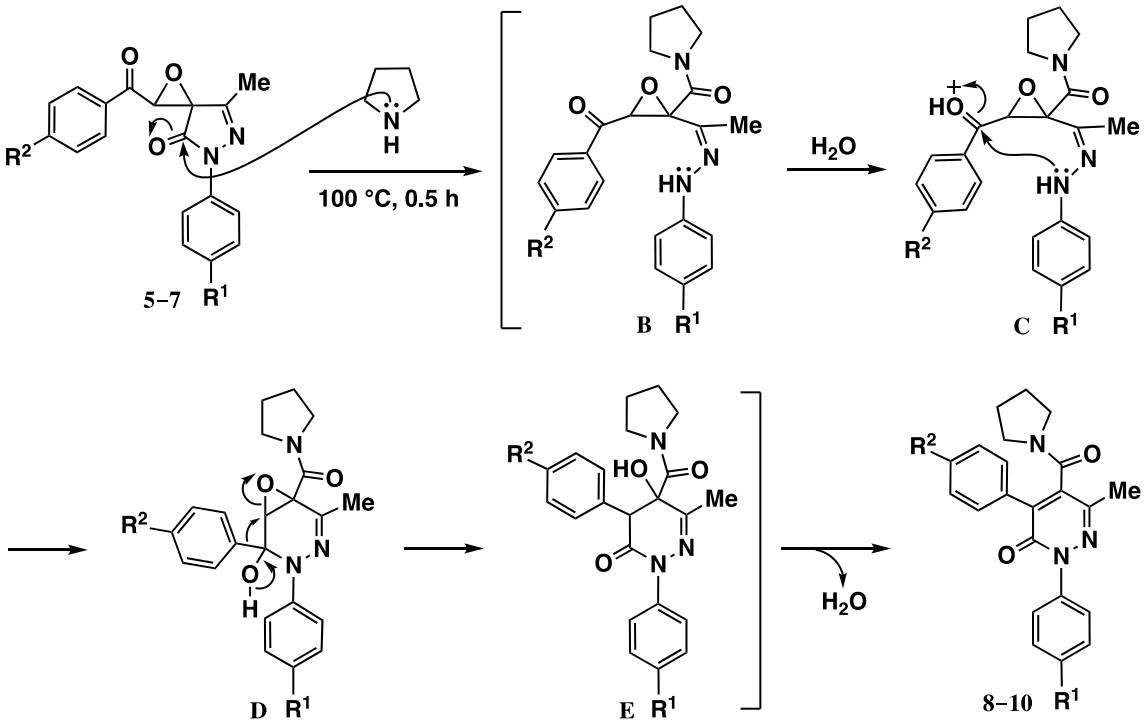
The formation of pyridazinones **8**–**10** could be explained by a plausible reaction mechanism presented in Scheme 1. Spiro epoxide-pyrazol-3-ones **5**–**7** would be reacted with pyrrolidine to give the key intermediate hydrazones **B** *via* a nucleophilic addition of the adjacent pyrrolidine nitrogen atom to the pyrazol-3-one carbonyl carbon. An intramolecular cyclization of **C**, which would be produced by a protonation of **B**, easily occurs, leading to intermediates **D**. An aryl migration[14] of **D** possibly proceeds to afford the intermediates **E**, which undergo elimination of H_2O to yield pyridazinone derivatives **8**–**10**.

Table 3. Ring transformation of spiro epoxide-pyrazol-3-ones **5-7** to pyridazinones **8-10**[a]



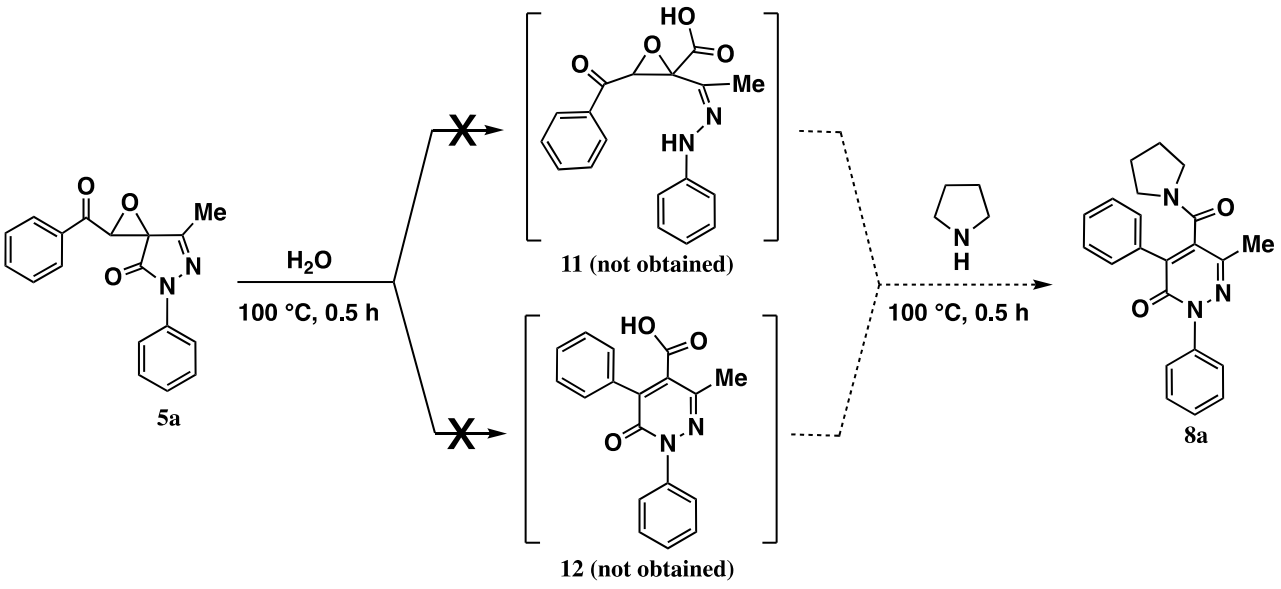
Entry	Substrate	R^1	R^2	Product	Yield (%)[b]
1	**5**	H	H	**8a**	66
2	**5**	H	F	**8b**	-
3	**5**	H	Cl	**8c**	58
4	**5**	H	Br	**8d**	49
5	**5**	H	Me	**8e**	57
6	**5**	H	OMe	**8f**	62
7	**5**	H	CF_3	**8g**	39
8	**5**	H	NO_2	**8h**	-
9	**6**	Me	H	**9a**	53
10	**6**	Me	F	**9b**	-
11	**6**	Me	Cl	**9c**	46
12	**6**	Me	Br	**9d**	36
13	**6**	Me	Me	**9e**	47
14	**6**	Me	OMe	**9f**	46
15	**6**	Me	CF_3	**9g**	24
16	**6**	Me	NO_2	**9h**	-
17	**7**	Cl	H	**10a**	77
18	**7**	Cl	F	**10b**	-
19	**7**	Cl	Cl	**10c**	75
20	**7**	Cl	Br	**10d**	80
21	**7**	Cl	Me	**10e**	60
22	**7**	Cl	OMe	**10f**	77
23	**7**	Cl	CF_3	**10g**	55
24	**7**	Cl	NO_2	**10h**	-

[a]Reactions were carried out with **5-7** (1 mmol), pyrrolidine (3 mL), and H_2O (one drop, 0.07 g).
[b]Isolated yield. [c]Reaction mixture was refluxed in a 100 ˚C oil bath.



Scheme 1

To clarify the details of the reaction mechanism, some control experiments were conducted. It was further found that spiro epoxide-pyrazol-3-one **5a** was not readily reacted with H_2O to furnish the ring-opening carboxylic acid **11** or pyridazine-5-carboxylic acid **12**. In fact, the reaction did not proceed at all and no compound **11** or **12** was obtained (Scheme 2). These findings suggest that **B** and **C** in Scheme 1 would be formed probably as the reaction intermediates.



Scheme 2

In conclusion, we have developed the method for the construction of spiro pyrazol-3-one derivatives containing oxirane moiety from pyrazole-4,5-diones and phenacyl bromides through the Darzens-type reaction. Furthermore, we have demonstrated the ring transformation of spiro compounds with pyrrolidine, giving pyridazinone derivatives. Pyridazinones are one of the most important subtypes of pyridazine heterocyclic family highly attractive in modern drug discovery and agrochemicals, such as Azelastine,[15] Lynparza,[16] Emorfazone,[17] Diclomezine,[18] and Flufenpyr.[19] Pyrazole and pyridazine are important building blocks for the preparation of biologically active compounds with interest in medicinal chemistry. Further synthetic applications for novel spiro pyrazole derivatives containing heterocyclic skeleton are in progress.

EXPERIMENTAL

All melting points are uncorrected. The IR spectra were recorded on a Thermo Fisher Scientific Nicolet iS5 FT-IR spectrometer equipped with an iD7 diamond ATR accessory. The ^{1}H and ^{13}C NMR spectra were measured with a JEOL JNM-ECZ600R/S1 spectrometer at 600.17 and 150.91 MHz, respectively. The ^{1}H and ^{13}C chemical shifts (δ) are reported in parts per million (ppm) relative to TMS as internal standard. Positive FAB MS spectra were obtained on a JEOL JMS-700T spectrometer. Elemental analyses were performed on YANACO MT-6 CHN analyzer. The substrates **1-3** were prepared in this laboratory according to the method reported procedure.[13]

General procedure for the preparation of spiro compounds 5a–h, 6a–h, 7a–h from 1–3, 4a–h, and Et$_3$N. A mixture of **1**–**3** (1.0 mmol), **4a**–**h** (2.0 mmol), and Et_3N (0.202 g, 2.0 mmol) in EtOH (10 mL) was stirred at rt for 1 h. The precipitate was collected by filtration, washed with H_2O, dried, and purified by recrystallization from an appropriate solvent to give **5a**–**h**, **6a**–**h**, and **7a**–**h.**

2-Benzoyl-7-methyl-5-phenyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (**5a**): Reaction was carried out with **1** (0.188 g, 1.0 mmol) and phenacyl bromide (**4a**) (0.398 g, 2.0 mmol). Colorless needles (0.247 g, 81%), mp 156–157 ˚C (acetone/petroleum ether); IR (ATR): ν 1713, 1690 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$): δ 1.88 (s, 3H, 7-Me), 4.80 (s, 1H, 2-H), 7.22–7.25 (m, 1H, Ph-H), 7.42–7.45 (m, 2H, Ph-H), 7.52-7.54 (m, 2H, Ph-H), 7.66–7.69 (m, 1H, Ph-H), 7.92–7.93 (m, 2H, Ph-H), 7.95-7.97 (m, 2H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 14.5 (7-Me), 62.4 (C-3), 64.2 (C-2), 118.5, 125.9, 128.6, 129.1, 129.4, 134.3, 135.2, 137.9 (Ph-C), 154.1 (C-7), 164.8 (C-4), 189.3 (*C*OPh); MS: *m/z* 307 $[M+H]^+$. Anal. Calcd for $C_{18}H_{14}N_2O_3$: C, 70.58; H, 4.61; N, 9.15. Found: C, 70.68; H, 4.61; N, 9.19.

2-(4-Fluorobenzoyl)-7-methyl-5-phenyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (**5b**): Reaction was carried out with **1** (0.188 g, 1.0 mmol) and 4-fluorophenacyl bromide (**4b**) (0.434 g, 2.0 mmol). Colorless needles (0.272 g, 84%), mp 169-170 ˚C (acetone/petroleum ether); IR (ATR): ν 1721, 1690 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$): δ 1.87 (s, 3H, 7-Me), 4.75 (s, 1H, 2-H), 7.19-7.25 (m, 3H, Ph-H), 7.41-7.45 (m, 2H,

Ph-H), 7.90-792 (m, 2H, Ph-H), 8.01-8.04 (m, 2H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 14.5 (7-Me), 62.3 (C-3), 64.1 (C-2), 116.7, 116.9, 118.5, 125.9, 129.1, 130.82, 130.84, 131.5, 131.6, 137.8 (Ph-C), 153.9 (C-7), 164.7 (C-4), 166.1, 167.8 (Ph-C), 187.9 (*C*O-4-F-C_6H_4); MS: *m/z* 325 $[M+H]^+$. Anal. Calcd for $C_{18}H_{13}FN_2O_3$: C, 66.66; H, 4.04; N, 8.64. Found: C, 66.66; H, 4.08; N, 8.65.

2-(4-Chlorobenzoyl)-7-methyl-5-phenyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (**5c**): Reaction was carried out with **1** (0.188 g, 1.0 mmol) and 4-chlorophenacyl bromide (**4c**) (0.467 g, 2.0 mmol). Colorless needles (0.302 g, 89%), mp 172-174 ˚C (acetone/petroleum ether); IR (ATR): ν 1721, 1686 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$): δ 1.86 (s, 3H, 7-Me), 4.75 (s, 1H, 2-H), 7.22-7.25 (m, 1H, Ph-H), 7.41-7.45 (m, 2H, Ph-H), 7.49-7.52 (s, 2H, Ph-H), 7.90-7.94 (m, 4H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 14.5 (7-Me), 62.3 (C-3), 64.0 (C-2), 118.5, 125.9, 129.1, 129.8, 130.1, 132.6, 137.8, 142.0 (Ph-C), 153.8 (C-7), 164.6 (C-4), 188.4 (*C*O-4-Cl-C_6H_4); MS: *m/z* 341 $[M+H]^+$. Anal. Calcd for $C_{18}H_{13}ClN_2O_3$: C, 63.44; H, 3.85; N, 8.22. Found: C, 63.39; H, 3.93; N, 8.24.

2-(4-Bromobenzoyl)-7-methyl-5-phenyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (**5d**): Reaction was carried out with **1** (0.188 g, 1.0 mmol) and 4-bromophenacyl bromide (**4d**) (0.556 g, 2.0 mmol). Colorless needles (0.349 g, 91%), mp 180-181 ˚C (acetone/petroleum ether); IR (ATR): ν 1721, 1685 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$): δ 1.86 (s, 3H, 7-Me), 4.74 (s, 1H, 2-H), 7.22-7.25 (m, 1H, Ph-H), 7.41-7.44 (m, 2H, Ph-H), 7.67-7.70 (m, 2H, Ph-H), 7.83-7.85 (m, 2H, Ph-H), 7.90-7.92 (m, 2H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 14.5 (7-Me), 62.3 (C-3), 64.0 (C-2), 118.5, 125.9, 129.2, 130.1, 130.9, 132.8, 133.0, 137.8 (Ph-C), 153.8 (C-7), 164.6 (C-4), 188.6 (*C*O-4-Br-C_6H_4); MS: *m/z* 385 $[M+H]^+$. Anal. Calcd for $C_{18}H_{13}BrN_2O_3$: C, 56.12; H, 3.40; N, 7.27. Found: C, 56.03; H, 3.51; N, 7.26.

7-Methyl-2-(4-methylbenzoyl)-5-phenyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (**5e**): Reaction was carried out with **1** (0.188 g, 1.0 mmol) and 4-methylphenacyl bromide (**4e**) (0.426 g, 2.0 mmol). Colorless needles (0.248 g, 77%), mp 149-150 ˚C (Et_2O/petroleum ether); IR (ATR): ν 1716, 1687 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$): δ 1.87 (s, 3H, 7-Me), 2.43 (s, 3H, CO-4-*Me*-C_6H_4), 4.77 (s, 1H, 2-H), 7.22-7.24 (m, 1H, Ph-H), 7.30-7.32 (m, 2H, Ph-H), 7.41-7.44 (m, 2H, Ph-H), 7.85-7.87 (m, 2H, Ph-H), 7.91-7.93 (m, 2H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 14.5 (7-Me), 22.0 (CO-4-*Me*-C_6H_4), 62.3 (C-3), 64.3 (C-2), 118.5, 125.8, 128.7, 129.1, 130.1, 131.9, 137.9, 146.6 (Ph-C), 154.3 (C-7), 164.9 (C-4), 188.8 (*C*O-4-Me-C_6H_4); MS: *m/z* 321 $[M+H]^+$. Anal. Calcd for $C_{19}H_{16}N_2O_3$: C, 71.24; H, 5.03; N, 8.74. Found: C, 71.14; H, 5.15; N, 8.65.

2-(4-Methoxybenzoyl)-7-methyl-5-phenyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (**5f**): Reaction was carried out with **1** (0.188 g, 1.0 mmol) and 4-methoxyphenacyl bromide (**4f**) (0.458 g, 2.0 mmol). Colorless needles (0.189 g, 56%), mp 125-126 ˚C (Et_2O/petroleum ether); IR (ATR): ν 1721, 1679 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$): δ 1.87 (s, 3H, 7-Me), 3.88 (s, 3H, CO-4-*Me*O-C_6H_4), 4.74 (s, 1H, 2-H), 6.96-6.99 (m, 2H, Ph-H), 7.21-7.25 (m, 1H, Ph-H), 7.41-7.44 (m, 2H, Ph-H), 7.91-7.93 (m, 2H, Ph-H),

7.94-7.97 (m, 2H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 14.5 (7-Me), 55.8 (CO-4-*Me*O-C_6H_4), 62.3 (C-3), 64.3 (C-2), 114.7, 118.5, 125.8, 127.4, 129.1, 131.2, 137.9 (Ph-C), 154.4 (C-7), 165.0 (Ph-*C*), 165.2 (C-4), 187.5 (*C*O-4-MeO-C_6H_4); MS: *m/z* 337 $[M+H]^+$. Anal. Calcd for $C_{19}H_{16}N_2O_4$: C, 67.85; H, 4.79; N, 8.33. Found: C, 67.66; H, 4.94; N, 8.36.

7-Methyl-5-phenyl-2-[4-(trifluoromethyl)benzoyl]-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (**5g**): Reaction was carried out with **1** (0.188 g, 1.0 mmol) and 4-(trifluoromethyl)phenacyl bromide (**4g**) (0.534 g, 2.0 mmol). Colorless needles (0.297 g, 79%), mp 151-152 ˚C (acetone/petroleum ether); IR (ATR): ν 1721, 1692 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$): δ 1.87 (s, 3H, 7-Me), 4.80 (s, 1H, 2-H), 7.23-7.27 (m, 1H, Ph-H), 7.42-7.45 (m, 2H, Ph-H), 7.79-7.81 (m, 2H, Ph-H), 7.89-7.91 (m, 2H, Ph-H), 8.09-8.11 (m, 2H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 14.5 (7-Me), 62.4 (C-3), 64.0 (C-2), 118.5, 122.3, 124.2, 126.0, 126.49, 126.51, 129.1, 129.2, 136.0, 136.2, 136.4, 136.7 (Ph-C), 136.8 (CO-4-*C*F_3-C_6H_4), 137.8 (Ph-C), 153.4 (C-7), 164.5 (C-4), 188.9 (*C*O-4-CF_3-C_6H_4); MS: *m/z* 375 $[M+H]^+$. Anal. Calcd for $C_{19}H_{13}F_3N_2O_3$: C, 60.97; H, 3.50; N, 7.48. Found: C, 60.90; H, 3.59; N, 7.48.

7-Methyl-2-(4-nitrobenzoyl)-5-phenyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (**5h**): Reaction was carried out with **1** (0.188 g, 1.0 mmol) and 4-nitrophenacyl bromide (**4h**) (0.488 g, 2.0 mmol). Yellow needles (0.316 g, 90%), mp 177-178 ˚C (acetone/petroleum ether); IR (ATR): ν 1717, 1694 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$): δ 1.86 (s, 3H, 7-Me), 4.80 (s, 1H, 2-H), 7.23-7.25 (m, 1H, Ph-H), 7.39-7.44 (m, 2H, Ph-H), 7.86-7.91 (m, 2H, Ph-H), 8.16-8.18 (m, 2H, Ph-H), 8.36-8.39 (m, 2H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 14.5 (7-Me), 62.5 (C-3), 63.9 (C-2), 118.5, 124.6, 126.0, 129.2, 129.9, 137.7, 138.4, 151.4 (Ph-C), 153.3 (C-7), 164.3 (C-4), 188.5 (*C*O-4-NO_2-C_6H_4); MS: *m/z* 352 $[M+H]^+$. Anal. Calcd for $C_{18}H_{13}N_3O_5$: C, 61.54; H, 3.73; N, 11.96. Found: C, 61.54; H, 3.91; N, 12.01.

2-Benzoyl-7-methyl-5-(4-methylphenyl)-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (**6a**): Reaction was carried out with **2** (0.202 g, 1.0 mmol) and phenacyl bromide (**4a**) (0.398 g, 2.0 mmol). Colorless needles (0.283 g, 88%), mp 156-157 ˚C (acetone/petroleum ether); IR (ATR): ν 1725, 1684 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$): δ 1.87 (s, 3H, 7-Me), 2.36 (s, 3H, 4-*Me*-C_6H_4), 4.79 (s, 1H, 2-H), 7.22-7.25 (m, 2H, Ph-H), 7.51-7.54 (m, 2H, Ph-H), 7.66-7.68 (m, 1H, Ph-H), 7.78-7.80 (m, 2H, Ph-H), 7.95-7.97 (m, 2H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 14.5 (7-Me), 21.1 (4-*Me*-C_6H_4), 62.4 (C-3), 64.2 (C-2), 118.6, 128.6, 129.4, 129.6, 134.3, 135.2, 135.5, 135.6 (Ph-C), 154.0 (C-7), 164.6 (C-4), 189.4 (*C*OPh); MS: *m/z* 321 $[M+H]^+$. Anal. Calcd for $C_{19}H_{16}N_2O_3$: C, 71.24; H, 5.03; N, 8.74. Found: C, 71.22; H, 5.10; N, 8.74.

2-(4-Fluorobenzoyl)-7-methyl-5-(4-methylphenyl)-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (**6b**): Reaction was carried out with **2** (0.202 g, 1.0 mmol) and 4-fluorophenacyl bromide (**4b**) (0.434 g, 2.0 mmol). Colorless needles (0.282 g, 83%), mp 172-173 ˚C (acetone/petroleum ether); IR (ATR): ν 1719, 1685 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$): δ 1.86 (s, 3H, 7-Me), 2.36 (s, 3H, 4-*Me*-C_6H_4), 4.74 (s, 1H, 2-H), 7.18-7.25 (m, 4H, Ph-H), 7.76-7.78 (m, 2H, Ph-H), 8.01-8.04 (m, 2H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 14.5

(7-Me), 21.1 (4-*Me*-C_6H_4), 62.3 (C-3), 64.0 (C-2), 116.7, 116.9, 118.6, 129.6, 130.8, 131.5, 131.6, 135.4, 135.7 (Ph-C), 153.8 (C-7), 164.5 (C-4), 166.1, 167.8 (Ph-C), 188.0 (*C*O-4-F-C_6H_4); MS: *m/z* 339 $[M+H]^+$. Anal. Calcd for $C_{19}H_{15}FN_2O_3$: C, 67.45; H, 4.47; N, 8.28. Found: C, 67.41; H, 4.53; N, 8.25.

2-(4-Chlorobenzoyl)-7-methyl-5-(4-methylphenyl)-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (**6c**): Reaction was carried out with **2** (0.202 g, 1.0 mmol) and 4-chlorophenacyl bromide (**4c**) (0.467 g, 2.0 mmol). Colorless needles (0.299 g, 84%), mp 182-183 ˚C (acetone/petroleum ether); IR (ATR): ν 1716, 1690 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 1.85 (s, 3H, 7-Me), 2.36 (s, 3H, 4-*Me*-C_6H_4), 4.74 (s, 1H, 2-H), 7.21-7.23 (m, 2H, Ph-H), 7.49-7.51 (m, 2H, Ph-H), 7.76-7.78 (m, 2H, Ph-H), 7.91-7.93 (m, 2H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 14.5 (7-Me), 21.1 (4-*Me*-C_6H_4), 62.3 (C-3), 64.0 (C-2), 118.6, 129.6, 129.8, 130.0, 132.6, 135.4, 135.7, 142.0 (Ph-C), 153.7 (C-7), 164.4 (C-4), 188.4 (*C*O-4-Cl-C_6H_4); MS: *m/z* 355 $[M+H]^+$. Anal. Calcd for $C_{19}H_{15}ClN_2O_3$: C, 64.32; H, 4.26; N, 7.90. Found: C, 64.43; H, 4.26; N, 7.92.

2-(4-Bromobenzoyl)-7-methyl-5-(4-methylphenyl)-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (**6d**): Reaction was carried out with **2** (0.202 g, 1.0 mmol) and 4-bromophenacyl bromide (**4d**) (0.556 g, 2.0 mmol). Colorless needles (0.348 g, 87%), mp 186-187 ˚C (acetone/petroleum ether); IR (ATR): ν 1716, 1689 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 1.85 (s, 3H, 7-Me), 2.36 (s, 3H, 4-*Me*-C_6H_4), 4.73 (s, 1H, 2-H), 7.21-7.23 (m, 2H, Ph-H), 7.66-7.68 (m, 2H, Ph-H), 7.76-7.78 (m, 2H, Ph-H), 7.83-7.85 (m, 2H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 14.5 (7-Me), 21.1 (4-*Me*-C_6H_4), 62.3 (C-3), 64.0 (C-2), 118.6, 129.7, 130.1, 130.9, 132.8, 133.0, 135.4, 135.7 (Ph-C), 153.7 (C-7), 164.4 (C-4), 188.7 (*C*O-4-Br-C_6H_4); MS: *m/z* 399 $[M+H]^+$. Anal. Calcd for $C_{19}H_{15}BrN_2O_3$: C, 57.16; H, 3.79; N, 7.02. Found: C, 57.07; H, 3.81; N, 7.00.

7-Methyl-2-(4-methylbenzoyl)-5-(4-methylphenyl)-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (**6e**): Reaction was carried out with **2** (0.202 g, 1.0 mmol) and 4-methylphenacyl bromide (**4e**) (0.426 g, 2.0 mmol). Colorless needles (0.233 g, 70%), mp 128-130 ˚C (Et_2O/petroleum ether); IR (ATR): ν 1716, 1688 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 1.86 (s, 3H, 7-Me), 2.36 (s, 3H, 4-*Me*-C_6H_4), 2.43 (s, 3H, CO-4-*Me*-C_6H_4), 4.76 (s, 1H, 2-H), 7.21-7.23 (m, 2H, Ph-H), 7.28-7.32 (m, 2H, Ph-H), 7.77-7.79 (m, 2H, Ph-H), 7.85-7.87 (m, 2H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 14.5 (7-Me), 21.1 (4-*Me*-C_6H_4), 22.0 (CO-4-*Me*-C_6H_4), 62.3 (C-3), 64.2 (C-2), 118.6, 128.7, 129.6, 130.1, 131.9, 135.5, 135.6, 146.6 (Ph-C), 154.1 (C-7), 164.7 (C-4), 188.9 (*C*O-4-Me-C_6H_4); MS: *m/z* 335 $[M+H]^+$. Anal. Calcd for $C_{20}H_{18}N_2O_3$: C, 71.84; H, 5.43; N, 8.38. Found: C, 71.75; H, 5.49; N, 8.39.

2-(4-Methoxybenzoyl)-7-methyl-5-(4-methylphenyl)-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (**6f**): Reaction was carried out with **2** (0.202 g, 1.0 mmol) and 4-methoxyphenacyl bromide (**4f**) (0.458 g, 2.0 mmol). Colorless needles (0.189 g, 54%), mp 120-121 ˚C (Et_2O/petroleum ether); IR (ATR): ν 1719, 1690 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 1.86 (s, 3H, 7-Me), 2.36 (s, 3H, 4-*Me*-C_6H_4), 3.88 (s, 3H, CO-4-*Me*O-C_6H_4), 4.73 (s, 1H, 2-H), 6.96-6.98 (m, 2H, Ph-H), 7.21-7.23 (m, 2H, Ph-H), 7.77-7.79 (m, 2H, Ph-H), 7.94-7.96 (m, 2H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 14.5 (7-Me), 21.8 (4-*Me*-C_6H_4), 55.8

(CO-4-*Me*O-C_6H_4), 62.3 (C-3), 64.3 (C-2), 114.6, 118.6, 127.5, 129.6, 131.1, 135.5, 135.6 (Ph-C), 154.2 (C-7), 164.8 (C-4), 165.1 (Ph-C), 187.6 (*C*O-4-MeO-C_6H_4); MS: *m/z* 351 $[M+H]^+$. Anal. Calcd for $C_{20}H_{18}N_2O_4$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.47; H, 5.22; N, 8.02.

7-Methyl-5-(4-methylphenyl)-2-[4-(trifluoromethyl)benzoyl]-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (**6g**): Reaction was carried out with **2** (0.202 g, 1.0 mmol) and 4-(trifluoromethyl)phenacyl bromide (**4g**) (0.534 g, 2.0 mmol). Colorless needles (0.331 g, 85%), mp 176-177 ˚C (acetone/petroleum ether); IR (ATR): ν 1718, 1693 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 1.86 (s, 3H, 7-Me), 2.36 (s, 3H, 4-*Me*-C_6H_4), 4.79 (s, 2H, 2-H), 7.22-7.25 (m, 2H, Ph-H), 7.76-7.81 (m, 4H, Ph-H), 8.09-8.11 (m, 2H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 14.5 (7-Me), 21.1 (4-*Me*-C_6H_4), 62.4 (C-3), 63.9 (C-2), 118.6, 122.4, 124.2, 126.47, 126.50, 129.1, 129.7, 135.4, 135.8, 136.0, 136.2, 136.4, 136.6 (Ph-C), 136.8 (CO-4-*C*F_3-C_6H_4), 153.4 (C-7), 164.2 (C-4), 188.9 (*C*O-4-CF_3-C_6H_4); MS: *m/z* 389 $[M+H]^+$. Anal. Calcd for $C_{20}H_{15}F_3N_2O_3$: C, 61.86; H, 3.89; N, 7.21. Found: C, 61.84; H, 3.89; N, 7.21.

7-Methyl-2-(4-nitrobenzoyl)-5-(4-methylphenyl)-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (**6h**): Reaction was carried out with **2** (0.202 g, 1.0 mmol) and 4-nitrophenacyl bromide (**4h**) (0.488 g, 2.0 mmol). Yellow needles (0.336 g, 92%), mp 180-181 ˚C (acetone/petroleum ether); IR (ATR): ν 1715, 1694 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 1.85 (s, 3H, 7-Me), 2.36 (s, 3H, 4-*Me*-C_6H_4), 4.80 (s, 1H, 2-H), 7.21-7.23 (m, 2H, Ph-H), 7.74-7.76 (m, 2H, Ph-H), 8.16-8.18 (m, 2H, Ph-H), 8.35-8.38 (m, 2H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 14.5 (7-Me), 21.1 (4-*Me*-C_6H_4), 62.5 (C-3), 63.9 (C-2), 118.6, 124.6, 129.7, 129.9, 135.3, 135.9, 138.4, 151.4 (Ph-C), 153.2 (C-7), 164.1 (C-4), 188.6 (*C*O-4-NO_2-C_6H_4); MS: *m/z* 366 $[M+H]^+$. Anal. Calcd for $C_{19}H_{15}N_3O_5$: C, 62.46; H, 4.14; N, 11.50. Found: C, 62.69; H, 4.18; N, 11.57.

2-Benzoyl-5-(4-chlorophenyl)-7-methyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (7a): Reaction was carried out with **3** (0.223 g, 1.0 mmol) and phenacyl bromide (**4a**) (0.398 g, 2.0 mmol). Colorless needles (0.304 g, 89%), mp 158-159 ˚C (acetone/petroleum ether); IR (ATR): ν 1714, 1692 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 1.87 (s, 3H, 7-Me), 4.80 (s, 1H, 2-H), 7.37-7.41 (m, 2H, Ph-H), 7.52-7.55 (m, 2H, Ph-H), 7.66-7.69 (m, 1H, Ph-H), 7.88-7.90 (m, 2H, Ph-H), 7.95-7.98 (m, 2H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 14.5 (7-Me), 62.3 (C-3), 64.3 (C-2), 119.6, 128.7, 129.2, 129.4, 131.0, 134.3, 135.3, 136.4 (Ph-C), 154.5 (C-7), 164.7 (C-4), 189.2 (*C*OPh); MS: *m/z* 341 $[M+H]^+$. Anal. Calcd for $C_{18}H_{13}ClN_2O_3$: C, 63.44; H, 3.85; N, 8.22. Found: C, 63.52; H, 3.78; N, 8.21.

5-(4-Chlorophenyl)-2-(4-fluorobenzoyl)-7-methyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (**7b**): Reaction was carried out with **3** (0.223 g, 1.0 mmol) and 4-fluorophenacyl bromide (**4b**) (0.434 g, 2.0 mmol). Colorless needles (0.324 g, 90%), mp 178-179 ˚C (acetone/petroleum ether); IR (ATR): ν 1721, 1687 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 1.86 (s, 3H, 7-Me), 4.74 (s, 1H, 2-H), 7.19-7.25 (m, 2H, Ph-H), 7.37-7.40 (m, 2H, Ph-H), 7.87-7.89 (m, 2H, Ph-H), 8.02-8.04 (m, 2H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 14.5 (7-Me), 62.3 (C-3), 64.1 (C-2), 116.8, 116.9, 119.6, 129.2, 130.8, 131.0, 131.6, 131.7, 136.4 (Ph-C),

154.3 (C-7), 164.6 (C-4), 166.1, 167.8 (Ph-C), 187.8 (*C*O-4-F-C_6H_4); MS: *m/z* 359 $[M+H]^+$. Anal. Calcd for $C_{18}H_{12}ClFN_2O_3$: C, 60.26; H, 3.37; N, 7.81. Found: C, 60.23; H, 3.47; N, 7.81.

2-(4-Chlorobenzoyl)-5-(4-chlorophenyl)-7-methyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (**7c**): Reaction was carried out with **3** (0.223 g, 1.0 mmol) and 4-chlorophenacyl bromide (**4c**) (0.467 g, 2.0 mmol). Colorless needles (0.338 g, 90%), mp 188-189 ˚C (acetone/petroleum ether); IR (ATR): ν 1725, 1688 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 1.86 (s, 3H, 7-Me), 4.74 (s, 1H, 2-H), 7.37-7.39 (m, 2H, Ph-H), 7.50-7.52 (m, 2H, Ph-H), 7.86-7.89 (m, 2H, Ph-H), 7.92-7.94 (m, 2H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 14.5 (7-Me), 62.3 (C-3), 64.1 (C-2), 119.6, 129.2, 129.9, 130.0, 131.0, 132.6, 136.4, 142.1 (Ph-C), 154.2 (C-7), 164.6 (C-4), 188.3 (*C*O-4-Cl-C_6H_4); MS: *m/z* 375 $[M+H]^+$. Anal. Calcd for $C_{18}H_{12}Cl_2N_2O_3$: C, 57.62; H, 3.22; N, 7.47. Found: C, 57.61; H, 3.33; N, 7.49.

2-(4-Bromobenzoyl)-5-(4-chlorophenyl)-7-methyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (**7d**): Reaction was carried out with **3** (0.223 g, 1.0 mmol) and 4-bromophenacyl bromide (**4d**) (0.556 g, 2.0 mmol). Colorless needles (0.373 g, 89%), mp 187-188 ˚C (acetone/petroleum ether); IR (ATR): ν 1724, 1688 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 1.86 (s, 3H, 7-Me), 4.74 (s, 1H, 2-H), 7.37-7.40 (m, 2H, Ph-H), 7.67-7.69 (m, 2H, Ph-H), 7.83-7.89 (m, 4H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 14.5 (7-Me), 62.3 (C-3), 64.0 (C-2), 119.6, 129.2, 130.1, 131.0, 131.1, 132.87, 132.94, 136.4 (Ph-C), 154.2 (C-7), 164.6 (C-4), 188.5 (*C*O-4-Br-C_6H_4); MS: *m/z* 419 $[M+H]^+$. Anal. Calcd for $C_{18}H_{12}BrClN_2O_3$: C, 51.52; H, 2.88; N, 6.68. Found: C, 51.33; H, 2.89; N, 6.62.

5-(4-Chlorophenyl)-7-methyl-2-(4-methylbenzoyl)-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (**7e**): Reaction was carried out with **3** (0.223 g, 1.0 mmol) and 4-methylphenacyl bromide (**4e**) (0.426 g, 2.0 mmol). Colorless needles (0.333 g, 94%), mp 173-174 ˚C (Et_2O/petroleum ether); IR (ATR): ν 1728, 1683 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 1.86 (s, 3H, 7-Me), 2.43 (s, 3H, CO-4-*Me*-C_6H_4), 4.77 (s, 1H, 2-H), 7.30-7.32 (m, 2H, Ph-H), 7.37-7.39 (m, 2H, Ph-H), 7.85-7.90 (m, 4H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 14.5 (7-Me), 22.0 (CO-4-*Me*-C_6H_4), 62.3 (C-3), 64.3 (C-2), 119.6, 128.8, 129.2, 130.1, 130.9, 131.9, 136.5, 146.7 (Ph-C), 154.6 (C-7), 164.9 (C-4), 188.7 (*C*O-4-Me-C_6H_4); MS: *m/z* 355 $[M+H]^+$. Anal. Calcd for $C_{19}H_{15}ClN_2O_3$: C, 64.32; H, 4.26; N, 7.90. Found: C, 64.38; H, 4.21; N, 7.93.

5-(4-Chlorophenyl)-2-(4-methoxybenzoyl)-7-methyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (**7f**): Reaction was carried out with **3** (0.223 g, 1.0 mmol) and 4-methoxyphenacyl bromide (**4f**) (0.458 g, 2.0 mmol). Colorless needles (0.327 g, 88%), mp 168-169 ˚C (acetone/petroleum ether); IR (ATR): ν 1727, 1686 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 1.87 (s, 3H, 7-Me), 3.88 (s, 3H, CO-4-*Me*O-C_6H_4), 4.73 (s, 1H, 2-H), 6.97-6.99 (m, 2H, Ph-H), 7.37-7.39 (s, 2H, Ph-H), 7.88-7.97 (m, 4H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 14.5 (7-Me), 55.8 (CO-4-*Me*O-C_6H_4), 62.2 (C-3), 64.4 (C-2), 114.7, 119.6, 127.4, 129.2, 130.9, 131.2, 136.5 (Ph-C), 154.8 (C-7), 165.0 (C-4), 165.2 (Ph-C), 187.4 (*C*O-4-MeO-C_6H_4); MS: *m/z* 371 $[M+H]^+$. Anal. Calcd for $C_{19}H_{15}ClN_2O_4$: C, 61.55; H, 4.08; N, 7.56. Found: C, 61.58; H, 3.98; N, 7.58.

5-(4-Chlorophenyl)-7-methyl-2-[4-(trifluoromethyl)benzoyl]-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (**7g**): Reaction was carried out with **3** (0.223 g, 1.0 mmol) and 4-(trifluoromethyl)phenacyl bromide (**4g**) (0.534 g, 2.0 mmol) for 0.5 h. Colorless needles (0.330 g, 81%), mp 146-147 ˚C (Et_2O/petroleum ether); IR (ATR): ν 1722, 1694 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 1.86 (s, 3H, 7-Me), 4.79 (s, 1H, 2-H), 7.38-7.40 (m, 2H, Ph-H), 7.80-7.82 (m, 2H, Ph-H), 7.87-7.89 (m, 2H, Ph-H), 8.10-8.12 (m, 2H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 14.5 (7-Me), 62.3 (C-3), 64.0 (C-2), 119.6, 122.3, 124.1, 126.50, 126.52, 129.1, 129.2, 131.1, 136.0, 136.27, 136.32, 136.5 (Ph-C), 136.8 (CO-4-*C*F_3-C_6H_4), 153.9 (C-7), 164.4 (C-4), 188.7 (*C*O-4-CF_3-C_6H_4); MS: *m/z* 409 $[M+H]^+$. Anal. Calcd for $C_{19}H_{12}ClF_3N_2O_3$: C, 55.83; H, 2.96; N, 6.85. Found: C, 55.66; H, 3.00; N, 6.87.

5-(4-Chlorophenyl)-7-methyl-2-(4-nitrobenzoyl)-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (**7h**): Reaction was carried out with **3** (0.223 g, 1.0 mmol) and 4-nitrophenacyl bromide (**4h**) (0.488 g, 2.0 mmol). Yellow needles (0.354 g, 92%), mp 171-172 ˚C (acetone/petroleum ether); IR (ATR): ν 1720, 1697 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 1.86 (s, 3H, 7-Me), 4.80 (s, 1H, H-2), 7.37-7.39 (m, 2H, Ph-H), 7.85-7.88 (m, 2H, Ph-H), 8.17-8.19 (m, 2H, Ph-H), 8.36-8.39 (m, 2H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 14.6 (7-Me), 62.4 (C-3), 63.9 (C-2), 119.6, 124.6, 129.3, 130.0, 131.2, 136.3, 138.3, 151.5 (Ph-C), 153.7 (C-7), 164.2 (C-4), 188.4 (*C*O-4-NO_2-C_6H_4); MS: *m/z* 386 $[M+H]^+$. Anal. Calcd for $C_{18}H_{12}ClN_3O_5$: C, 56.04; H, 3.14; N, 10.89. Found: C, 56.05; H, 3.20; N, 10.90.

General procedure for the preparation of pyridazinones 8-10 from 5-7 and pyrrolidine in the presence of H_2O. A mixture of **5-7** (1.0 mmol) and pyrrolidine (3 mL, 36 mmol) in the presence of H_2O (one drop, 0.07 g, 3.9 mmol) was stirred at 100 ˚C for 0.5 h. After removal of the solvent *in vacuo*, a 5% HCl solution (20 mL) was added to the reaction mixture with stirring and ice cooling. The resulting mixture was extracted with $CHCl_3$ (60 mL). The extract was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with $CHCl_3$-acetone (4:1) as the eluent to give **8a-h**, **9a-h**, and **10a-h.**

6-Methyl-2,4-diphenyl-5-(1-pyrrolidinylcarbonyl)-3(2*H*)-pyridazinone (8a): Yellow prisms (0.237 g, 66%), mp 267-268 ˚C (acetone/petroleum ether); IR (ATR): ν 1618, 1609 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 1.86-1.97 (m, 4H, pyrrolidinyl-H), 2.44 (s, 3H, pyridazine 6-Me), 3.27-3.77 (m, 4H, pyrrolidinyl-H), 7.19-7.34 (m, 10H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 19.7 (pyridazine 6-Me), 24.6, 25.9, 45.7, 46.3 (pyrrolidinyl-C), 125.6, 128.1, 129.2, 129.3 (Ph-C), 129.72 (pyridazine C-5), 129.74, 129.8, 130.5, 145.0 (Ph-C), 154.5 (pyridazine C-4), 155.9 (pyridazine C-6), 164.7, 165.1 (2C=O); MS: *m/z* 360 $[M+H]^+$. Anal. Calcd for $C_{22}H_{21}N_3O_2$: C, 73.52; H, 5.89; N, 11.69. Found: C, 73.43; H, 5.98; N, 11.58.

4-(4-Chlorophenyl)-6-methyl-2-phenyl-5-(1-pyrrolidinylcarbonyl)-3(2*H*)-pyridazinone (**8c**): Yellow needles (0.228 g, 58%), mp 244-245 ˚C (acetone/petroleum ether); IR (ATR): ν 1630 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 1.84-1.97 (s, 4H, pyrrolidinyl-H), 2.44 (s, 3H, pyridazine 6-Me), 3.26-3.77 (m, 4H,

pyrrolidinyl-H), 7.17-7.25 (m, 6H, Ph-H), 7.32-7.38 (m, 3H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 19.7 (pyridazine 6-Me), 24.6, 25.9, 45.7, 46.3 (pyrrolidinyl-C), 125.5, 127.6, 128.5, 129.5 (Ph-C), 129.9 (pyridazine C-5), 130.0, 132.0, 136.2, 144.8 (Ph-C), 153.2 (pyridazine C-4), 156.1 (pyridazine C-6), 164.6, 164.9 (2C=O); MS: *m/z* 394 $[M+H]^+$. Anal. Calcd for $C_{22}H_{20}ClN_3O_2$: C, 67.09; H, 5.12; N, 10.67. Found: C, 67.10; H, 5.19; N, 10.70.

4-(4-Bromophenyl)-6-methyl-2-phenyl-5-(1-pyrrolidinylcarbonyl)-3(2*H*)-pyridazinone (**8d**): Yellow needles (0.216 g, 49%), mp 229-230 ˚C (acetone/petroleum ether); IR (ATR): ν 1622 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$): δ 1.84-1.98 (m, 4H, pyrrolidinyl-H), 2.44 (s, 3H, pyridazine 6-Me), 3.26-3.77 (m, 4H, pyrrolidinyl-H), 7.10-7.12 (m, 2H, Ph-H), 7.20-7.25 (m, 2H, Ph-H), 7.33-7.39 (m, 5H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 19.7 (pyridazine 6-Me), 24.6, 25.9, 45.7, 46.3 (pyrrolidinyl-C), 124.6, 125.5, 128.1, 129.5 (Ph-C), 130.0 (pyridazine C-5), 130.1, 131.5, 132.1, 144.7 (Ph-C), 153.2 (pyridazine C-4), 156.1 (pyridazine C-6), 164.5, 164.9 (2C=O); MS: *m/z* 438 $[M+H]^+$; high-resolution MS: Calcd for $C_{22}H_{21}BrN_3O_2$ 438.0817, Found 438.0815. Anal. Calcd for $C_{22}H_{20}BrN_3O_2 \cdot 0.2H_2O$: C, 59.79; H, 4.65; N, 9.51. Found: C, 59.75; H, 4.63; N, 9.33.

6-Methyl-4-(4-methylphenyl)-2-phenyl-5-(1-pyrrolidinylcarbonyl)-3(2*H*)-pyridazinone (**8e**): Colorless needles (0.214 g, 57%), mp 248-249 ˚C (acetone/petroleum ether); IR (ATR): ν 1619 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$): δ 1.83-1.94 (m, 4H, pyrrolidinyl-H), 2.24 (s, 3H, 4-*Me*-C_6H_4), 2.43 (s, 3H, pyridazine 6-Me), 3.26-3.77 (m, 4H, pyrrolidinyl-H), 7.00-7.02 (m, 2H, Ph-H), 7.11-7.13 (m, 2H, Ph-H), 7.21-7.25 (m, 2H, Ph-H), 7.29-7.34 (m, 3H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 19.7 (pyridazine 6-Me), 21.5 (4-*Me*-C_6H_4), 24.6, 25.9, 45.7, 46.3 (pyrrolidinyl-C), 125.6, 126.2, 128.8, 129.30 (Ph-C), 129.32 (C-5), 129.6, 130.5, 140.2, 145.2 (Ph-C), 154.6 (pyridazine C-4), 155.8 (pyridazine C-6), 164.8, 165.2 (2C=O); MS: *m/z* 374 $[M+H]^+$. Anal. Calcd for $C_{23}H_{23}N_3O_2$: C, 73.97; H, 6.21; N, 11.25. Found: C, 73.91; H, 6.32; N, 11.12.

4-(4-Methoxyphenyl)-6-methyl-2-phenyl-5-(1-pyrrolidinylcarbonyl)-3(2*H*)-pyridazinone (**8f**): Yellow needles (0.242 g, 62%), mp 172-173 ˚C (acetone/petroleum ether); IR (ATR): ν 1617, 1603 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$): δ 1.86-1.94 (m, 4H, pyrrolidinyl-H), 2.42 (s, 3H, pyridazine 6-Me), 3.26-3.77 (m, 7H, 4-*Me*O-C_6H_4 and pyrrolidinyl-H), 6.71-6.73 (m, 2H, Ph-H), 7.19-7.25 (m, 4H, Ph-H), 7.31-7.33 (m, 3H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 19.7 (pyridazine 6-Me), 24.6, 25.9, 45.7, 46.3 (pyrrolidinyl-C), 55.3 (4-*Me*O-C_6H_4), 113.7, 121.1, 125.6 (Ph-C), 129.1 (pyridazine C-5), 129.3, 129.6, 132.4, 145.3 (Ph-C), 154.3 (pyridazine C-4), 155.7 (pyridazine C-6), 160.7 (Ph-C), 164.8, 165.3 (2C=O); MS: *m/z* 390 $[M+H]^+$; high-resolution MS: Calcd for $C_{23}H_{24}N_3O_3$ 390.1818, Found 390.1823. Anal. Calcd for $C_{23}H_{23}N_3O_3 \cdot 0.3H_2O$: C, 69.96; H, 6.02; N, 10.64. Found: C, 69.97; H, 6.26; N, 10.58.

6-Methyl-2-phenyl-5-(1-pyrrolidinylcarbonyl)-4-[4-(trifluoromethyl)phenyl]-3(2*H*)-pyridazinone (**8g**): Colorless needles (0.166 g, 39%), mp 233-234 ˚C (acetone/petroleum ether); IR (ATR): ν 1626,

1606 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 1.89-1.96 (m, 4H, pyrrolidinyl-H), 2.46 (m, 3H, pyridazine 6-Me), 3.27-3.78 (m, 4H, pyrrolidinyl-H), 7.21-7.25 (m, 2H, Ph-H), 7.32-7.39 (m, 5H, Ph-H), 7.47-7.49 (m, 2H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 19.7 (pyridazine 6-Me), 24.6, 25.9, 45.7, 46.3 (pyrrolidinyl-C), 122.7, 124.5, 125.08, 125.11, 125.5, 129.5, 130.3 (Ph-C), 130.4 (pyridazine C-5), 131.0, 131.2, 131.4, 131.7 (Ph-C), 133.0 (4-*C*F_3-C_6H_4), 144.5 (Ph-C), 152.7 (pyridazine C-4), 156.3 (pyridazine C-6), 164.5, 164.7 (2C=O); MS: *m/z* 428 $[M+H]^+$. Anal. Calcd for $C_{23}H_{20}F_3N_3O_2$: C, 64.63; H, 4.72; N, 9.83. Found: C, 64.39; H, 4.80; N, 9.77.

6-Methyl-2-(4-methylphenyl)-4-phenyl-5-(1-pyrrolidinylcarbonyl)-3(2*H*)-pyridazinone (**9a**): Yellow prisms (0.197 g, 53%), mp 277-278 ˚C (acetone/petroleum ether); IR (ATR): ν 1619, 1604 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 1.83-1.96 (m, 4H, pyrrolidinyl-H), 2.30 (s, 3H, 4-*Me*-C_6H_4), 2.43 (s, 3H, pyridazine 6-Me), 3.26-3.77 (m, 4H, pyrrolidinyl-H), 7.08-7.25 (m, 9H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 19.7 (pyridazine 6-Me), 21.2 (4-*Me*-C_6H_4), 24.6, 25.9, 45.7, 46.3 (pyrrolidinyl-C), 125.2, 128.1 (Ph-C), 129.4 (pyridazine C-5), 129.5, 129.72, 129.75, 130.5, 140.0, 142.7 (Ph-C), 154.4 (pyridazine C-4), 155.9 (pyridazine C-6), 164.8, 165.2 (2C=O); MS: *m/z* 374 $[M+H]^+$. Anal. Calcd for $C_{23}H_{23}N_3O_2$: C, 73.97; H, 6.21; N, 11.25. Found: C, 73.77; H, 6.42; N, 11.15.

4-(Chlorophenyl)-6-methyl-2-(4-methylphenyl)-5-(1-pyrrolidinylcarbonyl)-3(2*H*)-pyridazinone (**9c**): Yellow prisms (0.186 g, 46%), mp 242-243 ˚C (acetone/petroleum ether); IR (ATR): ν 1616 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 1.80-1.97 (m, 4H, pyrrolidinyl-H), 2.33 (s, 3H, 4-*Me*-C_6H_4), 2.43 (s, 3H, pyridazine 6-Me), 3.25-3.77 (m, 4H, pyrrolidinyl-H), 7.07-7.12 (m, 4H, Ph-H), 7.18-7.25 (m, 4H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 19.7 (pyridazine 6-Me), 21.2 (4-*Me*-C_6H_4), 24.6, 25.9, 45.7, 46.3 (pyrrolidinyl-C), 125.2, 127.8, 128.5 (Ph-C), 129.8 (pyridazine C-5), 130.0, 131.9, 136.0, 140.4, 142.5 (Ph-C), 153.1 (pyridazine C-4), 156.0 (pyridazine C-6), 164.6, 164.9 (2C=O); MS: *m/z* 408 $[M+H]^+$. Anal. Calcd for $C_{23}H_{22}ClN_3O_2$: C, 67.73; H, 5.44; N, 10.30. Found: C, 67.80; H, 5.54; N, 10.26.

4-(Bromophenyl)-6-methyl-2-(4-methylphenyl)-5-(1-pyrrolidinylcarbonyl)-3(2*H*)-pyridazinone (**9d**): Yellow prisms (0.165 g, 36%), mp 236-237 ˚C (acetone/petroleum ether); IR (ATR): ν 1618 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 1.88-1.95 (m, 4H, pyrrolidinyl-H), 2.33 (s, 3H, 4-*Me*-C_6H_4), 2.43 (s, 3H, pyridazine 6-Me), 3.25-3.77 (m, 4H, pyrrolidinyl-H), 7.07-7.13 (m, 6H, Ph-H), 7.35-7.37 (m, 2H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 19.7 (pyridazine 6-Me), 21.3 (4-*Me*-C_6H_4), 24.6, 25.9, 45.7, 46.3 (pyrrolidinyl-C), 124.5, 125.2, 128.3 (Ph-C), 129.8 (pyridazine C-5), 130.0, 131.4, 132.1, 140.4, 142.4 (Ph-C), 153.1 (pyridazine C-4), 156.0 (pyridazine C-6), 164.6, 164.9 (2C=O); MS: *m/z* 452 $[M+H]^+$. Anal. Calcd for $C_{23}H_{22}BrN_3O_2$: C, 61.07; H, 4.90; N, 9.29. Found: C, 61.04; H, 4.85; N, 9.22.

6-Methyl-2,4-bis(4-methylphenyl)-5-(1-pyrrolidinylcarbonyl)-3(2*H*)-pyridazinone (**9e**): Yellow prisms (0.183 g, 47%), mp 237-238 ˚C (acetone/petroleum ether); IR (ATR): ν 1623 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 1.88-1.95 (m, 4H, pyrrolidinyl-H), 2.25, 2.31 [s, 6H, 2(4-*Me*-C_6H_4)], 2.43 (s, 3H,

pyridazine 6-Me), 3.25-3.78 (m, 4H, pyrrolidinyl-H), 7.01-7.03 (m, 2H, Ph-H), 7.08-7.14 (m, 6H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 19.7 (pyridazine 6-Me), 21.2, 21.5 [2(4-*Me*-C_6H_4)], 24.6, 25.9, 45.7, 46.3 (pyrrolidinyl-C), 125.3, 126.2, 128.8 (Ph-C), 129.1 (pyridazine C-5), 129.8, 130.5, 140.0, 140.2, 142.8 (Ph-C), 154.5 (pyridazine C-4), 156.0 (pyridazine C-6), 164.4, 165.0 (2C=O); MS: *m/z* 388 $[M+H]^+$. Anal. Calcd $C_{24}H_{25}N_3O_2$: C, 74.39; H, 6.50; N, 10.84. Found: C, 74.33; H, 6.60; N, 10.73.

4-(4-Methoxyphenyl)-6-methyl-2-(4-methylphenyl)-5-(1-pyrrolidinylcarbonyl)-3(2*H*)-pyridazinone (**9f**): Yellow prisms (0.186 g, 46%), mp 228-229 ˚C (acetone/petroleum ether); IR (ATR): ν 1622 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$): δ 1.88-1.95 (m, 4H, pyrrolidine H), 2.31 (s, 3H, 4-*Me*-C_6H_4), 2.42 (s, 3H, pyridazine 6-Me), 3.25-3.84 (m, 7H, 4-*Me*O-C_6H_4 and pyrrolidinyl-H), 6.72-6.74 (m, 2H, Ph-H), 7.08-7.25 (m, 6H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 19.7 (pyridazine 6-Me), 21.2 (4-*Me*-C_6H_4), 24.6, 25.9, 45.7, 46.4 (pyrrolidinyl-C), 55.4 (4-*Me*O-C_6H_4), 113.7, 121.1, 125.3 (Ph-C), 128.9 (pyridazine C-5), 129.9, 132.4, 139.9, 142.9 (Ph-C), 154.1 (pyridazine C-4), 155.8 (pyridazine C-6), 160.7 (Ph-C), 164.4, 165.0 (2C=O); MS: *m/z* 404 $[M+H]^+$. Anal. Calcd for $C_{24}H_{25}N_3O_3$: C, 71.44; H, 6.25; N, 10.41. Found: C, 71.38; H, 6.37; N, 10.26.

6-Methyl-2-(4-methylphenyl)-5-(1-pyrrolidinylcarbonyl)-4-[4-(trifluoromethyl)phenyl]-3(2*H*)-pyridazinone (**9g**): Colorless prisms (0.108 g, 24%), mp 227-228 ˚C (acetone/petroleum ether); IR (ATR): ν 1615 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$): δ 1.89-1.95 (m, 4H, pyrrolidinyl-H), 2.32 (s, 3H, 4-*Me*-C_6H_4), 2.45 (s, 3H, pyridazine 6-Me), 3.26-3.77 (m, 4H, pyrrolidinyl-H), 7.08-7.13 (m, 4H, Ph-H), 7.36–7.38 (m, 2H, Ph-H), 7.48–7.50 (m, 2H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 19.7 (pyridazine 6-Me), 21.2 (4-*Me*-C_6H_4), 24.6, 25.9, 45.7, 46.3 (pyrrolidinyl-C), 124.5, 122.7, 125.07, 125.09, 125.2, 130.0 (Ph-C), 130.3 (pyridazine C-5), 131.0, 131.3, 131.5 (Ph-C), 133.1 (4-*C*F_3-C_6H_4), 140.7, 142.2 (Ph-C), 152.6 (pyridazine C-4), 156.3 (pyridazine C-6), 164.5, 164.8 (2C=O); MS: *m/z* 442 $[M+H]^+$. Anal. Calcd for $C_{24}H_{22}FN_3O_2$: C, 65.30; H, 5.02; N, 9.52. Found: C, 65.35; H, 5.08; N, 9.52.

2-(4-Chlorophenyl)-6-methyl-4-phenyl-5-(1-pyrrolidinylcarbonyl)-3(2*H*)-pyridazinone (**10a**): Colorless needles (0.303 g, 77%), mp 292-293 ˚C (acetone/petroleum ether); IR (ATR): ν 1621, 1605 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$): δ 1.82-1.94 (m, 4H, pyrrolidinyl-H), 2.43 (s, 3H, pyridazine 6-Me), 3.26-3.76 (m, 4H, pyrrolidinyl-H), 7.15-7.17 (m, 2H, Ph-H), 7.21-7.29 (m, 7H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 19.7 (pyridazine 6-Me), 24.6, 25.9, 45.7, 46.3 (pyrrolidinyl-C), 126.9, 128.3, 129.0, 129.5 (Ph-C), 129.9 (pyridazine C-5), 130.1, 130.5, 135.8, 143.4 (Ph-C), 154.5 (pyridazine C-4), 156.1 (pyridazine C-6), 164.6, 164.9 (2C=O); MS: *m/z* 394 $[M+H]^+$. Anal. Calcd for $C_{22}H_{20}ClN_3O_2$: C, 67.09; H, 5.12; N, 10.67. Found: C, 66.87; H, 5.18; N, 10.67.

2,4-Bis(4-chlorophenyl)-6-methyl-5-(1-pyrrolidinylcarbonyl)-3(2*H*)-pyridazinone (**10c**): Yellow prisms (0.323 g, 75%), mp 291-292 ˚C (acetone/petroleum ether); IR (ATR): ν 1616, 1603 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$): δ 1.88-1.99 (m, 4H, pyrrolidinyl-H), 2.43 (s, 3H, pyridazine 6-Me), 3.24-3.76 (m, 4H,

pyrrolidinyl-H), 7.15-7.26 (m, 6H, Ph-H), 7.29-7.33 (m, 2H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 19.7 (pyridazine 6-Me), 24.6, 25.9, 45.7, 46.3 (pyrrolidinyl-C), 126.8, 127.4, 128.7, 129.7 (Ph-C), 130.1 (pyridazine C-5), 131.9, 136.2, 136.5, 143.2 (Ph-C), 153.1 (pyridazine C-4), 156.2 (pyridazine C-6), 164.5, 164.7 (2C=O); MS: *m/z* 428 $[M+H]^+$. Anal. Calcd for $C_{22}H_{19}Cl_2N_3O_2$: C, 61.69; H, 4.47; N, 9.81. Found: C, 61.55; H, 4.43; N, 9.70.

4-(4-Bromophenyl)-2-(4-chlorolphenyl)-6-methyl-5-(1-pyrrolidinylcarbonyl)-3(2*H*)-pyridazinone (**10d**): Yellow prisms (0.379 g, 80%), mp 275-276 ˚C (acetone/petroleum ether); IR (ATR): ν 1712, 1622 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$): δ 1.88-1.96 (m, 4H, pyrrolidinyl-H), 2.42 (s, 3H, pyridazine 6-Me), 3.24-3.76 (m, 4H, pyrrolidinyl-H), 7.11-7.13 (m, 2H, Ph-H), 7.15-7.18 (m, 2H, Ph-H), 7.31-7.33 (m, 2H, Ph-H), 7.39-7.41 (m, 2H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 19.7 (pyridazine 6-Me), 24.6, 25.9, 45.7, 46.3 (pyrrolidinyl-C), 124.9, 126.8, 127.8, 129.7 (Ph-C), 130.2 (pyridazine C-5), 131.7, 132.1, 136.2, 143.2 (Ph-C), 1531.1 (pyridazine C-4), 156.2 (pyridazine C-6), 164.4, 164.7 (2C=O); MS: *m/z* 472 $[M+H]^+$. Anal. Calcd for $C_{22}H_{19}BrClN_3O_2$: C, 55.89; H, 4.05; N, 8.89. Found: C, 55.71; H, 3.92; N, 8.87.

2-(4-Chlorophenyl)-6-methyl-4-(4-methylphenyl)-5-(1-pyrrolidinylcarbonyl)-3(2*H*)-pyridazinone (**10e**): Yellow prisms (0.245 g, 60%), mp 239-240 ˚C (acetone/petroleum ether); IR (ATR): ν 1621 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$): δ 1.88-1.95 (m, 4H, pyrrolidinyl-H), 2.27 (s, 3H, 4-*Me*-C_6H_4), 2.43 (s, 3H, pyridazine 6-Me), 3.26-3.77 (m, 4H, pyrrolidinyl-H), 7.04-7.06 (m, 2H, Ph-H), 7.12-7.18 (m, 4H, Ph-H), 7.28-7.30 (m, 2H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 19.7 (pyridazine 6-Me), 21.5 (4-*Me*-C_6H_4), 24.6, 25.9, 45.7, 46.4 (pyrrolidinyl-C), 125.7, 126.9, 129.1 (Ph-C), 129.5 (pyridazine C-5 and Ph-C), 130.5, 135.8, 140.7, 143.5 (Ph-C), 154.7 (pyridazine C-4), 156.2 (pyridazine C-6), 164.2, 164.7 (2C=O); MS: *m/z* 408 $[M+H]^+$. Anal. Calcd for $C_{23}H_{22}ClN_3O_2$: C, 67.73; H, 5.44; N, 10.30. Found: C, 67.63; H, 5.57; N, 10.26.

2-(4-Chlorolphenyl)-4-(4-methoxyphenyl)-6-methyl-5-(1-pyrrolidinylcarbonyl)-3(2*H*)-pyridazinone (**10f**): Yellow prisms (0.328 g, 77%), mp 242-243 ˚C (acetone/petroleum ether); IR (ATR): ν 1621 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$): δ 1.88-1.95 (m, 4H, pyrrolidinyl-H), 2.41 (s, 3H, pyridazine 6-Me), 3.25-3.77 (m, 7H, 4-*Me*O-C_6H_4 and pyrrolidinyl-H), 6.75-6.76 (m, 2H, Ph-H), 7.16-7.21 (m, 4H, Ph-H), 7.29-7.31 (m, 2H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 19.7 (pyridazine 6-Me), 24.6, 25.9, 45.6, 46.3 (pyrrolidinyl-C), 55.4 (4-*Me*O-C_6H_4), 113.9, 120.8, 126.9 (Ph-C), 129.3 (pyridazine C-5), 129.5, 132.4, 135.6, 143.7 (Ph-C), 154.2 (pyridazine C-4), 155.8 (pyridazine C-6), 160.9 (Ph-C), 164.7, 165.1 (2C=O); MS: *m/z* 424 $[M+H]^+$. Anal. Calcd for $C_{23}H_{22}ClN_3O_3$: C, 65.17; H, 5.23; N, 9.91. Found: C, 65.16; H, 5.27; N, 9.79.

2-(4-Chlorophenyl)-6-methyl-5-(1-pyrrolidinylcarbonyl)-4-[4-(trifluoromethyl)phenyl]-3(2*H*)-pyridazinone (**10g**): Yellow prisms (0.255 g, 55%), mp 261-262 ˚C (acetone/petroleum ether); IR (ATR): ν 1618 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$): δ 1.90-1.98 (m, 4H, pyrrolidinyl-H), 2.45 (s, 3H, pyridazine 6-Me), 3.25-3.77 (m, 4H, pyrrolidinyl-H), 7.17-7.19 (m, 2H, Ph-H), 7.31-7.33 (m, 2H, Ph-H), 7.36-7.38 (m, 2H, Ph-H), 7.52-7.54 (m, 2H, Ph-H); ^{13}C NMR ($CDCl_3$): δ 19.7 (pyridazine 6-Me), 24.6,

25.9, 45.7, 46.3 (pyrrolidine C), 122.6, 124.4, 125.3, 125.4, 126.8, 129.8 (Ph-C), 130.6 (pyridazine C-5), 131.0, 131.5, 131.7, 132.0, 132.2 (Ph-C), 132.7 (4-*C*F_3-C_6H_4), 136.5, 142.9 (Ph-C), 152.7 (pyridazine C-4), 156.4 (pyridazine C-6), 164.4, 164.5 (2C=O); MS: *m/z* 462 $[M+H]^+$. Anal. Calcd for $C_{23}H_{19}ClF_3N_3O_2$: C, 59.81; H, 4.15; N, 9.10. Found: C, 59.55; H, 4.10; N, 9.08.

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